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Exploring the psychology and genetics of sensory processing sensitivity in multicultural South Africa

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EXPLORING THE PSYCHOLOGY AND GENETICS OF SENSORY PROCESSING SENSITIVITY IN MULTICULTURAL SOUTH AFRICA

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Abstract

Sensory Processing Sensitivity (SPS) is a personality trait charaterised by deep cognitive processing, heightened awareness of sensory stimulation, strong emotional reactivity and a propensity to feel overwhelmed. Individuals with high levels of SPS are referred to as Highly Sensitive Persons (HSPs) and are thought to comprise 20-35% of the population. A defining feature of HSPs is their permeability to environmental influence, rendering them susceptible to disproportionately negative behavioural outcomes in adverse contexts, but disproportionately positive outcomes in nurturant contexts, when compared to non-HSPs. Since its conceptualisation in the late 1990s, the SPS construct has gained significant traction in the scientific literature and has been recently merged into a cross-disciplinary metaframework known as Environmental Sensitivity (ES). Furthermore, because of the simplicity and accessibility of its attendant instrument (the Highly Sensitive Person Scale [HSPS]), and its intuitive explanation of human behavioural differences, SPS theory has garnered notable popularity in the public media. However, SPS was conceptualised, and has been further developed, using culturally homogeneous and mostly Caucasian-centric samples. To date, the trait has not been explored anywhere on the ethnically and culturally diverse African continent. To address this gap in the literature, this doctoral research aimed to provide an initial psychological and biological exploration of SPS, and the HSPS, in diverse South African samples. Four studies were conducted, namely:

1. a pilot investigation of the HSPS amongst university-level psychology students,
2. factor and latent class analysis of the HSPS,
3. an investigation into the association between SPS, the five-factor model of personality, and adjustment to the first year of university in a multi-ethnic student sample, and
4. a broad examination of the influence of SPS, and other physiological (birth weight, temperament) and genetic (5-HTTLPR and *DRD4*) markers of the larger ES framework, on childhood internalising and externalising behaviour amongst Black African members of the Birth to Twenty Plus cohort.

Across all studies, the HSPS demonstrated acceptable internal consistency reliability. The psychometric properties of the instrument aligned with previous reports, except for factor analysis which revealed a unique, five-factor structure. SPS correlations with the five-factor model of personality were all in predicted directions. In line with hypothesised expectations, HSPs were less well-adjusted to university (Study 3) and displayed more internalising and externalising

behavioral problems (Study 4) than their non-sensitive counterparts. Environmental mediation of outcomes for HSPs was inconsistent, neither fully supporting nor fully contradicting SPS theory. There was no clear association between SPS and genetic variation in the 5-HTTLPR, or in the *DRD4* gene. On balance, this exploratory doctoral research found evidence to support both SPS theory, and its attendant instrument, the HSPS. However, some of the results highlighted inconsistencies that will need to be resolved in future studies. Nevertheless, SPS appears to be a meaningful personality construct with important implications and thus deserves further research, especially in an African context.

Keywords: sensory processing sensitivity; Highly Sensitive Person Scale; university adjustment; childhood behaviour; 5-HTTLPR; *DRD4*; South Africa

Declaration

I, Andrew Keith May, declare that this thesis is my own unaided work. It is being submitted for the degree of Doctor of Philosophy at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other university.



Andrew Keith May

The 17th day of August 2020 in Johannesburg

Dedication

"There is a difference between knowing the path and walking the path"

To Marcia
For showing me the path
To Jane
For teaching me how to walk it

Acknowledgements

The most important lesson to be learnt from a PhD seems to have very little to do with writing ability, theoretical knowledge, critical thinking, data analysis, or any other academic skill. Rather, the crucial lesson that is consistently taught, from proposal to thesis submission, is that of identifying, connecting to and relying on other people who will help to lessen the burden of a monumental task. I was fortunate enough to find a number of individuals who helped turn a personal curiosity of mine into a fully-fledged research project, for which I owe all of them a tremendous debt of gratitude.

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Expanding the research to include a genetic component would not have been possible without Zané Lombard, who took on the difficult task of joining a research project that was already partway through. Zané's efficiency and resilience, even in the face of overwhelming challenges, are unmatched, and set a benchmark for all to aspire to. She has been a key figure in my academic and personal growth, long before this PhD commenced, and so I am exceptionally grateful to have her as a role model.

There is no possible way to measure the supportive contribution of my dearest friend, Tyler Morgan. Over and above academic aptitude, the success of a PhD relies on having a sufficient pool of tools and resources (both mental and physical). Tyler directed me to all the right tools (LaTeX, R, Visual Studio Code) and never once faltered in his provision of comforting reassurance and wise counsel. Tyler rarely ever receives the acknowledgement he so deserves, and this feeble attempt here remains woefully insufficient. I am forever in his debt.

I am very thankful to both Linda Richter and Shane Norris, who afforded me access to the renowned Birth to Twenty Plus (BTT+) cohort, which helped to elevate this research to new heights. Their plates were already overflowing with other important commitments before I added numerous requests of my own, so I consider myself exceptionally fortunate to have been

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For administering the Highly Sensitive Person Scale (alongside an exhausting battery of other assessments) to over 1000 study participants, I am indebted to Feziwe Mpondo and her team of research assistants. Despite her workload, which would have led even the hardiest individuals to despair, Feziwe remained delightfully pleasant in all my interactions with her, making her a true joy to work with.

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Completing a PhD while holding down a job requires several difficult compromises, so I am extremely thankful to Amanda Krause, for always being open to negotiate around my research and work responsibilities.

Words seem insufficient when it comes to acknowledging my international collaborators, Michael Pluess, Francesca Lionetti and Robert Keers, who not only provided valuable statistical support but also afforded me international travel experiences that I will cherish for the rest of my life.

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Lastly, I'd like to thank the funders that made this research possible. The National Health Laboratory Service and the Health and Welfare Sector Education and Training Authority are thanked for their generous funding contributions. The support of the DST-NRF Centre of Excellence in Human Development towards this research/activity is hereby acknowledged. Opinions expressed and conclusions arrived at, are those of the author and are not necessarily to be attributed to the CoE in Human Development.

Contents

Abstract i

Declaration iii

Dedication iv

Acknowledgements v

List of abbreviations xvi

1 Introduction 1

1.1 Overview . . . 1
1.2 Evolutionary background of sensory processing . . . 2
1.3 Human sensory processing . . . 6
1.3.1 Psychodynamic perspective . . . 6
1.3.2 Psychobiological perspective . . . 8
1.3.3 Developmental perspective . . . 10
1.3.4 The obfuscation of sensory processing . . . 12
1.4 Sensory processing sensitivity . . . 14
1.4.1 Discovery and conceptualisation . . . 14
1.4.2 The highly sensitive person . . . 15
1.4.2.1 Sensory awareness . . . 15
1.4.2.2 Depth of processing . . . 16
1.4.2.3 Inhibition . . . 18
1.4.2.4 Emotionality . . . 19
1.4.2.5 Other characteristics . . . 20
1.4.2.6 SPS and related sensory phenotypes . . . 21
1.4.2.7 Crossover interactions . . . 23
1.4.3 Revaluation of human sensitivity . . . 24
1.5 Diathesis-stress (transactional/dual risk theory) and differential susceptibility . 25
1.5.1 The diathesis-stress model . . . 25
1.5.1.1 Temperament . . . 26
1.5.1.2 Physiology . . . 27

1.5.1.3 Gene x environment studies . . . 28
1.5.1.3.1 Serotonin transporter . . . 28
1.5.1.3.2 Dopamine receptor D4 . . . 33
1.5.2 Differential susceptibility to the environment . . . 35
1.5.3 Relation to SPS . . . 39
1.6 Implications . . . 40
1.7 Measuring and detecting plasticity . . . 42
1.7.1 The highly sensitive person scale . . . 43
1.7.2 Detecting plasticity . . . 44
1.8 Study rationale . . . 46
1.8.1 The South African context . . . 46
1.8.2 Population diversity . . . 46
1.8.3 African genetic diversity . . . 47
1.8.4 Study aim and objectives . . . 48

2 Study 1 **50**
2.1 Brief introduction . . . 50
2.2 Methods . . . 52
2.2.1 Study participants . . . 52
2.2.2 Instruments . . . 52
2.2.2.1 The HSPS . . . 52
2.2.2.2 Miscellaneous items . . . 53
2.2.3 Procedure . . . 53
2.3 Results . . . 54
2.3.1 The HSPS . . . 54
2.3.1.1 Scale scoring and item interpretation . . . 54
2.3.1.2 Item correlation . . . 55
2.3.1.3 Convergent validity . . . 55
2.4 Discussion . . . 56

3 Study 2 **59**
3.1 Brief introduction . . . 59
3.2 Methods . . . 61
3.2.1 Participants . . . 61
3.2.2 Instrumentation . . . 61
3.2.3 Procedure . . . 62
3.3 Results . . . 62
3.3.1 The HSPS . . . 62
3.3.2 Exploratory factor analysis . . . 62
3.3.3 Confirmatory factor analysis . . . 68
3.3.4 Latent Class Analysis . . . 68

3.4 Discussion . . . 70

4 Study 3 **74**
4.1 Brief introduction . . . 74
4.2 Methods . . . 77
4.2.1 Study participants . . . 77
4.2.2 Instruments . . . 78
4.2.2.1 The HSPS . . . 78
4.2.2.2 The Student Adaptation to College Questionnaire - Modified 78
4.2.2.3 The Parental Bonding Instrument/The Measure of Parental Style . . . 79
4.2.2.4 The Big Five Inventory . . . 80
4.2.2.5 The Resistance to Peer Influence Scale . . . 81
4.2.3 Procedure . . . 82
4.3 Results . . . 83
4.3.1 Instruments . . . 83
4.3.1.1 Childhood care: the PBI/MOPS . . . 83
4.3.1.2 Personality attributes . . . 83
4.3.2 Hierarchical linear modelling . . . 86
4.3.3 Exhaustive linear modelling . . . 88
4.3.4 The interaction between childhood care and SPS . . . 89
4.4 Discussion . . . 91

5 Study 4 **97**
5.1 Brief introduction . . . 97
5.2 Methods . . . 102
5.2.1 Study participants . . . 102
5.2.2 Instrumentation . . . 102
5.2.2.1 The HSPS . . . 102
5.2.2.2 The South African Child Assessment Schedule . . . 102
5.2.2.3 Carey Infant Temperament Questionnaire . . . 104
5.2.2.4 Maternal education . . . 105
5.2.2.5 Socioeconomic status . . . 105
5.2.3 Genotyping . . . 106
5.2.3.1 DNA extraction and quantification . . . 106
5.2.3.2 PCR amplification . . . 106
5.2.3.3 Electrophoresis and genotype calling . . . 106
5.2.4 Procedure . . . 107
5.3 Results . . . 109
5.3.1 Neonatal variables . . . 109
5.3.2 The SACAS . . . 110

5.3.3 Genotyping . . . 112
5.3.4 Temperament . . . 113
5.3.5 The HSPS . . . 114
5.3.5.1 Descriptive statistics . . . 114
5.3.5.2 Psychometric results . . . 115
5.3.6 Linear modelling . . . 116
5.3.6.1 Neonatal variables as predictors of childhood behaviour . . . 116
5.3.6.1.1 Main effects . . . 116
5.3.6.1.2 Interaction effects . . . 117
5.3.6.2 Temperament as a predictor . . . 119
5.3.6.2.1 Main effects . . . 119
5.3.6.2.2 Interaction effects . . . 120
5.3.6.3 Genotype as a predictor . . . 120
5.3.6.3.1 Main effects . . . 120
5.3.6.3.2 Interaction effects . . . 125
5.3.6.4 Sensory processing sensitivity as a predictor . . . 129
5.3.6.4.1 Main effects . . . 129
5.3.6.4.2 Interaction effects . . . 129
5.3.6.5 SPS as an outcome variable . . . 132
5.3.7 Correlations between sensitivity markers . . . 132
5.4 Discussion . . . 133
5.4.1 Neonatal variables . . . 133
5.4.2 Temperament as a predictor . . . 135
5.4.3 Genotype as a predictor . . . 135
5.4.4 SPS as a predictor . . . 139
5.4.4.1 Psychometric results . . . 140
5.4.5 SPS as an outcome variable . . . 140
5.4.6 Correlations between sensitivity markers . . . 141
5.4.7 Implications . . . 141
5.4.8 Limitations . . . 143
5.4.9 Future directions . . . 146
5.4.10 Conclusion . . . 148

6 General Discussion **150**
6.1 Overview . . . 150
6.2 Summary discussion . . . 150
6.3 Critiques of SPS and Environmental Sensitivity . . . 154
6.4 Unanswered questions and future directions . . . 156
6.5 Conclusion . . . 160

7 Reference list **162**

Appendix A Ethics clearance **197**

Appendix B The Highly Sensitive Person Scale **202**

Appendix C Study instruments **204**

Appendix D List of manufacturers **226**

Appendix E Model diagnostics - Study 3 **227**

Appendix F Model diagnostics - Study 4 **230**

List of Figures

1.1 The diathesis-stress model 26
1.2 The *SLC6A4* gene structure and function 30
1.3 The dopamine receptor subtype D4 34
1.4 Prenatal programming of postnatal plasticity 38
1.5 The differential susceptibility model 39
1.6 The approximate allele frequency distribution of the S allele across Africa and Eurasia 42
1.7 *DRD4* VNTR lengths as a function of human migratory distance 43
1.8 Interaction models and their interpretation 45

2.1 A correlation heat map of HSP scale items and researcher-generated reverse-scored items 56
2.2 A scatter plot matrix for scale scores in Study 1 58

3.1 Factor extraction solutions for Study 2 64
3.2 Score distribution density plots for the three latent classes 69

4.1 Predicted university adaptation as a function of the interaction between SPS levels and childhood care 91

5.1 An overview of the available Black African BTT+ sample data 103
5.2 An example gel with genotype calls 107
5.3 A scatterplot matrix of demographic, neonatal and socioeconomic variables in Black African members of the Birth to Twenty Plus cohort 111
5.4 Combined density plots for the three latent classes 117
5.5 Potential birth weight x environmental interactions in predicting childhood behaviour 120
5.6 Potential temperament x environment interactions in predicting childhood behaviour 123
5.7 Box plots showing average behaviour scores per 5-HTTLPR genotype 125
5.8 Box plots showing average behaviour scores per *DRD4* genotype 126
5.9 Potential 5-HTTLPR x environment interactions in predicting childhood behaviour 129
5.10 Potential *DRD4* x environment interactions in predicting childhood behaviour . 132

5.11 Potential SPS x environment interactions in predicting childhood behaviour . . 133
5.12 Predicted HSPS average item score as a function of gestational age 134

E.1 Diagnostic plots for the university adjustment model (Study 3) 228
E.2 Diagnostic plots for the university adjustment model (Study 3) continued . . . 229

F.1 Internalising behaviour predicted by neonatal variables 231
F.2 Externalising behaviour predicted by neonatal variables 232
F.3 Total psychology scores predicted by neonatal variables 233
F.4 Internalising scores predicted by genotype 234
F.5 Externalising scores predicted by genotype 235
F.6 Total psychology scores predicted by genotype 236
F.7 Internalising scores predicted by temperament 237
F.8 Externalising scores predicted by temperament 238
F.9 Total psychology scores predicted by temperament 239
F.10 Internalising scores predicted by SPS 240
F.11 Externalising scores predicted by SPS 241
F.12 Total psychology scores predicted by SPS 242

List of Tables

2.1 Descriptive statistics for Study 1 55

3.1 Descriptive statistics for all annual student samples 63
3.2 Factor loadings based on the pattern matrix 66
3.3 Factor composition per sample 67
3.4 Fit comparison for different HSPS factor solutions 68
3.5 Latent class analysis results for Study 2 69

4.1 Descriptive statistics for Study 3 78
4.2 Instrument scoring results and comparison by sex 85
4.3 Disattenuated scale correlations 86
4.4 Correlations between the five factor model and the five factors of SPS 86
4.5 Hierarchical linear modelling results 87
4.6 Linear models with SPS divided into five factors 88
4.7 University adjustment regression model 89

5.1 PCR cycling conditions for the amplifcation of both 5-HTTLPR and *DRD4* exon III VNTRs 107
5.2 Demographic, neonatal and socioeconomic variables for the BTT+ study 110
5.3 Average item scores for the SACAS subscales 112
5.4 Birth to Twenty Plus participant allele frequencies, compared to other Black South African samples 113
5.5 Average item scores for temperament 114
5.6 Average item scores for the HSPS scale 115
5.7 Fit comparison for different HSPS factor solutions 116
5.8 Latent class analysis results 116
5.9 Models of behaviour regressed on neonatal variables 118
5.10 Models of behaviour regressed on neonatal variables with environmental interaction term 119
5.11 Temperament effects on behaviour 121
5.12 Temperament x environment effects on behaviour 122
5.13 Genotypic effects on behaviour 124
5.14 5-HTTLPR x environment effects on behaviour 127
5.15 *DRD4* x environment effects on behaviour 128

5.16 SPS effects on behaviour 130
5.17 SPS x environment effects on behaviour 131

D.1 List of manufacturers 226

List of abbreviations

5-HTT	5-hydroxytryptamine transporter
5-HTTLPR	5-hydroxytryptamine transporter linked polymorphic region
ACQ	Achenbach-Connors-Quay
ACTH	adrenocorticotropic hormone
AES	Aesthetic Sensitivity
AIC	Akaike Information Criterion
ARAS	ascending reticular activating system
AS	Aesthetic Sensitivity
ASD	Autism Spectrum Disorder
BAS	Behavioural Activation System
BFI	Big Five Inventory
BIC	Bayesian Information Criterion
BIS	Behavioural Inhibition System
bp	base pair
BTT+	Birth to Twenty Plus
CBT	cognitive behavioural therapy
CFA	confirmatory factory analysis
CITQ	Carey Infant Temperament Questionnaire
CNS	central nervous system
COMT	catechol-O-methyltransferase
CP	Careful Processing
CRH	corticotropin-releasing hormone
DMN	default mode network
DNA	deoxyribonucleic acid
DNAB	dorsal noradrenergic bundle
dNTPs	deoxyribonucleotide triphosphates
DRD4	dopamine receptor subtype D4
DS	differential susceptibility
E	extraversion-introversion
EFA	exploratory factor analysis
EOE	Ease of Excitation

ES	Environmental Sensitivity
fMRI	functional magnetic resonance imaging
GC	guanine-cytosine
GxE	gene x environment
HPA	hypothalamus-pituitary-adrenal axis
HSP	highly sensitive person
HSPS	Highly Sensitive Person Scale
kb	kilobase
kg	kilogram
L	long allele
LBW	low birth weight
LMIC	low and middle income country
LOESS	locally estimated scatter plot smoothing
LST	Low Sensory Threshold
MAOA	monoamine oxidase A
MOPS	Measure of Parental Style
mRNA	messenger ribonucleic acid
N	neuroticism-stability
NA	Negative Affectivity
NBW	normal birth weight
NGS	next generation sequencing
NS	Neural Sensitivity
NUA	negative university adjustment
OMIM	online Mendelian inheritance in man
OT	occupational therapy
p	page
P	psychoticism
PBI	Parental Bonding Instrument
PCR	polymerase chain reaction
PO	Propensity to Overwhelm
PSS	polygenic susceptibility score
PTSD	post-traumatic stress disorder
PUA	positive university adjustment
R	repeat
rGE	gene-environment correlation
RMSEA	Root Mean Square Error of Approximation
RPI	Resistance to Peer Influence

S	short allele
SACAS	South African Child Assessment Schedule
SACQ	Student Adustment to College Questionnaire
sd	standard deviation
SERT	serotonin transporter
SES	socioeconomic status
SLC6A4	solute carrier family 6, member 4
SPS	sensory processing sensitivity
SRMR	Standardised Root Mean square Residual
SSRI	selective serotonin reuptake inhibitor
TBE	Tris-Boric acid-Ethylenediaminetetraacetic acid
TLI	Tucker-Lewis Index
TMI	transmarginal inhibition
TUA	total university adjustment
US	United States
VIF	variance inflation factor
VNTR	variable number tandem repeat
XL	extra long allele

Chapter 1

Introduction

Our bodies have five senses: touch, smell, taste, sight, hearing. But not to be overlooked are the senses of our souls: intuition, peace, foresight, trust, empathy. The differences between people lie in their use of these senses; most people don't know anything about the inner senses while a few people rely on them just as they rely on their physical senses, and in fact probably even more.

- C. JoyBell C.

1.1 Overview

Why do humans differ in their ability to sense and process environmental stimulation, and how do these differences manifest behaviourally? To unpack this question, which is central to this doctoral research, the introduction commences with broad consideration of the importance of sensation and sensory processing to all living organisms. Drawing from animal research, sensory processing is acknowledged as a fundamental part of animal "personalities", the evolutionary reasoning for which is discussed. The varied but conflicting views on human sensory processing are then considered, beginning with early theoretical propositions by Jung, followed by empirical research by Eysenck, Gray, Kagan, Cheek and Buss, Thomas and Chess, Strelau and Mehrabian. The obfuscation of the role of human sensory processing amidst this previous research is examined.

With the historical foundation laid, focus shifts towards the first research to emphasise sensory processing as a basic personality trait in humans, conducted by Aron and Aron (1997). This trait, known as sensory processing sensitivity (SPS), is carefully detailed and couched within the wider literature, including the aforementioned animal research as well as medical and occupational therapy (OT) disciplines. The measurement of SPS, through the use of the

self-report Highly Sensitive Person Scale (HSPS) is described.

The development of a highly similar theory pertaining to human sensitivity, namely differential susceptibility to the environment (Ellis and Boyce, 2011), is also outlined. Although rooted in biological, rather than psychological reasoning, the theory is thought to coalesce together with SPS, forming a new cross-disciplinary metaframework for understanding human sensitivity, known as Environmental Sensitivity (Greven et al., 2019; Pluess, 2015). Marrying psychological and biological perspectives affords a brief discussion on genetic markers that might underpin sensory processing differences in humans.

Lastly, some implications of, and future research avenues in, the field of sensory processing are contemplated. The lack of multicultural work is acknowledged, and questions are raised about how sensitivity might operate in the unique South African context. This provides the rationale for this doctoral research, the aims and objectives of which close out the chapter.

1.2 Evolutionary background of sensory processing

Fundamental to all life is the ability to detect, integrate and respond to environmental stimulation (Jerome and Liss, 2005; Pluess, 2015; Wolf, Doorn, and Weissing, 2008). From unicellular to multicellular organisms (Baluška and Mancuso, 2009), survival is contingent upon the processing of sensory information from the surrounding context in order to guide adaptive behaviour (i.e. behaviour that ultimately maximises gene dispersal; Chiel and Beer, 1997; Prochiantz, 2010). It is, thus, unsurprising that the passage of evolution, from rudimentary to complex, is marked primarily by the development of the nervous system which elaborates an organism's ability to richly process and respond to their situational determinants (Arendt, Denes, Jékely, and Tessmar-Raible, 2008; Bucher and Anderson, 2015). Climbing the ranks of the animal kingdom steadily unveils increasingly advanced neural systems that enable complex patterns of behaviour which, in turn, afford greater capacity for adaptation (Prochiantz, 2010), culminating in globally-spread primates like macaques and humans (Dorus et al., 2004).

Within animal species, although nervous system structure is consistent across individuals, sensory processing ability is not, allowing phenotypic behavioural variation on which natural selection may operate (Wilson, Coleman, Clark, and Biederman, 1993). Amidst this variation, traditional evolutionary and behavioural ecology studies have sought to describe *mean* behavioural trends within species, under the assumption that natural selection would corral phenotypes towards an "optimum" for the given environment (stabilising selection; Sih, Bell, Johnson, and Ziemba, 2004), working antagonistically to the effects of random genetic mutation and recombination which would generate outliers to this optimum. Through this lens, the importance of individual differences in sensory processing ability has been regarded as unworthy of specific attention, and has thus been minimally emphasised (Sih et al., 2004; Wilson et al.,

1993).

Defining optimal behaviour for any context, however, has been a contentious topic of debate (Belsky, 1997a; Pluess and Belsky, 2013), fuelled by the awareness that there are often many paths towards reproductive fitness and adaptation. Moreover, these paths meander in accordance with the ever-changing environment. Contemporary animal research has thus reduced emphasis on mean behavioural trends (Gosling, 2001; Wilson et al., 1993), whilst bringing back into sharper focus the relevance of individual differences, by revealing contrasting but equally successful survival strategies at the intraspecies level. These strategies are the product of differing animal "personalities" which are fundamentally structured around sensory processing ability, and thus the extent to which behaviour is guided by environmental stimulation (Gosling, 2001; Koolhaas et al., 1999; Wolf et al., 2008).

Amongst the first research to reveal important animal personality differences, Wilson et al. (1993) examined pumpkinseed fish (*Lepomis gibbosus*) along the "shy-bold" continuum. Juvenile "shy" fish were less likely to approach novel objects (either wire minnow fish traps or human observers in the water), swam closer to other fish, harboured a different parasite profile and acclimated slower to a laboratory environment when compared to "bold" fish. Once acclimatised to the laboratory, however, shy behaviour declined. Considering this evidence together suggests the existence of a stably inherited genotypic difference that regulates the extent of responsiveness to the environment (Aron, Aron, and Jagiellowicz, 2012). A similar distinction occurs amongst fruit flies (*Drosophila melanogaster*), which can be either classified as "rovers" or "sitters" - a trait determined by the effects of a single gene (Renger, Yao, Sokolowski, and Wu, 1999). Neurologically, sitters evince greater neuron excitability, nerve plasticity and synaptic connectivity than their roving counterparts, suggesting a more thorough attendance to environmental stimuli (Renger et al., 1999). Observations of great tits (*Parus major*) reveal that some individuals persistently adhere to foraging tactics that have achieved success previously, whereas others modify their foraging behaviour to be pursuant with the prevailing situation (Verbeek, Drent, and Wiepkema, 1994). Similarly, a proportion of great tits have also demonstrated more flexibility in breeding time in response to global climate change, attempting to synchronise the hatching of their offspring with the emergence of their caterpillar prey (Nussey et al., 2005). Clear individual differences in response to environmental stimuli are currently documented for over 100 animal species (Wolf et al., 2008), including rats (Coppens, De Boer, and Koolhaas, 2010; Koolhaas et al., 1999), mice (Benus, Koolhaas, and Van Oortmerssen, 1987), goats (Lyons, 1989), pigs (Hessing, Hagelsø, Schouten, Wiepkema, and Van Beek, 1994), canids (Bekoff, 1977; Braem et al., 2017), squids (Sinn, Gosling, and Moltschaniwskyj, 2008), guppies (Bashey, 2006), and rhesus monkeys (Suomi, 2006), *inter alia*, although studied in the language of different terminologies, such as flexibility, reactivity, plasticity or coping style (Dingemanse, Kazem, Réale, and Wright, 2010; Wolf et al., 2008).

Overviewing the evidence, regardless of species, consistently reveals two distinct behavioural

approaches. Some organisms opt to "act first" (e.g. "bold" pumpkinseed fish; "roving" fruit flies), actively exploring the environment and taking advantage of opportunities as they arise, but often without regard to matters of efficiency or personal safety. Others "pause-to-check" (e.g. "shy" pumpkinseed fish; "sitter" fruit flies), preferring a cautious approach guided by thorough processing of the surrounding environment, although incurring substantive metabolic costs.

These two contrasting approaches arise from the combination of both *sensitivity* and *responsivity*; a pair of terms designed to unite research terminologies across species (Pluess, 2015). *Sensitivity* refers to the perception and processing of external stimulation (the input), thus "sensitive" organisms register much of the detail in their surrounding environment, processing this information to great depths, whilst the converse is true of "non-sensitive" organisms. *Responsivity* specifically refers to the behavioural output that follows internalising environmental cues (Pluess, 2015). Due to the unobservable nature of cognition, researchers must infer covert sensitivity from overt responsivity (Aron et al., 2012; Homberg, Schubert, Asan, and Aron, 2016; Mendaglio, 2003). However, behavioural responses can be additionally influenced by numerous other factors, which prompts the distinction between these closely aligned concepts (Pluess, 2015). Henceforth, "sensitivity" is used to imply both sensitivity and corresponding responsivity, although the subtle discrepancy between these terms should be borne in mind.

What advantage is conferred by the coexistence of two contrasting strategies to responding to environmental stimuli, rather than a single "optimal" type? Wolf et al. (2008) sought to answer this question through careful mathematical modelling, which produced a clear line of evolutionary-grounded reasoning. Consider a population of individuals homogeneous in their non-sensitive strategy to the environment, that is, behavioural changes are random, and independent of the context. Firstly, sudden environmental changes may threaten the existence of the entire population, due to a behavioural strategy unguided by context. Secondly, a sensitive individual introduced into the population is immediately positioned to enjoy extensive pay-offs. Through better appreciation of their milieu, the sensitive individual may consistently, rather than randomly, identify richer foraging areas, better capitalise on opportunities to mate, and/or react timeously and appropriately to the threat of predators, amongst other examples. These pay-offs ultimately strengthen the reproductive fitness of the individual, such that a sensitive genotype and phenotype are spread to the proceeding generation of the population. A sensitive strategy incurs costs, however, such as the metabolic costs of maintaining finely tuned sensation and carefully addressing a broader range of environmental stimuli, as well as time and mortality (in situations where sensitivity is a poor strategy) costs. As more sensitive individuals gather in the population, individual pay-offs for sensitivity steadily decrease, whilst costs remain the same. For similar reasoning then, a population of purely sensitive individuals is unlikely to be successful, and easily invaded by non-sensitive individuals (Wolf et al., 2008).

In order to advance the mathematical model further, it must be assumed that responsivity is

negatively frequency-dependent (Revelle, 1995; Wolf et al., 2008). Put differently, the pay-offs of responsivity outweigh its costs only if the number of responsive individuals in the population remains low, thus offering an adaptive edge by virtue of its rarity (Gosling, 2001). Computer simulations exactly support this assumption, aligning with the observation that responsive individuals compose approximately 20-25% of the population, regardless of species (Aron et al., 2012; Wolf et al., 2008). The inclusive fitness of the entire population benefits in this scenario, in that non-responsive individuals dominate under milder environmental conditions, but responsive individuals are better able to navigate changing environments, ensuring the survival of the population until a new equilibrium is reached (Wolf et al., 2008).

Wolf and colleagues (2008) further questioned why such behavioural syndromes of responsiveness and non-responsiveness are consistently adhered to, in that individuals stick to a single strategy only, without fluctuating between the two. Here, modelling revealed that once an individual has adopted a responsive strategy once, it can apply the same strategy in future contexts at either a lowered cost or to greater benefit (having become better at responsiveness through experience). This generates a positive feedback loop that encourages consistent responsivity. Meanwhile, originally unresponsive individuals do not enjoy such advantages when opting to attempt responsiveness in a new context, and are thus encouraged to continue their mixed/random strategy (Wolf et al., 2008). Modelling aside, it is reasonable to assume that, since each strategy might be underscored by characteristically different neural processing abilities (e.g. as seen in fruit flies), and that these abilities are the likely product of lengthy developmental maturation (Rice and Barone Jr, 2000), any attempts to switch strategy are sure to incur costs that prohibitively lower reproductive fitness. Sensory processing ability, therefore, appears to display *developmental plasticity*, being set early in organismal development with minimal alteration thereafter, more so than *activational plasticity*, that is, having the capacity to change flexibly to the immediate context (Bakermans-Kranenburg and van IJzendoorn, 2015).

In summary, recent decades have borne witness to a paradigm shift regarding sensory processing in animals. Spread along a continuum, sensory processing ability gives rise to behavioural differences that are not the *material* of natural selection, but rather the *product* (Gosling, 2001; Revelle, 1995; Wilson et al., 1993). Put differently, observed behavioural differences in animals are not due to a random assortment of sensory processing abilities still subject to refinement by selective pressures. Rather, behavioural differences reflect the product of generations of natural selection shaping adaptive sensory processing strategies. Specifically, two broad strategies are discernible – animals towards the "sensitive" end of the continuum (i.e. engaging in considerable sensory processing) display a considered hesitance, pausing to check before responding to their environment, whilst "non-sensitive" animals (i.e. engaging in shallow processing) abandon careful reflection in favour of action. Neither strategy holds a decisive fitness advantage over the other, given that they find success in contrasting circumstances, but their coexistence in a single population facilitates survival of the species through inclusive fitness.

1.3 Human sensory processing

Revelations regarding animal sensory processing have encouraged a reassessment of the topic in humans. Although historical research on human sensory processing has been extensive, the matter has been largely obscured amidst the competing schools of thought applied to personality research (Revelle, 1995). Perhaps the first explorations of human sensitivity lie in Carl Jung's proposal of "innate sensitiveness" – a purely theoretical concept couched within the psychodynamic tradition. Empirically demonstrable differences in sensitivity became the focus of later psychobiological research, beginning with Eysenck (1957) and Gray (1981). However, much of this early work was done under the umbrella of introversion-extraversion, a topic which encompasses more than just sensory processing (e.g. sociability). Other child developmental work on shyness (Cheek and Buss, 1981) and inhibitedness (Kagan, 1994) alludes to issues of sensory processing, but fails to appropriately emphasise them (Aron and Aron, 1997). Meanwhile, some developmental researchers have more successfully acknowledged sensory processing as a fundamental individual difference (as appreciated in animals), such as Mehrabian (1977), Thomas and Chess (1977) and Strelau (1974), but the notion failed to gather momentum until the late 1990s. Following below, each research perspective on human sensory processing is briefly detailed.

1.3.1 Psychodynamic perspective

Jung's theorising relating to sensitivity began as a means of identifying a constitutional, rather than experiential, reason for neurosis. Sigmund Freud's theory of hysteria placed limited emphasis on dispositional qualities (Jung, 1961, para 36), rather asserting that psychoneurosis was mostly a result of childhood psychosexual trauma (Jung, 1961, para 4, para 36). However, as Jung contested, "there are a great many people who experience traumata in childhood or adult life without getting a neurosis" (Jung, 1961, para 217). Jung rather proposed that "the individual must meet the trauma with a quite definite inner predisposition in order to make it really effective" (Jung, 1961, para 217). This inner predisposition Jung referred to as "innate sensitiveness", which he argued was the primary facilitator for neurosis, relegating experiences such as trauma to a secondary role. Careful not to advance only one side of the nature versus nurture debate, Jung particularly emphasises the interaction of constitution and experience. Wrote Jung:

> In reality, it is not a question of either one or the other [constitution or experience]. A certain innate sensitiveness produces a special prehistory, a special way of experiencing infantile events, which in turn are not without influence on the development of the child's view of the world. Events bound up with powerful impressions can never pass off without leaving some trace on sensitive people. Some

> of them remain effective throughout life, and such events can have a determining influence of a person's whole mental development. Dirty and disillusioning experiences in the realm of sexuality are especially apt to frighten off a sensitive person for years afterwards, so that the mere thought of sex arouses the greatest resistances (Jung, 1961, para 399).

Jung's theory is thought to stem from his own sensitive nature, the value of which was an apparent source of inner conflict (Aron, 2004), as is allegedly projected through his writings. Earlier descriptions are punitive, unashamedly describing sensitive individuals with adjectives such as "infantile", "ill-tempered", "quarrelsome" and "full of bitterness and malice". However, these are tempered with a number of more empathetic reflections, with Jung conceding that

> [t]his excessive sensitiveness very often brings an enrichment of the personality... [n]othing could be more mistaken, though, than to regard this excessive sensitiveness as itself a pathological character component. If that were really so, we should have to rate about one quarter of humanity as pathological (Jung, 1961, para 572)[1]

and acknowledging that those with "congenital sensitiveness" "tr[y] to go the more or less uncontrolled and half conscious way of normal people, not realizing that [their] own nature demands of [them] more effort than the normal person is required to exert" (Jung, 1961, para 572).

Over time, Jung's opinion on the matter of sensitivity seemed to garner a more decidedly positive slant. His descriptions of sensitiveness had, by and large, been incorporated into his conceptualisation of introversion. To Jung, an introvert was a person who directed psychic energy inward, away from external objects (Aron, 2004), which is appreciably different to the current view of introversion as low sociability (section 1.3.4). Possibly, he preferred the word "introvert" because the connotations were more neutral in comparison to "sensitive" (Aron, 2004; Aron et al., 2012). Referring to introverts, he wrote:

> From an extraverted and rationalistic standpoint, these types are indeed the most useless of men. But viewed from a higher standpoint, they are living evidence that this rich and varied world with its overflowing and intoxicating life is not purely external, but also exists within. These types are admittedly one-sided specimens of nature, but they are an object lesson for the man who refuses to be blinded by the intellectual fashion of the day. In their own way, they are educators and promoters of culture. Their life teaches more than their words... their lives teach the other possibility, the interior life which is so painfully wanting in our civilization (Jung, 1971, para 665).

[1] Recall that approximately one quarter of animals within a given species is considered sensitive (section 1.2).

Empirical support for the accuracy of Jung's theory on innate sensitiveness is perhaps only available from recent literature (section 1.4; Aron, 2004, 2006; Greven et al., 2019). His views seem otherwise neglected in the wake of the more popular topic of introversion-extraversion, which has enjoyed the support of extensive empirical investigation.

1.3.2 Psychobiological perspective

Hans J. Eysenck (1957, 1967, 1981) was amongst the first to acknowledge psychobiological differences pertaining to sensory processing, albeit within the broader context of his two-factor personality model. Eysenck strongly believed that personality traits were manifestations of individual differences in brain function (Matthews and Gilliland, 1999). Eysenck's initial supposition was that individuals could be separated along orthogonally positioned axes of extraversion-introversion (E) and neuroticism-stability (N). His attempts to couch E within psychobiology began with an inhibition theory, which proposed that the balance between two forces, namely inhibition and excitation, separated introverts from extraverts. Introversion arose as a consequence of being slow to inhibit, that is, introverts were slower to habituate to, or become bored with, repeated exposure to a stimulus, thus they often had to guard against the risk of overstimulation. In contrast, extraverts were quick to inhibit, and so sought out further stimulation to combat boredom (Aron and Aron, 1997).

Detailing the E dimension further through work on hysterics, Eysenck noted that the traits of impulsivity and sociability were important sub-factors (Aron and Aron, 1997; Eysenck, 1967; Jang, 1998). Impulsivity was initially considered the more crucial determinant for positioning individuals along the E dimension, but sociability steadily garnered more attention with further research. With the introduction of a third dimension, psychoticism (P), to his original model, and a shift of research focus towards psychotic patients, Eysenck argued that impulsivity correlated better with P, and so revised his personality inventory by transferring most impulsivity items to the P dimension, allowing E to be dominantly defined by sociability (Carver and White, 1994).

Further revisions to the theory saw a change to the psychobiological underpinnings of E, whereby levels of arousal superseded issues of inhibition and excitation (Eysenck, 1967, 1981). Using a simplified conceptual nervous system, Eysenck proposed that the E dimension corresponded to levels of cortical arousal mediated by a reticulo-cortical circuit (mapping largely to the ascending reticular activating system (ARAS) in the brainstem; Bullock and Gilliland, 1993; Eysenck, 1967; Matthews and Gilliland, 1999). Introverts were initially presumed to be consistently more aroused (having a higher basal level of brainstem arousal; Bullock and Gilliland, 1993) than extraverts. This lead introverts to seek out minimally stimulating activities, whilst extraverts sought highly stimulating activities, in order for each type to achieve an optimal level of arousal (Bullock and Gilliland, 1993; Hebb, 1955).

However, problems with these assumptions were soon evident. Arousal levels were discovered to be dynamic (Gale, 1973), varying as a function of numerous factors including sex, time of day, arousal-inducing properties of the environment (Gale, 1973) and individual strategies for managing stimulation. Moreover, once a threshold for excessive stimulation is crossed, a compensatory protective state of transmarginal inhibition (TMI) activates, reducing arousal (Bullock and Gilliland, 1993; Matthews and Gilliland, 1999; Rokhin, Pavlov, and Popov, 1963). Since this threshold is lower in introverts, arousal is maintained at a level lower than extraverts in contradiction with Eysenck's initial assumption. As a further blow to Eysenck's arousal theory, Stelmack's (1990) twenty year review of the relevant empirical literature failed to support different resting levels of arousal between introverts and extraverts. Additional complications for Eysenck's revised theory surfaced with continued research into impulsivity, which appeared to associate better with the biological differences underlying the extraversion-introversion continuum (Aron and Aron, 1997), undermining the shift of the impulsivity trait to the psychoticism superfactor.

In light of these complications, Eysenck's student, Jeffrey Gray (1970, 1981, 1991), proposed modifications to Eysenck's work, leading to an alternative theory. Gray reasoned that impulsivity, along with a second trait of anxiety, were substantial enough to warrant dimensions of their own, oriented 30 degrees to Eysenck's E and N dimensions (Matthews and Gilliland, 1999). Gray justified these amendments psychobiologically through the proposal of a modified conceptual nervous system. Arousal remained a core issue of Gray's personality model (Matthews and Gilliland, 1999), but the mechanism was ascribed to the more narrowly functioning dorsal noradrenergic bundle (DNAB). More important, however, are the Behavioural Inhibition System (BIS) and Behavioural Activation System (BAS) that are proposed to govern anxiety and impulsivity respectively (Fonseca and Yule, 1995). Gray posited that the BAS, consisting of the neurological pathways driven primarily by dopamine, regulated goal-directed behaviour by encouraging approach to appetitive stimuli (Carver and White, 1994; Gray, 1981). Meanwhile, the serotonin-sensitive BIS comprises the septohippocampus, which works in conjunction with the frontal lobes to attend to punishing and/or novel stimuli (Revelle, 1995). Activation of the system ceases behaviour, drawing full attention towards these cues. Thus, Gray's understanding of sensory processing involved the collaborative effort of both the BAS and the BIS, generating an approach or inhibitory response depending on the balance of power between these two systems (McNaughton and Gray, 2000). As an important aside, note that Gray developed the theory of these systems from animal model work, but they have repeatedly found application in human behavioural research.

In spite of the efforts of Eysenck, Gray and other adherents to frame inhibition within psychobiological reasoning, scholars of child behaviour (prior to the 1980s) had almost entirely attributed inhibited behaviour to early experience (Kagan, 1994; Kagan and Snidman, 1991). However, continued research implicated an undeniable role for innate, biological factors, often pertaining to sensory processing. For example, Daniels and Plomin (1985) noted a strong cor-

relation between biological mother shyness and the shyness of their adopted-away offspring at 24 months of age. Meanwhile, Kagan's research on the construct of inhibitedness had revealed that inhibited children had more allergies (Kagan, Snidman, Julia-Sellers, and Johnson, 1991), salivary cortisol, urinary norepinephrine and right hemisphere activation, along with lowered thresholds for activation of the amygdala and the hypothalamus (Aron and Aron, 1997; Kagan and Snidman, 1991). Rosenberg and Kagan (1987) even discovered that inhibited European-ancestry children, and their close relatives, are more likely to have blue eyes, whilst it was more probable for uninhibited children to have brown eyes. Such biological differences are difficult to incorporate into a context-exclusive line of reasoning for shy, inhibited behaviour, but rather speak to an innate predisposition to process stimulation to a fundamentally different extent. Kagan and Snidman (1991) reasonably advanced the notion that "[a]lthough shy, timid behaviour can be the product of specific experiences, independent of any temperamental bias, we believe that a small proportion of children begin life with a predisposition to develop such a profile, given specific environmental conditions". Similarly, leading shyness researcher Jonathan Cheek proposed that "early-developing shyness occurs in people born with a highly sensitive nervous system" (Cheek, 1989, p. 9).

Empirical psychobiological research had thus acknowledged that sensitivity was a contributing factor in constructs that pertained to individual differences such as introversion, shyness and inhibitedness, although its exact role was poorly articulated. Following below are examples of where researchers promoted sensory sensitivity as an individual difference in and of itself.

1.3.3 Developmental perspective

A landmark longitudinal study by Thomas and Chess conducted during the late 1950s aimed to elucidate the importance of childhood temperament (Thomas, Chess, and Birch, 1970). Significant curiosity, continuing until the present day (section 1.5.1), surrounds the observation that children differ in their outcomes even when exposed to highly similar environmental circumstances (Revelle, 1995); a phenomenon known as multifinality (Bakermans-Kranenburg, Dobrova-Krol, and van IJzendoorn, 2012; Cicchetti and Rogosch, 1996). For example, authoritarian parenting may induce anxiety and timidity in one child, but incite rebellion and anger in another (Thomas et al., 1970). To account for this discrepancy, the child's own temperament became an important focus in appreciating developmental psychology (as Jung had anticipated; section 1.3.1). Thomas and Chess (1977) were able to outline a constellation of nine personality traits, each graded along a three-point scale (low, medium, high) that collectively described a child's temperament.

Although numerous temperamental styles arise from the interaction between nine traits, Thomas and Chess proffered three broad categories of temperament, namely "easy", "slow to warm up", and "difficult" (Thomas and Chess, 1977). "Easy" children (40% of their sample)

display a regularity in behaviour, content to follow daily routines, but also readily adaptable to changes and eager to approach new environmental stimuli. "Slow to warm up" children (15%) adopt a modicum of caution when confronted with novelty, adapting slower to change and tempering an otherwise pleasant mood with slight negativity. "Difficult" children (10%) complete the other end of the temperamental spectrum, evincing a largely negative mood and inhibited, irregular behaviour, often reacting intensely to life, be that laughing loudly or crying inconsolably. These "difficult" children have proceeded to garner the lion's share of research attention (much of it in the form of shyness, as discussed previously; Thomas, Chess, Korn, and Korn, 1982), spurred on by Thomas and Chess's (1977) finding that about 70% of such children manifest behavioural problems; a worrisome figure when juxtaposed against the 18% of "slow to warm up" children developing similar issues.

Notably, one of the nine traits delineated by Thomas and Chess includes "threshold of responsiveness" - a measure of sensitivity to stimulation. Children are considered as having either high or low thresholds, reflecting an early example of sensitivity regarded as an individual difference in personality. However, threshold of responsiveness failed to correlate with temperamental style, with each style evincing examples of children with high and low thresholds (Thomas and Chess, 1977).

Mehrabian's (1977) research into stimulation screening offers a further attempt to account for individual differences related to sensory processing. Driven by the lack of support for the arousal theories advanced earlier by Eysenck and Gray (section 1.3.2), Mehrabian argued that the "orienting reflex" of an individual was more informative than discussions of an average arousal level. "Orienting reflex" describes the manner in which an individual responds to a sudden increase in the rate of information per unit time (a more useful consideration since changes in information rate alter arousal more predictability than changes in information volume). "Arousable" individuals increase their arousal significantly, followed by a gradual decline back to a baseline level. In contrast, "non-arousable" individuals evince a modest increase in arousal that rapidly reverts back to baseline. Mehrabian ascribed this individual difference to a matter of *stimulation screening* - arousable individuals struggled to screen out irrelevant information, and were thus termed "non-screeners", whilst "non-arousable" individuals were more selective in their attendance to environmental stimulation, disregarding information perceived as unimportant, and thus denoted as "screeners".

To empirically address stimulation screening, Mehrabian developed a 40-item instrument aimed to identify screeners from non-screeners. Results revealed that non-screeners, who were more commonly female than male, displayed more anxiety and neuroticism, had a greater tendency to affiliate, had heightened sensitivity to rejection, exhibited greater empathy and had less achievement orientation. Broadly, non-screeners were noted to more strongly adhere to the pleasure-arousal hypothesis, approaching pleasure and avoiding displeasure to greater degrees in comparison to screeners. Similar to Thomas and Chess, Mehrabian integrated his sen-

sory processing theorising into a broader framework of temperament. Mehrabian and O'Reilly (1980) posited that the majority of variances in personality could be accounted for by three broad emotional dimensions; arousal-nonarousal, pleasure-displeasure and dominance-submissiveness. Different combinations of these three dimensions generate eight temperament types, paired together to create four continua, namely exuberant-depressed, relaxed-anxious, disdainful-dependent and hostile-docile. Non-screening correlated with the poles of exuberant, anxious, dependent and hostile; a mix of traits that paint a largely negative picture of non-screeners.

Lastly, Strelau proposed a Regulative Theory of Temperament that was framed around individual differences in central nervous system functioning (Strelau, 1974; Strelau and Zawadzki, 1993). As part of this theory, six temperament traits were outlined, namely Briskness, Perseverance, Activity, Emotional Reactivity, Endurance and Sensory Sensitivity. Specifically, Sensory Sensitivity was defined by the reactivity of an individual towards stimulation of low stimulus value (Bridges and Schendan, 2019; Strelau, 1974). Although a corresponding inventory was developed to assess these six traits (Strelau and Zawadzki, 1993, 1995), the Sensory Sensitivity subscale proved problematic because of low validity and the inability to detail an underpinning mechanism for the trait (Bridges and Schendan, 2019). At least one recent study (Hintsa et al., 2016) abandoned the use of Sensory Sensitivity because of these issues, and Kantor-Martynuska (2012) suggested substantial revisions to the trait in light of more recent, and better supported theories of sensory processing and sensitivity (Section 1.4).

1.3.4 The obfuscation of sensory processing

Much other historical research can be brought to bear on the topic of human sensory processing, but the common theme underlying most such research is that the issue of sensory processing is often obscured and/or poorly emphasised. Sensory processing seems overlooked in favour of more popular discussions on introversion-extraversion and temperament, for example. Frank (1939, p. 389) noted "an initial difficulty in the study of personality is the lack of any clear-cut conception of what is to be studied", and so it would seem that in between different attempts to provide clarity, sensory processing has become obfuscated. Some of the pitfalls of this oversight are briefly acknowledged.

Although sensory processing differences between introverts and extraverts have been well documented, the distinction between these personality types remains a matter of sociability, rather than sensitivity. Over two decades of early research has demonstrated that introverts evince greater electrodermal lability (Crider and Lunn, 1971); have heightened sensitivity to pain (Haier, Robinson, and Williams, 1984), analgesics, caffeine (Bullock and Gilliland, 1993) and low auditory frequencies (Stelmack and Campbell, 1974); display greater awareness to subtle stimuli (e.g. Siddle, Morrish, White, and Mangan, 1969); prefer lower levels of noise (Geen, 1984); have more attentional vigilance, and are capable of more thorough learning with-

out awareness (Patterson and Newman, 1993). However, these clear sensory discrepancies are rarely leveraged to help distinguish introverts from extraverts - an oversight beginning with Eysenck's use of largely sociability items to address the E dimension (section 1.3.2) and extending to the more popular five-factor personality model (Costa and McCrae, 1992), which exclusively uses sociability as a measure of extraversion. The complication stemming from an over-reliance on sociability manifests when considering that the strategy of introversion (low sociability) can be selected for two quite different reasons. Indeed, it is a useful strategy for those who have a sensitive nervous system that is only further stressed by the demands of highly social situations, but it is also beneficial to those who have endured a number of aversive experiences, and are thus conditioned to socially withdraw as a matter of safety, regardless of innate sensitivity. Measures of introversion-extraversion, like the Revised NEO Personality Inventory (Costa and McCrae, 1992), are not capable of distinguishing between these two types of introverts because they are not particularly concerned with how a personality dimension might have *developed* (Bridges and Schendan, 2019). Rather, it is *observable* differences between these two categories that have received emphasis, at the expense of the internal, cognitive processing mechanisms (Aron et al., 2012; Bridges and Schendan, 2019). It is unremarkable then, that levels of inter-observer agreement on judging the presence of traits related to the five-factor personality model are highest for extraversion (Gosling, 2001; John and Srivastava, 1999), given how much focus has been directed towards observable features of personality, like sociability.

In the matter of shy behaviour, there has been difficulty delineating the exact role of sensory processing. Akin to the attempts of Freud and Jung at disentangling the complex interaction between constitutional factors and experience (section 1.3.1), shyness researchers have struggled to evenly emphasise the roles of both nature and nurture, resulting in the shyness construct often having to be deconstructed into categories such as acquired versus innate (Aron and Aron, 1997), and state versus trait (Asendorpf, 1989). Moreover, shyness is typically defined by *fearful sociability*, but such behaviour is observably similar to, but conceptually different from, *low sociability* (Aron and Aron, 1997). Those with "highly sensitive nervous systems", as Cheek proposed (section 1.3.2), might understandably seem shy, and may very well develop shyness based on experience, yet are similarly capable of welcoming social interaction, albeit infrequently to avoid overburdening their sensitive dispositions. Note also that shy behaviour, supposedly driven by sensitivity, is characteristic of children with a "difficult" temperamental style (Thomas and Chess, 1977). Yet the temperamental measure of sensitivity defined by Thomas and Chess, namely threshold of responsiveness, failed to correlate with any temperamental style, suggesting that sensitive children can also have "easy" temperaments. A thematically similar argument applies to inhibited behaviour. Again, inhibited behaviour is the observable response for either the child affording their heightened sensitivities important time to adjust, or the child conditioned by adversity (Aron and Aron, 1997). Delineating between such children (innately sensitive versus conditioned by adversity) requires careful elucidation of cognitive processes; an approach not evident in the vast majority of historical research on childhood inhibition.

That shyness and inhibition were considered symptomatic of a "difficult" temperament, and that sensory processing was linked to these negatively-viewed constructs, provides some of the reasoning behind the negativity bias that has only further obscured the issue of sensitivity (Aron and Aron, 1997; Belsky and Pluess, 2009c). The tendency to view sensitive behaviour as negative seems a long-standing feature of Western societal opinion, assuming Jung did indeed begin to use the neutral word "introvert" as a synonym for his theory of innate sensitiveness (section 1.3.1). This bias has coloured much of the literature, spurring on erroneous conclusions that continue to cast children (and adults) of sensitive disposition as exclusively vulnerable individuals - a matter discussed in more detail below (section 1.5.1).

To summarise, the confusion in the human sensory processing literature prior to 1997 appears to arise from a lack of clarity between what is primary, and what is secondary (Aron and Aron, 1997) in determining observable behaviour. Sensory processing has been subsumed as a *secondary* component of a number of related, but more observable constructs. Consequently, a sensitive disposition has been regarded as a characteristic marker of difficult temperament, or otherwise introverted, shy, inhibited behaviour. However, these assumptions stem from an overly-attentive examination of behavioural outcomes, to the detriment of cognitive process – a common critique levelled at this area of research (Bullock and Gilliland, 1993; Gale, 1987). A more parsimonious possibility, suggested through animal research findings (section 1.2), is that sensory processing differences are amongst the *primary* determinants of personality constructs. It is the threshold of responsiveness that facilitates the development of a particular temperamental style; the neural sensitivity that promotes an introverted or extraverted personality. Sensory processing is then itself, an important individual difference, rather than just a component of other behavioural differences.

1.4 Sensory processing sensitivity

1.4.1 Discovery and conceptualisation

In acknowledging the vague understanding of sensory processing, and wanting to confirm that it holds a primary rather than a secondary role in personality, Aron and Aron (1997) addressed the topic in more detail. Beginning with a series of qualitative interviews with self-defined "highly sensitive" individuals, Aron and Aron (1997) constructed a collection of core features that defined a high level of sensitivity. These were built into a self-report measure, named the Highly Sensitive Person Scale (HSPS; see Appendix B). Briefly, the HSPS consists of 27 items that tap both heightened awareness to sensory stimulation and rapid overwhelm to excessive sensory input (more detail on the instrument is offered in section 1.7.1). A series of six follow-up quantitative studies in diverse samples empirically validated the consistency of this core set of features, as assessed by the HSPS, suggesting the existence of a single coherent personality

construct pertaining to an individual difference in sensory processing, which Aron and Aron (1997) have termed *sensory processing sensitivity* (SPS).

Critically important was the finding that SPS was partially independent from social introversion and emotionality, considered both separately and together. Although the majority of those deemed to display SPS were introverted, an appreciable percentage (at least 20%; Aron et al., 2012) were extraverts (as determined by the Myers-Briggs Type Indicator [MBTI]; Briggs-Myers and Briggs, 1985). Furthermore, the items forming the HSPS did not correlate significantly with the MBTI (.14, $p < .10$), the Eysenck Personality Inventory (Eysenck and Eysenck, 1968), extraversion (as measured by the five-factor model, Costa and McCrae, 1992; John, Donahue, and Kentle, 1991), nor other stand-alone items aimed at addressing social introversion. Correlations with emotionality were stronger (average r = .52 over 3 studies, $p < .01$), but still well below one, and possibly inflated due to shared method variance. Correlation with both social introversion and emotionality taken together was similarly high (average r = .55), but again below unity, leaving at least 62% of the variance unaccounted for (Aron and Aron, 1997). Even considering a multiplicative interaction effect between social introversion and emotionality failed to appropriately explain sensitivity. In sum, these findings lent support to the speculation that the previous literature had understandably muddled the issue of sensory processing, which does indeed bear strong relevance to introversion, as well as the negative emotionality that can encourage a state of introversion, inhibitedness and/or shyness, but is nonetheless not synonymous with these constructs (section 1.3.4).

1.4.2 The highly sensitive person

With the matter of sensory processing disentangled from other personality dimensions, Aron and colleagues (Aron and Aron, 1997; Aron et al., 2012) clarified the behavioural profile of the highly sensitive person (HSP). Four characteristics emerged as pivotal in defining the HSP, including: 1) heightened sensory awareness, to the extent that a state of overstimulation is readily achieved; 2) behavioural inhibition following novel or conflicting stimulation; 3) in the sense of Craik and Lockhart (1972), deeper processing of sensory information and 4) strengthened emotional reactions, both positive and negative. Each of these is considered in more detail below.

1.4.2.1 Sensory awareness

At the root of the HSP's personality profile is a nervous system that is substantially more attuned to sensory stimulation. Stimulation is registered with greater ease, such that even very subtle stimulation can be detected, and with increased potency both at conscious and unconscious levels. As Aron (1999, p.4) explains,

> [m]ost people walk into a room and perhaps notice the furniture – that's about it. HSPs can be instantly aware, whether they wish to or not, of the mood, the friendships and enmities, the freshness or staleness of the air, the personality of the one who arranged the flowers.

Empirically supporting this notion, functional magnetic resonance imaging (fMRI) suggests those with high levels of SPS experience greater activation of the cingulate and insula areas, which together have been correlated to heightened moment-to-moment awareness (Craig, 2009); as well as the medial temporal gyrus, which centrally coordinates visual, auditory and language processing (Acevedo et al., 2014).

In stimulation-rich environments, there is a significant and continual engagement of the HSP's nervous system, imposing burdensome metabolic demands. Without relief, the nervous system can be easily overloaded, entering a state of transmarginal inhibition (Matthews and Gilliland, 1999; Rokhin et al., 1963; section 1.3.2) at noticeably lower thresholds than evidenced in non-sensitive individuals. During transmarginal inhibition, performance levels (cognitive and behavioural) decrease, and the state is often described by HSPs as feeling "over aroused" or "overwhelmed". Those HSPs interviewed by Aron and Aron (1997) commonly spoke of a frequent need to retreat, throughout the day, to environments of reduced stimulation to afford regeneration of their frayed nervous systems. They also acknowledged their limited ability to perform up to their regular standards when under scrutiny of observation by others, further indicating an inherently active and metabolically demanding nervous system that affords little opportunity for conscious control.

1.4.2.2 Depth of processing

In conjunction with heightened awareness of stimulation, HSPs process sensory information to greater depths. Deeper processing promotes careful reflection on situational determinants, often affording HSPs behavioural responses that are detail-oriented and accurate to context. Theirs is a more considered and cautious style, which Aron (1999) compares to the historical stereotype of a "royal advisor". Royal advisors have found success throughout history by balancing out the impulsive, and often confrontational tendencies of "warrior kings". Thus, it is common to find HSPs operating in the background, rather than at the forefront of a situation, where stimulation levels are minimised and opportunity for processing maximised. In career terms, HSPs find fulfilment in advisory capacities such as therapists, teachers, researchers and writers where they are able to leverage their extensively processed understandings of the wider context to great benefit (Aron, 1999).

Whilst thorough processing of sensory input typically heightens the contextual accuracy of behavioural output, the effect on response time varies with cognitive load. An fMRI study by

Jagiellowicz et al. (2011) revealed that SPS correlated with stronger activation in visual processing areas during a visual inspection task, in which both major and minor changes to a visual scene needed to be identified. HSPs took significantly longer when attempting to report back on minor versus major scene changes, whereas those lower on SPS responded at the same speed for both conditions. In contrast, Gerstenberg (2012) experimented with a less difficult visual inspection task (identifying a target against a background of visual distractors), finding that HSPs responded quicker, and with fewer errors than non-HSPs. Tangentially, only the trait of SPS predicted performance on this task - none of the dimensions of the five-factor personality model proved similarly informative, providing additional support for the independence of sensory processing sensitivity from other personality constructs. Together, these two imaging studies imply that HSPs respond faster and more accurately when under conditions of low cognitive load, but as load rises, accuracy is maintained at the expense of response speed, requiring lengthier pausing in order to resolve the larger cognitive burden.

There are other proposed cognitive consequences to the deep processing undertaken by HSPs, although these are more challenging to address empirically. HSPs collectively cite frequent, strongly guiding intuitive feelings whose origins escape articulation. Intuition is suspected to be the result of unconscious processing (Aron et al., 2012), and is thus reasonably strengthened amongst those with highly active nervous systems. Aron and colleagues (2012) speculate that such extensive processing may afford more useful dreams, in the psychoanalytic sense, and may also render HSPs more prone to suggestibility. On balance, HSPs characteristically present with richer, more varied cognition that manifests in complex inner lives and extensive meta-cognition (Aron, 1999; Lo, 2018). In at least partial support of these observations, Acevedo and colleagues (2014) observed increased activation of the angular gyrus and dorsolateral prefrontal cortex in those with high (vs. low) levels of SPS; areas of the brain known for cognition and the understanding of metaphor, and higher order cognition and decision making respectively.

Like heightened sensory awareness, improved processing contributes significantly to metabolic demand, further rationalising the low threshold for transmarginal inhibition in HSPs. That much of this processing occurs outside of conscious awareness explains why HSPs sometimes express symptoms of tiredness and overwhelm without having an external cause to attribute these symptoms to (Aron, 1999). Continual cognitive processing at the unconscious level may drain energy levels unexpectedly and so periods of stimulation relief, typically in solitude, must necessarily be frequent and lengthy to not only rejuvenate overtaxed neurons, but to also allow background processing to subside (Aron, 1999; Sand, 2016).

1.4.2.3 Inhibition

Strong behavioural inhibition is primarily observed in HSPs when encountering novel stimuli or when a high level of cognitive dissonance is experienced. Inhibition affords the additional time required to process environmental information and feedback to its fullest extent, in order to prepare, or adjust towards, a more accurate behavioural response (Patterson and Newman, 1993). Furthermore, inhibition can promote learning and thus better anticipation whenever similar environmental experiences reoccur (Patterson and Newman, 1993). Recall, then, that in familiar settings or those in which the level of stimulation is manageable, HSPs have the potential for responding *faster* than average, as witnessed in the research of Gerstenberg (2012; section 1.4.2.2). Inhibition is thus driven by a need to process information, and not necessarily due to fear of stimulation, or out of conditioning from past aversive experiences; a point of confusion that has previously muddled the literature (section 1.3.4). Acevedo and colleagues (2014) noted that HSPs (vs non-HSPs) show greater brain activity in the premotor area, in which action planning and behavioural control are thought to be regulated at an unconscious level. Similarly, HSPs demonstrate substantively more right hemispheric activity, including in the prefrontal cortex, which is known to control behavioural inhibition (Boyce, 2019; Revelle, 1995). Neural evidence thus supports the notion that, for HSPs, behavioural outputs follow only after significant preparation and reflection, typically afforded through inhibition.

The hesitant behaviour of HSPs fits agreeably within the conceptualisation of Gray's behavioural systems (section 1.3.2). Recall that the BIS (borne from animal model research) activates in response to cues of novelty and punishment (Carver and White, 1994). Initially, Gray reasoned that heightened sensitivity (as it was understood at the time) would be best explained by a strong BIS that produced chronic awareness of threatening stimulation, but confessed that such a state would "be torturous, assuming it viable at all" (Gray, 1981). Aron and Aron (1997) further Gray's reasoning by drawing from his later work (Gray, 1985), claiming that the role of the BIS is not to induce chronic awareness towards threat, but rather to serve as a checking system that contrasts reality and perception. Whilst expected and actual stimuli are compared, there is a brief "pause-to-check" phase – behaviour is resumed on completion of this comparison, unless there is a significant mismatch which only then results in complete behavioural inhibition. This synthesis of Gray's ideas better explains why HSPs are capable of both fast and slow reaction times, rather than presenting as continuously inhibited. The role of the BAS in HSPs is less evenly applied, given that HSPs can be both introverted, stimulation avoiders (low BAS activity) and extraverted, stimulation seekers (high BAS activity), albeit in small, manageable doses. However, exactly what behaviours constitute a strong BAS tendency has not been clearly conceptualised (Carver and White, 1994). Regardless of BAS strength, it is reasonable to conclude that, in Gray's terminology, the BIS principally drives HSP behaviour through its careful assessment of reality and perception.

Much like the benefits granted by heightened sensory awareness and deep processing are

counterbalanced by metabolic costs, inhibition offers equally weighted advantages and disadvantages. HSPs default "pause-to-check" response in the face of novelty or cognitive conflict allows for advantageous review of the environmental context in order to discern the best behavioural response. This is analogous to "testing the waters" rather than "diving in head first", a strategy which promotes survival in numerous contexts (Aron and Aron, 2013). However, inhibition exacts a heavy toll on resources, particularly time and energy. Addressing and managing this toll, especially in the face of the ever expanding set of responsibilities of adult living, is a lifelong challenge for HSPs (Aron, 2006; Lo, 2018; Sand, 2016). Moreover, pausing to check is unhelpful when fleeting opportunities - leveraged only by swift action - arise to promote reproductive fitness. Similarly, situations of imminent danger do not grant the luxury of carefully considered stratagems. Paired with a propensity to be easily overwhelmed, HSPs are likely to suffer survival disadvantages in panicked, life-threatening situations.

1.4.2.4 Emotionality

The highly reactive nervous system of HSPs also fosters increased emotional strength, both positive and negative, bearing with it a number of important consequences (Aron et al., 2012; Lo, 2018). Emotion research has clearly demonstrated that both memory and learning are improved when emotionally driven (Carver and White, 1994; Dirkx, 2001). Emotions prompt retrospective appraisal of the events in which they are grounded, facilitating the process of meaning-making (Cox and McAdams, 2014; Dirkx, 2001; Rowe, 2005). Through this process, individuals are often inclined towards the conditions necessary for positive mood states whilst avoiding those that engender negative feelings (Baumeister, Vohs, Nathan DeWall, and Liqing Zhang, 2007). Thus, emotions act as an important reference for learning about environmental stimulation (Baumeister et al., 2007; Dirkx, 2001). Increasing emotional strength serves to augment this process, implying that HSPs are not only guided with greater impetus by their environmental stimuli, but they also absorb more teachings from their surroundings, which are rapidly brought to mind whenever similar conditions are encountered (contributing to faster reaction times in certain contexts). Greater activation of the medial temporal gyrus (section 1.4.2.1) bears further relevance here, given its links to emotional meaning-making (Acevedo et al., 2014). Furthermore, HSPs display heightened activation of the ventral tegmental area (linked to the processing of several positive stimuli) as well as the insula (detection and interpretation of emotion) and inferior frontal gyrus (a component of the mirror neuron system) (Acevedo et al., 2014; Baumeister et al., 2007).

Across the emotional range, experiences of empathy are particularly common to HSPs (Aron et al., 2012; Greven et al., 2019; Lo, 2018). Heightened awareness, coupled with the human innate bias towards negativity (Baumeister et al., 2007), attunes HSPs to the suffering of others, whilst deep cognitive processing appears to strengthen an imagine-other perspective (Batson, 2009) that facilitates empathetic feelings (Lo, 2018). As previously outlined, neural imaging

studies confirm that those scoring high on the trait of SPS evince significantly stronger activation of the cingulate (section 1.4.2.1), but particularly within those areas repeatedly associated with empathy.

Emotional strength might heighten learning, memory and expressions of empathy, but it also promotes instability (Aron et al., 2012). As Baumeister and colleagues (2007) make clear, emotions exist to control us; attempts to reverse this dynamic (trying to control our emotions) are exceedingly difficult, made proportionally more challenging with the strength of the emotion. HSPs are thus regularly at the mercy of their emotions (Lo, 2018; Sand, 2016), which are capable of fluctuating between extremes of both positive and negative (as Jung explained regarding those with innate sensitiveness, "the explosion of affect is a complete invasion of the individual"; Jung, 1971). Such emotional reactivity can be detrimental in a number of present-day social interactions (Homberg and Lesch, 2011), and can contribute significantly to the burden of mental illness (Benham, 2006; Sand, 2016). Here again, metabolic demands must borne in mind, which are already significant at a basal level of neuronal functioning, let alone during emotionally exhausting periods.

1.4.2.5 Other characteristics

Aron and Aron (1997) note a number of additional, more specific features that appear common to HSPs, although their unanimity is questionable. For example, due to the propensity for overwhelm, combined with strong inhibition towards novelty, highly sensitive people typically reach lifetime milestones (e.g. moving out from the parental home, entering a committed relationship, settling on a career) later than average. Put differently, there is a tendency to delay the onset of adult responsibilities by maintaining a more childlike disposition, akin to the *puer aeternus* or *puella aeterna* complex ("the eternal child") from Jungian theory (Aron, 2006). HSPs commonly admit to welling up easily, which leads to frequent bouts of crying, as well as falling in love rapidly and with great intensity (Lo, 2018; Sand, 2016). Alcohol tolerance is usually minimal, as is tolerance of bright daylight. Dreams are often intense and well-remembered the morning after. Likewise, films (and other media) can be deeply impactful, depending on the subject matter, continuing to affect HSPs the day(s) after viewing. Lastly, if free to choose their living conditions, HSPs indicate a general preference towards a country lifestyle, likely because of the reduced stimulation it affords. Aron and Aron (1997) refer to these specific features as *sensitivity-related* variables, which await further empirical support before they can be declared accurate indices with which to judge the presence or absence of SPS.

The four characteristics described in the preceding sections are thus *sine qua non* to the conceptualisation of SPS. Importantly, it is only their co-occurrence together that warrants the label of HSP. Alone, these features may be maladaptive and more descriptive of disorder (Aron et al., 2012). Nevertheless, although Aron (1999) advances SPS as a neutral, non-pathological

personality trait, she notes (Aron, 2004) that it is unfortunately common for HSPs to be misdiagnosed with one of several different disorders, particularly autism, sensory defensiveness and sensory processing disorder (Acevedo, Aron, Pospos, and Jessen, 2018). Much akin to the obfuscation of sensitivity amidst other personality traits (section 1.3.4), these erroneous diagnoses are a possible consequence of the confusion that abounds pathological forms of sensitivity in the medical and occupational therapeutic literatures.

1.4.2.6 SPS and related sensory phenotypes

In the tradition of animal research, *sensitivity* has been used, heretofore, to describe a personality feature of being both alert and malleable to environmental influence. This is, by and large, a consequence of heightened *sensory* awareness and greater depth of *processing*, rationalising Aron and Aron's (1997) decision to adopt *sensory processing sensitivity* as a distinguishing label for the human equivalent of animal sensitivity.

A seemingly unavoidable drawback to the term *sensory processing sensitivity* is the particularly fertile ground it provides for jingle-jangle fallacies[2]. *Sensitivity*, *sensory processing* and *sensory sensitivity* are commonly used terms in medical, occupational therapeutic and psychological literature that may or may not overlap the particular set of qualities that SPS seeks to encapsulate. It is challenging then, to clearly delineate the boundaries that keep separate SPS from related sensory-based phenotypes. This issue has already been evident in disentangling introversion and shyness from SPS (sections 1.3.2, 1.3.4), but further examples warrant mention.

The SPS label is supposed to direct emphasis towards the aspect of *processing* (Aron and Aron, 2013), in order to elevate the personality construct above discussions of stimulus sensation, which primarily feature in the occupational therapy (OT) literature. However, much confusion still ensues. For example, the terms *sensory processing* and *sensory sensitivity* have seen a particular surge in use following the introduction of Dunn's model of sensory processing (Dunn, 1997), in the same year SPS was initially advanced. Dunn's model is designed to provide a theoretical framework for classifying the sensory profiles (i.e. how individuals manage information through their senses) of both children and adults (see Dunn, 2007 for review). Although Dunn strictly advances her model in non-pathological terms, an understanding of sensory profiles is fundamental to exploring appropriate remedial actions for when OT clients seek to better integrate their lifestyles with their preferred methods of stimulation management. This is a particularly challenging endeavour for individuals with heightened stimulus sensation, which is true of high levels of SPS (neutral/non-pathological) and a host of (pathological) phenotypes such as Autism Spectrum Disorder (ASD), post-traumatic stress disorder (PTSD),

[2] A jingle fallacy is the mistaken assumption that two different concepts are identical if they share the same (or highly similar) name. Conversely, a jangle fallacy is the mistaken assumption that two identical (or near-identical) concepts are different if they bear different names.

sensory processing disorder and schizophrenia *inter alia*.

Does Dunn's understanding of sensitivity and sensory processing coalesce with that of Aron and Aron or is this a jingle fallacy? Whilst some occupational therapists appear to suggest that both Dunn and Aron and Aron are speaking to equivalent individual differences in sensory processing (e.g. Liss, Timmel, Baxley, and Killingsworth, 2005; Meredith, Rappel, Strong, and Bailey, 2015), others have tried to stress conceptual differences. Levit-Binnun, Szepsenwol, Stern-Ellran, and Engel-Yeger (2014), for example, note that

> [t]he occupational therapy term sensory responsiveness should be distinguished from the broader psychological term sensory processing sensitivity. Sensory processing sensitivity refers not only to the sensitivity to sensory stimulation, but also to a deeper depth of processing involving higher emotional arousal and greater empathic abilities. On the other hand, sensory responsiveness, or sensory processing as it is sometimes referred to in the occupational therapy literature, is a more narrowly defined term, concerning only the way the brain processes and deals with incoming sensory information.

In other words, the authors argue along the same lines as Aron and Aron (1997): it is not only the ability to take on board a wealth of subtle sensory information that defines an HSP, but also the ability to rapidly integrate and process this information - an ability which is generally impaired in pathological conditions.

To garner evidence for the separation of SPS from pathological issues of sensation, Acevedo and colleagues (2018) reviewed fMRI studies on HS persons and individuals with ASDs, PTSD or schizophrenia. Despite common activation in neural areas important for consciously controlled movement (precentral gyrus), reward processing (the caudate), attention (thalamo-cingulate circuit), reflective thinking and cognitive control (areas of the default mode network [DMN]), there were important differences that characterised HSPs. Those with high levels of SPS showed unique activation of areas important for self-control (prefrontal cortex), empathy, self-other processing (inferior frontal gyrus, insula), awareness, reflective thinking (temporoparietal junction), reward processing (ventral tegmental area, substantia nigra), physiological homeostasis and pain control (hypothalamus, periaqueductal gray). Meanwhile, individuals with ASD, PTSD or schizophrenia displayed dysregulated responses in the DMN, insula and hippocampus, with these dysregulations being known to pose issues for sensory gating (Boyce, 2015). Moreover, at a behavioural level, individuals with any of these three diagnoses are known to minimally exhibit empathy, calmness and self-control - the exact qualities that likely promote survival and gene dispersal for HSPs (Acevedo et al., 2018). Additionally, note that HSPs are more consistent with Baron-Cohen's definition of empathisers (Baron-Cohen, Knickmeyer, and Belmonte, 2005), whilst other sensory types such as autistic individuals tend to occupy the opposite end of the scale as systemisers.

Approaching from a different angle, Mendaglio (2003) notes that gifted individuals (persons that are unusually talented) commonly display *heightened, multifaceted sensitivity*. Writes Mendaglio:

> Far from being a characteristic that refers only to one's feelings being easily hurt, sensitivity is usually described with awareness or perceptiveness at its core. This awareness is directed at self and others. Gifted people are described as having keen awareness of both cognitive and emotional content in self and others. [There] is [a] need to use descriptors such as heightened or greater when referring to sensitivity of the gifted. Implicit in these depictions of sensitivity is the notion that the gifted possess or display more sensitivity – they are more aware of themselves and their social environments – than their non-gifted counterparts (Mendaglio, 2003, p.73).

Whilst these same gifted individuals might also show features of maladaptive hypersensitivity in the OT sense (Neihart, 2000), Mengalio (2003) argues that such sensitivity should not be confused (i.e. a jingle fallacy) with the heightened, multifaceted sensitivity that bestows giftedness. Rather, Mendaglio draws parallels to SPS, which also speaks to a generally heightened, multifaceted sensitivity. Corroborating this idea, both Aron (1999) and Lo (2018) anecdotally report a degree of giftedness amongst HSPs. Similarly, Bridges and Schendan (2019) review a comprehensive body of literature to propose that HSPs are more creative due to their cognitive processing skills and openness (and/or permeability) to experience. If these suppositions are correct, SPS might facilitate aspects of giftedness (in tandem with favourable environmental conditions), and thus an attempt to distinguish the two labels (SPS and heightened, multifaceted sensitivity) might invoke a jangle fallacy.

Whilst further empirical evidence would provide valuable confirmation, one might possibly summarise that the OT and medical literatures, in the main, are concerned with those individuals that are overwhelmed by the *experience* of excessive sensation (autism, sensory defensiveness, PTSD etc.), whilst SPS speaks to those that are often overwhelmed by the *processing* of excessive sensation. What is increasingly evident is that although HSPs are prone to pathological sensory and mental health issues, they are also capable of demonstrating highly adaptive behaviour - a contrast to which emphasis now shifts.

1.4.2.7 Crossover interactions

Of particular interest among Aron and Aron's (1997) initial findings was the discovery of two distinct and meaningful sub-groups of sensitive individuals. Cluster analysis was performed on the data for individuals scoring in the top quartile on the HSPS. Of the two identified clusters, the smaller, comprising 30% of individuals, reported much higher levels of social introversion

and emotionality, but also correspondingly higher levels of unhappiness during childhood. The larger cluster of individuals remained equally as sensitive as the smaller, but scored similarly to non-sensitive individuals on measures of emotionality and introversion. This trend was particularly evident for male participants. From these observations, Aron and Aron (1997) conclude that sensitivity moderates the relation between parental environment and unhappy childhood, establishing a crossover interaction whereby sensitivity is linked to both favourable and unfavourable outcomes depending on environmental experience.

Similar crossovers have been observed in subsequent research. When provided feedback on academic performance, HSPs (vs non-sensitive subjects) evinced the greatest emotional reaction, both positive and negative, in accordance with the valence of the feedback (Aron, Aron, and Davies, 2005). Parallel to this finding, when subjected to a bogus college test in which half the participants received an elementary test, whilst the other half received an unfairly challenging test, HSPs completing the easy test demonstrated the most positive affect, whilst those completing the difficult test evinced significantly more negative affect (Aron et al., 2005). Slagt, Dubas, van Aken, Ellis, and Deković (2017) found that, amongst kindergarten children with high levels of SPS, those who experienced positive parenting had the *lowest* levels of externalising behaviour, but those experiencing negative parenting had the *highest* levels. These example crossover effects hint at a possible adaptive edge for individuals with highly sensitive nervous systems (especially in nurturant contexts), but this has rarely been acknowledged in historical research on sensitive individuals.

1.4.3 Revaluation of human sensitivity

Aron and Aron's research has afforded a new interpretation of human sensitivity which credibly synthesises a broad swathe of the biological and psychological literature, offering viable solutions to some of the thornier issues that have plagued personality research (section 1.3.4). The partial independence of SPS from other personality constructs suggests a potential confounding factor that has undermined much historical research, especially on extraversion-introversion (E). For example, where have highly sensitive extraverts complicated psychobiological assessments designed to delineate central nervous system (CNS) differences along the E scale? How might E and other personality constructs need to be reformulated in order to position sensory processing in a primary, rather than secondary role and what are the potential implications? That HSPs stably account for one quarter of the population, directly comparable to the proportion of sensitive animals, reveals a clear line of evolutionary reasoning that has been conspicuously absent from previous human personality theorising (Aron et al., 2012; Wilson et al., 1993). Lastly, the observation of not just worse-than, but also better-than average outcomes for HSPs calls unavoidable attention to the negativity bias which has clouded sensitivity research (Belsky and Pluess, 2009c).

1.5 Diathesis-stress (transactional/dual risk theory) and differential susceptibility

The reformulation of sensitivity as a neutral trait of human personality poses significant challenges for the once widely-embraced diathesis-stress theory (Monroe and Simons, 1991). Also known as the transactional (Sameroff, 1983) or dual-risk theory, diathesis-stress theorising holds that select individuals, termed "vulnerable", are characterised by genotypes, endophenotypes and/or phenotypes (risk 1/diathesis) that exclusively and disproportionately promote negative outcomes under adverse contextual factors (risk 2/stress; Slagt, Aken, Dubas, and Dekovi, 2016). Such reasoning has encouraged the pejorative view on sensitive behaviour, which has been considered a phenotype symbolic of vulnerability to adversity. Yet there has been increasing acknowledgement, beyond SPS research, that these same "vulnerable" individuals are capable of outcomes better-than-average, undermining the supposed exclusivity of their risk to hardship. Some evidence is now considered, followed by a discussion of the contemporary differential susceptibility to the environment theory (Ellis, Boyce, Belsky, and Bakermans-Kranenburg, 2011), which bears striking resemblance to sensory processing sensitivity.

1.5.1 The diathesis-stress model

The diathesis-stress line of reasoning was largely assembled on a foundation of evidence from childhood resilience studies, which began in the 1970s (Belsky and Pluess, 2013a). Developmental scholars had become increasingly cognisant of the multifinality (section 1.3.3) children displayed even when subjected to highly similar, if not identical, contextual factors. Consistently, it appeared that children could be broadly dichotomised into two groups - those that demonstrated resilience in the face of adversity and those that displayed vulnerability. This notion became the basis of theoretical framework known, interchangeably, as the transactional (Sameroff, 1983), or dual-risk, or diathesis-stress theory (Figure 1.1).

Diathesis-stress thinking, whether explicitly or implicitly, has served as a guiding framework for much of the scientific field (Belsky and Pluess, 2013a). Researchers spanning multiple disciplines have sought to identify the characteristic features that define vulnerable individuals. Yielding early success in this regard were three areas of research, namely temperament, physiology and genetics. Vulnerable children frequently present with difficult temperaments and highly reactive physiologies that appear consistently underpinned by selected genetic variation (Belsky et al., 2009; Belsky and Pluess, 2009a, 2013a). It is largely because of this preoccupation with diathesis-stress reasoning that sensitivity and its associated traits (e.g. neuroticism, inhibitedness, shyness) have accrued such negative connotations (Aron, 2004; Aron et al., 2012). However, these insights stem from often poorly replicated studies with narrow sampling of the environment, usually focusing on situations of adversity compared to a lack thereof, rather

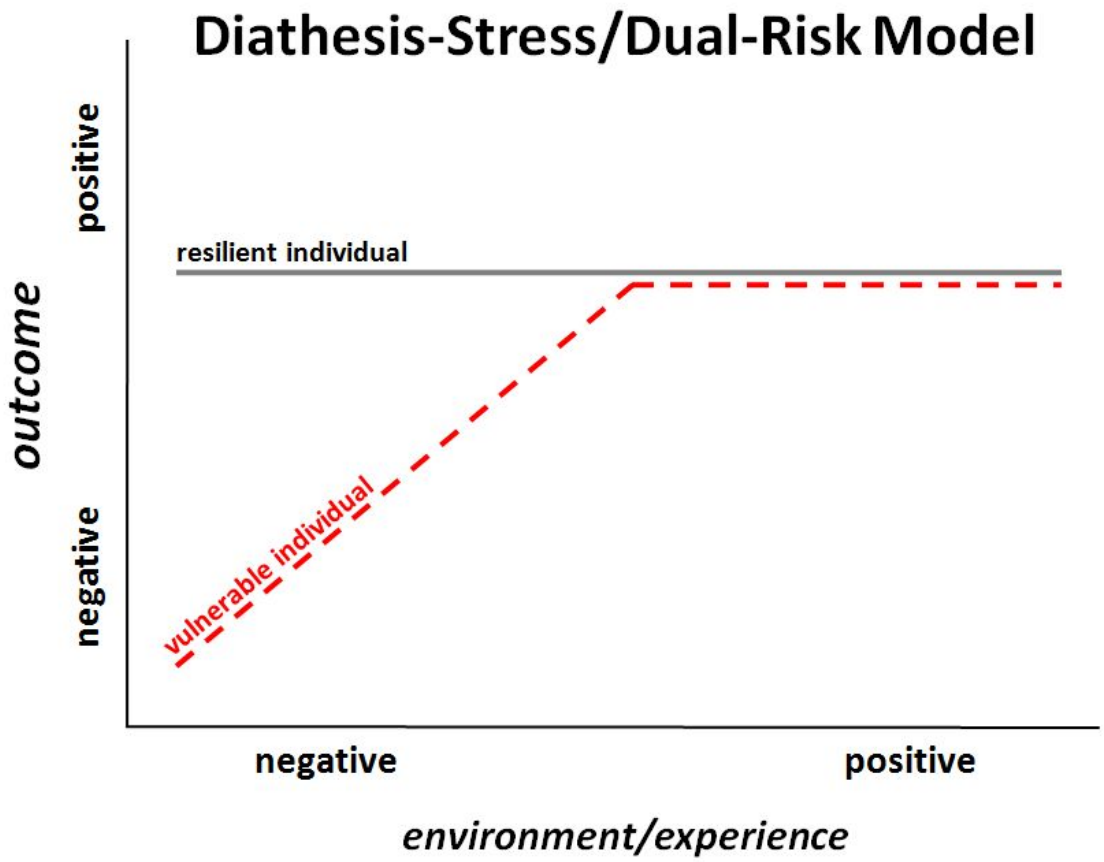


Figure 1.1: **The diathesis-stress model**. Diathesis-stress theorising contends that a subset of individuals are exclusively and disproportionately at risk to negative outcomes in the context of a negative environment. These "vulnerable" individuals are characterised by various markers, such as difficult temperament and reactive physiology. In nurturant environments, vulnerable individuals have comparable outcomes to resilient individuals, who are otherwise reasonably immune to environmental influence. Image available under a Creative Commons licence.

than comparing to situations of support and nurturance (Belsky et al., 2009; Belsky and Pluess, 2009a, 2009c). This negativity bias has been increasingly challenged over the past two decades, especially in light of gathering evidence that reveals vulnerable children tend to perform better than average when appropriately nurtured. Examples in each of the fields of temperament, physiology and genetics are briefly examined.

1.5.1.1 Temperament

The notion of "difficult temperament" refers to a constellation of features exhibited during childhood including, but not limited to, irregular physiology, a tendency to withdraw, resistance towards novelty and change, and intense negative emotionality (Bates, 1980; Thomas et al., 1982). A substantive body of research draws compelling correlations between early, difficult temperament and subsequent behavioural problems and pathology, aligning temperament with diathesis-stress thinking. For example, Lerner and Vicary (1984) found that features of diffi-

cult temperament, whether assessed at age five or early adulthood, predicted tobacco, alcohol and marijuana use in adolescence. Similarly, Windle (1991) found that adolescents exhibiting difficult temperaments had more depression, delinquent activity and substance abuse. Following a 10-year longitudinal study, Guerin, Gottfried, and Thomas (1997) reported that difficult temperament at 18 months predicted a higher frequency of attentional issues, thought problems and aggressive behaviour across the investigated period. However, non-replication of the link between difficult temperament and poor behavioural outcomes was also common (Daniels, Plomin, and Greenhalgh, 1984).

With more careful consideration for the modifying effects of the environment, Bradley and Corwyn (2008) discovered that six month old infants, regarded as difficult by their parents, were *most* likely to manifest behavioural difficulties in early childhood where parenting was poor. However, they were *least* likely to exhibit such issues where parenting was of high-quality, compared to children with easier temperaments. Pluess and Belsky (2009) identified a highly similar pattern in over 700 four-year-old children participating in the National Institute of Child Health and Human Development study. Children of difficult temperament, compared to easy temperament, earned the worst and best teacher ratings for socioemotional adjustment, directly contingent on whether they experienced high- or low-quality parenting respectively. Lastly, Roisman et al. (2012) showed, in a sample of 1306 primary school children, that difficult temperament (between 6 and 36 months) predicts the worst and best outcomes for measures of social, emotional and academic aptitude in direct relation to the sensitivity of parenting.

1.5.1.2 Physiology

Often underpinning a difficult temperament is a highly reactive physiology which augments a child's sensory awareness, and facilitates intense and expressive outbursts of negative emotion (Aron and Aron, 1997). Fearfulness is also heightened, as is a tendency to display behavioural inhibition and withdrawal, so as to avoid feelings of overwhelm (Aron and Aron, 1997). High physiological reactivity, which is rooted in an unusually receptive nervous system, is indicated through multiple proxies, such as elevated salivary cortisol, blood pressure, pulse and/or heart rate - factors which have been traditionally considered symbolic of "vulnerable" children (Obradović and Boyce, 2009). For example, higher internalising behavioural problems have been noted in children with high skin-conductance levels (Weems, Zakem, Costa, Cannon, and Watts, 2005) and high respiratory sinus arrhythmia (Boyce et al., 2001).

However, Boyce et al. (1995) revealed that children with the highest arterial blood pressure during a stress test (compared to those with lower pressure) were most prone to respiratory illness when the rearing environment was stressful, but suffer the least respiratory illness when childhood conditions were more benign. Meanwhile, children with elevated cortisol reactivity were rated by their teachers as either among the least or most prosocial, depending on the quality

of conditions under which the children lived (Obradović, Bush, Stamperdahl, Adler, and Boyce, 2010). Quas and colleagues (2004) found that children with high autonomic reactivity were able to accurately recall stressful events from a laboratory protocol two weeks prior when quizzed by a supportive interviewer. However, in the presence of an unsupportive interviewer, reactive children had the poorest memory for stressful events. Low reactive children did not display significant differences in memory regardless of the disposition of the interviewer. When investigating pubertal timing in young girls, Ellis, Shirtcliff, Boyce, Deardorff, and Essex (2011) noted that father absence predicts earlier onset of puberty, which is otherwise significantly delayed when fathers are present, but only in those girls with high physiological reactivity. Using high baseline respiratory sinus arrhythmia as a marker of physiological reactivity, Conradt and associates (2013) found that reactive, but securely attached infants demonstrated the least amount of problem behaviours at 17 months, but the most such behaviours when attached in a disorganised fashion. Again, low reactive children had moderate levels of behavioural problems regardless of attachment style.

1.5.1.3 Gene x environment studies

As argued by Belsky and Pluess (2013a), diathesis-stress theorising has likely had the greatest impact in the field of gene x environment research. Beginning in the early 2000s, a prominent research thrust to identify allelic variants promoting risk for poor outcomes under adverse conditions gained considerable following, spurred on by the apparent validity of the diathesis-stress model (e.g. Caspi et al., 2002; Caspi et al., 2003). Variants in and around genes such as the serotonin transporter (*SERT*), monoamine oxidase A (*MAOA*), catechol-O-methyltransferase (*COMT*) and dopamine receptor subtype D4 (*DRD4*) quickly became regarded as genotypic risk factors, in the same fashion in which reactive physiology and difficult temperament were acknowledged as endo- and phenotypic risk factors. Here again, however, there exists evidence to suggest these genetic "risk" factors also promote well-being in supportive contexts (Belsky et al., 2009). The serotonin transporter and dopamine receptor subtype 4 genes are used as detailed, illustrative examples.

1.5.1.3.1 Serotonin transporter

Serotonin (5-hydroxytryptamine; 5-HT) is a key monoamine neurotransmitter central to the serotonergic system, which has been highly conserved throughout evolutionary time (Homberg and Lesch, 2011). Found across all bilateral animals, serotonin primarily regulates gut function, but also moderates mood in response to resource availability. Similarly in humans, serotonin is linked to mood, appetite regulation, reproductive activity and sleep (Bouvette-Turcot et al., 2015; Esau, Kaur, Adonis, and Arieff, 2008; Lesch et al., 1997; Rasmussen and Werge, 2007). In accordance with Gray's conceptualisation of the behavioural inhibition system (section 1.3.2), serotonin is specifically noted to inhibit behavioural and emotional responses (Auer-

bach, Faroy, Ebstein, Kahana, and Levine, 2001; Soubrié, 1986). Low levels of serotonin are well correlated with depression and suicide ideation, whilst other alterations to serotonin level can invoke aggressive, violent behaviour in animals and humans (Åslund et al., 2013; Hemmings et al., 2018).

Serotonin's effects are, in part, contingent upon its rate of transport from the synaptic cleft back to the pre-synaptic neuron (De Neve, 2011; Esau et al., 2008; Way and Gurbaxani, 2008), as conducted by the membrane-bound serotonin transporter (SERT). Slower transport, and thus clearance of serotonin from the cleft, prolongs the neurotransmitter's inhibitory (and other) effects (Esau et al., 2008), which is known to heighten the chance of mood dysregulation, neuroticism, depression and anxiety-related traits (Homberg and Lesch, 2011). Pharmacological moderation of serotonin transporter availability has been leveraged through the design of the selective serotonin reuptake inhibitor (SSRI) class of drugs (e.g. Prozac) which are prescribed in the treatment of depression (Way and Taylor, 2010a). Meanwhile, inherent individual differences in the availability and efficiency of SERT are the result of the allelic diversity of the underlying gene (Way and Gurbaxani, 2008).

The serotonin transporter gene (solute carrier family 6, member 4; *SLC6A4*; alternatively, *SERT*, *5-HTT* or *HTT*; OMIM *182138) is a 31 kb sequence containing 14 exons, located at 17q11.2 (GRCh38 coordinates - 17:30 194 318-30 235 967; Esau et al., 2008; Online Mendelian Inheritance in Man, 2016; Figure 1.2). Approximately 1 kb upstream of the transcription start site, Heils et al., (1995; 1996) discovered an irregular repeat polymorphism (rs4795541), subsequently noted for its ability to regulate *SERT* expression. Named by Lesch et al. (1996) as the 5-HTT linked polymorphic region (5-HTTLPR), the locus is characterised by two principal alleles. The "long" (L) allele comprises 16 repeats of the 20-23 bp irregular sequence, whilst the "short" (S) allele consists of only 14 repeats due to a 43 bp deletion (Wendland, Martin, Kruse, Lesch, and Murphy, 2006). Other alleles as low as 13 repeats and as high as 20 repeats (extra-long: XL) are evident, but their frequencies are rare, and their functional impact poorly characterised (Murdoch, Speed, Pakstis, Heffelfinger, and Kidd, 2013).

Far clearer are the functional consequences of the long and short alleles, which are among the most well examined genetic variants to date. *In vitro* studies suggest (although not consistently so; Heinz et al., 2000; Murdoch et al., 2013; Parsey et al., 2006; van Dyck et al., 2004) that the short allele limits transcriptional efficiency of *SERT*, reducing available messenger RNA (mRNA) for translation and thus lowering transporter availability (Beach, Brody, Lei, and Philibert, 2010; Greenberg et al., 2000; Lesch et al., 1996; Stoltenberg et al., 2002). Accordingly, short allele homozygotes (denoted as S/S henceforth) demonstrate the lowest levels of serotonin turnover, followed by heterozygotes (S/L) and long allele homozygotes (L/L), although this pattern is potentially confounded by sex and ethnicity (van IJzendoorn, Belsky, and Bakermans-Kranenburg, 2012; Williams et al., 2003). What still remains unclear is whether a relationship of dominance or co-dominance is shared between the long and short alleles

(Alexander et al., 2012; Alexander et al., 2009; Bradley, Dodelzon, Sandhu, and Philibert, 2005; Way and Gurbaxani, 2008; Way and Taylor, 2010b).

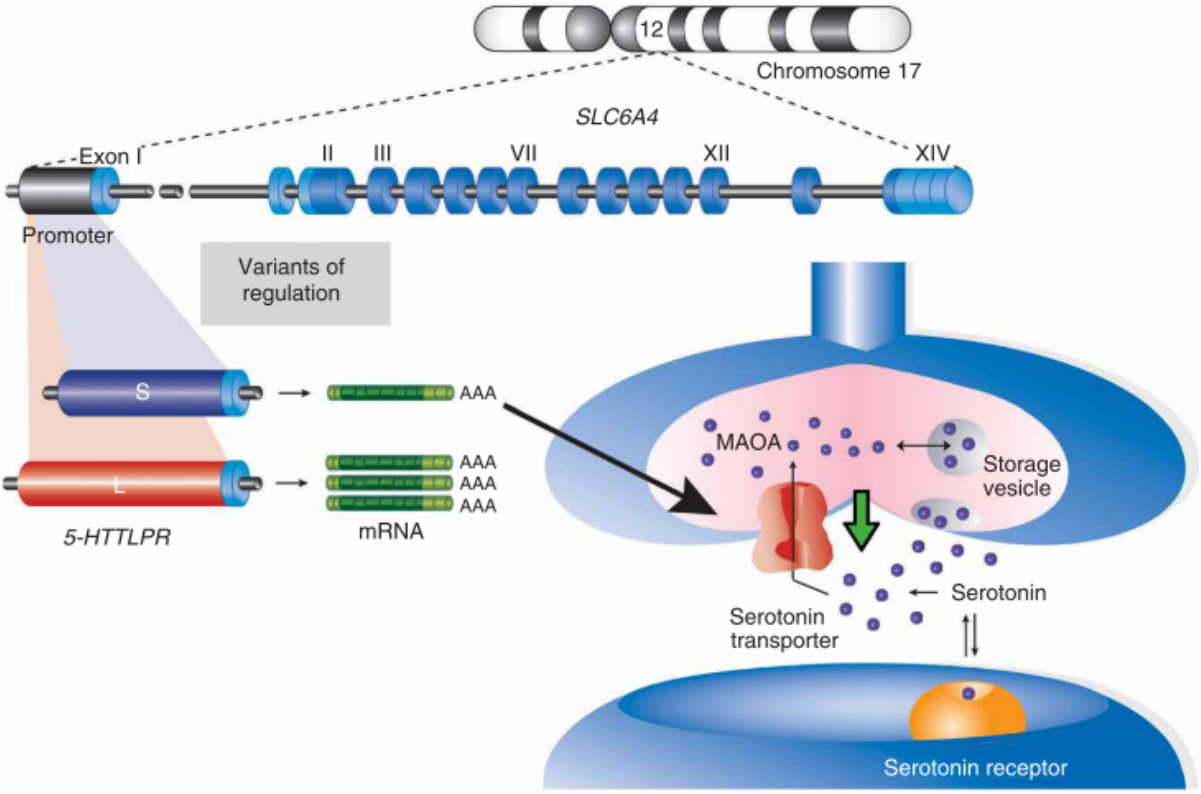


Figure 1.2: **The *SLC6A4* gene structure and function.** The *SLC6A4* gene is located at chromosome 17q11.2. The promoter region of the gene contains a linked polymorphic region (5-HTTLPR) with two commonly observed alleles distinguished by a 43 base pair insertion/deletion. Compared to the long allele, the short allele is transcriptionally less efficient, resulting in lower mRNA levels and translated protein receptors. The fewer the receptors, the slower the reuptake of serotonin neurotransmitter molecules from the synaptic cleft (after which they are either repackaged or metabolised by monoamine oxidase A [MAOA]). The rate of serotonin reuptake has important functional consequences, leading to distinct behavioural differences between short and long allele carriers. Reproduced, with permission (licence number: 4612431303642), from Canli and Lesch, 2007.

The serotonin transporter gene sits at a critical intersection between the stress and serotonergic systems (Way and Gurbaxani, 2008). Physiologically, stress is managed through the hypothalamus-pituitary-adrenal axis (HPA). Briefly, environmental stressors elicit the secretion of corticotropin-releasing hormone (CRH) by neurons in the paraventricular nucleus of the hypothalamus (Barr et al., 2004). In response to CRH (and other hormones), adrenocorticotropic hormone (ACTH) is released from the pituitary gland which subsequently influences the adrenal glands to secrete glucocorticoids (Barr et al., 2004). Glucocorticoids then exert catabolic-promoting effects on peripheral tissues in order to metabolically cope with the detected stressors. Most important among glucocorticoids is cortisol (the proxy by which stress levels are physiologically measured) which, when bound to its cognate glucocorticoid receptor, migrates into the nucleus where it upregulates expression of the *SERT* gene (and others). Notably, the short allele of the 5-HTTLPR appears less receptive to the effects of glucocorticoid

binding, resulting in diminished upregulation and thus fewer translated transporter molecules (Glatz, Mössner, Heils, and Lesch, 2003). Unsurprisingly then, S allele carriers have been noted for their increased startle responses, heightened reactivity to fearful faces, biased attention towards negatively-valenced words, and difficulty in diverting attention from threat-based stimuli (Homberg and Lesch, 2011) - all of which suggest a greater stress response. Note, however, that gene expression levels are often context and tissue specific. Several expression studies have confirmed that the S allele gives rise to fewer mRNA transcripts in lymphocytes, although the pattern isn't mirrored by post-mortem brain tissue (Way and Gurbaxani, 2008; Way and Taylor, 2010b). These contradictory findings are a reminder that the action of genes hinges on their cellular context and exposure to the environment (Way and Gurbaxani, 2008).

The serotonergic system has, since the 1960s, been acknowledged for its critical role in moderating aspects of the environment, especially those that are socially-relevant (Way and Gurbaxani, 2008; Way and Taylor, 2010a). For example, turnover of serotonin showed marked decreases amongst mice that were socially isolated (Garattini, Giacalone, and Valzelli, 1967). In serotonin transporter knockout mice and rats, anxiety-like behaviour and depression have been documented, especially in response to repeated bouts of stress (Caspi et al., 2010). Strikingly similar results have been observed in species of monkeys that possess the 5-HTTLPR S allele (Alexander et al., 2012; Caspi et al., 2010), with particularly noticeable effects in monkeys with poor rearing experiences (Bennett et al., 2002). In a landmark gene x environment study in humans, Caspi et al. (2003) discovered that short allele carriers (especially homozygotes) bore more negative outcomes (e.g. severe depression) following stressful life events. In the three years following this initial discovery, more than 300 articles were published regarding the possible impacts of the 5-HTTLPR, spanning behavioural, psychiatric and pharmacogenetic disciplines (Caspi et al., 2010; Wendland et al., 2006). With stress and other trying environmental circumstances as the focal point, the emergent pattern was that the S allele exclusively conferred vulnerability to poor outcomes, having been further linked to drug use (Covault et al., 2007), alcohol dependence, poor coping mechanisms (Wilhelm et al., 2007), excessive internet use, obesity, increased smoking, pathological gambling (Homberg and Lesch, 2011), suicide (Esau et al., 2008), violent behaviour (Reif et al., 2007), bipolar disorder, and obsessive compulsive disorder (Caspi et al., 2010; Rasmussen and Werge, 2007; Way and Gurbaxani, 2008). These findings were backed, in some cases, by meta-analytic evidence (Feinn, Nellissery, and Kranzler, 2005; Li and He, 2007; Lin, 2007). However, inconsistency in findings was commonplace and reported effect sizes (even in meta-analytic investigations) were less than convincing (Risch et al., 2009). That the S allele only existed to confer vulnerability to stress was an equally unconvincing theoretical position that has struggled to find place in an evolutionary framework (section 1.2).

Adding further confusion were study results that directly contradicted perceptions of the S allele as a vulnerability factor. Carriers were repeatedly observed to display improved cognition (Homberg and Lesch, 2011), in the forms of vigilant decision-making (Roiser, Rogers, Cook,

and Sahakian, 2006) and, based on superior performance on an affective go/no-go task (Roiser, Müller, Clark, and Sahakian, 2007), improved memory recall. Amongst adolescents, those harbouring at least one ("risky") short allele were hypothesised to have the highest number of sexual partners, especially when religious attendance was low (Halpern, Kaestle, Guo, and Hallfors, 2007). However, no such association was found. Rather, short allele carriers with high religious attendance were noted to have 30% *fewer* sexual partners than long allele homozygotes (Halpern et al., 2007), suggesting that S allele carriers were more heavily influenced by religious pressure against promiscuity and thus exhibited unexpectedly low-risk behaviour. Bachner-Melman and colleagues (2005) revealed that short allele carriers are rated as more creative dancers which is an important talent in light of the role of dance in courtship matings throughout human history. Carriers have also been found to have improved verbal creativity (Volf, Kulikov, Bortsov, and Popova, 2009) and more recently, S allele homozygotes were found to have a significantly higher intelligence quotient (Volf, Sinyakova, Osipova, Kulikov, and Belousova, 2015). Lastly, S allele carriers were noted to show better response to social support (Brummett, Boyle, Siegler, Kuhn, and Williams, 2008; Kaufman et al., 2004; Taylor et al., 2006). Eley and colleagues (2012; 2004) noted that cognitive behavioural therapy (CBT) worked better on anxious children that where homozygous for the short allele (although this finding was not replicated in adults with recurrent depression; Bockting, Mocking, Lok, Koeter, and Schene, 2013).

Of specific interest is the observation that the S allele is linked to numerous crossover interactions. For example, Kochanska, Kim, Barry, and Philibert (2011) found that S allele carrying children (compared to L/L homozygotes) had worse moral internalisation when their mothers were considered unresponsive, but far better moral internalisation when reared by responsive mothers. Similarly, Hankin et al. (2011) found that young adolescents (9-15 years) homozygous for the S allele evinced greater levels of positive affect when raised by supportive, positive parents but low levels of such affect when parents were negative and unsupportive. Children exposed to early maltreatment were more likely to develop antisocial behaviour if in possession of an S allele, but S allele carriers (versus non-carriers) also had the fewest antisocial tendencies in the absence of maltreatment (Cicchetti and Rogosch, 2012). Verschoor and Markus (2011) found that students homozygous for functional S alleles exhibited increased tension, negative mood and perceived stress on the day of an examination, but reported the lowest levels of such negative affect on a control day when contrasted with L allele homozygotes. Whilst the aforementioned studies were all specific to European-ancestry participants, Brody et al. (2011) have noted a similar crossover effect in African Americans. Adolescents carrying S alleles that perceived high levels of racial discrimination were most likely to display conduct problems, but had the fewest such problems (compared to L/L genotypes) where perceptions of racial discrimination were low. Perhaps most noteworthy is that a re-examination of the pioneering, aforementioned study by Caspi and colleagues (2003) reveals that S/S homozygotes displayed the *fewest* negative outcomes in the absence of stressful life events – a result that seemed overshadowed by negativity bias. All considered, functional definitions of the S allele have been

necessarily adjusted to reflect a more balanced view, whereby the S allele is now regarded to afford carriers greater vigilance towards the social environment, which can allow for several advantages not predicted by diathesis-stress theorising (Homberg and Lesch, 2011; Way and Gurbaxani, 2008; Way and Taylor, 2010a).

1.5.1.3.2 Dopamine receptor D4

Dopamine is a neurotransmitter of the catecholamine family that participates in a range of broad, non-specific functions. Principally, dopamine moderates attentional, motivational and reward-approach behaviour (Auerbach et al., 2001; Bakermans-Kranenburg, van IJzendoorn, Pijlman, Mesman, and Juffer, 2008) via the mesolimbic pathway which is linked to the experience of pleasurable sensations (Zillmer, Spiers, and Culbertson, 2008). However, dopamine signalling is also implicated in a range of other cognitive (e.g. verbal ability and learning) and motor (especially voluntary) functions (Zillmer et al., 2008). Dopaminergic effects are mediated through two diverse families (encompassing five different subtypes) of G-coupled receptor proteins, named the D1-like and D2-like families.

Of particular research interest has been a member of the dopamine D2-like family, namely dopamine receptor D4 (Figure 1.3c). The receptor first garnered attention from psychiatric and pharmaceutical disciplines following the discovery that it is the primary site of action for clozapine, an antipsychotic option available for the management of schizophrenia (Chang, Kidd, Livak, Pakstis, and Kidd, 1996; Van Tol et al., 1991). Schizophrenics, incidentally, present with elevated levels of D4 receptor in their brain tissue (Chang et al., 1996; Seeman, Guan, and Van Tol, 1993). Early research thus highlighted the potential importance of D4 receptors in behaviour (both normal and abnormal), prompting investigation into protein structural variations and their underpinning genetic code.

The dopamine receptor D4 gene (*DRD4* or *D4DR*; OMIM *126452), located at 11p15.5 (GRCh38 coordinates – 11:637 304-640 705; Figure 1.3a; Online Mendelian Inheritance in Man, 2012), consists of four exons and displays high allelic diversity. On balance, the gene encodes a 387 amino acid protein with seven transmembrane domains. However, amino acid chain length can vary due to an imperfect 48 bp variable number tandem repeat (VNTR) occurring in exon 3 (Figure 1.3b). These repeat sequences code for a proline-rich domain in the third cytoplasmic loop (Figure 1.3c), with repeat number putatively affecting ligand binding ability and/or signal transduction capabilities (Lichter et al., 1993). Repeat sizes range from 2 to 11 repeats, with the 7-repeat allele notably coding for a less reactive receptor (as compared to the more common 4-repeat allele; confirmed through both *in vitro* and *in vivo* tests) that dilutes intracellular dopamine signalling (i.e. a hypodopaminergic effect; Beach et al., 2010). The functional impact of other repeat lengths remains poorly understood (Beach et al., 2010).

The worldwide distribution of *DRD4* alleles bearing different repeat sizes is remarkably

varied. Chang et al. (1996) were amongst the first to investigate the population genetics of this VNTR by typing 1327 individuals across 36 populations. The 4-, 7- and 2-repeat alleles were observed most commonly, with global frequencies of 64.3%, 20.6% and 8.2% respectively. However, only the 4-repeat allele appeared in every population sampled. Other repeat lengths were scattered worldwide without significant patterning. From these observations, the authors reasoned that selective effects, if operating, were not strongly favouring one repeat size over another, despite possible functional discrepancies (Chang et al., 1996).

Early investigations into the effects of repeat length on psychopathology harmonised to support the 7-repeat (7R) allele as a vulnerability factor for a suite of externalising behaviours and psychopathologies including aggression, attention-deficit hyperactivity disorder (DiMaio, Grizenko, and Joober, 2003), alcohol use (Conner, Hellemann, Ritchie, and Noble, 2010), and compulsive and addictive behaviour (Bakermans-Kranenburg and van IJzendoorn, 2007; Bakermans-Kranenburg et al., 2008). Auerbach and associates (1999) were among the first to reveal ties between the 7R allele and difficult temperament. But in the same vein as research on the 5-HTTLPR, hypothesising that the 7R allele conferred exclusive vulnerability was inconsistent with evolutionary reasoning. Furthermore, closer inspection of results and wider sampling of the environment revealed a number of crossover effects that paint a picture less consistent with the diathesis-stress model.

To highlight but a few examples, the 7R allele has been associated, for better and for worse with: childhood externalising behaviour in response to maternal sensitivity (Bakermans-Kranenburg and van IJzendoorn, 2006); adolescent substance abuse following intervention or a lack thereof (Beach et al., 2010); prosocial behaviour in children as a result of maternal positiv-

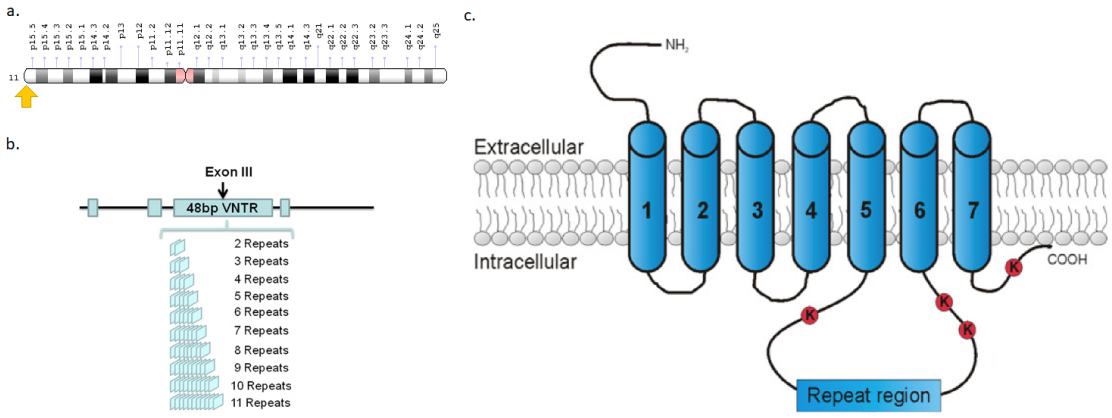


Figure 1.3: **The dopamine receptor subtype D4**. a) The *DRD4* gene is located on the p arm of chromosome 11 (image source: National Center for Biotechnology Information). b) In the third exon of the gene exists a variable number tandem repeat, ranging in size from 2-11 repeats, although 2, 4 and 7 repeat units are most commonly observed (adapted from Jiang, Chew, and Ebstein (2013)). c) The gene encodes a G-coupled receptor protein with seven transmembrane domains. The exon III VNTR affects the length of the third cytoplasmic loop, which has subsequent effects for ligand binding and signal transduction (adapted from Skieterska, Rondou, and Van Craenenbroeck, 2016).

ity (Knafo, Israel, and Ebstein, 2011); externalising behaviour in connection to childcare quality (Belsky and Pluess, 2013b,) young adult alcohol dependence in relation to childhood adversity (Park, Sher, Todorov, and Heath, 2011) and adolescent negative arousal as a function of contextual support (Beach et al., 2012). Meta-analytic investigation has served to strengthen and confirm the existence of these crossover effects (Bakermans-Kranenburg and Van Ijzendoorn, 2011). That these findings stem from both European-ancestry and African American samples (much like crossover interactions for 5-HTTLPR) suggests that the 7R allele functions similarly across these (and possibly other) ethnicities, although further investigation is warranted.

1.5.2 Differential susceptibility to the environment

Drawing together the consistent crossover effects observed in the areas of physiology, temperament and gene x environment research has lead two independent research groups to advance new theories that compensate for the limitations of the diathesis-stress model. Belsky and colleagues have steadily developed, beginning with Belsky, Steinberg, and Draper (1991), a theory of "differential susceptibility" (reviewed in Belsky and Pluess, 2009b), whilst Boyce and colleagues offered a theory of "biological sensitivity to context" (reviewed in Boyce and Ellis, 2005). Such was the overlap between these two lines of theoretical reasoning that they were subsequently amalgamated into a single framework denoted "differential susceptibility to the environment" (Ellis, Boyce, et al., 2011). The central purpose of this theory has been to address two broad questions that have gone unanswered throughout the resilience/vulnerability era of research. Firstly, why are geno-, endopheno- and phenotypes supposedly symbolic of vulnerability so frequent in the human population, when they should otherwise be removed by selective pressures? Secondly, why should vulnerable children excel in nurturant environments, well beyond the capabilities of their resilient counterparts?

To satisfy these questions, differential susceptibility to the environment theory invokes an evolutionary argument claiming that genetics employs a bet-hedging strategy to maximise successful gene dispersal (Belsky, 1997a, 1997b; Belsky et al., 1991). Since the future will forever remain inherently uncertain, no parent, past or present, could accurately identify child-rearing practices that would ensure continued survival of their genetic lineage (Pluess and Belsky, 2011). At best, family units must comprise offspring whose combined potential for reproductive success covers a wide gamut of environmental circumstances. Specifically, at least one child should be minimally influenced by their contextual input (a "fixed" or "conditional" strategy) so that if the selected child-rearing practices proved suboptimal relative to the requirements needed to survive the unfolding future, the developmentally fixed child would be negligibly affected (having demonstrated "resilience" toward parental influence). Thus, the fixed child still possesses a chance of successful reproduction regardless of the "mistake" in parental judgement. At least one other child should be thoroughly permeable to the inputs of their milieu (a "plastic" or "alternative" strategy), so that if the selected child-rearing practices promoted

behavioural traits apt for the future environment, the developmentally plastic child would have more fully absorbed these teachings, consequently enjoying improved odds at successful reproduction over their developmentally fixed sibling. In either scenario, kin selection operates, guaranteeing the continued longevity of at least some gene copies (i.e. inclusive fitness). Parents capable of producing both types of offspring are surely favoured through natural selection (Pluess and Belsky, 2011), explaining the continued and stable presence of both fixed (previously "resilient") and plastic (previously "vulnerable") individuals in modern society.

Pluess and Belsky (2011) further this evolutionary argument by speculating (based on a summary of substantial evidence) that *in utero* gene x environment interactions may be critical in the initial programming of a child's plasticity or fixedness (Figure 1.4). Signals received by the fetus during the prenatal period, whether consistently positive (nutrient sufficiency, calm and relaxed maternal physiology) or consistently negative (nutrient scarcity, maternal stress, anxiety and/or depression), may modify gene expression profiles, promoting the development of an active CNS that produces high physiological reactivity (section 1.5.1.2) and/or a difficult temperament (section 1.5.1.1), which are phenotypes that are indicative of an alternative (plastic) strategy. Consistency in pre-natal signalling suggests to the fetus that the post-natal environment is stable in its characteristics (whether positive or negative). Thus, it behoves the child to be maximally receptive to context, either to completely immerse themselves in the benefits of nurturant care, or to fully assimilate the dangers of a hostile environment such that a hyper-alert disposition can be readied. Such reasoning directly stems from the Barker hypothesis (see Barker and Osmond, 1986), also known as the thrifty phenotype hypothesis (Bateson et al., 2004; Vaag, Grunnet, Arora, and Brøns, 2012), which claims that the early fetal environment can modify adult (especially health) outcomes. This hypothesis has been well supported in both human and animal (e.g. Bashey, 2006) studies (Bateson et al., 2004; Vaag et al., 2012).

Importantly, physiological reactivity and difficult temperament are not merely passive products of heightened CNS activity, but also active tools with which the child can interrogate caregivers about the quality of the post-natal environment (Pluess and Belsky, 2011). In situations where the interrogation reveals a post-natal environment that fails to match pre-natal signalling, the child is still developmentally malleable enough to incur a switch in gene expression towards a conditional (fixed) strategy. The inconsistency in environmental cues suggests that the child would rather benefit from a resilience towards the capricious nature of the surrounding context. Similarly, where the prenatal environment begins as an inconsistent mix of helpful and harmful cues, fixedness is promoted immediately, possibly shifting towards plasticity if inconsistencies are resolved in the post-natal milieu (Pluess and Belsky, 2011).

Some nuances to the development of differential susceptibility must be borne in mind. Firstly, these speculations rest on the assumption that the fetus carries at least some genotypes (e.g. the 5-HTTLPR S allele, the *DRD4* 7R allele) facilitating sensitivity to the environment, and is thus receptive to the features of the *in utero* context. Where such genotypes are ab-

sent, the fetus is presumably forced to continue along a conditional (fixed) trajectory, without options to switch (Figure 1.4). Secondly, birth order may be a critical factor, given that genetics' bet-hedging strategy rests on the presence of both one fixed and one plastic child per family unit. Thirdly, the determination of a fixed or plastic approach is likely restricted to the developmentally sensitive period ranging from conception to early childhood. Any attempts to switch strategy thereafter are sure to invoke prohibitive fitness costs (Bateson et al., 2004); a notion consonant with the mathematical reasoning of Wolf and colleagues (2008), which reveals that playing a single consistent strategy generates a positive feedback loop that otherwise discourages attempts to change (section 1.2). In other words, differential susceptibility appears to speak to an example of developmental plasticity, rather than activational plasticity (much like sensitivity in animals; section 1.2; Bakermans-Kranenburg and van IJzendoorn, 2015), although empirical studies are needed for confirmation. Lastly, whilst a plastic strategy may be encouraged in harsh environments for adaptive reasons (further explained below), there are boundaries to the extent to which such theorising applies – conditions of severity (e.g. malnutrition, trauma and hypoxia) will foremostly hamper normal development without any compensating survival advantage (Bateson et al., 2004).

The above postulations make significant headway into resolving the questions that inspired them. "Vulnerable" children remain commonplace because they represent plastic individuals who have prepared themselves for difficult contexts. Where nutrients are scarce, social support is unreliable and threats are continuously present, it is advantageous to be impulsive; to display antisocial qualities; to be hyper-aroused and to be sexually promiscuous. Disabling consequences of poor mental (e.g. depression) and physical (e.g sexually transmitted diseases) health are the long term disadvantages that ultimately balance short-term benefit. This is referred to as a "live fast, die young" strategy, which still adequately disperses genes even if it does not fit within the social construction of "optimal" living (Belsky and Pluess, 2013a; Ellis and Del Giudice, 2014). Phenotypes of vulnerability (and their associated genotypes) are also characteristic of individuals hailing from high quality contexts where their heightened CNS reactivity has allowed them to absorb benefit to the point of reduced stress and health problems, whilst also affording masterful display of traits considered apt in current society (e.g. addiction-free, attentive, morally guided, prosocial). In differential susceptibility terms, plastic individuals are said to incur outcomes "for better and for worse" (Belsky, 2016; Belsky and Bakermans-Kranenburg, 2007). Together, the concepts of fixed and plastic children better align biological investigations of physiology, temperament and genetics with evolution, which overcomes the major limitation of the diathesis-stress model.

In summary, Boyce (2015) defines differential susceptibility to the environment as:

> the disproportionate, neurobiological sensitivity ["neurosensitivity"] of an individual, group or demographic subpopulation to the developmental and health consequences of both imperilling and protective environments. Differential suscepti-

> bility to socioemotional and physicochemical environments is acquired early in development, is an interactive product of genetic proclivities and contextual attributes, and is adaptive in the sense of maximising survival and reproductive success within extant environmental conditions (Boyce, 2015, p.1).

Note that differential susceptibility to the environment was not advanced in order to supplant diathesis-stress theorising. There remain research findings that are better explained by the diathesis-stress model, rather than differential susceptibility (Belsky and Pluess, 2009a), and so both theories must be considered when examining human development.

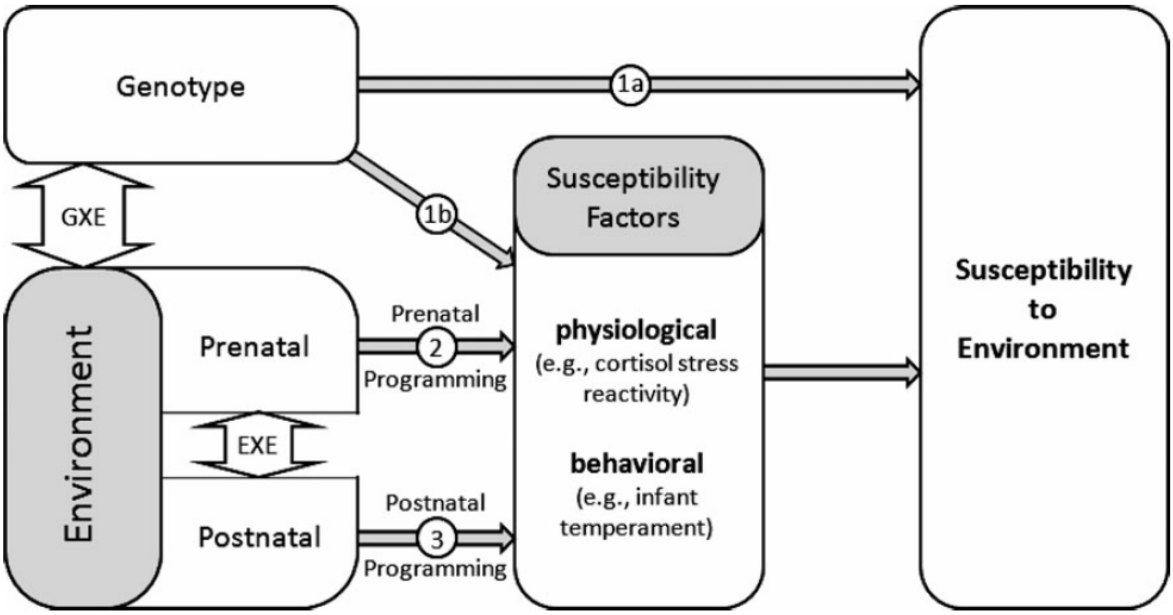


Figure 1.4: **Prenatal programming of postnatal plasticity.** The overall plasticity an individual is likely determined by a complex set of pre- and/or post-natal factors and their interactions with environmental context. Genotype is the primary determinant and may single-handedly decide susceptibility to the environment given a sufficient number of alleles consistently supporting either a fixed or plastic phenotype (path 1a). Alternatively, genotype may strongly encourage the onset of susceptibility factors such as high physiological and behavioural reactivity that allow the child to better interrogate the post-natal environment (path 1b) before calibrating to a final level of sensitivity. Genotypic effects, however, are often subordinate to environmental influence (gene x environment interaction; GxE), beginning *in utero*. Consistently poor or consistently nurturant environmental signals might program gene expression towards heightened plasticity, and thus equip the infant with the necessary susceptibility factors to continually question their environmental context (prenatal programming - path 2). In contrast, inconsistent signalling from the pre-natal environment would presumably shift gene expression towards a resilient, fixed phenotype. Before settling on a final level of sensitivity, however, it is in the child's best interests to compare pre- and post-natal environments (environment x environment interactions; ExE). Notable discrepancy between these two environments may program the onset of susceptibility factors to afford further, final sampling of the child's context (postnatal programming) before nervous system thresholds are set. Image reproduced, with permission (licence number 4612460233007) from Pluess and Belsky, 2011.

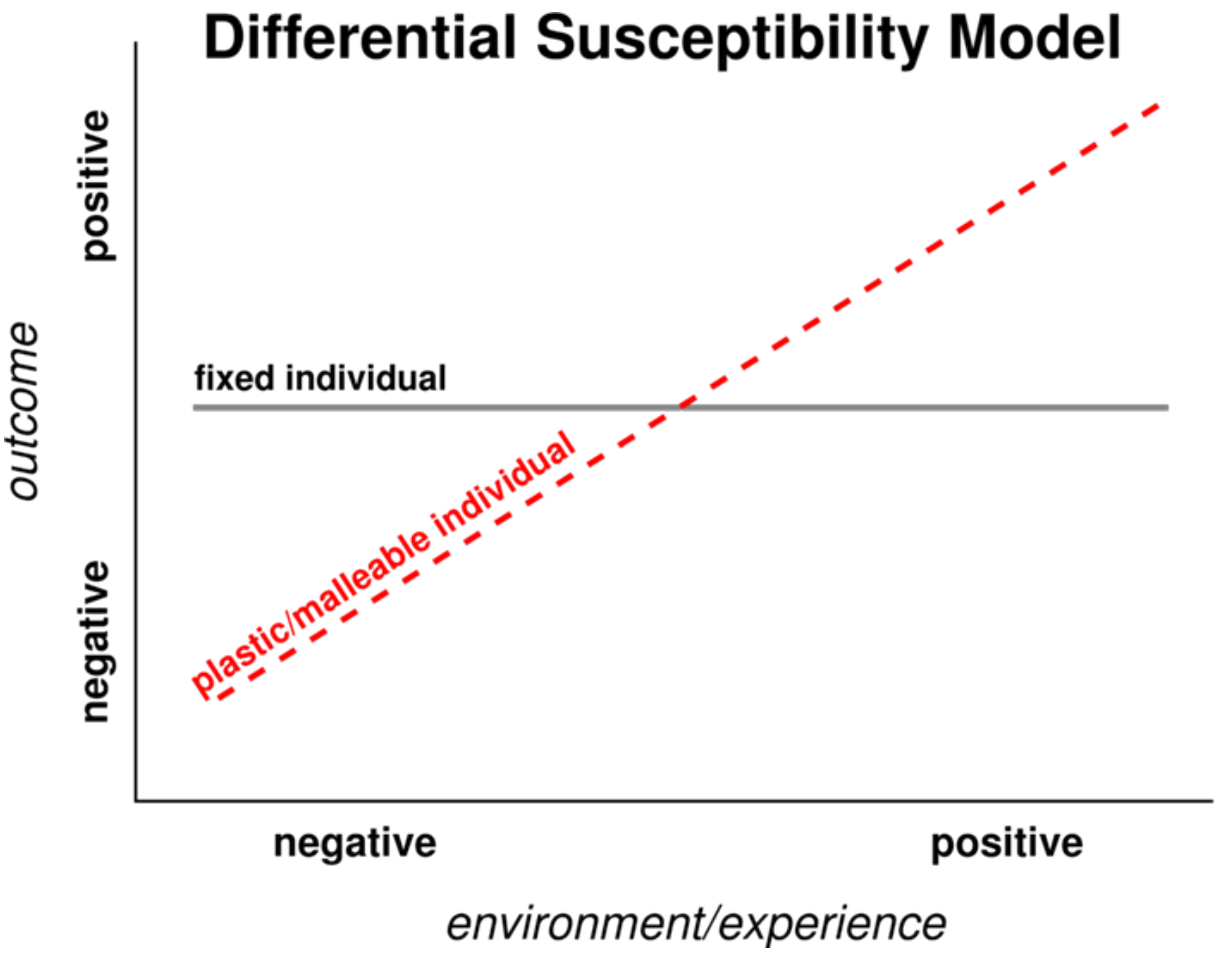


Figure 1.5: **The differential susceptibility model**. The differential susceptibility model proposes that the same individuals who experience disproportionately negative outcomes following negative experiences also enjoy disproportionately positive outcomes following positive experiences. These individuals are malleable/plastic towards their environmental context, whereas fixed individuals display stable outcomes regardless of environmental influence. Image available under a Creative Commons licence.

1.5.3 Relation to SPS

Given their overlapping focus on temperament, reactive physiology, heightened central nervous system processing and crossover effects, SPS and differential susceptibility theory are acknowledged as being largely equivalent, discerned mainly by their direction of approach. Both theories are rooted in evolutionary reasoning, but differential susceptibility theory draws its supporting evidence from childhood development, whilst SPS is premised on cognitive processing differences amongst adults. This is not an uncommon occurrence for personality research, which has been historically characterised by isolated child or adult theorising (Revelle, 1995). Nevertheless, Aron and colleagues (see Pluess et al., 2018) have found place for SPS theory amongst children, and Pluess and Boniwell (2015) have demonstrated that SPS aligns to differential susceptibility theorising in female adolescents overcoming depression.

Genetic and brain-imaging research appears to similarly tie these two theories together.

For example, Licht et al., (2011) noted a significant preponderance of 5-HTTLPR S alleles in a sample of Dutch HSPs, whilst Chen et al. (2011) suggest that variation in dopaminergic system genes is strongly associated to levels of SPS. Augmenting these findings, Assary and colleagues (in preparation) found SPS to be moderately heritable (Greven et al., 2019). Neuroimaging reveals that S allele carriers, during an inhibition task, have increased activity in the prefrontal cortex (Fallgatter, Jatzke, Bartsch, Hamelbeck, and Lesch, 1999); an area of the brain that is strongly active in HSPs (section 1.4.2.3). Way and Taylor (2010b) noted that S allele homozygotes, during a social evaluation task, evince greater diastolic blood pressure (a marker of reactive physiology), which took longer to return to baseline, possibly due to difficulties in emotional regulation (a challenge common to HSPs). As described previously, the S allele is linked to greater reactivity of the HPA axis (section 1.5.1.3.1), which is a mechanism by which to increase sensitivity to contextual stimuli as is characteristic of HSPs. A particular point of overlap is the insula, the region of the brain considered as the potential seat of consciousness (Craig, 2009), which demonstrates heightened activity in both HSPs and S allele carriers (section 1.4.2.1; Homberg et al., 2016). Homberg and colleagues (2016) summarise a comprehensive body of evidence that further highlights the striking similarities between the 5-HTTLPR S allele and SPS. Thus, there is convincing empirical support to believe that SPS and differential susceptibility speak to the same phenomenon, that is, that human sensory processing is an example of developmental plasticity. In other words, a fixed or plastic strategy is engendered (through gene x environment interactions) early in human development, and subsequently maintained through adult life – fixed individuals present as non-sensitive, whilst plastic individuals present as sensitive. Both theories conceptualise human sensory processing in a manner that aligns parsimoniously with animal research (section 1.2), speaking further to their shared theoretical framework.

Regardless of age, biomarker and/or direction of approach, researchers in these fields have shared a common focus on different levels of individual "neurosensitivity" (Pluess, 2015; Pluess and Belsky, 2013). In an effort to further unite the many lines of convergent evidence, Pluess (2015) summarised these ideas under the umbrella term "Environmental Sensitivity" (Greven et al., 2019). Note then that, henceforth, the terms differential susceptibility (DS), Environmental Sensitivity (ES) and neurosensitivity are used somewhat interchangeably.

1.6 Implications

The convergence of evidence across the broad disciplines of psychology and biology towards an integrated theory regarding environmental sensitivity (which, as Ellis and colleagues [2011] note, has occurred much like evolutionary convergence towards a single phenotypic solution) has profound consequences for our understanding of human nature. As alluded to previously (section 1.4.3), much historical research on personality must be reassessed in light of sensitivity

differences, as must significant biological research in the wake of potential plasticity (rather than vulnerability) differences. Moving forward, there are a wealth of specific research questions that should be addressed to better appreciate how to leverage these new insights into human development. For example, what is the domain-generality or domain-specificity of sensitivity (Ellis and Boyce, 2011)? That is, can individuals be sensitive to only a handful of inputs or contexts (domain-specific), or are sensitive individuals inherently receptive to all forms of environmental input (domain-general)? To what extent can plasticity or fixedness be pre- and post-natally programmed by interacting genetic and environmental influences (Pluess and Belsky, 2011)? How are different markers of differential susceptibility (temperament, physiology, genetics) mechanistically coupled? Lastly, how should treatment and intervention differ (if at all) when working with individuals of different neurosensitivity levels (Belsky and van IJzendoorn, 2015)?

The question of whether sensitivity manifests differently across geographical regions is also important to consider (Belsky and Pluess, 2009b). One of the fundamental goals of heightened neurosensitivity is to improve adaptation to changing environments. Recall, for example, the earlier cited animal research on *Parus major* (section 1.2) that revealed favourable selection of the plastic or sensitive birds capable of adjusting their breeding routine to accommodate for global climate change (Belsky and Pluess, 2009b; Nussey et al., 2005). It is reasonable to anticipate then, that neurosensitivity may exhibit population and region-specific idiosyncrasies. Interestingly, the frequency of the S allele increases with distance from Africa (Figure 1.6), producing a wide range of global allele frequencies. Across the African continent, the allele has a stable frequency between 20-30%, but this increases to almost 80% in the Far East. This observation reinforces again that the S allele cannot be solely regarded as a vulnerability factor, but rather, it may have helped early migratory humans adapt to new environments. Indeed, the short allele of 5-HTTLPR has only been documented in the two species capable of inhabiting widely different biomes, namely humans and rhesus macaques, which have been appropriately dubbed "weed species" (Dobson and Brent, 2013; Suomi, 2006). Similarly, *DRD4* VNTR alleles have a notably varied pattern of frequencies (section 1.5.1.3.2), but the general expansion of allele sizes (from 2 to 11 repeats) has been found to proportionately correlate with migratory distance from Africa as well (Figure 1.7; Chen, Burton, Greenberger, and Dmitrieva, 1999). Of particular note, the *DRD4* 7R allele appears to be an evolutionary recent addition to human genomic variation (arising 40 000 years ago; Ding et al., 2002). These observations seemingly imply critical roles for such plasticity-promoting alleles, but whether they function identically under all circumstances or across all ethnicities remains to be seen. For example, Eisenberg and colleagues (2008) examined the distribution of 7R alleles amongst two sub-groups (one pastoral, one nomadic) of the Kenyan Ariaal people. Whilst both pastoral and nomadic groups harboured the 7R allele at equal frequency (approximately 20%, in line with the proportion of HSPs and sensitive animals), phenotypic correlations were exactly opposite. Nomadic carriers of the 7R allele constituted the best nourished individuals of the group, yet pastoral carriers were undernourished in comparison to the rest of the group. Although a "for better and for worse" scenario is still in effect, these findings suggest that it may not always be easy to predict

how the 7R - and other sensitivity markers - respond in differing contexts.

On balance, because of it's relatively recent introduction to the scientific literature, Environmental Sensitivity theorising requires significantly more exploration. Since the theory hinges on person x environment interactions, the wider the selection of participants and environments for study, the better able researchers will be to understand and apply the potentially beneficial implications.

1.7 Measuring and detecting plasticity

Continued research on human sensory processing and its attendant implications will require accurate classification methods for positioning individuals along a fixed-plastic spectrum. As outlined above (section 1.5.1), there are several markers of a more sensitive, plastic disposition, including difficult temperament, reactive physiology and specific alleles of neurologically-relevant genes such as 5-HTTLPR and *DRD4*. However, these markers, because they aren't substantially interlinked nor completely diagnostic of plasticity, are fairly isolated and distal (Boyce, 2015; Lionetti et al., 2018). In contrast, sensory processing sensitivity theory was directly structured around individual differences in neurosensitivity levels, and thus the presence or absence of the SPS personality trait remains, to date, the most proximal indicator of human

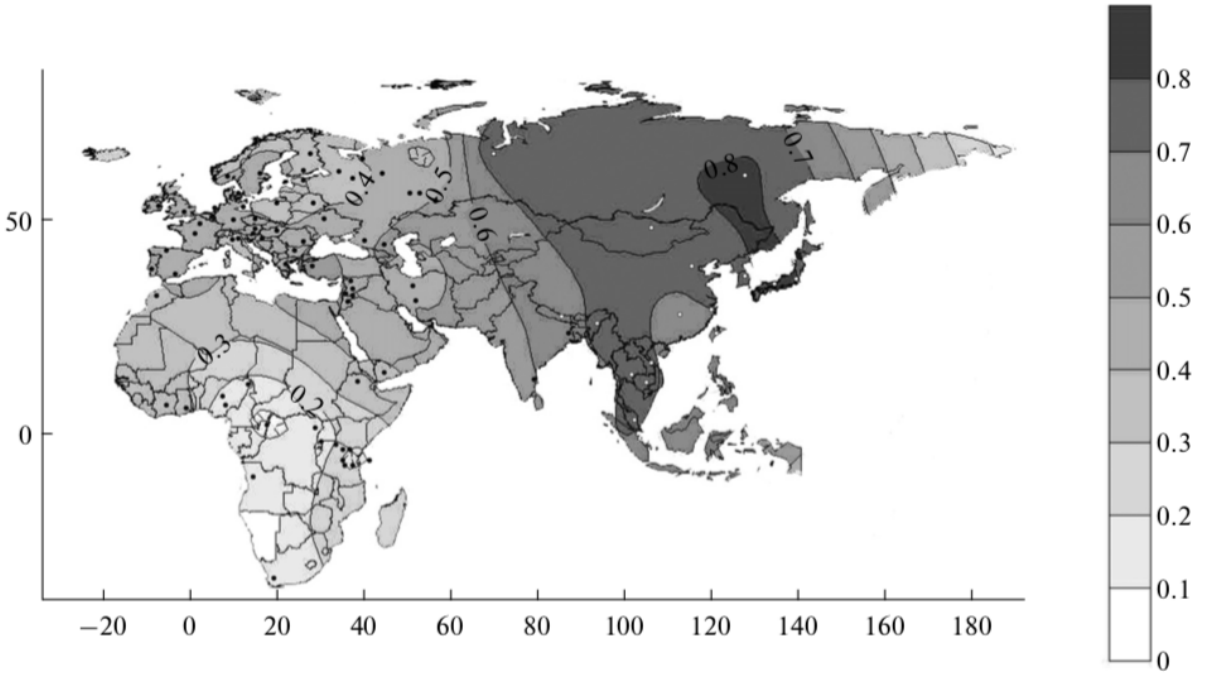


Figure 1.6: **The approximate allele frequency distribution of the S allele across Africa and Eurasia.** The frequency of the 5-HTTLPR S allele increases with migratory distance from Africa. Frequencies on the African continent range between 20-30%, but increase up to 80% in Far East countries like Japan. Image reproduced, with permission (licence number 4612450895590), from Gureyev et al. (2016).

neurosensitivity levels (Lionetti et al., 2018).

1.7.1 The highly sensitive person scale

Determination of SPS level is currently conducted through the administration of the Highly Sensitive Person Scale (HSPS), developed by Aron and Aron (1997) in parallel with their conceptualisation of the personality trait. Recall that the 27-item self-report instrument (Appendix B) taps behavioural responses across two broad domains, namely sensitivity to stimulation and rapid onset of overwhelm (transmarginal inhibition; section 1.4.2). Items are assessed along a 7-point scale, all scored in the same direction, creating a total score range of 27-189. No specific score cut-off is used to discern those with and without the personality trait, rather, the entire distribution of scores across a sample is considered and a high-low breakpoint is defined

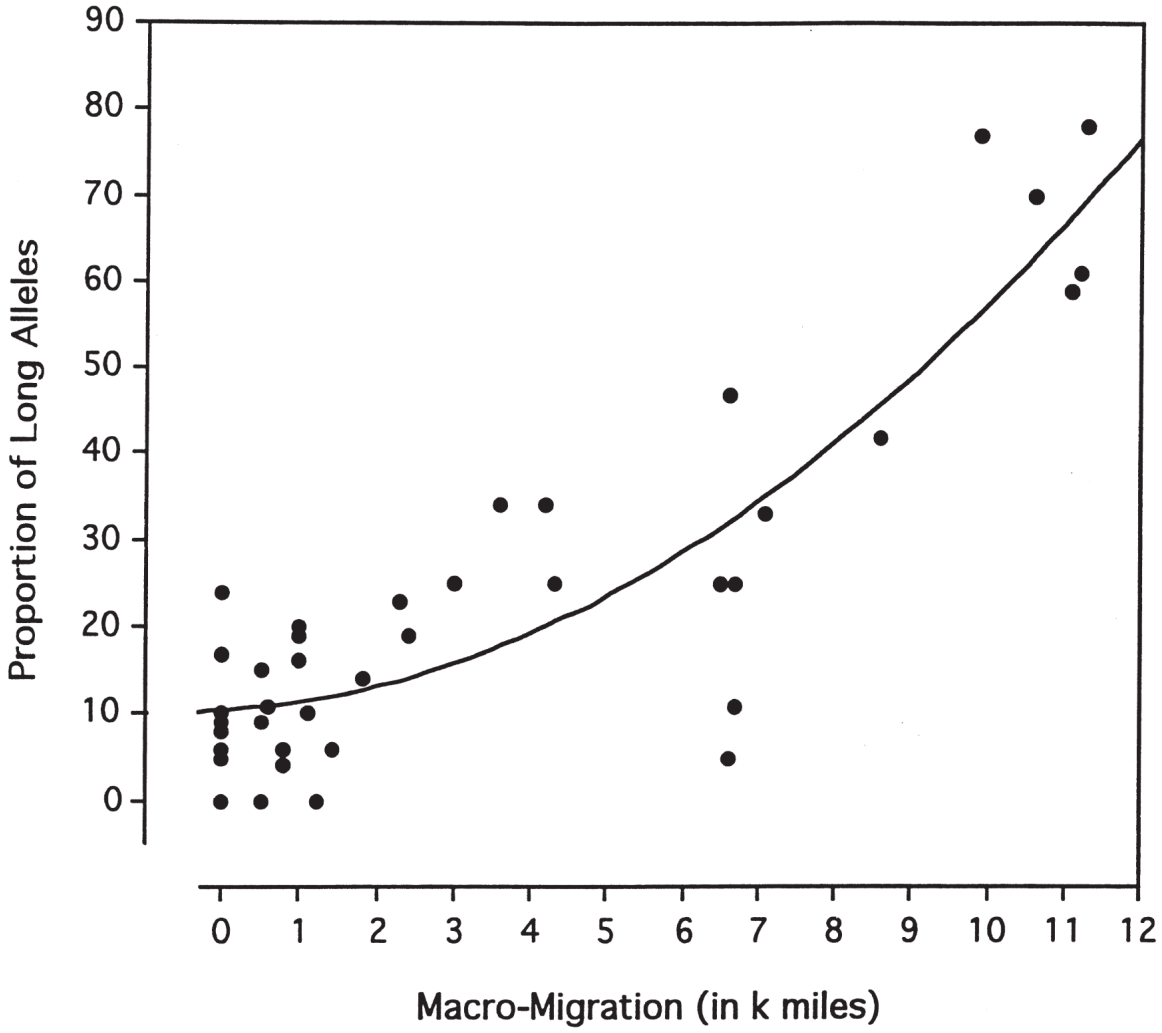


Figure 1.7: ***DRD4* VNTR lengths as a function of human migratory distance.** With migratory distance from Africa (in 1000 mile increments), the frequency of longer *DRD4* VNTR lengths (more than 4 repeats) increases proportionally. Image reproduced with permission (licence number 4622421392790) from Chen, Burton, Greenberger, and Dmitrieva (1999).

at the 70th-85th percentile (Aron and Aron, 2013). Those in the "high" range of scores would be regarded as highly sensitive persons. When psychometrically assessing the instrument in more detail, Lionetti et al. (2018) reported that there are usually three classes of responders to the HSPS. In addition to those scoring consistently high on each of the items (6-7 on the item scale), their is also a distinct group of individuals who indicate modest levels of sensitivity (3-5) and a group who exhibit low levels of sensitivity (1-2). In a popular analogy, these three classes of individuals are colloquially referred to as "orchids" (high sensitivity, plastic individuals, who, like orchids, only thrive under specific conditions), "dandelions" (low sensitivity, fixed individuals, who, like dandelions, are capable of growing under any conditions) and "tulips" (medium sensitivity individuals akin to modestly sensitive tulips; Boyce, 2019; Lionetti et al., 2018).

Although the HSPS has been widely used, and continues to garner evidence for both its reliability and validity, the vast majority of research has occurred in developed countries using participants homogeneous in their ethnicity and/or culture. Because of the confusion surrounding the word sensitivity and its many cultural interpretations, there have been repeated calls for the HSPS to be explored in more diverse samples and cultures (Pluess et al., 2018).

1.7.2 Detecting plasticity

Whether using SPS levels, or some other marker of neurosensitivity, statistical interaction models serve to usefully discern differential susceptibility (DS) from diathesis-stress (and other) effects (Aron et al., 2012; Pluess, 2015). Initially, DS was suggested to be in effect based on simple visual examinations of these interaction plots (Belsky and Bakermans-Kranenburg, 2007; Belsky et al., 2015). If the linear models representing fixed and plastic individuals (however defined) crossed over at roughly the midpoint of the environmental/experiential index, in a pattern commensurate with theory, this was considered sufficient evidence for differential susceptibility (Figure 1.8a). Conversely, if the predicted cross-over point only occurred at the far right of the environmental/experiential index (the most positive context sampled), then diathesis-stress (Figure 1.8d) was considered as a more likely explanation (Belsky et al., 2015; Widaman et al., 2012). Subsequently, far more stringent guidelines for detecting differential susceptibility have been proposed and debated to reduce the risk of Type I error (Belsky et al., 2015; Belsky, Pluess, and Widaman, 2013; Roisman et al., 2012; Widaman et al., 2012). For example, an additional guideline is that simple slopes analysis should reveal a significant slope for the linear model representing plastic individuals, but a non-significant slope for fixed individuals. Although these guidelines are still being actively debated, the core set of criteria for declaring differential susceptibility effects (and thus accurately identifying a case of plasticity vs fixedness) include:

1. the susceptibility moderator (M) is antecedent in time to an independent environmental/experiential variable (V)

2. V and M are not strongly correlated
3. V and M have similar potency in influencing the outcome variable
4. the influence of V as a risk factor is different for the two subgroups delineated by M (i.e. plastic and fixed) when determining the outcome.

With these criteria in place, researchers have both the necessary markers and the formal statistical conditions for studying human neurosensitivity and its interactions with the environment (Boyce, 2015).

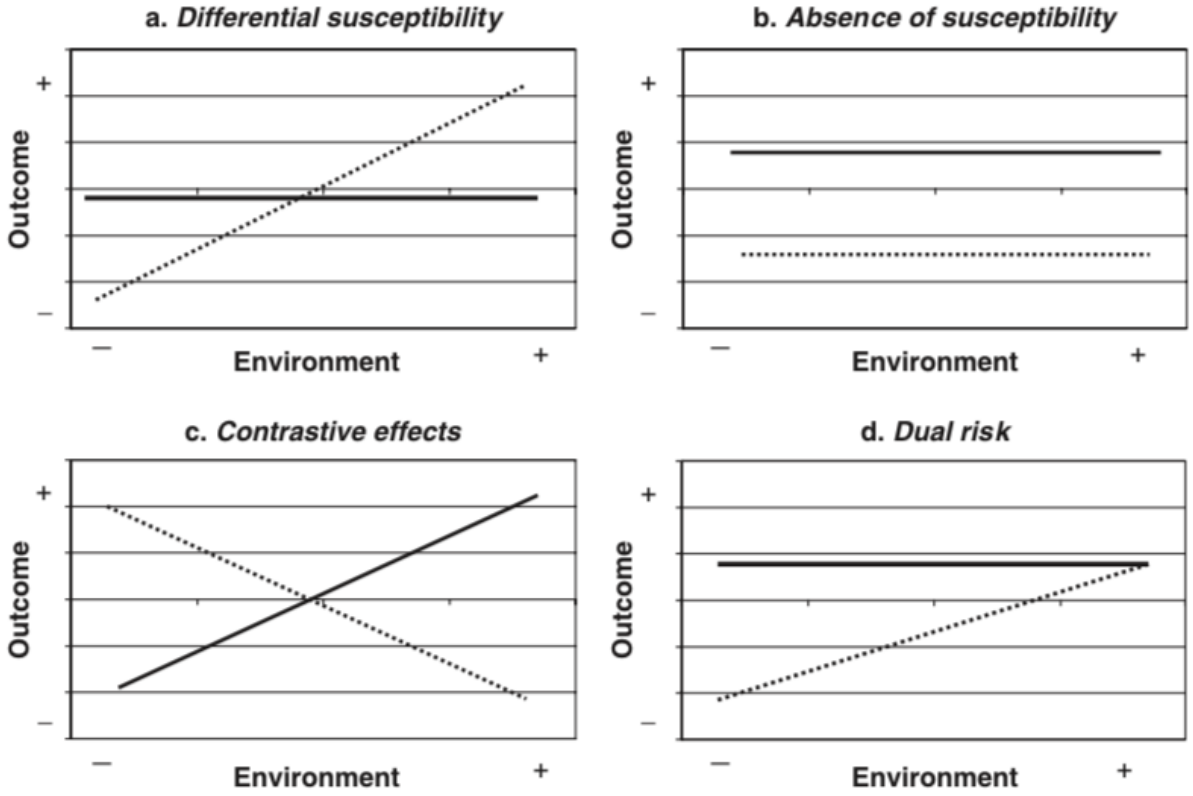


Figure 1.8: **Interaction models and their interpretation**. a) A differential susceptibility effect is identified when a crossover interaction between sensitive/plastic (dotted line) and non-sensitive/fixed (solid line) individuals occurs at roughly the midpoint of the environmental measure (x-axis), for the given outcome (y-axis). Simple slopes analysis should ideally reveal a significant slope for plastic individuals, but a non-significant slope for fixed individuals. b) Where regression lines are mostly parallel, no susceptibility (neither differential susceptibility nor diathesis-stress) can be concluded. c) Regression lines that are directly opposite in slope suggest contrastive effects. d) If the anticipated intersection point between regression lines is near to the most positive end of the sampled environmental spectrum, then a diathesis-stress effect is likely in operation. Image adapted from Belsky and Bakermans-Kranenburg, 2007.

1.8 Study rationale

For several reasons, an investigation of human sensitivity in the context of South Africa is well-positioned to address a number of the gaps in human sensitivity knowledge. Following below, these reasons are briefly explored.

1.8.1 The South African context

South Africa affords a particularly unique setting that offers an unusual combination of environmental factors. The country is characterised by an unparalleled culture of violence, which accounts for almost half of all injury-related deaths per year (Seedat et al., 2009). At least 55 000 rape cases are reported to police per year; a number which is thought to be nine times lower than the actual number of rapes occurring across the country (Seedat et al., 2009). Worldwide, South Africa ranks high in rates of homicide and gender-based harm (Gass, Stein, Williams, and Seedat, 2011; Ward et al., 2012). Age-standardised homicide rates have reached as high as 60 per 100 000 (Prinsloo, Matzopoulos, Laubscher, Myers, and Bradshaw, 2016), and are approximately seven times the global average (Ward et al., 2012). Such pervasive and excessive violence embeds South African citizens in an environment of trauma, to the extent that a significant proportion of individuals are subjected to multiple traumas across their lifespan (Williams, Williams, Stein, Jackson, and Moomal, 2007). Trauma serves to exacerbate other health-related issues including mental health disorders, substance abuse, HIV and other sexually transmitted diseases (Seedat et al., 2009). High levels of unemployment, poverty, xenophobia and inequity further degrade the social milieu, and carry significant detrimental consequences for both South African adults and children alike (Barbarin and Richter, 2001a; du Plessis, Kaminer, Hardy, and Benjamin, 2015; Richter, Mathews, Kagura, and Nonterah, 2018; Treves-Kagan et al., 2019). Applying the new research perspective on human sensitivity against this difficult backdrop may reveal important psychosocial insights that might modify approaches to education, employment and health care.

1.8.2 Population diversity

The South African demographic comprises substantial representation from a number of different ethnicities (Statistics South Africa, 2012). Note, however, that racial and ethnic classification is a point of considerable debate and controversy, particularly in South Africa (Erasmus, 2012), but also more globally (Aspinall, 2007). Establishing a single nomenclature for universal use is an unrealistic prospect, given that different terms for race and ethnicity will be of different weight and value to different people (Ellison and de Wet, 1997). For the purposes of this thesis, race is categorised using the terms appearing in a recent government-led commu-

nity survey in South Africa (Statistics South Africa, 2016). These terms include Black African, Coloured, Indian/Asian, and White. Since race is a social construct that has little biological (especially genetic) basis (Barbujani and Colonna, 2010), terms such as African-, mixed-, Asian- and European-ancestry are used as broader synonyms for the aforementioned racial categories, respectively. These terms are used in a strictly scientific and impartial sense, and are not meant to have any essentialist implications with regard to ethnic (and other) identities, morals, values, language and culture.

In addition to rich interethnic diversity, there is also significant intraethnic diversity, especially amongst Black Africans. Although predominantly of southeastern Bantu-speaking extraction, South Africa plays host to immigrants from across the African continent, which is home to more than 2000 ethnolinguistic groups (Fan et al., 2019; Ramsay, Tiemessen, Choudhury, and Soodyall, 2011). Furthermore, the South African Black population is in the midst of a rural to urban transition, and historical patterns of predominantly collectivist culture are increasingly subject to the more individualistic influences present in urbanised centres (Burgess, Harris, and Mattes, 2002). Thus, South Africa's eclectic citizenship is an ideal source of heterogeneous study samples with which to further scrutinise human sensitivity, which has otherwise been investigated amongst predominantly European-ancestry samples of Western culture (Pluess et al., 2018).

1.8.3 African genetic diversity

African-ancestry individuals harbour the most genetic diversity, with interindividual variation outweighing interethnic variation (Fan et al., 2019; Yu et al., 2002). This is particularly true of the San and Khoe peoples still resident on the southernmost reaches of the African continent, which is a potential birthplace of modern *Homo sapiens sapiens* (Schlebusch et al., 2012). Since all other populations have been found to possess only subsets of the genetic variation present in Africans, genetic studies on the African continent are poised to be maximally informative (Ramsay et al., 2011). However, extensive diversity can be challenging to address, especially with respect to achieving accurate population stratification in order to avoid confounding allele frequency differences between ethnicities (Teo, Small, and Kwiatkowski, 2010). Thankfully, although southeastern Bantu-speaking South Africans are genetically diverse, they remain homogeneous enough to roughly regard as a single ethnolinguistic group (May et al., 2013) if they are sampled from a single geographic area (Choudhury et al., 2017).

Some data pertaining to the frequency of plasticity alleles in Black South Africans are available. The frequency distribution of *DRD4* alleles was examined amongst 80 Bantu-speaking South Africans by Chang and colleagues (1996). The 4R allele predominated with a frequency of 61%, followed by the 7R allele at a frequency of 19%. Similarly, Esau and colleagues (2008) investigated frequencies of the S and L alleles of the 5-HTTLPR in mixed-ancestry, White and

Black South Africans. Amongst Black South Africans, the S allele accounted for 16.18% of the observed alleles (substantially lower than the 39.06% seen in Whites). Although a useful starting point, these frequencies are undermined by small sample sizes, leaving significant room for further investigation into an otherwise understudied population (Teo et al., 2010). Moreover, in Black South Africans, these alleles have only once before been examined with reference to human sensitivity research (Morgan et al., 2017).

1.8.4 Study aim and objectives

Without previous explorations of SPS in South Africa, the present study aimed to provide a robust, foundational assessment of the theory of sensory processing sensitivity and its attendant instrumentation, the Highly Sensitive Person Scale, within the country. Specific objectives included:

1. Assessing the comprehension, reliability and validity of the HSPS in an ethnolinguistically diverse South African sample.
2. Examining the psychometric properties of the HSPS through both factor and latent class analyses, and comparing these outcomes to published reports.
3. Determining the relationship between SPS levels and one or more behavioural outcomes, with and without an environmental modifier.
4. Comparing the extent to which SPS levels cohere with other putative markers of neurosensitivity, both in terms of their co-occurrence and their ability to equivalently predict behavioural outcomes, with and without an environmental modifier.

The task of achieving these objectives was divided across four different studies, linked together by their common use of the HSPS. Each of these studies is named and briefly outlined below:

- **Study 1: A pilot investigation of the HSPS in South Africa**
  Using a small sample of psychology undergraduate university students, the comprehension, reliability and validity of the HSPS was briefly explored (objective 1).
- **Study 2: Psychometric analysis of the HSPS using a culturally and ethnically diverse South African sample**
  A more in-depth examination of the HSPS, using both factor and latent class analyses, was conducted on a large sample of first-year psychology undergraduates (objective 2).

- **Study 3: The associations between SPS, other personality traits, and student adaptation to university**
  University adjustment in first-year students was examined in relation to SPS, the Big Five personality traits, and resistance to peer influence. Parental care during childhood was entered as an environmental modifier (objective 3).

- **Study 4: Individual differences in neurosensitivity in the Birth to Twenty Plus cohort and their association with childhood behaviour at age 7**
  A large, multi-faceted study examining complex interrelationships between neurosensitivity markers (SPS, candidate genes, infant temperament), and behavioral outcomes,ß amongst members of a longitudinal cohort. Socioeconomic status was examined as a possible environmental modifier (objectives 3 and 4). This study also offered a second opportunity to gauge the performance of the HSPS in an independent, non-student, sample (objectives 1 and 2).

Chapters 2, 3, 4 and 5 describe studies 1, 2, 3 and 4 respectively. Each chapter begins by briefly introducing the background and context of the study, followed by the methods, results and a study-specific discussion. Chapter 6 then provides a general discussion which draws from all four studies to critically evaluate sensory processing sensitivity in the South African context.

Chapter 2

Study 1: A pilot investigation of the HSPS in South Africa

Equipped with his five senses, man explores the universe around him and calls it Science.
- Edwin Powell Hubble

2.1 Brief introduction

The Highly Sensitive Person Scale (HSPS; see Appendix B) is a 27-item instrument that taps both a general sensitivity to stimulation, as well as a propensity to become easily overwhelmed in situations applying substantial stress to the nervous system (section 1.7). During its development, the instrument attained Cronbach's alphas ranging from .64 to .75 across six different, age-diverse samples drawn from the United States (US) population (Aron and Aron, 1997). Subsequent research has consistently attained alphas greater than .80, suggesting the instrument carries a high level of internal consistency reliability (Aron and Aron, 2013). Regarding convergent validity, the HSPS correlated well (r = .64) with Mehrabian's measure of sensory screening (Mehrabian, 1977) and the Behavioural Inhibition System scale (Carver and White, 1994; Smolewska, McCabe, and Woody, 2006), which are the most closely aligned measures to SPS (Aron and Aron, 1997). Lower correlations have been observed with items measuring social introversion (e.g. Eysenck and Eysenck's EPI measure; extraversion items from the five-factor personality model) and neuroticism, which suggests good discriminant validity, given arguments that sensitivity is at least partially independent from both these traits (Aron and Aron, 1997; Gerstenberg, 2012; Lionetti et al., 2018).

However, the HSPS was not developed within strongly cross-cultural samples, and there have been few subsequent attempts to confirm its cross-cultural transportability and freedom

from biases (Byrne and van de Vijver, 2010; Mylonas et al., 2014). When first published, no detailed account or justification was provided for the item phrasing employed, other than that, "items were based on observations from [an interview-based study] and previous theory and research that seemed relevant to the construct of sensory processing sensitivity" (Aron and Aron, 1997, p 352). Notable in this regard is that the instrument relies on language that is both colloquial (or at least relatively informal and culturally-loaded) and technical/sophisticated. An *a priori* analysis of the scale's language reveals a number of words and phrases whose accessibility and interpretability are questionable outside of American or Anglo-American populations, and in populations where multilingualism is the norm and English not necessarily the home language of participants. These words and phrases include "frazzled" (item 11), "rattled" (item 14), "shake you up" (item 21), "overwhelmed" (items 1 and 7), "subtleties" (item 2), and "conscientious" (item 12).

A compounding problem is the lack of reverse-scored HSPS items. The use of reverse-scored items is a recommended practice in most psychometric test construction, and assists in discouraging or detecting acquiescence (tendency to agree) and dissent (tendency to disagree) response sets, and certain patterns of random responding (Kaplan and Saccuzzo, 2012; Murphy and Davidshofer, 2005). Indeed, a number of HSPS items are evaluatively loaded, and could be thought to encourage a 'faking good' response set and/or socially desirable responding (Aron and Aron, 2013; Tourangeau, Rips, and Rasinski, 2009). These issues become doubly problematic when administering the instrument to participants less familiar with English and/or having responses that are culturally-influenced since there is even greater scope for inaccurate response sets, but no possible means to be alerted to such issues.

Prior to a more substantial psychometric assessment (Chapter 3), a small pilot study was conducted to assess the HSPS in a culturally-diverse assortment of South African students. Psychology undergraduate students, between the ages of 18-26, were invited to participate. In addition to the original HSPS, three researcher-generated reverse-scored items were added to the scale. The aim of this study was to ascertain whether the HSPS performed comparably to other samples by confirming that a) the scale maintained a high degree of internal consistency reliability ($\alpha > .70$); b) SPS was at least partially independent from introversion and neuroticism; c) females scored higher than males; d) there were no significant language issues that undermine the scale's performance and e) researcher-generated reverse-scored items correlated in anticipated directions with original HSPS items.

2.2 Methods

2.2.1 Study participants

Study participants were drawn from psychology undergraduate classes (first, second and third year) at the University of Witwatersrand, during the 2015 academic year. First year psychology students were able to earn course credit through a student research participation programme (second and third year students did not have access to this incentive). No exclusion criteria were enforced, given that the primary aim was to gather commentary on comprehension and language-based issues. Demographically, the population of psychology students at the University is ethnically and linguistically diverse and predominantly female.

Of the 117 participants that responded to the invitation to participate (approximately 5% of psychology undergraduates - a low response rate), 94 participants completed the 27 item HSPS with five or fewer missing items ($<$ 20% of items). The majority of these participants were in first year, likely due to the incentive of course credit. As anticipated, based on the general demographic of psychology students at the University, the majority of respondents were Black African and female. Over half of the respondents (51.07%) did not speak English as their home-language (detailed descriptive statistics are reported in Table 2.1)

2.2.2 Instruments

2.2.2.1 The HSPS

The pilot survey comprised the original 27 items of the HSPS (Aron and Aron, 1997), along with three researcher-generated, reverse-scored items, all of which were scored along a 7-point scale where 1 = Not at all, 4 = Moderately and 7 = Extremely. As described previously, the HSPS demonstrates strong reliability, with alphas $>$ .80 in a number of independent samples (Aron and Aron, 2013) and has good convergent and discriminant validity. Following each item of the HSPS, participants were asked to note any issues (via an open-ended response) they had in comprehending the language of the item (Did you have any problems with this statement [e.g. difficult to understand; confusing words; unclear meaning]? Please explain as clearly as possible). This option was designed to give participants, especially those whose home language was not English, a chance to air their uncertainty about any of the items.

To address the lack of negatively-phrased items, three reverse-scored items were generated based on the "sensitivity-related variables" (section 1.4.2.5) identified by Aron and Aron (1997). Sensitivity-related variables were discerned from highly informative items originally used in the development of the HSPS, but that were ultimately not selected for the final instrument for

various reasons (e.g. brevity; Aron and Aron, 1997). These items related to love intensity, lifestyle preference (country/rural versus urban) and reaction to personal criticism. Typically, HSPs demonstrate high levels of love intensity; prefer a calmer, country lifestyle; and struggle to receive personal criticism. Based on these claims, the reverse-scored items were: 1) 'Do you often feel less emotional than other people (e.g. you cry less; you don't fall in love as easily etc.)?, 2) Do you prefer your life to be very fast-paced (filled with activity)? and 3) Do you find personal criticism easy to deal with?. These items served as an additional safeguard, not only against instances of malingering and random responding, but also to ensure that participants correctly understood what the original HSPS items were asking of them.

2.2.2.2 Miscellaneous items

In attempting to validate that SPS is partially independent of introversion and neuroticism, a small selection of items assessing these traits were also included. A two item scale was used to gauge introversion (1. Do you prefer to go out with one or two friends [versus a larger group]?; 2. Do you like having just a few close friends [as opposed to a large circle of friends]?), whilst a three item scale was used to measure neuroticism (1. Are you prone to fears?; 2. Are you a tense or worried person by nature?; 3. Are you prone to depression?). Given the importance of early environment in relation to levels of SPS (section 1.4.2.7), a four item scale assessing childhood care was also included (1. Were you close to your primary caregiver [mother, father or legal guardian] as a child? 2. Was your primary caregiver [mother, father or legal guardian] fond of infants and small children [liking to hold and cuddle them; have them around]? 3. Would you say your childhood was difficult or troubled? 4. During your childhood, did you feel like you were dominated by others much of the time [for example, by siblings, parents, other relatives, friends etc.]?). For the sake of consistency, all of these miscellaneous items were adapted from ones used (and recommended) by Aron and Aron (1997; 2013) in their research on sensitive individuals.

2.2.3 Procedure

Following ethical approval (clearance certificate number H15/08/30, Appendix A), an invitation to participate in research examining sensory processing differences was extended (via an email notification and a brief in-class presentation) to first, second and third year psychology undergraduates. After confirming their informed consent, participants completed the research survey independently (i.e. without assistance from a researcher), and electronically via SurveyMonkey®. No pencil-and-paper surveys were administered. Item order was randomised per participant to mitigate context effects (Tourangeau et al., 2009). Prior to the survey items, participants were presented with optional demographic questions that elicited information on their age, sex, ethnicity and home language. No other identifying information was recorded.

For the purposes of descriptive statistics, participants were removed if they had over 20% missing data (for participants with less than 20% missing data, missing item responses were replaced with the arithmetic mean for that item), but retained all responses to the open-ended questions regarding item comprehension. Data analysis was performed using R (version 3.5.1), RStudio (version 1.1.456) and the *psych* (version 1.8.4; Revelle, 2018) and *ggplot2* (version 3.0.0; Wickham, 2016) packages.

2.3 Results

2.3.1 The HSPS

2.3.1.1 Scale scoring and item interpretation

The 27-item HSPS demonstrated good Cronbach's α and Guttman's λ^6 values (.87 and .93 respectively), suggesting high internal consistency reliability in line with other published reports. Inter-item correlations were largely positive (average r = .20), as were item by scale correlations (average r = .47). Only three items had scale correlations $<$.30, namely items 2, 4 and 18. Total HSPS scores were normally distributed (W = .99, p = .43), with a high average of 121.95. The mean item score and standard deviation (sd; 4.52 $\pm$ .77) fell between scores from United States (3.96 $\pm$ .71) and German samples (4.54 $\pm$ .94; Aron and Aron, 2013). There was no significant difference in HSPS score between male and female respondents (Wilcoxon rank sum test: W = 682, p = .36, effect size r = .10), although the number of male respondents (n = 15) was notably small.

Only a relatively small number of open-ended responses were offered by students, and these were analysed by way of open-coding to identify common responses for each item, as well as any useful higher-order commonalities and overlaps in the issues raised. This examination revealed common difficulties in two areas. Firstly, difficulties in comprehension were noted for the words "frazzled", "subtleties" and "conscientious", along with the phrase "inner life". Secondly, there were difficulties in understanding the scope of selected terms, namely "sensory input", "pain" and "changes". Students were unsure what the phrase "sensory input" encompassed; whether it referred to any one sense in particular or any otherwise valid combination of senses. When asked about their sensitivity to "pain", several students questioned whether pain referred to physical or emotional pain, or both. In a similar vein, when asked if "changes" in their life shook them up, a number of respondents queried what magnitude (small or large) and nature (positive or negative) of change they should use as their frame of reference.

Table 2.1: Descriptive statistics for Study 1

Criterion	Study 1 (mean ± sd)
n	94
Age	22.36 (6.36)
Ethnicity	**%**
Black African	47.88
White	34.04
Indian	17.02
Mixed Ancestry	1.06
Other	0
Sex (% female)	84.04
Home language	**%**
English	48.93
Non-English	51.07
Total HSPS score	121.95 (20.87)
Mean item score	4.52 (0.77)
Cronbach's α	.87
Guttman's λ^6	.93

2.3.1.2 Item correlation

Correlation values between items, including the researcher-generated reverse scored items were all in expected directions. Researcher-generated reverse-scored items all had negative or near-zero correlations with HSPS items, except where a social desirability bias may have been in effect (for example, items 10, 15 and 22 and reverse items 2 and 3), creating small areas of discrepant colouring on the correlation heat map (Figure 2.1). On their own, reverse-scored items attained an α = .45, and were weakly correlated to each other (.16 - .29). When scored together with HSPS items, the 30-item scale maintained an α = .87, but item by scale correlations for the reverse-scored items were weak (-.21 to -.29).

2.3.1.3 Convergent validity

Introversion, neuroticism and childhood care scales were totalled and are compared to HSPS totals in Figure 2.2. HSPS scores were moderately, but significantly correlated with both neuroticism and introversion, but bore a negligible linear relationship with childhood care. Notably, the correlation between childhood care and neuroticism was significantly negative, supporting a degree of independence from SPS.

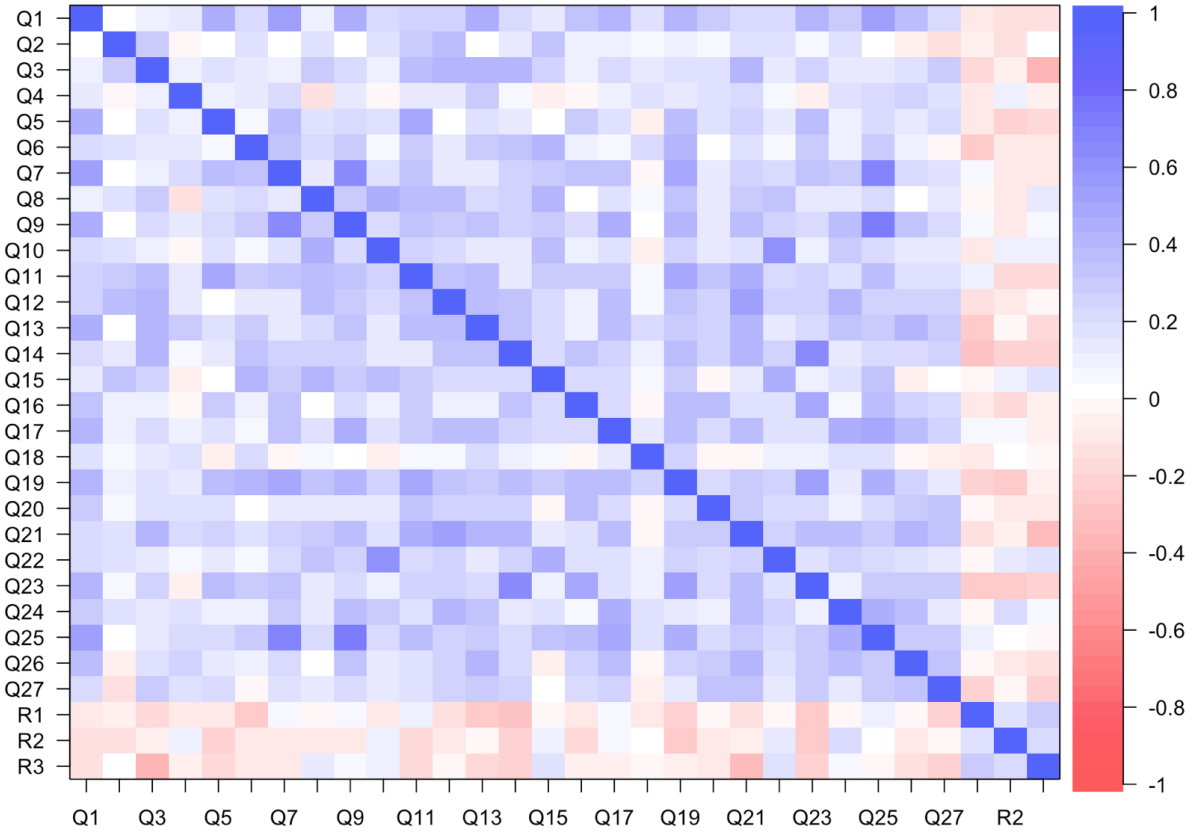


Figure 2.1: **A correlation heat map of HSP scale items and researcher-generated reverse-scored items**. On balance, HSPS items correlated positively with each other, but negatively with the researcher-generated reverse-scored items. Discrepant correlations are potentially attributed to social desirability bias. Q = HSPS question number; R = reverse-scored item number.

2.4 Discussion

Due to limited previous administration in culturally diverse settings, the HSPS was piloted on a small group of South African psychology undergraduates to assess scale performance and identify possible language and comprehension issues. On balance, the scale performed comparably to other published reports, both in terms of internal consistency reliability and average item score. Partial independence of SPS from both introversion and neuroticism (Aron and Aron, 1997) was replicated in these findings.

Regarding HSPS item comprehension, students expressed difficulty in understanding several terms, either as a consequence of their broad nature or because of their presumable absence from routine English conversation in South Africa. Importantly, none of these issues could be ascribed to particular ethnic or language groups. Since the University of Witwatersrand offers courses exclusively in English, all undergraduates are suitably proficient in the language to handle the demands of tertiary education. Coupled with a small sample size, this limited the ability to accurately identify causal reasons for particular comprehension issues. Some of the wording of the HSPS could certainly be argued as being imprecise (“subtleties”, “changes”) and collo-

quial (“frazzled”), but comprehension issues might have also spoken to the general education and maturity level of young undergraduates. Nevertheless, this remains, to date, the first attempt to interrogate and comment on the comprehension of HSPS items, and suggests some scope for improvement, especially in cross-cultural contexts.

Similarly, there have, to the best of the author’s knowledge, been no prior attempts to address the lack of negatively-phrased HSPS items. The few reverse-scored items generated for this study performed adequately, and appeared to integrate with the HSP scale with negligible adverse consequences. Importantly, two of these items (R2 and R3) raised suspicions of a socially desirable response set (Tourangeau et al., 2009), given their unexpectedly positive correlation with select HSPS items (e.g 10, 15 and 22), which possibly weakens the scale’s ability to delineate sensitive from non-sensitive. This risk of socially desirable responses has been acknowledged by Aron and Aron (2013), but they argue that this risk is offset by other items which tap possibly undesirable qualities (e.g. Are you easily overwhelmed by strong sensory input?). Although at the cost of a longer overall instrument, reverse-scored items would help to better detect and mitigate response biases (Kulas, Klahr, and Knights, 2018), and may prove especially useful as the scale finds application in increasingly diverse samples and contexts. This would be particularly important for any context in which it might be might be advantageous or socially desirable to present as sensitive, which the scale too readily facilitates. However, reverse-scored items can have unintended effects like increasing respondent frustration and cognitive load, and may also result in factor analysis artefacts (Kulas et al., 2018). These issues will need to be balanced against the need to avoid acquiescence or socially desirable response sets. The three reverse-scored items used here provide a suitable starting point for future exploration, but could admittedly be improved, especially because they are based only on sensitivity-related features (Aron and Aron, 1997; section 1.4.2.6) that are not central to the conceptualisation of the highly sensitive person, possibly explaining their weak item by scale correlations.

In summary, the pilot results identify possible areas of improvement for the HSPS instrument, which remains both unchanged (except for briefer [Aron and Aron, 2013] and translated versions [Ershova, Yarmotz, Koryagina, Shlyakhta, and Tarnow, 2018; Konrad and Herzberg, 2019]) and unchallenged as the primary psychological instrument for gauging environmental sensitivity. Regardless, in its current form, the HSPS performed robustly even in an ethnically and culturally diverse sample, albeit one suitably proficient in English. Admittedly, the study sample was predominantly female, which limits the generalisability of these pilot findings, but psychometric examination of the HSPS in a more sex-balanced sample is the focus of Chapter 5 (Study 4). For the second study, aimed at factor and latent class analysis, clarification was provided for language-based issues (“subtleties”, “frazzled” and “conscientious”) before administering the HSPS to a larger number of undergraduates. No clarification of broad terms (“changes”, “pain”, “sensory input” and “inner life”) was offered over concerns that this might make the instrument too prescriptive.

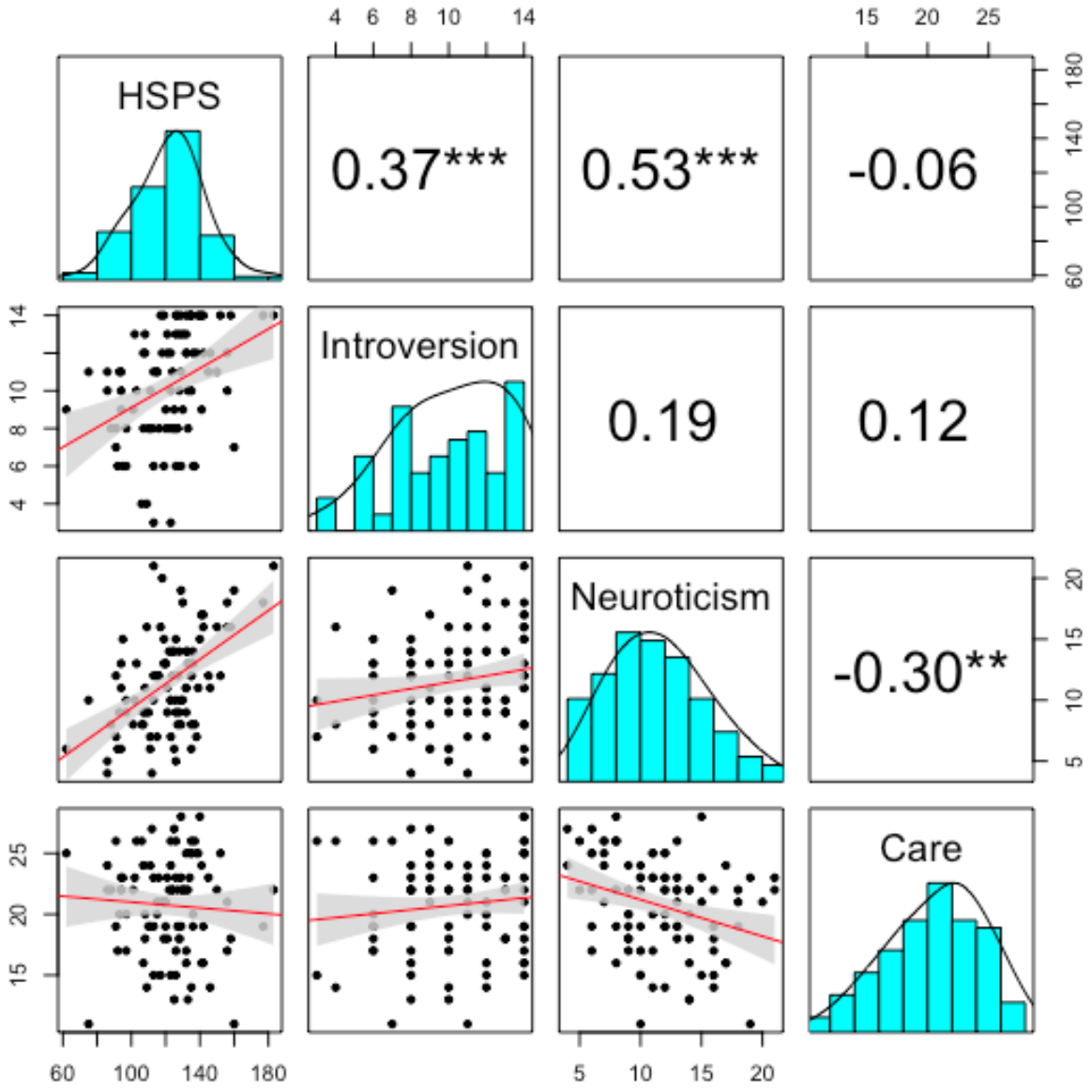


Figure 2.2: **A scatter plot matrix for scale scores in Study 1**. Distribution of the total scores for the Highly Sensitive Person Scale (HSPS), introversion, neuroticism and childhood care are shown along the diagonal via histogram and density curves. Pearson's correlation values are shown above the diagonal and regression lines with 95% confidence intervals below. SPS levels were significantly positively correlated to both introversion and neuroticism, but bore no relationship to parental care. Neuroticism was significantly negatively correlated to parental care. $***$ = $p < .001$; $**$ = $p < .01$.

Chapter 3

Study 2: Psychometric analysis of the HSPS using a culturally and ethnically diverse South African sample

All our knowledge begins with the senses, proceeds then to the understanding, and ends with reason. There is nothing higher than reason.
- Immanuel Kant, *Critique of Pure Reason*

3.1 Brief introduction

The pilot study confirmed that the HSPS, aside from minor comprehension issues, performs comparably in South African students versus other, primarily European-ancestry samples in developed countries. However, several questions still surround the psychometric properties of the HSPS. Aron and Aron (1997) offer few details on the psychometric principles that guided the scale's development, or of any psychometric analyses carried out on early variants of the scale, besides internal consistency reliability and factor analysis. Based on a significant decline between the first and second eigenvalues in their principle component analyses of the scale, along with rotated two-factor solutions they found to be "not obviously interpretable", Aron and Aron (1997) have argued for a single factor solution best conceptualised as "sensitivity". However, a subsequent analysis (Smolewska et al., 2006) used confirmatory factor analysis to demonstrate that a three-factor solution fits significantly better - a finding replicated by others (Booth, Standage, and Fox, 2015; Lionetti et al., 2018; Sobocko and Zelenski, 2015) and incorporated into the development and characterisation of a child version of the HSPS on which the Arons collaborated (Pluess et al., 2018). These three factors have been labelled Ease of

Excitation (EOE), Low Sensory Threshold (LST) and Aesthetic Sensitivity (AES). Meanwhile, for theoretical reasons, Evans and Rothbart (2008) preferred a two-factor solution representing orienting sensitivity and negative affect as orthogonal constructs. Lastly, Meyer and associates (2005) arrived at a four-factor solution when using the instrument as part of a larger examination of adults with borderline and avoidant features.

A notable limitation of the aforementioned factor analyses is the lack of sample heterogeneity (Lionetti et al., 2018; Smolewska et al., 2006). Results were primarily based on participants of European-ancestry of a generally Western culture. In response to this limitation, Şengül-İnal and Sülmer (2017) administered a translated HSPS to Turkish individuals of a relatively collectivist culture, and arrived at a unique four factor solution (Sensitivity to Overstimulation, Sensitivity to External Stimulus, Aesthetic Sensitivity and Harm Avoidance) that outperformed two and three factor models. Part of the uniqueness of this solution was tentatively ascribed to cultural differences, which the authors, and others (Pluess et al., 2018) have encouraged as a future avenue of investigation.

Also requiring further investigation are the latent classes of responders to the HSPS. Recall that Lionetti et al. (2018) found evidence for a three class solution, comprising high, medium and low sensitivity responders. These different classes of responders have been termed "orchids", "tulips" and "dandelions" respectively (Boyce, 2019; Greven et al., 2019). However, this recent finding has not been subjected to many replication efforts, especially within non-European ancestry samples.

Given the potential of the HSPS to distinguish between individuals most susceptible to the potentially advantageous and disadvantageous aspects of their early childhood (and adulthood) environment, it could serve as an ideal tool in low and middle income countries (LMICs) in which poverty, inequality and inadequate access to services constitute significant environmental stressors (Black et al., 2017). However, in the absence of resources for developing a locally appropriate equivalent (Laher and Cockcroft, 2017), researchers in LMICs will need assurance that the HSPS is applicable across geographical, socioeconomic, cultural and linguistic contexts.

Motivated by these concerns, the aim of this study was to further interrogate SPS theory and its attendant instrumentation, the HSPS, through factor and latent class analysis. Three ethnically and culturally diverse student samples were recruited and analysed separately using exploratory factor analysis. Results were then compared to a combined sample of all student participants (n = 750). The final factor structure was then compared to other published solutions using confirmatory factor analysis. Latent class analysis was used to test one to four-class solutions.

3.2 Methods

3.2.1 Participants

Three sets of participants were drawn exclusively from first year psychology students at the University of the Witwatersrand during the 2016 (n = 262), 2017 (n = 168) and 2018 (n = 240) academic years. An age range of 18-25 years was enforced to avoid possible age-related effects on levels of sensitivity. Again, students were able to claim 1% course credit for participation. Furthermore, participants were entered into a prize draw for a monetary voucher.

In line with Study 1, the majority of participants per academic year were Black African and female. Demographic variance was within reasonable limits, and important psychometric criteria (Cronbach's α, average scale total score, average item score, average item by scale and average inter-item correlations) remained stable across samples. Given this stability, a combined sample was prepared, which also included responses from participants younger than 26 from Study 1 (n = 80). Descriptive statistics for each independent sample, and the combined sample (n = 750), are reported in Table 3.1.

3.2.2 Instrumentation

The HSPS (and the reverse-scored item set) was included as part of a larger survey assessing personality and university adjustment. Select clarifications were added to HSPS items 2, 11 and 12 based on Study 1 results. The items themselves were not modified in any way; rather, a bracketed statement was placed after the item to offer clarification of problematic words (as suggested by Tourangeau et al., 2009). Clarifications were as follows:

- Item 2: Do you seem to be aware of subtleties in your environment? (By "subtleties" I mean very small details [e.g. a soft sound; a slight change in temperature; a brief movement; a light touch to your skin and so on] that most people would find hard to see or detect)
- Item 11: Does your nervous system sometimes feel so frazzled that you have to go off by yourself? (By "frazzled" I mean tired out and completely exhausted)
- Item 12: Are you conscientious? (By "conscientious" I mean doing your work very carefully and thoroughly; paying lots of attention to detail).

3.2.3 Procedure

Following ethical clearance (certificate number H16/05/34, Appendix A), an invitation was extended to first-year undergraduates and the same administration procedure was followed as detailed in Study 1. Participants with over 20% missing item responses were removed. Remaining missing values were imputed with the arithmetic mean per item. To afford a more rigorous assessment of the factor structure, separate exploratory factor analyses (EFA) were conducted and compared across the 2016, 2017, 2018 and combined samples. Confirmatory factor analysis (CFA) was performed on the combined dataset, with results compared against other published factor solutions. Finally, one to four class models were explored using latent class analysis on the combined sample. All data analysis was performed using R (version 3.5.1) and RStudio (version 1.1.456). Packages employed included *psych* (version 1.8.4; Revelle, 2018), *nFactors* (version 2.3.3; Raîche, Walls, Magis, Riopel, and Blais, 2013), *lavaan* (version 0.6-3; Rosseel, 2012), and *poLCA* (version 1.5.0; Linzer and Lewis, 2011).

3.3 Results

3.3.1 The HSPS

Each independent, annual sample performed comparably and in line with observations from Study 1, which are reproduced again for ease of reference in Table 3.1. In the combined sample, scale total scores were normally distributed (W = .99, p = .38). There was a significant difference in average scale total between males and females (t = 4.91, p = 1.89×10^{-6}) of moderate effect size (r = .33, Hedges' g = .47). Inter-item correlations (average = .18) and item by scale correlations (average = .46) were similar to Study 1; however, items with scale correlations below .30 were different (items 8,12 and 15 compared to 2, 4 and 18 from Study 1).

3.3.2 Exploratory factor analysis

In each of the four samples (2016, 2017, 2018 and combined), EFA was preceded by several preparatory checks. For all samples, the Kaiser-Meyer-Olkin (KMO) test suggested the sample size was appropriate (KMO $>$ .80; all annual samples had a sample to variable ratio $>$ 5:1 , whilst the combined sample had a ratio $>$ 25:1), and Bartlett's test of sphericity confirmed that items were sufficiently correlated for factor analytic procedures ($p < .01$). The determinant of the correlation matrices was consistently greater than the recommended minimum of 1×10^{-5}. In line with other results (Aron and Aron, 2013), an inspection of eigenvalues revealed a large

Table 3.1: Descriptive statistics for all annual student samples

Criterion	Pilot (2015)	2016	2017	2018 †	Combined
n	94	262	168	240	750
Age *	22.36 (6.36)	19.33 (1.21)	19.24 (1.28)	19.32 (1.29)	19.38 (1.30)
Ethnicity (%)					
Black African	47.88	51.53	47.62	38.33	45.87
White	34.04	30.15	26.19	32.92	30.53
Indian	17.02	11.07	17.26	17.08	15.20
Mixed Ancestry	1.06	5.73	4.17	7.92	5.60
Other	0	1.53	4.76	3.33	2.67
Sex (% female)	84.04	81.68	77.98	84.17	82.00
Home language (%)					
English	48.93	50.00	55.95	59.17	54.27
Non-English	51.07	50.00	44.05	40.83	45.60
Total HSPS score *	121.93 (20.87)	121.74 (20.62)	124.21 (21.08)	122.41 (21.64)	122.61 (20.84)
Females	122.22 (20.77)	123.40 (20.54)	126.52 (20.08)	123.87 (21.75)	124.30 (20.70)
Males	120.53 (22.04)	114.33 (19.51)	116.05 (22.79)	114.68 (19.53)	114.97 (19.85)
Mean item score	4.52 (0.77)	4.51 (.76)	4.60 (.78)	4.53 (.80)	4.54 (.77)
Cronbach's α	.87	.86	.85	.86	.86
Guttman's λ^6	.93	.89	.90	.89	.88

† In the 2018 sample, one participant chose not to report their ethnicity.
* Values reported as mean ($\pm$ standard deviation)

first eigenvalue (6.31 - 6.60 across samples) that accounted for $\pm$ 24% of the variance, followed by a second, much smaller eigenvalue of 1.99 - 2.44, accounting for $\pm$ 8% of the variance.

Choosing the number of factors to extract was based on a weight of evidence across multiple methods (Ford, MacCallum, and Tait, 1986), including parallel analysis, optimal coordinates, sample size adjusted Bayesian Information Criterion (BIC), Velicer Minimum Average Partial test and the distribution of residuals (Figure 3.1)[1]. A five-factor solution was most commonly suggested, except for the 2018 sample in which a four-factor solution received more support. Four- and five-factor solutions were subsequently explored, first without rotation, and then with factors extracted via a minimum residual approach (which produces outcomes similar to maximum likelihood extraction even for unrobust matrices [Revelle, 2018]) and rotated obliquely using oblimin rotation, given that SPS (like other personality traits) is known to have environmental and genetic correlates (Aron and Aron, 1997), thus latent factors are unlikely to be independent (Kline, 1994; Tinsley and Tinsley, 1987). A cut-off value of .30 was used to identify significant item loadings but any cross-loading items were removed. Across samples, the five-factor solution was easiest to interpret and cohered best with the theoretical understanding of highly sensitive persons. Factor loadings for the combined sample (n = 750) produced the clearest separation of factors and are reported in Table 3.2. Note that these loadings were derived from a Pearson correlation matrix - results were negligibly different when using a polychoric correlation matrix (Holgado-Tello, Chacón-Moscoso, Barbero-García, and Vila-Abad, 2010).

[1] A range of factor extraction methods were explored because, individually, each method has limitations, and rarely do they lead to identical results. For example, scree plots can have multiple inflection points, making interpretation prone to ambiguity and subjectivity (Hayton, Allen, and Scarpello, 2004)0.

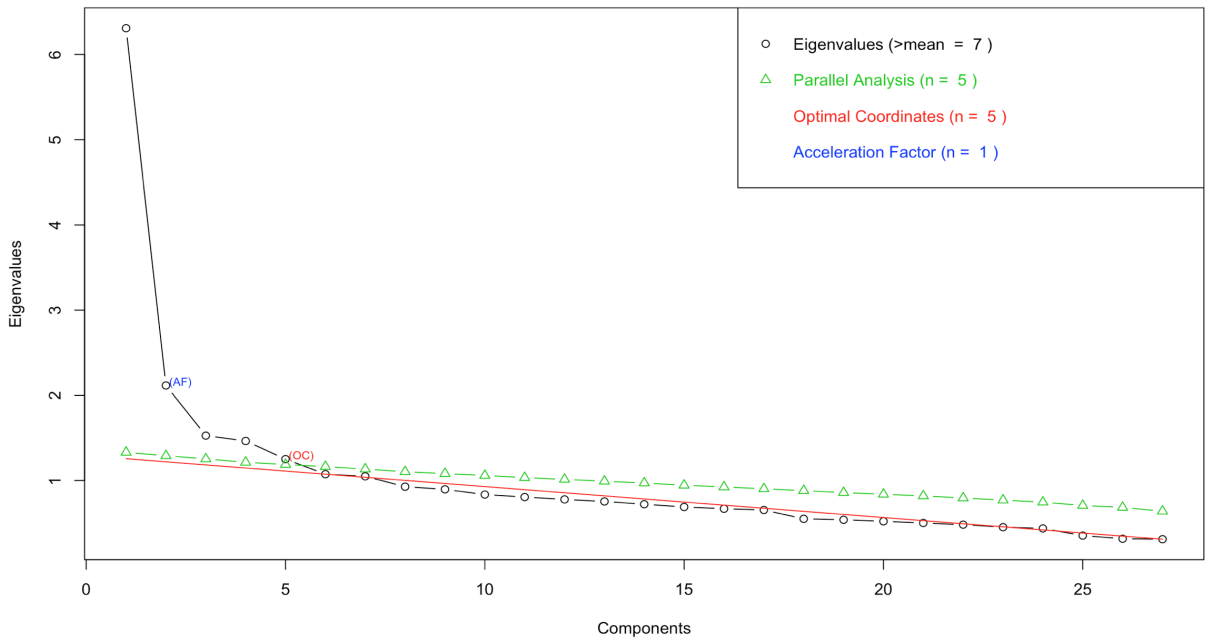


Figure 3.1: **Factor extraction solutions for Study 2**. A scree plot of eigenvalues is shown with overlays for several non-graphical solutions for factor extraction. In all but the 2018 sample, both optimal coordinates and parallel analysis suggested five-factor extraction, which also afforded the lowest Bayesian Information Criterion (BIC) value (not shown).

Based on the theme of their member items, the five factors were named Negative Affectivity (NA), Neural Sensitivity (NS), Propensity to Overwhelm (PO), Aesthetic Sensitivity (AS) and Careful Processing (CP). The item composition of these factors, per sample, is displayed in Table 3.3. Three of the five factors, namely PO, AS and CP, demonstrated high cross-sample stability. The NS and NA factors were less consistent in their composition with several items alternating between these factors from sample to sample. The delineation between NA and NS improved in the larger, combined sample where all factors attained acceptable to good reliability estimates (Table 3.2).

The final factor solution retained 20 items that loaded significantly, each onto only a single factor. Only one item was excluded due to cross-loading; "Are you easily overwhelmed by strong sensory input?" loaded moderately onto both the Propensity to Overwhelm (.40) and Neural Sensitivity (.38) factors. The other six items (2, 6, 15, 18, 27) that were excluded failed to load sufficiently onto any of the extracted factors. Inter-factor correlations ranged from .01 (between NA and AS) to .46 (between NA and NS). The lack of correlation between NA and AS supports other studies which have found these to be two distinct features of HS persons (Sobocko and Zelenski, 2015). Meanwhile, the moderate correlation between NA and NS possibly explains why select items alternated between these two factors across different samples.

Reverse-scored items continued to perform in line with expectations from Study 1. To further interrogate their appropriateness, EFA was rerun with the inclusion of reverse-scored items in the combined student sample (data not shown). A five factor solution was again suggested.

Reverse items 1 (Do you often feel less emotional than other people?) and 3 (Do you find personal criticism easy to deal with?) loaded negatively on to the Neural Sensitivity factor, replacing HSPS items 11 and 5. Reverse item 2 (Do you prefer your life to be very fast-paced?) loaded negatively on the Negative Affectivity factor. These additions modestly lowered the reliability of the NA (.74 down from .75) and NS (.61 down from .69) subscales, as well as the entire scale (.85 down from .86).

Table 3.2: Factor loadings based on the pattern matrix

Item	NA *	NS	PO	AS	CP	h^2
23. Do you find it unpleasant to have a lot going on at once?	.78					.67
16. Are you annoyed when people try to get you to do too many things at once?	.65					.47
14. Do you get rattled when you have a lot to do in a short amount of time?	.58					.49
26. When you must compete or be observed while performing a task, do you become so nervous or shaky that you do much worse than you would otherwise?	.37					.22
21. Do changes in your life shake you up?	.32					.31
20. Does being very hungry create a strong reaction in you, disrupting your concentration or mood?	.30					.16
13. Do you startle easily?		.57				.40
4. Do you tend to be more sensitive to pain?		.56				.31
3. Do other people's moods affect you?		.38				.23
11. Does your nervous system sometimes feel so frazzled that you just have to go off by yourself?		.38				.41
5. Do you find yourself needing to withdraw during busy days, into bed or into a darkened room or any place where you can have some privacy and relief from stimulation?		.30				.35
9. Are you made uncomfortable by loud noises?			.77			.56
25. Are you bothered by intense stimuli, like loud noises or chaotic scenes?			.73			.63
7. Are you easily overwhelmed by things like bright lights, strong smells, coarse fabrics, or sirens close by?			.57			.41
19. Do you become unpleasantly aroused when a lot is going on around you?			.31			.39
10. Are you deeply moved bu the arts or music?				.76		.57
22. Do you notice and enjoy delicate or fine scents, tastes, sounds, works of art?				.74		.55
12. Are you conscientious?					.60	.35
24. Do you make it a high priority to arrange your life to avoid upsetting or overwhelming situations?					.59	.38
17. Do you try hard to avoid making mistakes or forgetting things?					.59	.43
Rotated sum of squared loadings	2.41	2.11	2.24	1.48	1.43	
Explained variance (%)	9	8	8	5	5	
Cronbach's α	.75	.69	.76	.74	.62	

* NA = Negative Affectivity; NS = Neural Sensitivity; PO = Propensity to Overwhelm; AS = Aesthetic Sensitivity; CP = Careful Processing

Table 3.3: Factor composition per sample

Item	2016	2017	2018	Combined *
1. Are you easily overwhelmed by strong sensory input?	NS/PO	NS/PO	PO	NS/PO
2. Do you seem to be aware of subtleties in your environment?	NS	PO	AS	-
3. Do other people's moods affect you?	NS	NS	-	NS
4. Do you tend to be more sensitive to pain?	NS	NS	NS	NS
5. Do you find yourself needing to withdraw during busy days, into bed or into a darkened room or any place where you can have some privacy and relief from stimulation?	NS	NA	NA	NS
6.Are you particularly sensitive to the effects of caffeine?	-	NS	-	-
7. Are you easily overwhelmed by things like bright lights, strong smells, coarse fabrics, or sirens close by?	PO	PO	PO	PO
8. Do you have a rich, complex inner life?	-	NS	-	-
9. Are you made uncomfortable by loud noises?	PO	PO	PO	PO
10. Are you deeply moved by the arts or music?	AS	AS	AS	AS
11. Does your nervous system sometimes feel so frazzled that you just have to go off by yourself?	NS	NA	NA	NS
12. Are you conscientious?	CP	CP	CP	CP
13. Do you startle easily?	NS	NA/NS	NS	NS
14. Do you get rattled when you have a lot to do in a short amount of time?	NA	NA	NA	NA
15. When people are uncomfortable in a physical environment do you tend to know what needs to be done to make it more comfortable (like changing the lighting or the seating)?	-	-NS	CP	-
16. Are you annoyed when people try to get you to do too many things at once?	NA	NA	NA	NA
17. Do you try hard to avoid making mistakes or forgetting things?	CP	CP	CP	CP
18. Do you make a point to avoid violent movies and TV shows?	-	NS/CP	NS	-
19. Do you become unpleasantly aroused when a lot is going on around you?	NA	NA	-	PO
20. Does being very hungry create a strong reaction in you, disrupting your concentration or mood?	NA	NS	-	NA
21.Do changes in your life shake you up?	NA	NA	-	NA
22. Do you notice and enjoy delicate or fine scents, tastes, sounds, works of art?	AS	AS	AS	AS
23. Do you find it unpleasant to have a lot going on at once?	NA	NA	NA	NA
24. Do you make it a high priority to arrange your life to avoid upsetting or overwhelming situations?	CP	CP	CP	CP
25. Are you bothered by intense stimuli, like loud noises or chaotic scenes?	PO	PO	PO	PO
26. When you must compete or be observed while performing a task, do you become so nervous or shaky that you do much worse than you would otherwise?	NA	NA	NA	NA
27. When you were a child, did your parents or teachers seem to see you as sensitive or shy?	-	NA	-	-

* NA = Negative Affectivity; NS = Neural Sensitivity; PO = Propensity to Overwhelm; AS = Aesthetic Sensitivity; CP = Careful Processing

3.3.3 Confirmatory factor analysis

To interrogate the validity of the five-factor solution, the model fit was compared with other published factor solutions using CFA. The one-factor (Aron and Aron, 1997), two-factor (Evans and Rothbart, 2008), three-factor (Smolewska et al., 2006), and four-factor (Şengül-İnal and Sümer, 2017) solutions were forced on the dataset (there was not sufficient information to test Meyer and colleagues [2005] four-factor solution). Furthermore, a bifactor model was tested whereby all items were allowed to load onto a general factor of sensitivity as well as the three specific factors from the three-factor model (Smolewska et al., 2006). For the bifactor model, factors were constrained to be orthogonal (Lionetti et al., 2018). Model fit was compared to the five-factor solution using several indices. These included: the Standardised Root Mean square Residual (SRMR), where values $<$ .08 suggest a good fit; the Root Mean Square Error of Approximation (RMSEA), where values $<$.01, $<$.05 and $<$.08 represent excellent, good and mediocre fits respectively; the Tucker-Lewis Index (TLI), where values $>$.90 and $>$.95 suggest marginal and excellent fits respectively, and the BIC and Akaike Information Criterion (AIC) for which lower values represent better model fits. Since the chi-square statistic is sensitive to sample size, the statistic was divided by the degrees of freedom (df) to produce a ratio for which values between 2-3 are tentatively considered as acceptable fits (Schermelleh-Engel, Müller, and Moosbrugger, 2003). These fit indices, per factor solution, are compared in Table 3.4.

The five-factor model displayed good fit metrics across all indices. Moreover, its fit (for the combined student dataset) was noticeably better than other published solutions, enjoying a 10,000 - 20,000 point reduction in AIC and BIC values depending on the particular model comparison. The five-factor solution was the only model to achieve "good" and "marginal" fits for the popular RMSEA and TLI indices respectively. Similarly, only the five-factor model achieved a χ^2/df ratio between 2 and 3.

Table 3.4: Fit comparison for different HSPS factor solutions

Model	Reference	χ^2	df	χ^2/df	p value	SRMR *	RMSEA	TLI	AIC	BIC
One factor	Aron & Aron, 1997	1908.54	324	5.89	$<.001$	.070	.081	.644	74786	75161
Two factor	Evans & Rothbart, 2008	1428.51	274	5.21	$<.001$	.076	.073	.722	68908	69260
Three factor	Smolewska et al., 2006	1138.35	227	5.02	$<.001$	.081	.073	.703	64219	64551
Four factor	Gulbin & Sumer, 2017	1282.47	293	4.38	$<.001$	.054	.062	.767	74009	74490
Bifactor	Lionetti et al., 2018	1085.23	301	3.61	$<.001$	.054	.062	.810	74009	74490
Five factor	Study 2 (combined sample)	454.68	160	2.84	$<.001$	.047	.050	.909	53977	54300

* SRMR = Standardised Root Mean square Residual; RMSEA = Root Mean Square Error of Approximation; TLI = Tucker-Lewis Index; AIC = Akaike Information Criterion; BIC = Bayesian Information Criterion

3.3.4 Latent Class Analysis

Measures of fit for one to four class solutions are displayed in Table 3.5. Several fit statistics supported a four-class solution (including the log-likelihood, likelihood ratio and AIC), but this solution made little theoretical sense. Specifically, there were no detectable themes by which to

separate the four identified classes. Differences between the four classes appeared to be driven by a small number of items, rather than by patterns of responding that were visible across the instrument. Three classes were suggested by both a low BIC and high entropy score. Based on combined density plots (Figure 3.2), these three classes reflected low-, medium- and high-sensitivity groups akin to "dandelion", "tulip" and "orchid" theorising. Accordingly, 24.13% of students ranked as dandelions, 39.07% tulips, and 36.80% orchids, with a cut-off average item score of 4.03 separating dandelions from tulips and 4.82 separating tulips from orchids.

Table 3.5: Latent class analysis results for Study 2

Model	residual df	log-likelihood	likelihood ratio	AIC	BIC	Entropy
One class	588	-36301.56	57444.19	72927.12	73675.57	-
Two class	425	-34961.80	55000.32	70573.59	720750.12	.892
Three class	262	-34310.62	53740.04	69597.23	**71851.83** *	**.904**
Four class	99	**-33978.18**	**53132.32**	**69258.37**	72266.04	.900

* Values representing the best fit, per fit statistic, are shown in bold. Lower (closer to zero) values suggest better model fits for all criteria except entropy, for which higher values are preferred.

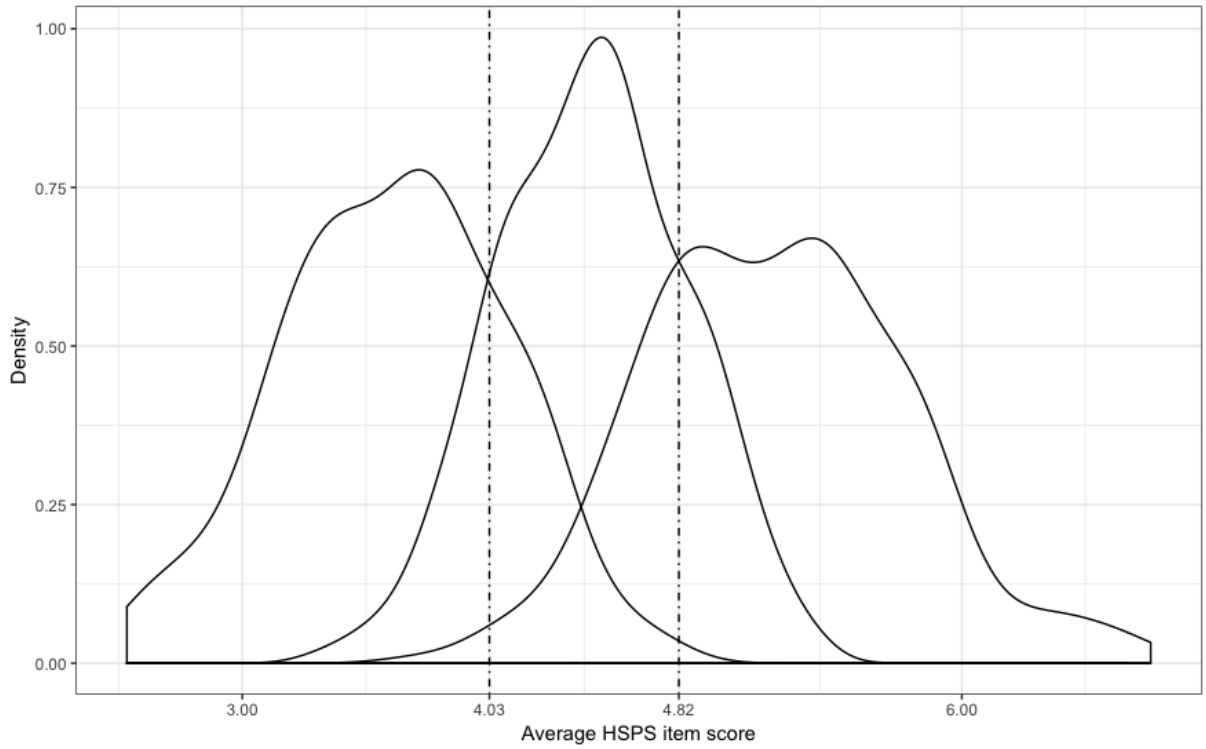


Figure 3.2: **Score distribution density plots for the three latent classes.** Amongst psychology students, relatively high cut-off values separated dandelions from tulips (4.03) and tulips from orchids (4.82). This is in keeping with the previous findings that psychology students rate themselves more sensitive than members of the general population (Aron and Aron, 2013).

3.4 Discussion

The HSP scale was designed and psychometrically assessed in developed countries of a largely individualistic culture. Not only has factor analysis of the instrument yielded inconsistent results across studies, these studies were potentially limited by homogeneous, primarily Caucasian samples. This study aimed to address this limitation by psychometrically assessing the HSPS in South Africa, which is both ethnically diverse and has good representation of both idiocentric and allocentric cultures (Johnston, 2015, Burgess et al., 2002). Overall, the psychometric performance of the instrument (across all student samples) aligned with previously published results, however, exploratory factor analysis revealed a five-factor solution that has never before been reported. Moreover, based on several fit measures, the five-factor solution was found to be a better fit than other published solutions (save for the four-factor solution by Meyer and colleagues [2005], which was not tested). Admittedly, however, the solution failed to achieve an ideal TLI value, although the attained value was higher than all other models tested.

One advantage of the five-factor solution is that it appears to overcome perceived weaknesses in the theoretical strength of other factor solutions. In the three-factor solution (EOE, AES and LST; Smolewska et al., 2006), which appears to have been most widely adopted (e.g. Ahadi and Basharpoor, 2010; Gerstenberg, 2012; Lionetti et al., 2018; Liss, Mailloux, and Erchull, 2008; Sobocko and Zelenski, 2015), several items seem conspicuously incongruous with the latent factor they supposedly measure. Some examples include: item 17 (Do you try hard to avoid making mistakes or forgetting things?) and item 27 (When you were a child, did your parents or teachers seem to see you as sensitive or shy?) as measures of ease of excitation (EOE); and item 12 (Are you conscientious?) and item 5 (Do you find yourself needing to withdraw during busy days, into bed or into a darkened room or any place where you can have some privacy and relief from stimulation?) as measures of aesthetic sensitivity (AES). Moreover, the AES factor is known to have low reliability (α = .55 - .61; Liss et al., 2008; Sobocko and Zelenski, 2015). Meanwhile, the two-factor solution (Negative Affectivity and Orienting Sensitivity; Evans and Rothbart, 2008) makes arguably unfair assumptions that items such as "Do you startle easily?", "Do you tend to be sensitive to pain?" and "Are you made uncomfortable by loud noises?" reflect an individual's level of negative affectivity, rather than simply reflecting greater physiological sensitivity. In addition, the reliability of the orienting sensitivity subscale was found to be weak (α = .51 - .56) in two samples of Canadian undergraduate students (Sobocko and Zelenski, 2015). Equivalent issues appear to affect the four-factor structure identified in a Turkish sample. For example, a modified item 4 ("I tend to be very sensitive to pain") loads incongruously on the Aesthetic Sensitivity factor (unless one construes "pain" in an emotional sense, the sort portrayed in the dramatic arts). Meanwhile, the weakly reliable ($\alpha = .55$) Harm Avoidance factor applies a seemingly negative label to an item set reflecting behaviour that can also be argued as wisely cautious.

In contrast to these weaknesses, the five-factor solution appears to better align to the theoretical conceptualisation of a highly sensitive person. Aron (2019) cites four fundamental and (*a priori*) neutral characteristics of the HS person, namely: 1) stronger emotional reactions, both positive and negative; 2) heightened awareness of sensory information; 3) deep cognitive processing of this information and 4) high susceptibility to overstimulation (section 1.4.2). Similarly, the factor solution of the HSPS in the current study appears to make distinctions along these lines, in that Negative Affectivity (NA) and Aesthetic Sensitivity (AS) reflect positive and negative emotionality (1); Neural Sensitivity (NS) relates to heightened sensory awareness (2); Careful Processing (CP) indicates deep and thorough processing (3) whilst Propensity to Overwhelm (PO) encapsulates the tendency for overwhelm (4). Encouragingly, the five factors attained robust reliability estimates, with the possible exception of CP (α = .62). However, that two of the five factors are comprised of a small number (two to three) of items is potentially unideal.

The exact determinants of this study's unique factor solution remain unclear, although several possibilities bear mention. Most likely, the unique factor structure can be attributed to the greater sample diversity, knowing that ethnic and/or cultural differences have been noted to affect factor structure in other instrumentation (e.g. Allen, DeVellis, Renner, Kraus, and Jordan, 2007; Asner-Self, Schreiber, and Marotta, 2006; Mylonas, 2009). South Africa is highly multicultural with strong individualist and collectivist influences. On one hand, the African philosophy of "Ubuntu" (a person becomes a person through other people) has fostered collectivist trends evident amongst the value orientations of all of the country's inhabitants, whilst on the other hand, forces of migration, urbanisation and affluence have been driving shifts towards individualism (Burgess et al., 2002). This is especially pertinent to urban Black South Africans (the majority of respondents in this study) who, at least anecdotally, juggle both the collectivist influence of traditional African culture and the individualism characteristic of much of urban living. These opposing cultural views are, at the broadest level, well known to value and perceive individuals of sensitive disposition in opposite fashion - sensitivity is mostly frowned upon amongst individualists, but highly praised amongst collectivists (Aron, 2004). However, sensitivity is an umbrella construct that encompasses an array of different cognitive, physiological and behavioural features (Liss et al., 2008; section 1.5.1). It is conceivable that more nuanced relationships exist between culture and sensitivity - sub-facets of sensitivity may be differentially valued in a manner that isn't captured by merely distinguishing opinion on sensitive and non-sensitive individuals. That SPS might encompass a larger number of latent factors may point towards a finer discrimination among attributes of sensitivity, and how these are differentially viewed and valued by a sample of people stemming from significantly different backgrounds. Similar reasoning was offered by Şengül-İnal and Sümer (2017) for the lack of fit of one-, two- and three-factor models in their Turkish sample.

A further possibility explaining the larger factor structure is that language issues inflated item-response variance, which then prompted the need for more factors to be extracted. How-

ever, special effort was made to try address language issues beforehand, using a pilot study (Chapter 2). Based on this pilot, supporting statements were added in order to aid the comprehension of some items. Of the three items that did require some clarification, two (items 11 and 12) loaded on to thematically-appropriate factors, whilst the remaining item (item 2) was discarded due to poor loadings across all extracted factors. Correlations with reverse-scored items were also in the expected direction and their inclusion as part of EFA did not destabilise the five-factor structure. Although many South Africans do not have English as their first or home language (Statistics South Africa, 2012), the studied sample of students are proficient enough to manage tertiary-level education in English. It thus seems reasonable to assume that the HSP scale was interpreted exactly as intended, especially given that all other psychometric properties (such as Cronbach's α and the average item score) were comparable to other studies. Whilst the possibility of language-based issues cannot be fully discounted, these do not appear to be the most parsimonious explanation for the unique factor solution.

As previously highlighted in Study 1, some items are prone to a social desirability bias (e.g. "Do you notice and enjoy delicate or fine scents, tastes, sounds, works of art?") which might explain some of the instability in factor structure across different studies (Aron and Aron, 2013). The researcher-generated reverse-scored items that were additionally explored as part of this doctoral research appeared to strengthen suspicions of social desirability bias (Study 1; Figure 2.1). The inclusion of these items in a separate EFA (data not shown) did not appear to destabilise the five-factor structure of the HSPS, and so reverse-scored items might be a worthwhile option for strengthening the instrument overall. However, future studies will need to explore this avenue in significantly more detail, as reverse-scored items have been known to confound factor analytic structure (Kulas et al., 2018).

A final possibility is that the five-factor solution reinforces cautions already expressed by Aron and Aron (2013) . For several reasons, it has been suggested that the HSPS is not completely amenable to factor analysis. Most importantly, the instrument is targeted towards only 20-35% of the population, meaning that the bulk of the sample variance in scale item response is attributable to less sensitive individuals (dandelions and tulips). Furthermore, there exists a sex bias in that females tend to score higher than males (although the proportion of male and female HSPs is equal; Aron and Aron, 1997). This bias is likely a further consequence of cultural differences in the ways males and females are socialised (Aron, 2006; Aron and Aron, 2013). In support of sex differences, a significant difference was found between scale total averages for males and females. The unique five-factor solution might be testament to these issues, which manifest differently across different samples, perhaps exacerbated by the present study sample's heterogeneity. Combining these issues with the common acknowledgement that factor analysis tends to be poorly performed and interpreted (Ford et al., 1986; Kline, 1994) might further justify why there has been such inconsistency in factor analytic results for this instrument.

Encouragingly, the results of the latent class analysis align with those previously published. In subsamples of US psychology students, Lionetti and associates (2018) also obtained varied degrees of support for either a three or four class solution, with the balance of evidence favouring a three class solution. The cut-off scores for this study were only marginally higher (4.03 and 4.82 vs 3.71 and 4.66) and the sample comprised, on average, fewer dandelions but more orchids. This possibly reflects the larger percentage of female participants in the study sample (82.00% vs 62.30%), or otherwise hints at a greater level of sensitivity amongst South African psychology students (or more openness in admitting sensitive behaviour) versus US students. Regardless, the distribution of orchid, tulip and dandelion individuals was within currently accepted estimates (Greven et al., 2019).

Some limitations of the study warrant discussion. Firstly, the student samples were heavily biased towards females which may have unfairly skewed the results. This also limits the generalisability of the findings, although attempts to validate these results in a more general, sex-balanced sample are documented in Chapter 5. Secondly, the HSPS relies solely on participant self-report. Additional genetic, physiological and/or behavioural data would have helped to confirm the accuracy of reported SPS levels. Thirdly, no attempt was made to exclude participants based on any history of disorder (e.g. sensory processing disorder; autism spectrum disorders) or medication use that may have impacted upon measures of sensitivity. Such individuals may have biased the results, but were presumed to be minimal in number. Lastly, factor solutions were not compared by first returning all excluded items to their highest-loading factor (Şengül-İnal and Sümer, 2017). This meant that the number of items per factor solution was not consistent which may have biased comparisons between them.

In conclusion, the HSPS remains a sufficiently reliable instrument, even in a more heterogeneous setting, although there exists room for further development and improvement. The instrument has generated varied factor solutions, none of which have received consistent support. This most likely reflects the complex relationship between culture and sensitivity as well as the historical confusion in defining "sensitivity" and its attendant features and behaviours (section 1.3.4). Additionally, item phrasing has not been significantly interrogated for flaws, which might also contribute to factor structure instability. The current lack of reverse-scored items limits identification of possible issues in respondent comprehension or response set bias. However, the inclusion of reverse-scored items could create problems for factor analysis (Kulas et al., 2018). These issues will need to be considered as the HSPS finds application in diverse settings. Nevertheless, SPS theory is underpinned by strong cross-disciplinary support and the stratification of participants by levels of sensitivity continues to offer unique insights. Short of a locally developed equivalent, some minor clarifications can help make the HSPS accessible to cross-cultural samples and so South African researchers should consider seriously the addition of the HSPS in future studies.

Chapter 4

Study 3: The associations between SPS, other personality traits, and student adaptation to university

The senses, being the explorers of the world, open the way to knowledge.
- Maria Montessori

4.1 Brief introduction

Recall that, as a consequence of heightened neural sensitivity, HSPs are rendered more malleable to environmental forces, for better and for worse (Belsky and Bakermans-Kranenburg, 2007; Ellis, Boyce, et al., 2011; section 1.4.2.7). Of particular importance is early parental environment, which Aron and Aron (1997) found to roughly dichotomise HSPs. Where early parental experiences are largely warm and nurturant, HSPs tend to enjoy unusually successful personal and professional lives, however, in the context of adversity and poor parenting, HSPs are disproportionately affected by mental health burdens (e.g. anxiety, depression) which often result in long histories of psychotherapy and/or psychopathology (Aron, 2006). As Aron (2004) concedes, the difficulties are a necessary result of what also affords the benefits – heightened awareness and processing sharpens attention to, and the felt experience of, both positivity and negativity, with supporting evidence from a number of fMRI studies (Acevedo et al., 2014; Acevedo et al., 2018; Acevedo, Jagiellowicz, Aron, Marhenke, and Aron, 2017; Jagiellowicz et al., 2011). Thus, crossover interactions appear characteristic of SPS, which has been reasonably argued (Aron et al., 2012; Ellis, Boyce, et al., 2011; Wolf et al., 2008) to balance out as a neutral, evolutionarily stable trait that fits within the larger conceptual framework of Environmental Sensitivity (Pluess, 2015).

Despite these arguments, SPS has been more commonly noted for its modest correlations to a range of negative, "sub-optimal" outcomes (Booth et al., 2015; Brindle, Moulding, Bakker, and Nedeljkovic, 2015; Sobocko and Zelenski, 2015). When compared to low levels of SPS, high levels of SPS appear to engender more social phobia (Neal, Edelmann, and Glachan, 2002), agoraphobic avoidance, harm avoidance (Hofmann and Bitran, 2007), anxiety, depression (Bakker and Moulding, 2012; Liss et al., 2008; Liss et al., 2005), work stress, burnout (Evers, Rasche, and Schabracq, 2008) communication apprehension (Gearhart and Bodie, 2012), and avoidant and borderline features (Meyer et al., 2005; Meyer and Carver, 2000). On balance, then, SPS has drawn more attention for its inherent weaknesses, with far less acknowledgement of paired strengths.

Whilst these findings seem persuasive, in part due to their volume, two key considerations must be borne in mind. Firstly, negative outcomes are not necessarily maladaptive or sub-optimal. As Belsky and colleagues have argued, negative mental health outcomes can be signatures of a "live fast, die young" strategy (Belsky and Pluess, 2013a; Belsky et al., 1991). Since SPS facilitates greater plasticity to environmental influence, HSPs raised in threatening, adverse environments may possibly undergo accelerated sexual maturation (Ellis, 2004; Ellis, Boyce, et al., 2011), and are inclined to develop avoidant, phobic responses that might safeguard them from danger, although at the cost of long-term burdens such as anxiety and depression. Secondly, and more importantly, almost all of the aforementioned findings (save for Liss et al., 2005) failed to control for either early parental environment or neuroticism (Aron et al., 2012). A lack of acknowledgement for early childhood experiences prohibits the uncovering of possible crossover interactions (Aron et al., 2012), whilst inattention to levels of neuroticism prevents a clear distinction of how much variance is uniquely owed to sensitivity, rather than the negative affectivity it can sometimes engender (Aron and Aron, 2013). In support of this latter notion, SPS has been observed as sharing only moderate correlations with neuroticism, suggesting that sensitivity is related to, but nonetheless not equivalent to, neuroticism (Aron and Aron, 1997; Sobocko and Zelenski, 2015). In Study 1, a brief measure of neuroticism shared a modestly strong correlation to SPS levels in the pilot sample.

To investigate further, this study assessed the relationship between levels of SPS and university adjustment. Typically, university adjustment is a multi-faceted process in which young, emerging adults (Arnett, 2000, 2015) must balance and harmonise a range of academic, social and personal development pressures (Baker and Siryk, 1984; Bowman, Jang, Jarratt, and Bono, 2019; Crede and Niehorster, 2012; Petersen, Louw, and Dumont, 2009). The first year at university is particularly challenging in this regard (Bowman, 2010; Kurtz, Puher, and Cross, 2012; Lapsley, Rice, and Shadid, 1989; Reason, Terenzini, and Domingo, 2006), given both the unfamiliarity of the setting and the wealth of changes that must be simultaneously managed, from changes in personal identity and social networks to changes in living arrangement, financial management, and academic pace (Bowman et al., 2019; Crede and Niehorster, 2012; Dyson and Renk, 2006). These vicissitudes are a source of significant stress and psychologi-

cal disturbance (Cushman and West, 2006; Fisher and Hood, 1987; Lidy and Kahn, 2011), the navigation and management of which has far-reaching consequences. University adjustment is considered to have notable predictive power regarding students, mainly in terms of academic performance but also in terms of personality attributes, behavioural outcomes, and mental and physical wellness (Kurtz et al., 2012; Pritchard, Wilson, and Yamnitz, 2007). Positive adjustment portends greater overall success in both academic and personal mastery, whilst negative adjustment forewarns difficulties such as anxiety, depression, suicide ideation, and alcohol and drug abuse *inter alia* (Crede and Niehorster, 2012; Dyson and Renk, 2006; Furr, McConnell, Westefeld, and Jenkins, 2001; Hingson, 2010; Hingson, Heeren, Winter, and Wechsler, 2005; Labrie, Ehret, Hummer, and Prenovost, 2012).

Overall, university adjustment has a complex array of influences, including demographic factors, prior achievement, social support, relationship with parents, and personal attributes (Crede and Niehorster, 2012). Personal attributes, especially personality and affective traits, have been well-investigated in this regard. For example, neuroticism, loneliness and interpersonal mistrust predict greater depression amongst college students (Rich and Scovel, 1987). Depression is also common in students with perfectionism tendencies, which also induce various health problems (Pritchard et al., 2007; Rice and Mirzadeh, 2000; Vincent and Walker, 2000). Features of burnout were common in students ranking high in neuroticism and/or low in extraversion (Morgan and de Bruin, 2010). In contrast, highly extraverted, agreeable, optimistic, hardy, conscientious, emotionally stable and/or open students are known to have better university adjustment, academic performance and corresponding health outcomes (Crede and Niehorster, 2012; Lidy and Kahn, 2011; Poropat, 2009; Pritchard et al., 2007). With regards to family and parental relationships, students from cohesive families, with secure attachment and/or high levels of autonomy tend to cope better at university. Those students with authoritarian or abusive parents, and families marked by significant conflict, fare much worse in their adjustment (Crede and Niehorster, 2012; Holmbeck and Wandrei, 1993).

Much less is known about the influence of SPS on university adjustment. With their acute sensitivity to environmental pressures, adjustment is possibly even more taxing for HSPs. Highly sensitive persons tend to be deeply distressed by change and are rattled by the pressures of multitasking (Aron and Aron, 1997) - both of which are necessary aspects of university adjustment. Having a propensity for strong emotional responses, HSPs may struggle with low emotional stability and thus lean more heavily towards emotion-focused coping, both of which have been linked to worse outcomes (although not consistently so; Lidy and Kahn, 2011; Pritchard et al., 2007). On the other hand, given their ability for rapid and deep cognitive processing (Aron and Aron, 1997; Aron et al., 2012), HSPs might be better enabled to cope academically and rapidly acquire the necessary skills required for appropriate university adjustment. That both university adjustment and high sensory processing sensitivity are strongly influenced by early parenting makes adjustment in this subset of individuals particularly relevant and interesting.

SPS and university adjustment also lack significant investigation against diverse ethnocultural backgrounds; the sort afforded, for example, by South African universities. In the last five years, further adjustment pressures have been placed on South African students owing to a number of violent protests and disruptions (known as the #Feesmustfall movement) that have placed significant strain on students and the tertiary education sector (Hodes, 2017; Luescher, Loader, and Mugume, 2017; Molefe, 2016). These protests are the culmination of several aggravating factors. Firstly, student enrolment at South African universities has rapidly increased to levels that are not well sustained by current infrastructure (Hodes, 2017; Petersen et al., 2009). Secondly, the overwhelming majority of students hail from disadvantaged backgrounds, and enter university with the prospect of substantial financial hurdles and significant educational gaps that must be overcome (Petersen et al., 2009). Lastly, the ruling political party in South Africa (the African National Congress) has often promised equity of access and opportunity in the tertiary sector, but the realisation of this ideal has been frustratingly slow in the eyes of students, who have unequivocally demanded free tertiary education as part of the protests (Naicker, 2016). Thus, for South African students, a tense, uncertain, and at times violent atmosphere has further complicated adjustment to university, the full effects of which are still to be tallied (Langa, 2017).

This climate of uncertainty and adversity, along with the traditional challenges of university adjustment should, theoretically, be most strongly felt by HSPs. For this study, it was hypothesised that, in a sample of first year university students, levels of SPS would correlate negatively with overall university adjustment. This would align with previously published reports of typically negative outcomes for HSPs. However, when accounting for parental environment and partialing out neuroticism (as recommended by Aron and Aron (2013)), the power of SPS levels to predict university adjustment would likely drop. In keeping with previous trends, it was also predicted that childhood care would moderate the adjustment success of highly sensitive students in a for better and for worse manner (Belsky and Bakermans-Kranenburg, 2007). Lastly, comparisons were made between the association of SPS to university adjustment versus other personality features, namely the Big Five (John et al., 1991) and resistance to peer influence (Steinberg and Monahan, 2007).

4.2 Methods

4.2.1 Study participants

Study participants were a subset of the same first-year psychology students, at the University of the Witwatersrand, sampled in Study 2 (Chapter 3, section 3.2.1). Of these students, 744 attempted to complete additional instruments (beyond the HSPS from Study 2) pertaining to university adjustment and personality. Participants were excluded if they failed to indicate their

age, were over 25 years of age or had more than 20% missing information in total across all five of the survey instruments (n = 164). The final sample size was 580 individuals. As per Studies 1 and 2, students were incentivised to participate via the research participation programme. In addition, students (per academic year) were entered into a prize draw for a monetary voucher. Participant demographics were similar to those previously described (Study 2 methods; section 3.2.1) and are summarised in Table 4.1.

Table 4.1: Descriptive statistics for Study 3

Criterion	Study 3 (mean ± sd)
n	580
Age	19.27 (1.23)
Ethnicity	**%**
Black African	44.83
White	30.52
Indian	15.00
Mixed Ancestry	6.38
Other	3.10
Sex (% female)	81.03
Home language	**%**
English	55.69
Non-English	44.31

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4.2.2 Instruments

All study instruments are available in Appendix C.

4.2.2.1 The HSPS

The HSPS was used as described previously (Study 2; section 3.2.2; Appendix B).

4.2.2.2 The Student Adaptation to College Questionnaire - Modified

Baker and Siryk's (1984) Student Adustment to College Questionnaire (SACQ) comprises 67 items, answered on a 9-point Likert scale, that interrogate student adjustment across four categories, namely academic, personal, social and institutional adjustment. Over three decades later, it remains one of the most widely used measures for university adjustment (Crede and Niehorster, 2012). Despite evidence of overall adequate reliability and validity across a large

number of studies, the four-subscale structure of the SACQ has been criticised (Taylor and Pastor, 2007) for low levels of reliability.

In research by LaBrie and colleagues (2012), the SACQ was modified by removing 12 items that strictly pertained to commuter students (which were not pertinent to the authors' investigation), and exploratory factor analysis of the remaining items revealed a two-factor solution. These two factors represented positive and negative university adjustment, and attained excellent alpha values (.93 and .92 respectively). Given these improved subscale reliabilities, and this study's similar indifference to commuting aspects of adjustment, these modifications to the SACQ were also adopted.

A total university adjustment score was calculated by reverse scoring items reflecting negative university adjustment so that their values could be added together with items measuring positive university adjustment. For this combined metric, higher values thus represent better adaptation to university life.

4.2.2.3 The Parental Bonding Instrument/The Measure of Parental Style

Early family environment and childhood care was assessed with two different, but related instruments. In the 2016 sample, students completed the Measure of Parental Style (MOPS), whilst samples from the two subsequent years completed the Parental Bonding Instrument (PBI). Both of these instruments have been used previously in SPS research (Acevedo et al., 2017; Aron et al., 2005).

The 25-item self-report PBI (Parker, Tupling, and Brown, 1979) requires respondents to reflect on the levels of 1) care and 2) overprotection they experienced, from each parent, during their first 16 years. Items for each of the two subscales are scored on a four-point scale (0-3) and tallied such that higher scores represent greater levels of care and overprotection. The instrument has been extensively used and demonstrates good validity and test-retest reliability for both maternal and paternal assessment (Parker et al., 1997; Wilhelm, Niven, Parker, and Hadzi-Pavlovic, 2005). Instrument scores were found to be stable across a 20 year period and showed no vulnerability to issues of participant gender, participant mood state or attitudinal change as a product of life experience (Wilhelm et al., 2005). Evidence suggests the PBI is a good measure of both perceived and actual parenting (Parker, 1983; Parker and Gladstone, 1996).

Critiques of the PBI include its lack of items covering abuse (sexual or physical) and its potential to confuse some respondents through the use of positive and negatively expressed items (Gamsa, 1987). To address these issues, Parker and colleagues (1997) redesigned the instrument using a set of 15 refined items (still scored on a four-point scale) that captured the PBI domains of care and overprotection in addition to a dimension of parental abuse (Parker et al., 1997).

The purpose of this redesigned instrument, named The Measure of Parenting Style (MOPS), was to better capture the elements of parenting known to engender later psychopathology. To this end, and to unify item expression, all MOPS items are expressed in a negative direction, such that higher scores indicate more dysfunctional parenting on the three subscales of indifference, overcontrol and abuse. Alpha reliabilities for these subscales, for either parent, were acceptable (.76 - .93) and scores were not influenced by age or social class (Parker et al., 1997).

Importantly, the correlation between the MOPS indifference subscale and the PBI care subscale was significantly strong (-.76), as was the correlation between the overprotection and overcontrol subscales (.71). This suggested that the MOPS indifference and overcontrol dimensions, although measured with smaller item sets, are still reasonable estimates of the PBI care and overprotection dimensions respectively, to the extent that the MOPS can be seen as an abbreviated version of the PBI (both of which have identical instructions and scoring, further supporting their interchangeability). However, a notable difference between scales is that PBI scores showed largely normal distributions, but MOPS scores were skewed by a high proportion of zero-scored items (Parker et al., 1997).

In administering the PBI and MOPS, participants in this study were only requested to evaluate whoever they deemed their primary caregiver. Many South African youths are raised in family units that do not comprise a mother and a father, mostly as a consequence of the disruptive influences of migration, violence, poverty and disease (Barbarin and Richter, 2001b). Siblings, great-grandparents, grandparents, aunts and uncles have also been noted to fulfil the role of primary caregiver, or otherwise care-giving is a responsibility distributed across multiple relatives (Barbarin and Richter, 2001b). Obtaining information on a single primary caregiver was thus a strategy to improve consistency in the assessment of care-giving as far as possible.

To increase the available sample size and facilitate merging of the data, scores from the MOPS and PBI were standardised. Specifically, only the care (PBI) and indifference (MOPS) subscale scores were used, as these appear to be more stable dimensions than overprotection/overcontrol (Parker et al., 1997; Wilhelm et al., 2005). Firstly, the MOPS indifference subscale was reversed so that higher scores reflected less indifference (more care). Subscale total scores were then converted to their z-score equivalent. Thus, all participants had a comparable z-score for childhood care.

4.2.2.4 The Big Five Inventory

The Big Five Inventory (BFI; Benet-Martinez and John, 1998; John et al., 1991; John, Naumann, and Soto, 2008) is a widely used, 44-item self-report measure of five dimensions of personality (openness to experience, conscientiousness, extraversion, agreeableness and neuroticism). The instrument was developed to meet demand for a shorter assessment tool than the gold-standard NEO Personality Inventory, Revised (Costa and McCrae, 1992), which com-

prises 240 items. Despite this brevity, the BFI retains excellent psychometric properties. Alpha reliabilities average at .80, and three month test-retest reliabilities average at .85. Moreover, the instrument strongly mirrors the convergent and discriminant validities of other five-factor model instruments (John and Srivastava, 1999). Items are scored on a five-point Likert scale, with 7-10 items per subscale.

4.2.2.5 The Resistance to Peer Influence Scale

To assess at least one dimension of the social pressure during university adjustment, the Resistance to Peer Influence (RPI) scale (Steinberg and Monahan, 2007) was included. The RPI is a self-report instrument in which respondents must decide which one, of a pair of statements (10 pairs in total), is more representative of their personal behaviour. Each pair includes one statement reflecting conformity to peer pressure, whilst the other reflects independence from such pressure (e.g. Some people take more risks when they are with their friends than they do when they are alone BUT Other people act just as risky when they are alone as when they are with their friends). Once respondents have selected a statement, they must declare if it is "sort of true" or "really true" for them. Thus, each pair of items is scored on a four point scale and the total score is divided by the number of completed items (with 7 being the desired minimum). Higher scores indicate a greater resistance towards peer influence.

The RPI was developed and tested in an eclectic set of samples that varied widely in age, socioeconomic status, ethnicity and levels of criminality (Steinberg and Monahan, 2007). Both cross-sectional and longitudinal analyses were conducted. On balance, RPI scores were strongly influenced by age of respondent, but only slightly by socioeconomic status. Older individuals, females and African-Americans tended to score higher, whilst younger respondents, males, serious criminal offenders, and Asian individuals scored lower (Sumter, Bokhorst, Steinberg, and Westenberg, 2009). From 18 to 30 years of age, there were no significant differences in scores (Steinberg and Monahan, 2007), suggesting a degree of stability in responding to peer influence for this age range which is pertinent to this study. Factor analysis of the instrument reveals a one-factor structure (Sumter et al., 2009). Regarding reliability and validity, internal consistency reliability for the RPI across multiple samples was adequate (.70 - .76; Monahan, Steinberg, and Cauffman, 2009; Monahan, Steinberg, Cauffman, and Mulvey, 2009; Stautz and Cooper, 2014). Reliability remained stable regardless of the age of respondents, including young adolescents from 10-18 years of age (Sumter et al., 2009). Scores correlated negatively to measures of impulsivity and antisocial risk-taking, but positively with impulse control and IQ (Steinberg and Monahan, 2007). Moreover, RPI scores were found to logically coalesce with fMRI results that assessed brain activation and morphology in pre-teens and adolescents (Grosbras et al., 2007; Paus et al., 2008).

4.2.3 Procedure

Following ethical clearance (Appendix A), all five instruments were compiled into a single survey, administered electronically via SurveyMonkey. Instruments were presented in the same order, beginning with the HSPS, but item order per instrument was randomised to reduce context effects (Tourangeau et al., 2009). Since the primary outcome variable of this study was university adaptation, an invitation to participate was advertised in the second half (July-December) of each academic year (2016, 2017 and 2018). This ensured that first-year students, per year, had all engaged with the stressors of university life for at least six months.

As per both Study 1 and Study 2, descriptive statistics, scale scoring and sex comparisons per instrument (following suitable assumption tests) were performed using R (version 3.5.1) and RStudio (version 1.1.456), along with the *psych* package (version 1.8.4; Revelle, 2018).

To explore the relationship between the measured predictors and the outcome variable of university adjustment, three different linear modelling strategies were conducted in the following order:

1. Hierarchical linear modelling

A baseline model of university adjustment regressed on levels of SPS was established. This baseline was then compared against a second model in which parental care and neuroticism were entered hierarchically in order to partial out their effects prior to entering HSPS scores into the model.

2. Exhaustive modelling

To determine which combination of measured predictors best accounted for variation in university adjustment, an exhaustive selection algorithm was applied through the use of the *leaps* package (version 3.0; Lumley, 2017). Exhaustive selection combines the benefits of both backward elimination and forward selection of predictors (Faraway, 2015), but such automated predictor selection is generally reserved for exploratory analyses where the sample size is at least 40 times greater than the total number of predictors (Cohen, Cohen, West, and Aiken, 2003; Faraway, 2015), as is the case in the present study. Algorithm results determined the best order in which to add predictors to the model. Thereafter, several fit statistics were examined to determine what number of predictors provided the most explanatory power (i.e. the best model fit).

3. Interaction modelling

To determine the potential moderating effect of parental care on SPS levels, an interaction term of HSPS and parental care scores was included and model fit re-examined.

Models were assessed for fit using the BIC, adjusted R^2, residual sum of squares (RSS) and Mallow's C_p criteria. To visualise regression models, predicted values were plotted using the

sjPlot package (version 2.6.1; Ludecke, 2017).

4.3 Results

4.3.1 Instruments

4.3.1.1 Childhood care: the PBI/MOPS

In the 2016 sample (n = 224), the MOPS indifference subscale achieved an alpha of .84, whilst in the combined 2017/2018 sample (n = 356), the PBI care scale attained an alpha of .91. Scores on neither scale were normally distributed. After standardising the scores and merging the two samples, scores remained negatively skewed with most participants (65%) reporting high levels of childhood care (z score > 0). There was no significant difference in childhood care detected between males and females (W = 24559, p = 0.41, negligible effect size).

4.3.1.2 Personality attributes

Results for the various personality scales used are summarised in Table 4.2. All instruments attained good internal consistency reliability scores (with the exception of a moderate score for agreeableness), particularly the university adjustment scales (α = .90 - .94). Only HSPS, positive adjustment and total adjustment scores were normally distributed based on the Shapiro-Wilk test.

Instrument score comparisons by sex revealed that males and females significantly differed except on measures of conscientiousness, agreeableness and resistance to peer influence. Females had significantly *higher* SPS levels, negative university adjustment (NUA) scores and neuroticism than males. In contrast, females had significantly *lower* positive university adjustment (PUA) scores, total university adjustment (TUA) scores, openness, and extraversion. Because the sample size of males and females was unequal, effect sizes were calculated using Hedges' g, a variant of Cohen's d (Maher, Markey, and Ebert-May, 2013), where values of .2, .5 and .8 reflect small, medium and large effect sizes respectively. Sex differences in neuroticism were of large effect size whilst the remainder of comparisons were small to negligible.

Inter-scale correlations, corrected for scale reliability (except in the case of the z-standardised childhood care scores), are summarised in Table 4.3. In line with previous literature, HSPS scores correlated positively with neuroticism but negatively with extraversion (Greven et al., 2019; Lionetti et al., 2019). Furthermore, many studies have found positive correlations between HSPS and openness, but no significant relationships to either conscientiousness or agree-

ableness (Greven et al., 2019; Lionetti et al., 2019) - observations which were also seen here. HSPS scores were positively correlated to NUA, but inversely correlated to positive and total university adjustment. PUA shared prominent positive correlations with conscientiousness and extraversion but associated negatively with neuroticism. These relationships were reversed when considering NUA, which correlated particularly well with neuroticism. The modifier variable, childhood care, was modestly correlated to other variables (except openness and resistance to peer influence). Better childhood care correlated with better adjustment to university.

For a more detailed examination of the relationship between SPS and the five-factor model, SPS was deconstructed into the five factors identified in Study 2. Correlations are shown in Table 4.4. Negative Affectivity, Neural Sensitivity and Propensity to Overwhelm correlated positively with neuroticism, but negatively (or negligibly) to the rest of the five factor model. In contrast, Aesthetic Sensitivity and Careful Processing had positive correlations to openness and conscientiousness (especially in the case of Careful Processing).

Table 4.2: Instrument scoring results and comparison by sex

Criterion	HSPS	PUA	NUA	TUA	O	C	E	A	N	RPI*
Cronbach's α	.86	.90	.91	.94	.72	.83	.81	.60	.83	.79
Guttman's λ^6	.92	.94	.95	.97	.83	.88	.88	.76	.89	.84
Average total (n = 580)	122.75 (21.42)	135.86 (31.90)	134.32 (40.72)	301.55 (64.82)	35.89 (5.62)	29.94 (6.33)	23.88 (6.10)	32.24 (4.81)	25.80 (6.48)	3.02 (.58)
Observed minimum	68	54	37	110	17	10	8	14	8	1.2
Observed maximum	183	213	247	452	50	45	40	43	40	4
Normality (p-value)	.43	.07	$< .01$	.08	.01	$< .01$	$< .01$	$< .01$	$< .01$	$< .01$
Females (n = 470)	124.53 (21.07)	133.95 (32.18)	137.31 (40.23)	296.64 (64.77)	35.49 (5.60)	29.91 (6.47)	23.60 (6.15)	32.19 (4.89)	26.76 (6.10)	3.02 (.58)
Males (n = 110)	115.16 (21.35)	144.04 (29.41)	121.52 (40.72)	322.52 (61.02)	37.65 (5.37)	30.05 (5.73)	25.11 (5.75)	32.47 (4.41)	21.68 (6.49)	2.99 (.57)
Test statistic	t(163.43) = 4.15	t(175.46) = -3.18	W = 31 722	t(171.3) = -3.96	W = 19 926	W = 25 714	W = 21 724	W = 25 327	W = 37 284	W = 27 047
p-value	$< .01$	$< .01$	$< .01$	$< .01$	$< .01$	.93	$< .01$	.74	$< .01$	.45
Effect size *r*	.31	.23	.15	.29	.16	$< .01$	.11	.01	.30	.03
Hedges' *g*	.44	.32	.39	.40	.39	.02	.25	.06	.82	.05

* HSPS = Highly Sensitive Person Scale; PUA = Positive University Adjustment; NUA = Negative University Adjustment; TUA = Total University Adjustment; O = Openness; C = Conscientiousness; E = Extraversion; A = Agreeableness; N = Neuroticism; RPI = Resistance to Peer Influence.

Table 4.3: Disattenuated scale correlations

Instrument[a]	1	2	3	4	5	6	7	8	9	10	11
1. HSPS	-										
2. PUA	-.14**	-									
3. NUA	.49***-.65***	-									
4. TUA	-.37***.94***-.99***	-									
5. O	.10	.29***-.18***.25***	-								
6. C	-.08	.54***-.53***.59***.25***	-								
7. E	-.31***.39***-.28***.36***.21***.24***	-									
8. A	-.08	.28***-.34***.35***.15*	.44***.11	-							
9. N	.67***-.35***.64***-.57***-.15***-.29***-.41***-.46	-									
10. RPI	-.07	.21***-.24***.25***.24***.27***.16**	.10*	-.10	-						
11. Care[b]	-.10*	.20***-.22***.24***.00	.16***.14 ***	.11	-.15***.04	-					

[a] HSPS = Highly Sensitive Person Scale; PUA = positive university adjustment; NUA = negative university adjustment; TUA = total university adjustment; O = openness; C = conscientiousness; E = extraversion; A = Agreeableness; N = Neuroticism; RPI = resistance to peer influence.
[b] Standardised care scores are not attenuated for scale reliability. *** = $p < .001$; ** = $p < .01$; * = $p < .05$

Table 4.4: Correlations between the five factor model and the five factors of SPS

Instrument [a]	1	2	3	4	5	6	7	8	9	10
1. Openness	-									
2. Conscientiousness	.19***	-								
3. Extraversion	.16***	.20***	-							
4. Agreeableness	.10*	.31***	.08	-						
5. Neuroticism	-.12***-.24***-.34***-.33***	-								
6. Negative Affectivity	-.14**	-.26***-.25***-.16***.57***	-							
7. Neural Sensitivity	.03	-.19**	-.25***-.12***.62***.60***	-						
8. Propensity to Overwhelm	.01	-.09*	-.26***-.08	.38**	.51***.57***	-				
9. Aesthetic Sensitivity	.52***	.02	.01	.08	.10*	.13**	.20***.18***	-		
10. Careful Processing	.10*	.43***-.03	.07	.20**	.24***.28***.32***.17***	-				

[a] *** = $p < .001$; ** = $p < .01$; * = $p < .05$

4.3.2 Hierarchical linear modelling

Prior to investigating more complex models, a baseline model in which total university adjustment was regressed on SPS levels revealed a significant, negative linear relationship in which a roughly one point increase in SPS predicted a one point decrease in total university adjustment (Table 4.5). Sex was entered as a fixed effect, given the significantly different levels of SPS between males and females. These variables were able to account for 12% of the variation in adjustment.

To partial out the effects of childhood care and neuroticism, in keeping with recommendations by Aron & Aron (2013), these effects were entered into the model sequentially before

Table 4.5: Hierarchical linear modelling results

	R^2	B	95% CI	SE B	β	p-value*
Baseline	.12					$< .001$
Constant		416.02		15.18		$< .001$
Sex (Male)		16.9	[4.05; 29.75]	6.54	.10	.01
HSPS		-.96	[-1.19; -.72]	.12	-.32	$< .001$
Step one	.07					$< .001$
Constant		296.97		2.88		$< .001$
Sex (Male)		24.11	[11.13; 37.10]	6.61	.15	$< .001$
Care		14.93	[9.83; 20.03]	2.60	.23	$< .001$
Step two	.27					$< .001$
Constant		424.04		10.37		$< .001$
Sex (Male)		.47	[-11.16; 12.54]	6.15	.00	.94
Care		10.77	[6.21; 15.34]	2.32	.17	$< .001$
Neuroticism		-4.75	[-5.49; -4.01]	.38	-.48	$< .001$
Step three	.28					$< .001$
Constant		439.83		14.18		$< .001$
Sex (Male)		.50	[-11.55; 12.56]	6.14	.00	.94
Care		10.69	[6.13; 12.25]	2.32	.17	$< .001$
Neuroticism		-4.36	[-5.23; -3.48]	.45	-.44	$< .001$
HSPS		-.21	[-.47; .04]	.13	-.07	.10

* B = unstandardised regression coefficient; CI = confidence interval; SE = standard error; β = standardised regression coefficient.

entering HSPS scores. Model parameters are summarised in Table 4.5. Sex was maintained as a fixed effect throughout the stepwise modelling. Standardised z-scores for parental care were entered first, which were significantly positively correlated to university adjustment explaining 7% of the variance. Neuroticism scores were then added, revealing a significant negative association that explained a further 20% of variance for a combined total of 27%. Notably, accommodating for levels of neuroticism appeared to render sex differences inconsequential. With these effects partialed out, the addition of HSPS scores to the model proved non-significant and only explained a further 1% of the variance in adjustment scores. Each one point increase in HSPS score only predicted a .21 decline in university adjustment score.

To better understand which aspects of the SPS trait were driving the negative relationship with TUA, a second baseline model was created with SPS deconstructed into its five component factors (Table 4.6). Both NA (B = -2.87; $p < .001$) and NS (B = -2.66; $p < .001$) predicted significant declines in total adjustment scores whilst CP (B = 3.61; $p < .001$) predicted improved adjustment. Neither AS (B = .24; p = .79) nor PO (B = -.29; p = .61) showed significant relationships to adjustment scores. The overall model fit was significant, $F(573) = 30.24$; $p < .001$, and explained 23% of the variance in adjustment scores ($R^2 = .23$). Both neuroticism and parental care were then partialed out (Table 4.6). Compared to the baseline model described above, Negative Affectivity remained significant (B = -1.96; $p < .001$) but predicted a smaller decline in adjustment. Careful Processing was also significant (B = 3.54; $p < .001$) with a

coefficient only marginally smaller than the preceding model. Neural Sensitivity fell short of significance (B = -1.01; p = .07), whilst Aesthetic Sensitivity (B = .25; p = .77) and Propensity to Overwhelm (B = -.14, p = .80) continued to have negligible influence on adjustment scores. The model fit was significant, F(571) = 36.86; p $<$ .001, explaining 33% of the variance in adjustment scores.

Table 4.6: Linear models with SPS divided into five factors

	R^2	B	95% CI	SE B	β	p-value*
Baseline	.23					$<$ .001
Constant		393.52		15.27		$<$ .001
Sex (Male)		8.20	[-4.12; 20.51]	6.27	.05	.19
Negative Affectivity		-2.87	[-3.77; -1.97]	.46	-.30	$<$ .001
Neural Sensitivity		-2.66	[-3.76; -1.56]	.56	-.24	$<$ .001
Propensity to Overwhelm		-.29	[-1.40; .83]	.57	-.02	.61
Aesthetic Sensitivity		.24	[-1.52; 2.00]	.89	.01	.78
Careful Processing		3.61	[2.18; 5.04]	.73	.19	$<$ .001
Including care and neuroticism	.33					$<$ .001
Constant		417.5		14.77		$<$ .001
Sex (Male)		-1.28	[-13.01; 10.44]	5.97	.01	.83
Care		10.90	[6,49; 15.32]	2.25	.17	$<$ .001
Neuroticism		-3.40	[-4.32; -2.49]	.47	-.34	$<$ .001
Negative Affectivity		-1.96	[-2.84; -1.07]	.45	-.20	$<$ .001
Neural Sensitivity		-1.01	[-2.12; .09]	.56	-.09	.07
Propensity to Overwhelm		-.14	[-1.18; .91]	.53	-.01	.80
Aesthetic Sensitivity		.25	[-1.39; 1.89]	.84	.01	.77
Careful Processing		3.54	[2.20; 4.88]	.68	.19	$<$ .001

* B = unstandardised regression coefficient; CI = confidence interval; SE = standard error; β = standardised regression coefficient.

4.3.3 Exhaustive linear modelling

Using an exhaustive selection algorithm, predictor variables were suggested for entry into the regression model in the following approximate order: conscientiousness, neuroticism, childhood care, extraversion, sensory processing sensitivity, openness, resistance to peer influence, sex and lastly, agreeableness. Fit statistics (BIC, adjusted R^2 and Mallow's C_p) were optimal with the first seven variables (plus the intercept), which thus eliminated the need for sex and agreeableness as predictors. The final model is presented in Table 4.7. All predictors attained significant p-values ($<$ .05). Standardised β values suggested conscientiousness, neuroticism, SPS and childhood care had the largest influence on adjustment scores. The model fit was significant, F(572) = 69.62; p $<$ .001, and explained 45% of the variation in adjustment scores.

Table 4.7: University adjustment regression model

	R^2	B	95% CI	SE B	β	p-value *
Without interaction	.47					$< .001$
Constant		228.85		22.54		$< .001$
Conscientiousness		3.82	[3.17; 4.48]	.34	.38	$< .001$
Neuroticism		-3.04	[-3.81; -2.26]	.40	-.30	$< .001$
Care		7.12	[3.16; 11.08]	2.04	.11	$< .001$
Openness		1.01	[.28; 1.74]	.38	.09	$< .001$
HSPS		-.35	[-.57; -.12]	.12	-.12	$< .001$
RPI		8.75	[1.76; 15.73]	3.60	.08	.01
Extraversion		.70	[.01; 1.40]	.36	.07	.04
With interaction	.47					$< .001$
Constant		293.99		3.84		$< .001$
Conscientiousness		24.24	[20.09; 28.40]	2.12	.38	$< .001$
Neuroticism		-22.10	[-26.67; -17.54]	2.33	-.34	$< .001$
Care		-1.13	[-7.80; 5.54]	3.40	-.02	.74
Openness		5.13	[1.08; 9.17]	2.06	.08	.01
SPS level (Low)		10.86	[1.58; 20.15]	4.73	.08	.02
RPI		4.90	[.88; 8.91]	2.04	.08	.02
Extraversion		4.56	[.37; 8.75]	2.13	.07	.03
Care*SPS level		12.72	[4.57; 20.88]	4.15	.20	.002

* B = unstandardised regression coefficient; CI = confidence interval; SE = standard error; β = standardised regression coefficient.

4.3.4 The interaction between childhood care and SPS

Before examining the moderating effect of childhood care on SPS levels, the sample was first dichotomised into "high" sensitive and "low" sensitive individuals as recommended by Aron and Aron (2013) and practiced elsewhere in the literature (e.g. Pluess and Boniwell, 2015). Dichotomisation results in a loss of information, but does afford the comparison of separate regression slopes for particular groups of interest, such as high and low sensitive individuals. Theoretically, highly sensitive persons account for 20-35% of the population (Aron and Aron, 1997; Greven et al., 2019), therefore, a high-low breakpoint was established at the 70th percentile of HSPS scores. This boundary was selected based on a visual inspection of HSPS score distribution, and given the fact that samples of psychology students likely contain a higher proportion of HSPs than the general population (Aron and Aron, 2013). Highly sensitive individuals (n = 176) had a mean HSPS score of 147.39, whilst low sensitivity individuals (n = 404) had a mean of 112.02. This difference was significant (W = 71104, $p < .001$) and of large effect size (Hedges g = 2.88, r = .80). In terms of total university adjustment, highly sensitive persons averaged 278.22, whilst low sensitivity individuals attained an average of 311.71. Again, this difference was significant, t(348.77) = -5.99, $p < .001$, and of moderate effect size (Hedges g = 0.54, r = .31).

The categorical sensitivity variable (high vs low) was then entered as a replacement for

continuous HSPS scores in the final model, along with interaction term involving childhood care scores. All other variables were centred to ease interpretation of the interaction model (Cohen et al., 2003). Results are reported in Table 4.7. The interaction between childhood care and SPS levels was found to be significant. For low sensitivity individuals, each unit increase in standardised childhood care score corresponded to an approximate 12 point increase in total university adjustment (Figure 4.1a). Simple slopes analysis revealed that this was a significant gradient ($p < .01$). Conversely, high sensitivity individuals had an approximate one point decrease in adjustment for each unit increase in childhood care, resulting in a non-significant slope ($p = .76$).

Because the cutoff between high and low sensitivity individuals is somewhat arbitrarily defined, latent class analysis was also used to statistically segregate respondents into the three known categories of sensitivity, namely "dandelions", "tulips" and "orchids" representing high, medium and low sensitivity respectively. The same interaction model was applied to dandelion and orchid individuals ($n = 357$; model parameters not shown) revealing a similar, significant interactive effect between sensitivity class and childhood care (Figure 4.1b).

An examination of the diagnostics for all linear models reported revealed six potentially problematic cases (see Appendix E for a selection of diagnostic plots). Two participants had childhood care scores that were five standard deviations below average, marking them as potential outliers. Further investigation of these participants confirmed that scores on the other parental sub-scales (abuse, overcontrol) were similarly poor, suggesting unfortunately abusive and sub-par care-giving. One participant had a residual value that was significantly outlying, even after Bonferroni correction (adjusted $p = .04$). Meanwhile, three other participants had leverage values twice as great as the sample average leverage. However, none of these six respondents had Cook's distances greater than 0.03, suggesting they were not unfairly biasing the regression models. Removal of the participant with a significantly outlying residual slightly improved model fit and was thus the only change made following diagnostic checks. Aside from these minor issues, there was good evidence to suggest the models met with all necessary assumptions. Based on an examination of variance inflation factor (VIF) and tolerance statistics, there was no evidence of multicollinearity between predictors (mean VIF = 1.26, tolerance $>.60$ for all predictors) and the Durbin-Watson test suggested no significant autocorrelation ($d = 1.93$, $p = .42$).

When comparing the regression lines to locally estimated scatter plot smoothing (LOESS) curves (Figure 4.1c), there was evidence to suggest a quadratic relationship between childhood care and university adjustment. Note that to avoid unfairly influencing the LOESS curve, the two participants with outlying childhood care scores were first removed. When childhood care was entered as a second order term, this did not appear to substantially change the interpretation of the results (Figure 4.1d; model parameters not shown). Similarly, an ordered normal transformation of parental care scores made no significant change to the model or its interpretation

(not reported).

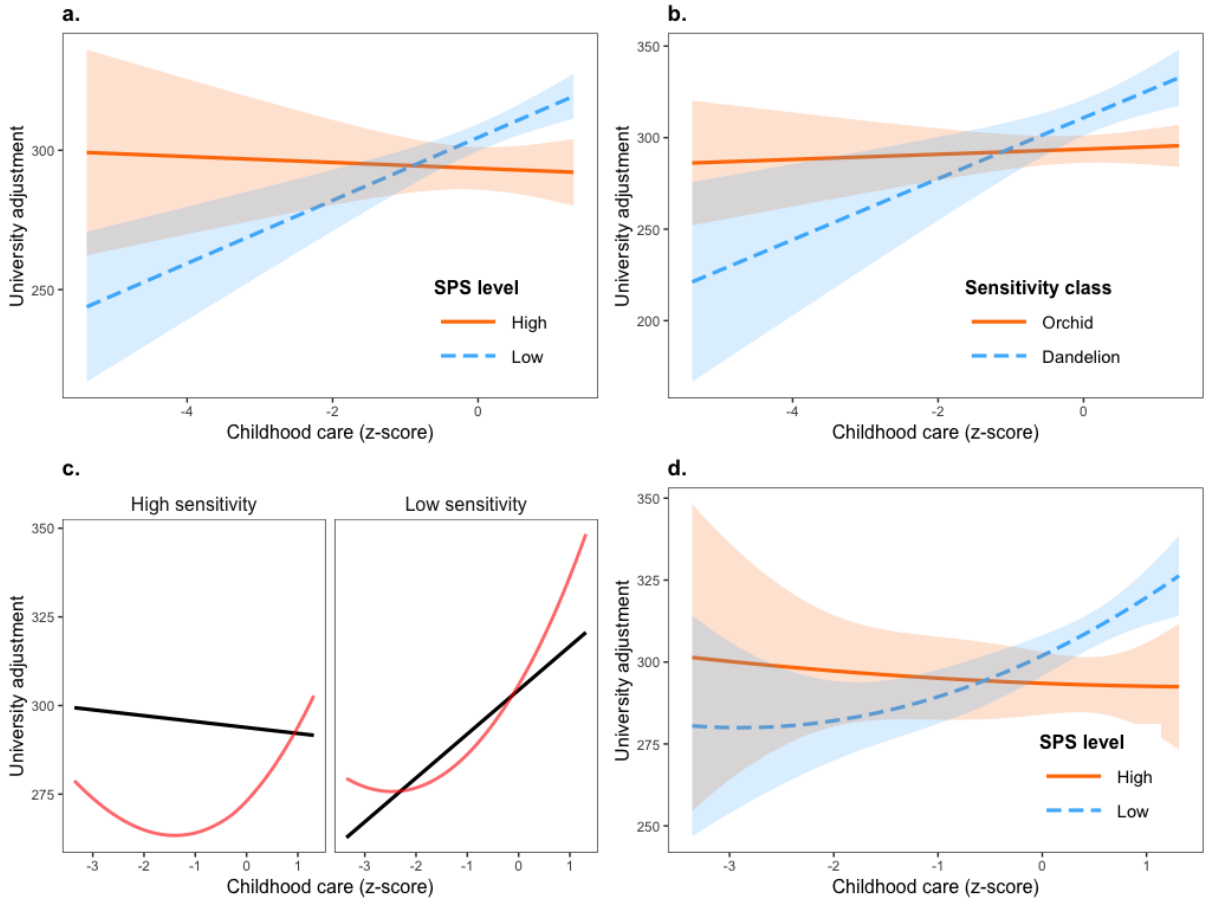


Figure 4.1: **Predicted university adaptation as a function of the interaction between SPS levels and childhood care**. a. Based on a 70/30 split, individuals with high levels of SPS appeared more stably adjusted to university regardless of levels of childhood care experienced. In contrast, those with low levels of SPS had significantly better adjustment with increasing levels of childhood care. b. A similar interaction was seen when using latent class analysis to statistically separate respondents into orchid and dandelion classes. c. Regression lines (black) are plotted with LOESS smoothed lines (red). The shape of the smoothed lines possibly suggests that childhood care is better represented as a quadratic term. d. When childhood care is entered as a quadratic term, the interpretation of the regression model is not substantially changed.

4.4 Discussion

Personality attributes are well known determinants of university adjustment and the identification of stable effects of personality on adjustment can be useful for prediction and intervention purposes (Kurtz et al., 2012). Although much is known about the role of the "big five" domains of personality in the university setting, less research has been done on SPS, which is a sufficiently distinct but seemingly fundamental aspect of personality (Aron et al., 2012; Wolf et al., 2008). This study found SPS to be a significant predictor in explaining the adjustment of a sample of psychology first year students, with higher levels of SPS suggesting more difficulty

in university adjustment. However, this effect was relatively small in size and appeared to be moderated by parental care.

Considered in isolation, SPS had moderate zero-order correlations with total (-.37) and negative (.49) university adjustment, and was a significant predictor of worsening university adjustment following linear regression modelling. This effect was largely driven by two of the main characteristic features of highly sensitive persons, namely high neural sensitivity and strong emotional reactivity (particularly, in this case, negative affectivity). In contrast, the tendency of highly sensitive persons towards carefully processed, considered behaviour facilitated *improved* university adjustment. Such behaviour is possibly a variant of conscientiousness, given that the Careful Processing (CP) subscale had a zero-order correlation of .43 with BFI conscientiousness. However, total HSPS score did not correlate well with conscientiousness (-.06), and HSPs did not score any differently on conscientiousness to non-HSPs (data not shown). The hierarchical analysis confirmed that by partialing out neuroticism, the suggested negative effect of SPS on university adjustment was notably diminished. Neuroticism clearly accounted for some of the effects of sub-factors negative affectivity and neural sensitivity, whose regression coefficients were appreciably reduced. Importantly, there was no substantial change to the positive effects of careful processing after partialing out neuroticism. Others have also noted contrasting patterns of association when using sub-factors of the HSPS. For example, Evers et al. (2008) found the HSPS sub-factors of Ease of Excitation (EOE) and Low Sensory Threshold (LST) to correlate with a lowered sense of coherence, lower self-efficacy and a higher sense of alienation. The more positive Aesthetic Sensitivity (AES) factor did not, however, share these correlations. Similarly, Liss et al. (2008) found that the higher the AES score, the lower the likelihood HSPs would present with symptoms of autism and alexithymia.

Considered together with personality and other variables, SPS remained an important determinant of lowered university adjustment, although of relatively small effect. In agreement with meta-analytic evidence (Crede and Niehorster, 2012), conscientiousness was found to be, by far, the strongest predictor of university adjustment, followed closely by neuroticism. Indeed, all "big five" traits correlated in the same directions and of similar magnitudes to this same meta-analysis. Openness and extraversion continued to demonstrate an important influence on adjustment, in line with other findings (Poropat, 2009). The only factor without an apparent role in adjustment was agreeableness, although this factor is known to have at least a small effect on academic performance (Poropat, 2009). Parental care, and the ability to resist peer influence were also important in explaining the variance in university adjustment.

That SPS remained an important variable even in the presence of the five major factors of personality supports contentions raised by Aron and Aron (1997), who have argued that SPS level is an *antecedent* to many personality variables (section 1.4). That is, the reactivity of one's nervous system establishes the framework around which other personality traits (e.g. the five-factor model) are structured, making it an important individual difference in its own right.

According to these results, SPS levels still carried some explanatory power (albeit relatively minor) in terms of university adjustment over and above the five-factor model. Others (e.g Gerstenberg, 2012; Lionetti et al., 2019) have also found SPS to predict outcomes independently of the five-factor model. As Aron and Aron (1997) have argued, careful consideration must thus be given to what is primary and what is secondary in terms of personality development. This seems particularly true of neuroticism and its relation to SPS. Although also the potential result of many environmental influences, neurotic behaviour is, at the very least, facilitated by a low-threshold nervous system, which explains its moderately strong correlation with SPS (.67 in this study). But results from this study support the claim that the tendency towards negative affect is but one aspect of highly sensitive persons, whose low threshold nervous system can also provide significant benefit. In the case of this study, the benefit accrued from careful processing, a form of conscientious-like behaviour (CP had a .43 correlation with conscientiousness), which can be plausibly argued as advantageous in multiple aspects of university adjustment. The secondary propensity HSPs have for disruptive negative emotion/emotional instability seems to overshadow an equal propensity for beneficial detail-oriented and diligent behaviour, although this behaviour is not well captured by the BFI conscientiousness scale alone. Previous SPS research has tended to highlight only the inclination towards negative affect and the problems it can engender (anxiety, depression, social phobia, and here, poorer university adjustment), without consideration of the strengths SPS affords. Partialing out neuroticism, and deconstructing SPS into appropriate factors, appears to be one method of better unpacking the influence of SPS on behaviour (Bridges and Schendan, 2019).

One known determinant of where the balance lies between the strengths and weakness of SPS is early parental environment. Here, it was hypothesised that parental care would modify university adjustment outcomes for highly sensitive participants in a for better or worse manner (e.g. Figure 1.8a). However, study findings were directly opposite to this supposition. Individuals with *low* levels of SPS showed significant differences in university adjustment as a function of their parental care, whilst those ranking *high* on SPS seemed to have a stable level of adjustment regardless of parental care. There are several possible explanations for this observation. Firstly, one potential indicator of university adjustment is prior academic achievement (Crede and Niehorster, 2012). Students who have performed well academically prior to university tend to find the adjustment to tertiary education easier. Since good prior achievement is typically reflective of high cognitive functionality and conscientiousness, which are alleged strengths of HSPs (given their alleged propensity for "giftedness"; Section 1.4.2.6), the university context might act as filter for those HSPs that have successfully leveraged these advantages. Such students would not only be able to rapidly adjust to the new academic structure of university, but may also apply their cognitive flexibility to quickly acquire the practical skills needed for non-academic adjustment pressures. Secondly, that these HSPs are in psychology classes may speak (at least, anecdotally) to particularly high levels of personal awareness and metacognition, such that they have been better able to integrate their childhood upbringing in a constructive, psychologically healthy manner. In other words, an ascertainment bias might exist, in which

university psychology classes attract highly functional HSPs, regardless of early care-giving, whereas those HSPs that were significantly troubled by their parental experiences are not well represented. An alternative, or otherwise compounding, reason is that poorly coping students may be less likely to participate in surveys, or may not declare their difficulties honestly (Crede and Niehorster, 2012). Since the study survey was administered in the third (of four) semesters, many poorly coping students may have already dropped out. Lastly, these results might undermine, or otherwise challenge the claims of SPS theory. Perhaps not all HSPs are particularly permeable to parental influence, and perhaps high levels of SPS do not always result in outcomes "for better and for worse". This would suggest that SPS might be more domain-specific, rather than domain-general (section 1.6, discussed further in section 6.2), and further research is required before generalisations are made about the functioning of highly sensitive persons.

Although some important complexities have been explored, it must still be acknowledged that individuals high on SPS apparently struggle more with university adjustment than those with low SPS levels. Research has repeatedly shown that the university setting tends to favour those with robust emotional stability, high levels of extraversion and strong perceptions of social support (Lidy and Kahn, 2011). That HSPs feel emotion more deeply, that the majority (70%) are introverted, and that the generally low frequency of HSPs in the population (15-30%) may apply a degree of minority stress (Hayes, Chun-Kennedy, Edens, and Locke, 2011), all portends greater adjustment challenges for HSPs. As Jung contended, for those of sensitive disposition "[their] own nature demands of [them] more effort than the normal person is required to exert" (Jung, 1961, para. 572), and it would appear that university adjustment is one such area where these demands are made.

For these reasons, SPS might be a particularly important trait to consider for university counsellors (Holmbeck and Wandrei, 1993; Pritchard et al., 2007). Given that levels of university stress are on a concerning upward trend according to longitudinal investigation (Beiter et al., 2015; Mackenzie et al., 2011; Sax, 1997), and that the modern world becomes increasingly saturated with excessive stimulation (Rothbart and Posner, 2015), the pressures facing highly sensitive students are set to increase. South African students are additionally burdened with the current ripple effects of the #Feesmustfall movement (Langa, 2017), the strains of which are likely borne most noticeably on the shoulders of HSPs. Identifying highly sensitive students may be informative, not merely because they may find university more challenging (as suggested by these results), but also because they may be likely to respond better to intervention (Belsky and van IJzendoorn, 2015; Pluess and Boniwell, 2015). Even simple strategies may yield noticeable improvements, so long as they encourage HS students to construct habits and environments for themselves that lower the disadvantages of negative affect and high neural sensitivity, but accentuate the advantages of careful and thorough cognition. Some examples include, quieter, calmer study settings, focusing on uni- rather than multi-tasking (Carrier, Rosen, Cheever, and Lim, 2015) and mentally, physically and emotionally centering practices such as meditation and yoga (Acevedo et al., 2017). Connecting with other sensitive individuals (per-

haps through counsellor-led support groups) may help to improve perceived social support and diminish the unwanted strains of minority stress. Of course, some level of difficulty at university is desirable (Crede and Niehorster, 2012), since this forces students to expand and develop their capabilities, but this difficulty may require different strategies of approach for those with low threshold nervous systems, lest it become problematically overwhelming.

The results of this study should be viewed in light of several limitations. Firstly, this was an exploratory, observational, cross-sectional study based on convenience sampling and thus no causal relationships can be inferred, nor can our linear models be generalised for predictive purposes. The cross-sectional nature of the study design also fails to address the high temporal variance that university adjustment is likely to display. Secondly, the measure of parental care was possibly weak. A combination of two different, but related measures was used, that was necessarily scored based on a broadly defined "primary caregiver", rather than the traditional approach of independent scores for a mother and a father. In addition, the measures were self-report and based on retrospective recall of events, which is prone to both social desirability and recall biases (Tourangeau et al., 2009), possibly explaining the noticeably negatively skewed (more high quality parenting) scores. However, the PBI is one of the most consistently used measures of parenting (Wilhelm et al., 2005) and demonstrates robust psychometric properties (which extend to the MOPS) including long-term stability. That the participants in this study are not much older than the 16 years over which they had to recall their parental experience hopefully implies a high level of accuracy. Whether transforming the parental care variable via an ordered normal transformation, or entering it as a polynomial term, the modifying effect of care on SPS remained stably interpretable. Thirdly, by reducing the multidimensional process of university adjustment to simply "positive" and "negative" adjustment, there may have been an important loss of information and nuance. Fourthly, the measure of parental care only reflects a degree of personal socioeconomic status (SES). No acknowledgement of any form of household/financial SES was made, which is otherwise well known to influence adjustment (Bowman, 2010; Crede and Niehorster, 2012; Ostrove and Long, 2007). Fifthly, the length of the study survey (> 100 items) may have generated considerable fatigue amongst participants, undermining the accuracy and completeness of their responses. Finally, an automated selection algorithm was leveraged to inform the order of predictor entry into the overall regression model. This approach is generally not advised (Faraway, 2015), but seemed sufficient for an exploratory investigation and still yielded outcomes in line with other research. However, cross-validation of these results in an independent sample would be ideal (Cohen et al., 2003).

Future studies might consider some additional extensions to this work. For example, it may be of benefit to examine HSPs in traditionally more demanding undergraduate programs such as law or medicine (Pritchard et al., 2007), where they may not be as well represented as psychology classes. This study considers university adjustment, broadly defined, and pays no attention to, for example, educational or motivational theories, university persistence (Robbins et al., 2004) and academic performance (Poropat, 2009), which may be of interest. It may

also be interesting to consider pre-university personality data, including SPS, and compare outcomes after adjustment to university (Kurtz et al., 2012). Lastly, more investigation on potential modifier variables is needed, or otherwise third variables that can moderate the parental care x sensitivity interaction (e.g. household SES) (Poropat, 2009).

In conclusion, levels of SPS may be an important consideration amongst university students, as well as in personality research more broadly. Assuming that nervous system threshold is a primary determinant for secondary personality traits, HSPs appear capable of both high levels of neuroticism and conscientious-like behaviour, which have notably opposite influences on university adjustment. Clearly, HSPs struggle with the demands imposed by university life, but given their receptiveness to intervention (Pluess and Boniwell, 2015), highly sensitive students may be ideal targets for university support programs which can help accentuate their strengths while mitigating their weaknesses. This line of thought can be reasonably extrapolated to HSPs in other contexts (e.g. the workplace), and thus further research on SPS is well warranted.

Chapter 5

Study 4: Individual differences in neurosensitivity in the Birth to Twenty Plus cohort and their association with childhood behaviour at age 7

If a child is to keep alive his inborn sense of wonder, he needs the companionship of at least one adult who can share it, rediscovering with him the joy, excitement and mystery of the world we live in.
- Rachel Carson

5.1 Brief introduction

The above studies have exclusively focused on SPS, which is but one component of the larger framework of Environmental Sensitivity (section 1.5.3). Recall that other consistently supported, albeit more distal markers of high neurosensitivity include physiological reactivity, difficult temperament and the 5-HTTLPR (S allele, section 1.5.1.3.1) and *DRD4* (7 repeat allele, section 1.5.1.3.2) VNTRs, amongst others (sections 1.5.1, 1.5.2). Thus, sensitivity to the environment is detectable at different organismic "layers", starting from observable phenotypes and behaviour as the uppermost layer, followed by cognition and brain activity, physiological reactivity and finally genetic variation (Boyce, 2015).

Based on the argument that post-natal plasticity may be prenatally programmed (Pluess and Belsky, 2011; Section 1.5.2), in accordance with the Barker hypothesis (Barker, 1998; Barker and Osmond, 1986), birth weight and gestational age may also bear relevance to infant

sensitivity. Given its general indication of poor intra-uterine environment, low birth weight has been robustly linked to internalising behavioural problems and a wide range of health issues in adulthood (Boyce, 2015; Pettersson, Larsson, D'Onofrio, Almqvist, and Lichtenstein, 2019). For example, van Os et al. (2001) found higher behavioural problems in 10 year old children (using the Child Behaviour Checklist; Achenbach and Ruffle, 2000) that had low birthweight. In a study of 546 894 sibling pairs from Sweden, Pettersson et al. (2019) found a small but significant effect of reduced fetal growth on later risk for adult psychiatric disorder.

Although an evident risk factor for poorer outcomes, birth weight and gestational age have also been observed as potential markers of differential susceptibility (DS). Poehlmann and colleagues (Poehlmann et al., 2012; Poehlmann et al., 2011) found that pre-term, low birth weight infants had the most externalising behavioural problems at two years old when receiving angry and critical parenting but the least such behaviour when raised by more supportive parents. The authors postulate that pre-term, low birth weight children have more issues with emotional self-regulation and thus rely more heavily on their parents for aid. The quality of parenting they receive establishes a scenario for differential effects to emerge. However, Jaekel, Pluess, Belsky, and Wolke (2015) found only evidence for diathesis-stress reasoning when examining the academic performance of eight year old children. Children with low birth weight, born to mothers who displayed low levels of maternal sensitivity were academically poorer than normal birth weight children whose mothers were insensitive. Where maternal sensitivity was high, low birth weight children were roughly equivalent in academic performance to normal birth weight children. Low birth weight might only serve as a marker of differential susceptibility for selected phenotypic outcomes, although significantly more research is required.

Empirical support for plasticity markers has mostly been accrued through cross-sectional studies examining a particular marker in isolation. Far fewer studies have attempted to examine multiple markers within a single sample. Belsky and Beaver (2011) conducted the first DS study to examine multiple genetic loci simultaneously. In a nationally representative sample of American youths (n = 1586), the authors examined the effects of five known plasticity alleles on adolescent self-regulation. Plasticity alleles included the 10-repeat allele of *DAT1*, the A1 allele of *DRD2*, the 2- and 3-repeat alleles of *MAOA*, the 7R allele of *DRD4* and the short allele of 5-HTTLPR. A basic polygenic susceptibility score (PSS) was calculated by adding the number of plasticity alleles present per individual. Self-regulation was then regressed on PSS, a measure of parenting quality and an interaction term (PSS x parenting quality). Race was entered as a fixed effect. Results revealed a differential susceptibility effect for males (but not females). The more plasticity alleles male participants carried, the more likely they were to demonstrate high levels of self-regulation in the context of supportive parenting, but low levels of self-regulation in the context of unsupportive parenting. Chhangur et al. (2017) examined five genes pertinent to the dopaminergic pathway (*DRD2*, *DRD4*, *DAT1*, *MAOA* and *COMT*) in 4-8 year old children with moderate-to-high externalising behavioural issues, whose parents were then randomly assigned to an intervention or control group. Boys (but not girls) with a high PSS benefited substantively

more from the intervention, according to a parent-reported externalising behaviour measure, than those with a low PSS. These studies suggested that genetic variants may, through additive or other epistatic effects, cumulatively heighten individual plasticity.

Also lacking in the literature are longitudinal investigations of both SPS and DS. To date, there have been no studies that have examined the long-term stability of SPS, nor examinations of what childhood factors might predict adult levels of SPS (Greven et al., 2019). Regarding DS, Keers and Pluess (2017) examined sensitivity to psychological distress in the longitudinal National Child Development Study. Based on numerous factors, a single cumulative score for childhood environmental quality, and one for adult environmental quality, were used as predictors together with a PSS comprising the S allele of 5-HTTLPR and eight additional SNP alleles known to promote plasticity. The authors were able to identify a gene x environment x environment (GxExE) effect adhering to the differential susceptibility hypothesis. Specifically, children with high genetic plasticity were more prone to psychological distress as adults if their childhood environment had been poor, but demonstrated greater resilience to distress where their childhoods had been of high environmental quality. These results adhere to the idea of individual differences in sensory processing remaining fairly stable after childhood (i.e. developmental plasticity; section 1.2), however, further longitudinal explorations are needed.

In addition to limited multi-marker and longitudinal studies, few DS studies have been conducted using non-European ancestry participants, especially continental Africans. Where African individuals have been investigated, they have been mostly African-American (e.g. Beach et al., 2012). An ideal opportunity to address these shortfalls lies with the Birth to Twenty Plus (BTT+) cohort. The multidisciplinary BTT+ study is South Africa's largest longitudinal study, aimed at examining the developmental trajectories of a group of South African youths (mostly Black African), from birth to 20 years of age and beyond (Barbarin and Richter, 2001b; Richter, Norris, and De Wet, 2004). Cohort members were recruited by inviting participation from mothers who gave birth to singleton children in selected hospitals in the Soweto-Johannesburg metropolitan region, during a 7-week period from April 23 to June 8, 1990 (Barbarin and Richter, 2001b; Richter et al., 2004). To maximise retention, mothers needed to remain residents of the metropole until the child was at least 6 months of age. Of the 5449 recorded births during the enrolment period, 3273 met the study inclusion criteria (51.39% female infants; Barbarin and Richter, 2001b; Richter et al., 2004). Except for an under-representation of White individuals, this initial sample was approximately representative of the South African demographic at the time, with 78.5% of participants being Black African, 12% Coloured (mixed ancestry), 6% White and 3.5% Indian (Richter, Norris, Pettifor, Yach, and Cameron, 2007).

The aim of the BTT+ study has been to provide a comprehensive lifespan-overview of cohort member development (Barbarin and Richter, 2001b; Richter et al., 2004). Investigations began antenatally (e.g. recording the context and details of mothers' pregnancies) and from

birth onwards, follow-up data collection waves were conducted on a near-annual basis. The data captured during each wave changed to accord with the developmental progress of cohort members. For example, early collection waves focused on nutrition, growth and development, with focus slowly shifting to behaviour, cognitive ability, school performance, psychosocial adjustment, puberty, sexual experimentation and drug and alcohol use, *inter alia*, as members matured through primary and high school (Richter et al., 2007). The most recent collection wave (beginning 2018, the year in which members turned 28) has focused on cognitive performance and other variables pertinent to adult life.

Importantly, cohort members were born during a period of dramatic change to the South African sociopolitical landscape, which was a major motivating force behind the rationale of the BTT+ study (Barbarin and Richter, 2001b). By 1990, the year of Nelson Mandela's release from prison, the Apartheid regime was under tremendous pressure, with its once stringent frameworks for ethnic segregation rapidly collapsing. Rural Black Africans had begun to quickly populate previously White city spaces, largely through the establishment and expansion of unplanned townships like Soweto (Barbarin and Richter, 2001b; Richter et al., 2007). Such was the speed of this urbanisation that the potential effects (both positive and negative) on health and development for the next generation of children became an important consideration. Whilst these children would be in closer proximity to high quality health care and educational facilities, they would be raised in densely populated areas that struggled under the shifting weight of urban stressors, high disease burdens and unprecedented socio-cultural changes (Barbarin and Richter, 2001b; Richter et al., 2007). Consequently, BTT+ members have had highly heterogeneous upbringings, which has made for a particularly interesting research sample.

Unfortunately, conducting a longitudinal study in such an uncertain sociopolitical climate brought with it significant challenges that must be acknowledged prior to researching this cohort (Richter et al., 2007). In trying to maintain multidisciplinary value against an unpredictable background, no single investigator was charged with the overall management and resourcing of the BTT+ study (Richter et al., 2007). This meant that available funding, along with human and other resources (e.g. time) were constant concerns that had variable impact on the study throughout the years, often affecting data capture, comprehensiveness and cleaning. Maintaining contact with cohort members and their families, given their high mobility and their residence in townships that generally lacked street names, house numbers and telephones, was a particularly substantial challenge (Richter et al., 2004). Precious time and financial resources had to be invested in reconnecting with "lost" members, sometimes at the cost of suspending further data collection. As a result, attrition rate and participation per data collection wave fluctuated over the course of the study (Barbarin and Richter, 2001b; Richter et al., 2004). Nevertheless, over the first two decades, attrition was kept to a relatively low 30% (Richter et al., 2007).

Despite these important limitations, BTT+ is still a rich and comprehensive resource that includes both environmental and sensitivity-related variables on a robust sample size of partici-

pants. Records exist for member birth weight and gestational age, and infant temperament was briefly scored at six months and one year (Barbarin and Richter, 2001b; Richter et al., 2007). During adolescence, members provided blood samples for deoxyribonucleic acid (DNA) extraction and storage in lieu of genetic studies. A multitude of behavioural outcomes have been recorded during childhood and adolescence, especially internalising (e.g. depression, anxiety) and externalising (e.g. aggression, oppositional defiance) behaviours. These behaviours are of considerable research interest, especially during childhood, given their concerning prevalence (Bayer et al., 2011; Crijnen, Achenbach, and Verhulst, 1997) and the substantial economic costs they impose (Buchanan-Pascall, Gray, Gordon, and Melvin, 2018). Moreover, internalising and externalising behaviours are important predictors of academic performance, social adjustment and general mental health (Bayer, Hiscock, Ukoumunne, Price, and Wake, 2008; Margetts, 2005; Masten et al., 2005). Because such behaviours can perpetuate from one generation to the next (Bijleveld and Farrington, 2009), they are the target of extensive intervention efforts (Buchanan-Pascall et al., 2018; Hektner, August, Bloomquist, Lee, and Klimes-Dougan, 2014). These maladaptive behavioural outcomes are especially pertinent to investigate in low socioeconomic status (SES) neighbourhoods (Dearing, McCartney, and Taylor, 2006; Slopen, Fitzmaurice, Williams, and Gilman, 2010). Residents of such neighbourhoods either exhibit, or are exposed to, more aggression, violence and criminal behaviour, which establishes a high-stress environment (Åslund et al., 2013; Richter et al., 2018). Within this context, HPA activity is likely to be affected (section 1.5.1.3.1). Similarly, the 5-HTTLPR S allele has been found to interact with low SES to modify serotonergic activity in the brain (Åslund et al., 2013). As suggested above, these individual x environment effects likely begin *in utero* (Braithwaite et al., 2013), and may have more profound effects on individuals with high levels of SPS, which has also been recently recorded for BTT+ members. All considered, the BTT+ cohort provides a potentially informative context in which to examine differential susceptibility and diathesis stress effects (section 1.5.1).

The aim of this study was to explore both the main and interactive effects of available markers of Environmental Sensitivity on childhood behaviour amongst BTT+ cohort members. To supplement existing cohort data, as part of this doctoral study, the HSPS was administered to members during the most recent data collection wave. In addition, 5-HTTLPR and *DRD4* exon III VNTR genotypes were determined. In sum, five sensitivity-related predictors were examined, namely birth weight, temperament, SPS, 5-HTTLPR and *DRD4* genotypes. Other available predictors included sex, ethnicity, gestational age and maternal education. The main outcome variables were internalising, externalising and total psychology scores tallied from the South African Child Assessment Schedule, which caregivers completed when cohort members were seven years old. As this is a retrospective, observational and cross-sectional study, only a basic exploratory data analysis strategy was adopted involving two-step linear modelling. In an initial step, the main effects of sensitivity markers on behaviour were examined. Thereafter, a measure of household SES was included as part of an interaction term with the relevant sensitivity marker, given that SES has been noted to produce the most robustly consistent effects on

mental and physical health (Way and Taylor, 2010b). Interaction models were then plotted and examined for diathesis-stress and/or differential susceptibility effects (section 1.7, Figure 1.8).

5.2 Methods

5.2.1 Study participants

Participants for this study were all Black African members of the BTT+ cohort. Historical data on member birth weight, gestational age, maternal education, socioeconomic status, temperament (6-12 months) and behaviour ratings at age 7 were obtained with permission from the cohort's principal investigators. As part of this doctoral study, genotypes were determined at two loci (5-HTTLPR and *DRD4*), and the HSPS was included as a part of the 2018/2019 data collection wave under ethical clearance M160232 (see Appendix A).

For each of the available variables, the sample size varies for reasons outlined in the brief introduction. As variables were merged to address different research questions, sample size continued to vary. Figure 5.1 summarises the participants available for different combinations of variables.

5.2.2 Instrumentation

All study instruments are presented in Appendix C.

5.2.2.1 The HSPS

The minimally modified HSPS, derived from Study 1 and described previously, was the primary instrument for this study (Appendix B).

5.2.2.2 The South African Child Assessment Schedule

The South African Child Assessment Schedule (SACAS) is a structured, caregiver-report questionnaire aimed at assessing developmental milestones in the maturation and social demands of children aged 5-10 years (Barbarin and Richter, 2001a). Specifically, the instrument was developed to capture information on four key issues:

1. The child's overall adjustment to the demands of school

2. The child's ability to communicate and express feelings and thoughts

3. The child's relationship with peers

4. The child's mental health and general social competence.

Items were developed by scaffolding upon several previously validated scales, including the Achenbach-Connors-Quay (ACQ; Achenbach, Howell, Quay, and Conners, 1991), the Achen-

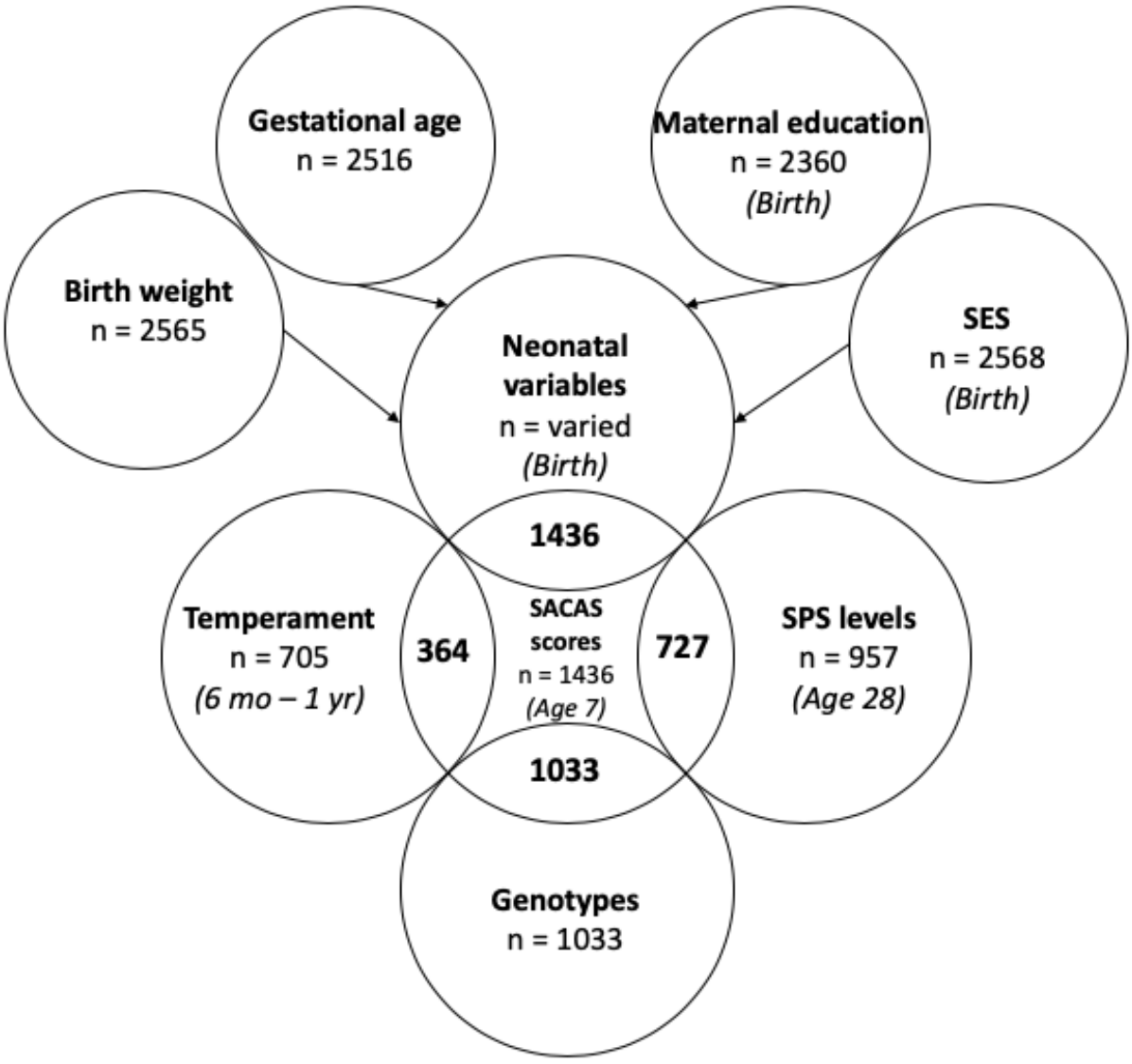


Figure 5.1: **An overview of the available Black African BTT+ sample data.** At inception, the BTT+ cohort had 3273 enrolments, 78.5% of which were Black African individuals who were specifically investigated in this study. The most complete data records were for variables captured at birth ("neonatal variables"), including birth weight, gestational age, maternal education and household socioeconomic status (SES). As part of this study, genotypes at two loci and SPS levels (age 28) were assessed. Historical data on infant temperament (6-12 months) was also available for a small subset of cohort members. These individual datasets were overlapped with caregiver rated internalising, externalising and total psychology scores (age 7) derived from the South African Child Assessment Schedule (SACAS). The bolded numbers between overlapping circles represent final sample sizes available for linear modelling.

bach Child Behaviour Checklist (Achenbach and Ruffle, 2000), the Problem Behaviour Index (Peterson and Zill, 1986), the Health Resources Inventory (Gesten, 1976), and the National Center for Education Statistics' Kindergarten Teacher Survey on Student Readiness (National Center for Education Statistics, 1993). Items drawn from these various scales were supplemented with items that tapped the diagnostic criteria for mental disorders based on the international statistical classification of diseases and related health problems (ICD-10; for the latest version, see World Health Organisation, 2016). All items were then commented on by a panel of South African mothers, who offered suggestions on improved wording and additional items they felt were necessary to capture deviant child behaviour. The final item set comprised 86 items, scored on a three-point scale, from 0 to 2 (not all items are scored in the same direction; Barbarin and Richter, 2001a; Barbarin and Richter, 2001b)[1].

Psychometrically, the SACAS has demonstrated acceptable levels of reliability (α = .6-.8, depending on how the instrument is sub-scaled) and sufficient validity (Barbarin and Richter, 2001a; Barbarin and Richter, 1999; Verkuijl et al., 2014). Validity was supported through a principal components factor analysis, along with high levels of convergence with other well validated and widely administrated measures of child health (Barbarin and Richter, 2001a). Furthermore, scores were higher for a clinical sample in comparison to a non-clinical sample (Barbarin and Richter, 2001a; Verkuijl et al., 2014).

Due to the wealth of items, the SACAS can be sub-scaled in a variety of ways. Regarding behaviour at the broadest level, overall scores for internalising behavioural problems (32 items) and externalising behavioural problems (34 items) can be tallied, where higher scores indicate more problematic behaviour (Barbarin and Richter, 2001a; Verkuijl et al., 2014). Within these sub-scales, are several smaller, nested sub-scales, for example Anxiety-Depression (12 items), Self-Regulation (9 items), Aggression (11 items) and Opposition-Defiance (4 items). There are three further, mostly non-nested subscales that examine Attention-Deficit behaviour (10 items), Thought Problems (7 items) and Social Difficulties (12 items). Tallying all these behavioural items together provides a general psychological adjustment score (total psychology; 86 items), with higher scores reflecting worse psychological adjustment. Due to their higher reliability estimates ($\alpha > .8$), the internalising, externalising and total psychological adjustment scores were used in this research.

5.2.2.3 Carey Infant Temperament Questionnaire

The Carey Infant Temperament Questionnaire (CITQ, Carey, 1970; Carey and McDevitt, 1978) was developed to serve as a simple, convenient tool for assessing infant temperament characteristics, between 4-8 months old, for both clinical and research purposes. The questionnaire originally comprised 70 statements, each followed by three choices. This was later revised

[1]Given that the SACAS was administered in 1997, prior to the present study, it is difficult to anticipate what influence the large number of SACAS items may have had on respondent fatigue.

(Carey and McDevitt, 1978) to 90 items with six options each, ranging from "almost always" to "almost never". Mothers complete the questionnaire by indicating to what extent each item is an accurate reflection of their child's behaviour. Scores are tallied in the nine categories of temperament outlined by Thomas and Chess (1977). The instrument has achieved good test-retest (.84 for a two-week interval) and internal consistency (.83) reliability (Carey and McDevitt, 1978).

For numerous reasons, only ten of the 90 CITQ items were selected for use in the BTT+ study. Many items posed translation difficulties, or were unsuitable for the local South African context (L. Richter, personal communication; Barbarin and Richter, 2001b; Richter, Dev Griesel, and Barbarin, 2000). Moreover, the questionnaire had to be necessarily abbreviated to afford time for the range of other pertinent variables that needed recording (L. Richter, personal communication; Barbarin and Richter, 2001b; Richter et al., 2000). The ten selected items were administered to primary caregivers during the 6 month data collection wave. Only eight of these ten items were carried forward to the 12 month data collection wave. To maximise the available sample size for this research, cohort members were included if they had at least one set of caregiver responses for the eight temperament items, whether at 6 months or 12 months. For cohort members that had item responses at both ages, the 6 month responses were given preference given that the number of observations at 12 months was notably low. All items were scored on a three-point scale (very like, not really and very unlike/different).

5.2.2.4 Maternal education

Maternal education was recorded on a six-point scale based on the highest grade passed at school. A score of 1 reflected no formal schooling whatsoever, whilst a score of 6 indicated the mother had some level of post-high school education. This simple metric was used solely as an indicator of education status and could also be framed as a measure of *personal* socioeconomic status, as opposed to *household* SES described in the following section. As a reflection of status, the metric makes no inferences or assumptions about actual intelligence or cognitive ability.

5.2.2.5 Socioeconomic status

Over a two year data collection period from infant birth to two years of age, mothers were asked to provide information on their household amenities and appliances. Specifically, mothers indicated if their household had electricity, a landline telephone, a fridge, a microwave, a washing machine, a television, a video recorder and/or a car (Barbarin and Khomo, 1997; Feeley, Musenge, Pettifor, and Norris, 2013). These household durables were scored in a binary manner (durable present = 1; durable absent = 0) and tallied together to create a basic metric for socioeconomic status. Note that total scores were supplied to the researcher in a z-standardised format, prohibiting any detailed comparison of household durables between cohort members.

5.2.3 Genotyping

5.2.3.1 DNA extraction and quantification

BTT+ cohort members were invited to provide blood samples for DNA extraction in their early adolescence. DNA from these samples was previously extracted using the salting out method (Miller, Dykes, and Polesky, 1988). Extracted DNA has since been stored in Tris-EDTA (TE) buffer at 4 °C.

At the outset of the study, DNA stock concentrations were quantified using the Nanodrop Spectrophotometer ND-1000 (see Appendix D for a list of manufacturer details). A standardised $50\,\mathrm{ng/\mu L}$ aliquot for each sample was prepared using TE buffer as the diluent.

5.2.3.2 PCR amplification

Both the 5-HTTLPR and the *DRD4* exon III VNTR loci have high guanine-cytosine (GC) content (Chang et al., 1996) which can limit traditional polymerase chain reaction (PCR) amplification. To improve amplification, a slow-down PCR procedure (Frey, Bachmann, Peters, and Siffert, 2008) was leveraged using Accuprime GC-rich polymerase (Invitrogen). PCR reaction mixtures contained 1 unit of *Taq* polymerase, primers (forward and reverse) at 0.2 μM, 1X Accuprime GC-rich buffer A (containing thermostable AccuPrime proteins, deoxyribonucleotide triphosphates [dNTPs] and $MgSO_4$), 100 μg DNA template and double distilled water up to a final reaction volume of $25\,\mu\mathrm{L}$. Cycling conditions are displayed in Table 5.1. The ramp speeds for heating and cooling were set at $2.5\,^{\circ}\mathrm{C/s}$ and $1.5\,^{\circ}\mathrm{C/s}$ respectively. All PCRs were conducted on BioRad T100 thermocycler instruments.

Primer sequences for both 5-HTTLPR (Heils et al., 1996) and *DRD4* (Lichter et al., 1993) amplification were obtained from previously published sources. For 5-HTTLPR, the amplicon sizes were 469 bp (14-repeat short allele) and 512 bp (16-repeat long allele). For *DRD4*, amplicon sizes ranged from 379 bp (2-repeat allele) to 811 bp (11-repeat allele) in 48 bp increments.

5.2.3.3 Electrophoresis and genotype calling

All amplicons were resolved via gel electrophoresis on a 2% agarose gel run at $5\,\mathrm{V/cm}$ in 1X Tris-Boric acid-Ethylenediaminetetraacetic acid (TBE). Amplicons were sized using a 50 bp ladder. Gels were viewed using the OmegaFluor gel documentation system and software (Figure 5.2).

Genotypes were called independently by two researchers. In the case of discrepant or uncertain calls, amplicons were resolved again alongside samples of similar genotype to improve the

Table 5.1: PCR cycling conditions for the amplifcation of both 5-HTTLPR and *DRD4* exon III VNTRs

Step	Temperature	Time (minutes)	Cycles
Initial denaturation	95°C	5:00	1
Denaturation	95°C	0:30	
Annealing	70°C (-0.4°C per cycle)	0:30	48
Extension	72°C	0:40	
Denaturation	95°C	0:30	
Annealing	53°C	0:30	15
Extension	72°C	0:40	
Final Extension	72°C	5:00	1

accuracy of detecting small (one unit) repeat size differences, especially in the case of *DRD4*. Where genotypes could still not be called with confidence, samples were reamplified until either a call could be made, or the sample was removed from the study due to repeated lack of amplification.

5.2.4 Procedure

As part of a larger battery of tests and questionnaires assessing the lives and cognitive performance of BTT+ cohort members at ages 28-29 (2018-2019), the HSPS was administered via one-on-one interviews at the Developmental Pathways to Health Research Unit at Chris Hani Baragwanath Academic Hospital, starting from June 2018. Interviewers briefly explained the instrument and its response scale and then proceeded to read out each item individually, giving the interviewee a chance to respond on the 7-point Likert scale. Interviewers captured responses using electronic tablet devices and data were stored on an electronic database.

Each individual dataset (HSPS, SACAS, temperament, and neonatal variables) was independently cleaned and analysed prior to merging in different combinations. Individuals were

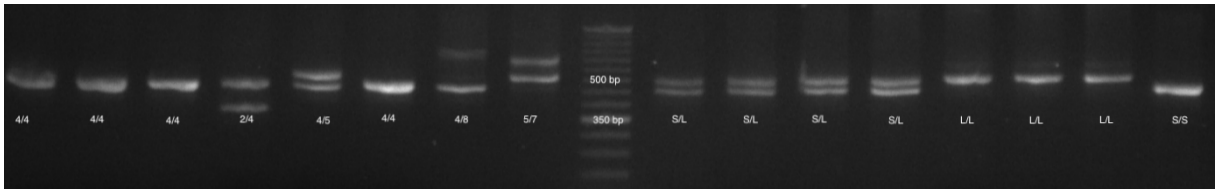


Figure 5.2: **An example gel with genotype calls.** Genotypes for eight BTT+ individuals, at both the 5-HTTLPR and *DRD4* loci, are shown. To the left of the 50 bp molecular weight marker, *DRD4* genotype results are displayed. Possible alleles ranged in repeat number from 2 to 11 repeats (distinguished in size by 48 bp increments), although 2-, 4- and 7-repeat alleles were most commonly observed. To the right of the ladder, 5-HTTLPR results are visible. Long alleles (512 bp) were more frequent than short alleles (469 bp).

removed only in the case of excessive missingness of item responses ($> 20\%$). Any remaining missing values were not imputed to avoid potential bias, given that the majority of predictor and outcome variables already had skewed distributions. Most of the continuous variables (birth weight, gestational age, HSPS, temperament, internalising, externalising, total psychology and z-standardised SES scores) had outlying observations, but these were retained for descriptive statistics purposes. Their potential influence was examined in more detail when considering case-wise diagnostics for the subsequent regression models.

Descriptive statistics were prepared for all available participants, regardless of ethnicity. However, only individuals of Black African ancestry (maximum n = 2568/3273) were retained for linear modelling purposes for three reasons. Firstly, the sample size per ethnicity was notably unbalanced. Secondly, as a possible consequence of the first issue, heterogeneity of variance was detected between ethnicities for select variables, which violates the assumptions of many statistical procedures. Lastly, because some of the linear models include genetic markers, focusing on a single ethnicity was necessary to avoid issues of population stratification (Cardon and Palmer, 2003). Previous analysis of the genotype-derived principal components for 94 Black African members of the BTT+ study suggested the cohort members were of adequately similar ancestry (May et al., 2013). Descriptive statistics on members of other ethnicities, where available, are nevertheless provided to better understand the position of Black African participants in relation to other cohort members.

When merging datasets ahead of inferential statistics, individuals were only retained if they had measurements available for the pertinent variables in each merged dataset. The degree of overlap between separate datasets varied considerably (Figure 5.1), thus the examination of different combinations of variables involved markedly different subsets of individuals. To compensate for this issue, an exploratory analysis strategy was adopted. For each sensitivity marker under investigation, an exhaustive selection algorithm (using the *leaps* package; version 3.0; Lumley, 2017) was used to determine the best combination of predictors per outcome variable. As noted previously (section 4.3.3), exhaustive selection combines the benefits of backward elimination and forward selection (Faraway, 2015), but use of such automated predictor selection methods is only encouraged in exploratory settings, where sample size is at least 40 times greater than the total number of predictors (Cohen et al., 2003). A regression model was selected based on the best compromise between four fit statistics, namely the BIC, adjusted R^2, RSS and Mallow's C_p. Case-wise diagnostics were then examined and highly influential or outlying cases were removed to generate a final main effects model. To this final model, SES was entered as part of an interaction term with the sensitivity-related variable to explore potential interactive effects. Continuous variables were centred to avoid issues of multicollinearity (Cohen et al., 2003).

To maximise the contrast between fixed (non-sensitive) and plastic (sensitive) individuals and their response to SES, sensitivity markers were dichotomised in all situations that improved

model interpretation. Although dichotomisation of a continuous variable can result in the loss of valuable information, it has been used frequently in differential susceptibility research to highlight characteristic differences between individuals at the extreme ends of the fixed-plastic continuum (e.g. Pluess and Boniwell, 2015). The cut-off value for dichotomising participants was, as far as possible, informed by theory and/or suggestions from the literature.

Lastly, since no studies (to date) have examined the stability and possible early prediction of future SPS levels (Greven et al., 2019), SPS was investigated as an outcome variable, rather than a predictor of behaviour, by regressing the trait onto other available variables. The frequency of co-occurence of different sensitivity markers was also examined via contingency table testing using the chi-square test. All analyses were conducted using R (version 3.5.1) and RStudio (1.1.456). Plots were prepared via the *ggplot* (version 3.0.0, Wickham, 2016) and *sjPlot* (version 2.6.1; Lüdecke, 2018) packages. Other packages employed included *bestNormalize* (version 3.4.1, Peterson, 2017) and *car* (version 3.0-2, Fox and Weisberg, 2011).

5.3 Results

A total of 12 variables were available for this investigation of BTT+ cohort members. Below, results and descriptive statistics for each variable, in turn, are provided. Thereafter, the possible main and interactive effects of predictor variables on behavioural outcomes (internalising, externalising and total psychology scores) are reported. Lastly, the potential predictors of high sensory processing sensitivity are examined, along with correlations between environmental sensitivity markers.

5.3.1 Neonatal variables

These variables, namely birth weight, gestational age, sex, ethnicity, household SES and maternal education were recorded on almost all cohort members and are summarised in Table 5.2. None of the continuous variables were normally distributed, in total or by sex, (Shapiro-Wilk test $p < .05$), but no transformation procedure was predicted to substantively improve variable distribution (using the *bestNormalize* package). Between sexes, there was no difference in variance. The average cohort member birthweight was 3.07 kg ($\pm$ .51), with males weighing significantly more than females (W = 1508500, $p < .001$), although of small effect size (r = .11). No other sex differences were observed. Differences by ethnicity were prominent for maternal education and household SES which, according to Levene's test, did not display equal variances across ethnic categories. White mothers had the highest education status (with a median value of 6 on the six-point scale, meaning most mothers had at least some tertiary education) and SES; Black African mothers had the lowest (with a median of 4 for maternal education, meaning that

most mothers had education up to Grade 8-10). Black African infants also had significantly reduced gestational age (compared to all ethnicities) and were significantly lighter (compared to White infants; Bonferroni-adjusted $p < .01$).

When dichotomising birth weight, cohort members were separated into "low" and "normal" categories. Medically, low birth weight (LBW) is defined by a weight of 2.5 kg and lower. LBW children (for the whole cohort: n = 386/3267; 11.82%. For Black Africans: n = 293/2565; 11.42%) had significantly shorter gestational periods regardless of ethnicity (W = 483480, $p < .001$, r = .30), but otherwise displayed no significant differences in levels of maternal education nor household SES when compared to normal birth weight (NBW) children.

Table 5.2: Demographic, neonatal and socioeconomic variables for the BTT+ study

	Birth weight (kg)	Gestational Age (weeks)	Maternal Education	Household SES
Cohort (n = 3273)	3.07 ± .51	38.14 ± 1.92	4.27 ± 1.08	0.00 ± 1.00
By sex				
Males (n = 1591)	3.12 ± .52**	38.16 ± 1.89	4.27 ± 1.08	-0.03 ± 1.01
Females (n = 1682)	3.02 ± .50	38.13 ± 1.94	4.27 ± 1.08	0.02 ± .98
By ethnicity[a]				
Black African (n = 2568)	3.08 ± .50**	37.94 ± 1.83	4.17 ± 1.08	-0.09 ± 1.00
White (n = 207)	3.20 ± .55***	39.04 ± 1.67***	5.39 ± 0.74***	0.60 ± 0.64***
Indian (n = 115)	2.91 ± .48	38.82 ± 1.72***	4.96 ± 1.02***	0.54 ± 0.78***
Mixed ancestry (n = 383)	3.01 ± .54*	38.92 ± 2.27***	4.30 ± 0.86	0.11 ± 0.90
Missing entries	6	102	341	0

[a] Bonferoni adjusted significance is indicated for values that are significantly different to the lowest value per category. *** = $p < .001$; ** = $p < .01$; * = $p < .05$

To pre-empt issues of collinearity in linear modelling, the pairwise relationship between variables was examined amongst Black African members (Figure 5.3). Birth weight and gestational age were moderately correlated, as were maternal education and SES. There was a small positive correlation between birth weight/gestational age and maternal education. However, none of the correlations were strong enough to suggest significant issues of collinearity. Moreover, the combined use of these predictors in subsequent linear models never resulted in variance inflation factors (VIFs) larger than 1 (A VIF larger than 5 is considered problematic) nor tolerance statistics (1/VIF) less than .10 (Cohen et al., 2003).

5.3.2 The SACAS

None of the three behaviour subscales were normally distributed, whether considered for all participants or per sex, however, there was no evidence to suggest that transformation procedures would have beneficially improved score distributions. Variance between sexes was homogeneous. Regarding score differences between sexes, internalising scores were only marginally higher in girls (p = .10), but both externalising behaviour (W = 460490, $p < .001$) and total psychology scores (W = 438020, p = .03) were significantly higher in boys at the 5% level.

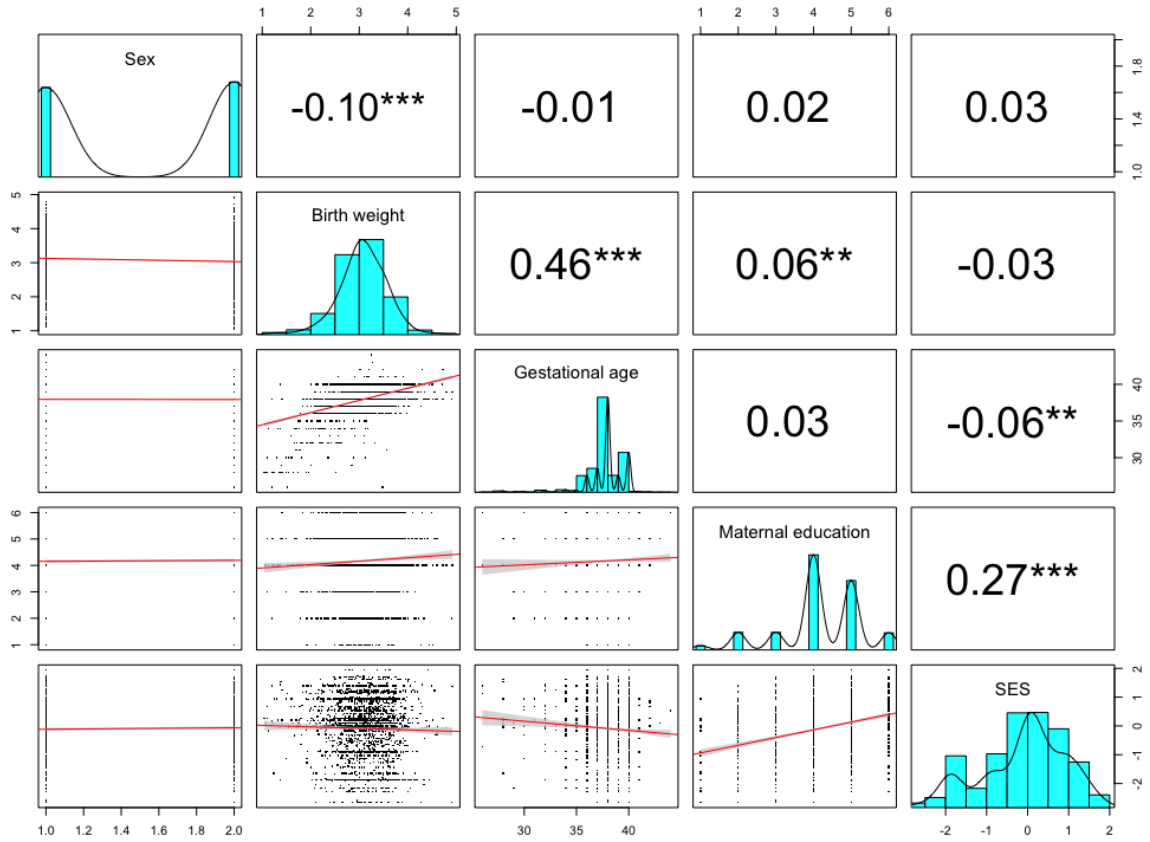


Figure 5.3: **A scatterplot matrix of demographic, neonatal and socioeconomic variables in Black African members of the Birth to Twenty Plus cohort.** Along the diagonal, histograms and density curves are plotted for each variable. Pearson's correlations are shown above the diagonal with bivariate scatter plots and trend lines shown below. Modest correlations were detected between sex and birth weight; birth weight and gestational age and maternal education and SES. Small correlations were noted between birth weight and maternal education, and between gestational age and SES. Since no correlation value exceed .5, there was little evidence to suggest that variables would be colinear (Cohen, Cohen, West, and Aiken, 2003). $***$ = p $<$ .001, $**$ = p $<$ .01.

However, for all comparisons, the effect size was minimal (r = .03 - .09). Between ethnicities, there was notable heterogeneity of variance, and Kruskal-Wallis testing (with post-hoc Bonferroni correction) confirmed significant ethnic differences between average item scores across all three behaviours. White children had the lowest scores, with Black African children scoring significantly higher than all other ethnicities.

Internal consistency reliability estimates (α) for the three subscales were moderate (internalising = .75, externalising = .82 and total psychology = .86, corrected for item overlap). Average item correlations were fairly low, in keeping with the broad nature of each scale (.09, .11 and .07 for internalising, externalising and total psychology respectively).

Table 5.3: Average item scores for the SACAS subscales

	Internalising	Externalising	Total psychology
All respondents (n = 1822)	0.46 ± .21	0.64 ± .28	0.57 ± .18
By sex			
Males (n = 863)	0.45 ± .20	0.67 ± .29***	0.58 ± .18*
Females (n = 959)	0.47 ± .21	0.61 ± .59	0.56 ± .18
By ethnicity[a]			
Black African (n = 1436)	0.46 ± .21**	0.66 ± .29***	0.58 ± .18***
White (n = 80)	0.39 ± .19	0.44 ± .23	0.44 ± .15
Mixed ancestry (n = 244)	0.47 ± .18**	0.60 ± .27***	0.56 ± .18***
Indian (n = 62)	0.50 ± .18**	0.55 ± .22***	0.54 ± .16***

[a] Bonferoni adjusted significance is indicated for values that are significantly different to the lowest average item score per category (internalising, externalising, total psychology). *** = $p < .001$; ** = $p < .01$; * = $p < .05$

5.3.3 Genotyping

Genotypic information was successfully determined for 1238 individuals out of a possible 1300 (95.23% success rate). Of these, 1033 were of Black African ancestry and were exclusively used in genetic analyses to avoid issues of population stratification[2]. However, nine individuals only had 5-HTTLPR genotypes, whereas one individual only had a *DRD4* genotype. Allele frequencies were similar to other published reports on African populations (Table 5.4) and in keeping with global distribution patterns for the S allele (Section 1.5.1.3.1, Figure 1.6). Hardy-Weinberg equilibrium was checked using GENEPOP (Raymond and Rousset, 1995; Rousset, 2008). Briefly, the Hardy-Weinberg law suggests (after several preliminary assumptions) that genotypic and allelic frequencies for an indefinitely large population should remain relatively stable (i.e. in equilibrium) from one generation to the next (Mayo, 2008). Where observed allele frequencies are not in line with those estimated through the Hardy-Weinberg law, two explanations exist. Either the observed locus and its various alleles are undergoing frequency shifts as a result of evolutionary forces (e.g. migration, non-random mating, population bottlenecks), or, more concerningly, there has been an error in determining or recording allele frequencies (Mayo, 2008). Laboratory-determined allele frequencies are thus checked for Hardy-Weinberg equilibrium as a safeguard against this latter possibility. In this study, genotypes for 5-HTTLPR were in equilibrium, but the same was not true for *DRD4*.

[2]Allele frequencies differ widely between populations, both for evolutionary (e.g. bottlenecks, assortative mating, migration) and stochastic (e.g. genetic drift) reasons. When attempting to associate a genotype with a phenotype, it is imperative to recruit study participants who are all of the same ethnolinguistic classification and from the same geographical area, so that any detectable allele frequency differences are relevant to the phenotype under study. A failure to heed this strategy might lead to the false conclusion that allele frequency differences that explain population ancestry are somehow implicated in differences in the phenotype of interest. In other words, when participants in a study can be stratified into groups that have allele frequency differences attributable to simple background population diversity, rather than for any meaningful reason that relates to the measured phenotype, a study is said to have population stratification (Cardon and Palmer, 2003)

Table 5.4: Birth to Twenty Plus participant allele frequencies, compared to other Black South African samples

	Frequency (%)		
5-HTTLPR	Present study n = 1237	Esau et al., 2008 n = 68	Morgan et al., 2017 n = 220
14	21.58	16.18	23.64
16	78.41	83.82	76.36
DRD4	Present study n = 1229	Chang et al., 1996 n = 80	Malan, 2014 n = 49
2	5.21	5.00	3.10
3	1.18	0.00	0.00
4	65.58	61.00	67.30
5	5.41	4.00	3.10
6	0.98	0.00	2.00
7	17.33	19.00	17.40
8	3.95	11.00	6.10
10	0.37	0.00	1.00

5.3.4 Temperament

A total of 705 cohort members had available temperament scores for between 6-12 months old. With a score range of 8-23, the average temperament score was 13.94 ($\pm$ 2.48), corresponding to an average item score of 1.74 ($\pm$ .31). Scores were not normally distributed, but showed no significant differences between sexes (W = 65806, p = .16). Variance in temperament scores between ethnicities was homogeneous, but Black African infants (n = 562) had significantly higher scores than other ethnicities following Kruskal-Wallis testing with post-hoc Bonferroni correction.

Reliability estimates were poor, given that the selection of items (eight of a possible 90) was based on broadly assessing multiple aspects of temperament, rather than selecting homogeneous items assessing one underlying factor. Cronbach's α for the scale was .38 and the average item correlation just .07.

When dichotomising temperament scores, participants in the 80th percentile and above were regarded as having a difficult temperament, in keeping with the same percentile cutoff used for SPS (see below, section 5.3.5.1). Wilcoxon rank sum testing showed no significant differences between difficult and non-difficult infants (whether amongst all infants or Black African infants only) in terms of birth weight, gestational age, maternal education or SES.

5.3.5 The HSPS

5.3.5.1 Descriptive statistics

By March 2019, 1081 BTT+ cohort members had completed the HSPS. The scale performed reliably (Cronbach's α = .85), in line with studies in previous chapters. The average item correlation was .18 and the average item score (out of 7) was 3.92 ($\pm$ .85), which was similar to a United States community score (3.96 $\pm$ .71; Aron and Aron, 2013). Scores were normally distributed for females (W = .996, p = .26) but not for males (W = .990, p = .003), nor for the overall sample (W = .996, p = .007). The lack of normality was attributable to a small number of male individuals who had scored very low on the instrument (average item score $<$ 1.85). Scores differed significantly between sexes (W = 108830, p $<$ .001, effect size r = .22), with males scoring lower than females. Black African individuals accounted for the vast majority of the sample (88.53%, n = 957/1081) which prohibited meaningful inter-ethnic comparisons.

As per the previous student study (Study 3), participants were dichotomised into highly sensitive and non-highly sensitive persons. For this study, participants in the 80th percentile and above (an HPS score $\geq$ 124) were regarded as highly sensitive. A more stringent cut-off was used on the assumption that the proportion of HSPs would be lower in the more general BTT+ sample compared to psychology students. Amongst Black African individuals (n = 957), highly sensitive persons (n = 213) had significantly lower birth weight (W = 86755, p = .03) than non-sensitive individuals. No other differences were detected.

Roughly one fifth of participants (240/1081) restricted the overwhelming majority of their item responses to just 1, 4, and 7 on the 7-point scale. Coincidentally, these are the three scale points that are descriptively labelled (1 = not at all, 4 = moderately, 7 = extremely) as per the

Table 5.5: Average item scores for temperament

	Temperament
All respondents (n = 705)	1.74 $\pm$ .31
By sex	
Males (n = 341)	1.76 $\pm$ .30
Females (n = 364)	1.73 $\pm$ .32
By ethnicity[a]	
Black African (n = 562)	1.79 $\pm$ .28***
Caucasian (n = 14)	1.46 $\pm$ .27
Mixed ancestry (n = 107)	1.58 $\pm$ .34
Indian (n = 22)	1.51 $\pm$ .35

[a] Bonferroni adjusted signicance is indicated for values that are significantly different to the lowest average item score. *** = p $<$ .001

Table 5.6: Average item scores for the HSPS scale

	HSPS
All respondents (n = 1081)	3.92 ± .85
By sex	
Males (n = 502)	3.71 ± .83
Females (n = 579)	4.10 ± .83
By ethnicity	
Black African (n = 957)	3.92 ± .85
Caucasian (n = 1)	4.93 ± NA
Mixed ancestry (n = 3)	3.86 ± .91
Indian (n = 22)	4.12 ± .79

original HSPS (Aron and Aron, 1997). There are two speculated, non-mutually exclusive explanations for this behaviour: 1) cohort members were experiencing high degrees of test fatigue given the battery of other assessments they were expected to complete and/or 2) participants may have found it easier to work within a 3-point scoring system, especially if there was any sense of anxiety about answering personal questions posed in a language that was not their default. To investigate if these responses were a potential source of bias, their internal consistency reliability was examined separately and found to be adequately high (α = .75). For the purposes of CFA, these individuals and their responses were retained in order to maximise sample size. However, in order to avoid the artefactual identification of these individuals as a latent class, all item responses were collapsed to a 3-point scale for the latent class analysis (original item responses were coded as follows: 1-2 = 1; 3-5 = 2 and 6-7 = 3).

5.3.5.2 Psychometric results

To validate the previous psychometric findings amongst student participants in Study 2, confirmatory factor analysis using the five factor model and latent class analysis for one to four classes were conducted (with 30 repeats). Results are displayed in Tables 5.7 and 5.8, with student results reprinted for ease of reference. The five factor solution continued to demonstrate stable fit statistics, although it was more closely challenged by the bifactor model which had better χ^2 $/df$ and RMSEA values.

Results for latent class analysis revealed an identical pattern to student results from Study 2, despite the response scale being collapsed to just three points. The BIC and entropy criteria favoured a three-class solution, which was more interpretable than a four-class solution (for the same reasons offered in Study 3). Cut-off average item scores were calculated from the intersection points of the different distributions which are compared, alongside the student results, in Figure 5.4. Cut-off scores were notably lower in the BTT+ cohort in agreement with the lower average item score compared to students. Regarding the sample composition, 29.79%

were classed as dandelions, 35.33% tulips and 34.88% orchids. Note that these latent classes could have also served as useful descriptive categories for HSPS respondents in subsequent regression modelling, instead of the aforementioned dichotomisation strategy. However, the dichotomisation strategy was given preference since the latent classes overlap considerably in terms of average item scores (Figure 5.4) and because dichotomisation is a recommended strategy (Aron and Aron, 2013) implemented elsewhere in the literature (e.g. Pluess and Boniwell, 2015).

Table 5.7: Fit comparison for different HSPS factor solutions

Model	Reference	χ^2	df	χ^2/df	p value	SRMR	RMSEA	TLI	AIC	BIC[a]
Students										
One factor	Aron & Aron, 1997	1908.54	324	5.89	$< .001$	.070	.081	.644	74786	75161
Two factor	Evans & Rothbart, 2008	1428.51	274	5.21	$< .001$	.076	.073	.722	68908	69260
Three factor	Smolewska et al., 2006	1138.35	227	5.02	$< .001$	.081	.073	.703	64219	64551
Four factor	Gulbin & Sumer, 2017	1282.47	293	4.38	$< .001$	.054	.062	.767	74009	74490
Bifactor	Lionetti et al., 2018	1085.23	301	3.61	$< .001$	.054	.062	.810	74009	74490
Five factor	Study 2	454.68	160	**2.84**	$< .001$	**.047**	**.050**	**.909**	**53977**	**54300**
Birth to Twenty Plus										
One factor		1704.54	324	5.26	$< .001$	.059	.063	.721	115404	115808
Two factor		1328.70	274	4.85	$< .001$	.056	.060	.772	106720	107099
Three factor		1104.04	227	4.86	$< .001$	.061	.060	.759	99025	99384
Four factor		1161.67	293	3.97	$< .001$	.056	.052	.817	110486	110905
Bifactor		910.52	301	**3.03**	$< .001$	.044	**.043**	.867	114656	115174
Five factor	Study 4	536.86	160	3.36	$< .001$	**.041**	.047	**.894**	**84691**	**85040**

[a] SRMR = Standardised Root Mean square Residual; RMSEA = Root Mean Square Error of Approximation; TLI = Tucker-Lewis Index; AIC = Akaike Information Criterion; BIC = Bayesian Information Criterion
Values in bold represent the best fit, per fit statistic.

Table 5.8: Latent class analysis results

Model	residual df	log-likelihood	likelihood ratio	AIC	BIC	Entropy[a]
Students						
One class	588	-36301.56	57444.19	72927.12	73675.57	-
Two class	425	-34961.80	55000.32	70573.59	720750.12	.892
Three class	262	-34310.62	53740.04	69597.23	**71851.83**	**.904**
Four class	99	**-33978.18**	**53132.32**	**69258.37**	72266.04	.900
Birth to Twenty Plus						
One class	505	-17560.68	26313.58	35445.35	36174.8	-
Two class	342	-16718.21	24637.60	34086.42	35549.82	.853
Three class	179	-16061.77	23344.06	33099.54	**35296.91**	**.870**
Four class	16	**-15890.93**	**23004.55**	**33083.85**	36015.17	.862

[a] df = degrees of freedom; AIC = Akaike Information Criterion; BIC = Bayesian Information Criterion.
Values representing the best fit, per fit statistic, are shown in bold. Lower (closer to zero) values suggest better model fits for all criteria except entropy, for which higher values are preferred.

5.3.6 Linear modelling

5.3.6.1 Neonatal variables as predictors of childhood behaviour

5.3.6.1.1 Main effects

Analysis of the potential predictors of childhood behaviour began with neonatal variables. Fit statistics were maximised based on the inclusion of sex, birth weight and maternal education

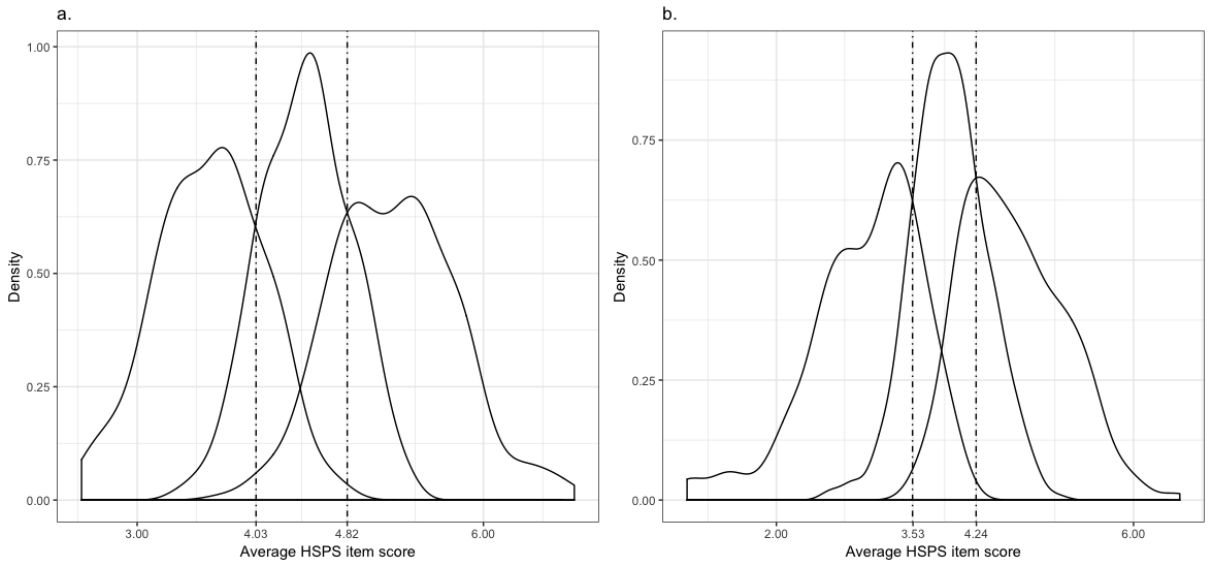


Figure 5.4: **Combined density plots for the three latent classes**. a) Class distributions from the student study (Study 2) are reproduced for ease of reference. b) Compared to psychology students, cut-off average item scores between the dandelion, tulip and orchid classes were much lower in the more general BTT+ cohort sample.

variables. Neither gestational age nor household socioeconomic status were found to have appreciable main effects.

For two of the three behaviour sub-scales (externalising and total psychology), increased birth weight significantly predicted lower average item scores (Table 5.9). Improved maternal education was also seen to significantly lower scores. The internalising regression model did not achieve a significant fit and was of minimal effect size, even after five participant entries were excluded following an examination of case-wise diagnostics (two participants had significantly outlying residual values following Bonferroni correction. The remaining three samples had high Cook's distance values). The regression model for externalising behaviour was of small effect size. Diagnostic plots revealed no issues (all diagnostic plots for this study are shown in Appendix F). Lastly, the total psychology model was also of small effect size. Three participants were removed for high Cook's distance. In all three models, examination of the VIF, tolerance statistics and autocorrelation (via the Durbin-Watson test) revealed no apparent issues.

5.3.6.1.2 Interaction effects

The z-scores for SES were entered as part of an interaction term with the dichotomised form of birth weight. Although no significant interactions were observed (Table 5.10), plots of predicted behaviour as a function of birth weight x SES revealed greater variability for LBW individuals (Figure 5.5). Meanwhile, NBW individuals demonstrated no substantive change in behaviour in response to changing SES. The form of the plot resembled a differential susceptibility effect (Figure 1.8a) but opposite to the hypothesised direction. Behavioural issues amongst LBW children appeared to *worsen* with improving SES. Notably, confidence intervals

Table 5.9: Models of behaviour regressed on neonatal variables

	Dependent variable:		
	Internalising	Externalising	Total psychology
	B (95% confidence intervals)		
Females	0.011	−0.070***	−0.070***
	(−0.013, 0.034)	(−0.101, −0.040)	(−0.101, −0.040)
Birth weight	−0.017	−0.033**	−0.033**
	(−0.039, 0.006)	(−0.063, −0.003)	(−0.063, −0.003)
Maternal education	−0.008	−0.017**	−0.017**
	(−0.020, 0.004)	(−0.032, −0.001)	(−0.032, −0.001)
Constant	0.543***	0.866***	0.867***
	(0.458, 0.628)	(0.754, 0.978)	(0.755, 0.980)
Observations	1,333	1,337	1,336
R^2	0.004	0.021	0.021
Adjusted R^2	0.002	0.019	0.019
Residual Std. Error	0.214 (df = 1329)	0.282 (df = 1333)	0.282 (df = 1332)
F Statistic	1.760 (df = 3; 1329)	9.561*** (df = 3; 1333)	9.552*** (df = 3; 1332)
Note:			*p<0.1; **p<0.05; ***p<0.01

Table 5.10: Models of behaviour regressed on neonatal variables with environmental interaction term

	Dependent variable:		
	Internalising	Externalising	Total psychology
	B (95% confidence intervals)		
Females	0.011	−0.068***	−0.024**
	(−0.012, 0.034)	(−0.099, −0.038)	(−0.044, −0.005)
Maternal education	−0.009	−0.022**	−0.015***
	(−0.022, 0.004)	(−0.039, −0.005)	(−0.026, −0.004)
SES	−0.002	0.005	0.001
	(−0.015, 0.010)	(−0.011, 0.021)	(−0.009, 0.012)
Low birth weight	0.023	0.022	0.016
	(−0.013, 0.060)	(−0.026, 0.069)	(−0.015, 0.047)
SES:Low birth weight	0.017	0.032	0.021
	(−0.019, 0.053)	(−0.015, 0.079)	(−0.010, 0.051)
Constant	0.455***	0.689***	0.587***
	(0.438, 0.472)	(0.667, 0.712)	(0.573, 0.602)
Observations	1,333	1,337	1,336
R^2	0.005	0.021	0.012
Adjusted R^2	0.001	0.017	0.008
Residual Std. Error	0.214 (df = 1327)	0.282 (df = 1331)	0.181 (df = 1330)
F Statistic	1.273 (df = 5; 1327)	5.733*** (df = 5; 1331)	3.270*** (df = 5; 1330)
Note:			*p<0.1; **p<0.05; ***p<0.01

were large due to the smaller proportion of LBW infants, but the pattern of results appeared consistent across the three different behavioural outcome variables. Simple slopes analysis revealed that only the slope of externalising behaviour in LBW children trended towards significance, but only at the 10% level (p = 0.1).

5.3.6.2 Temperament as a predictor

5.3.6.2.1 Main effects

As a continuous variable, temperament scores were poor predictors of behavioural outcomes. However, when participants were dichotomised, difficult temperament predicted significant increases in externalising and total psychology scores (Table 5.11), although of small effect size (Adjusted R^2 = .03). The model fit for internalising behaviour did not achieve signif-

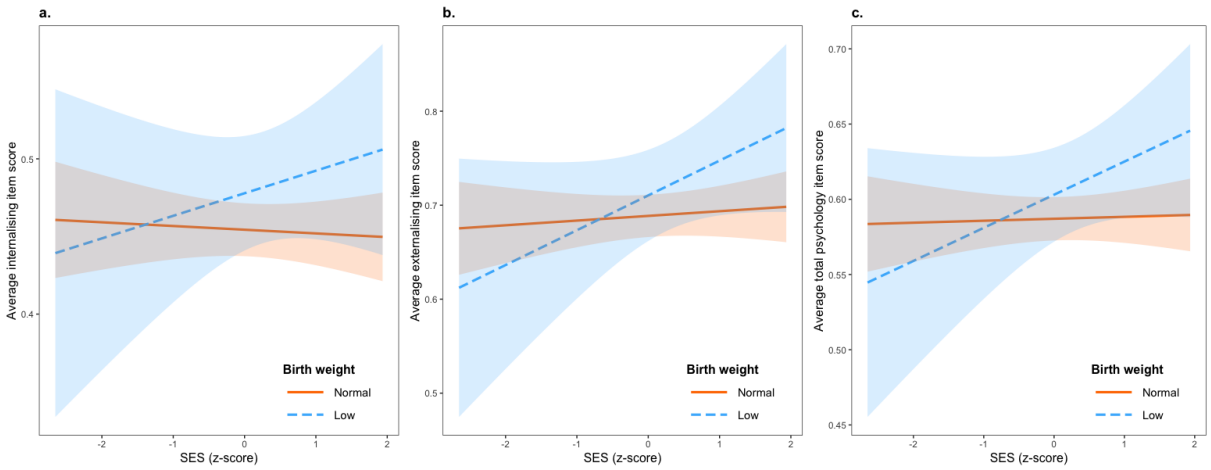


Figure 5.5: **Potential birth weight x environmental interactions in predicting childhood behaviour.** a) Low birth weight children tended to have increased internalising behaviour scores (age 7) with increasing SES levels recorded at birth, which was also true of b) externalising and c) total psychology scores. For normal birth weight infants, behaviour did not change with changing SES. Visual inspection alone suggests a potential differential susceptibility effect, given that the crossover point is near the midpoint of the environmental index, although theory would have predicted improved behaviour with higher SES.

icance which cautions against interpretation of the coefficient for difficult temperament within this model (Cohen et al., 2003). Supporting this caution, when testing the average internalising item scores between difficult and non-difficult children using Wilcoxon rank sum testing, no significant difference was observed (p = .08).

5.3.6.2.2 Interaction effects

Temperament x SES effects were non-significant (Table 5.12), and plots of the interaction did not reveal any noteworthy or consistent patterns (recall, for example, Figure 1.8b) other than confirming the generally higher behavioural scores for difficult temperament infants at all values for SES (Figure 5.6). For all models, there were no issues with VIF, tolerance or autocorrelation according to the Durbin-Watson test. Simple slopes analysis did not reveal any significant results. Given the small sample size of this dataset, the identification of interactive effects was substantively underpowered.

5.3.6.3 Genotype as a predictor

5.3.6.3.1 Main effects

Prior to regression modelling, the relationship between genotypes, neonatal predictor variables and behavioural outcomes were briefly explored. Importantly, there was no correlation between genotypes and sex, birth weight, gestational age, SES or maternal education (-.03 $\leq$ r $\geq$ .03). Box plots of genotype versus behaviour suggested an important role for the 14-repeat

Table 5.11: Temperament effects on behaviour

	Dependent variable:		
	Internalising	Externalising	Total psychology
	B (95% confidence intervals)		
Birth weight	−0.003		
	(−0.050, 0.043)		
Females		−0.076***	−0.026
		(−0.132, −0.020)	(−0.062, 0.010)
Maternal education	−0.003	−0.027*	−0.016
	(−0.027, 0.022)	(−0.058, 0.004)	(−0.036, 0.005)
Difficult temperament	0.059**	0.065**	0.058***
	(0.011, 0.107)	(0.004, 0.126)	(0.018, 0.098)
Constant	0.465***	0.805***	0.644***
	(0.298, 0.633)	(0.663, 0.947)	(0.551, 0.737)
Observations	360	362	362
R^2	0.016	0.040	0.034
Adjusted R^2	0.008	0.032	0.026
Residual Std. Error	0.210 (df = 356)	0.270 (df = 358)	0.176 (df = 358)
F Statistic	1.959 (df = 3; 356)	4.941*** (df = 3; 358)	4.195*** (df = 3; 358)
Note:			*p<0.1; **p<0.05; ***p<0.01

Table 5.12: Temperament x environment effects on behaviour

	Dependent variable:		
	Internalising	Externalising	Total psychology
	B (95% confidence intervals)		
Females		−0.076***	−0.025
		(−0.132, −0.020)	(−0.062, 0.011)
Maternal education	−0.003	−0.025	−0.014
	(−0.031, 0.026)	(−0.061, 0.010)	(−0.038, 0.009)
Birth weight	−0.002		
	(−0.026, 0.022)		
SES	−0.004	−0.009	−0.009
	(−0.030, 0.023)	(−0.043, 0.025)	(−0.031, 0.013)
Difficult temperament	0.057**	0.066**	0.057***
	(0.008, 0.105)	(0.005, 0.128)	(0.016, 0.097)
SES:Difficult temperament	0.014	−0.003	0.011
	(−0.032, 0.059)	(−0.061, 0.055)	(−0.027, 0.048)
Constant	0.444***	0.690***	0.577***
	(0.418, 0.470)	(0.646, 0.734)	(0.549, 0.606)
Observations	360	362	362
R^2	0.017	0.041	0.036
Adjusted R^2	0.003	0.028	0.022
Residual Std. Error	0.210 (df = 354)	0.270 (df = 356)	0.176 (df = 356)
F Statistic	1.240 (df = 5; 354)	3.044** (df = 5; 356)	2.641** (df = 5; 356)
Note:			*p<0.1; **p<0.05; ***p<0.01

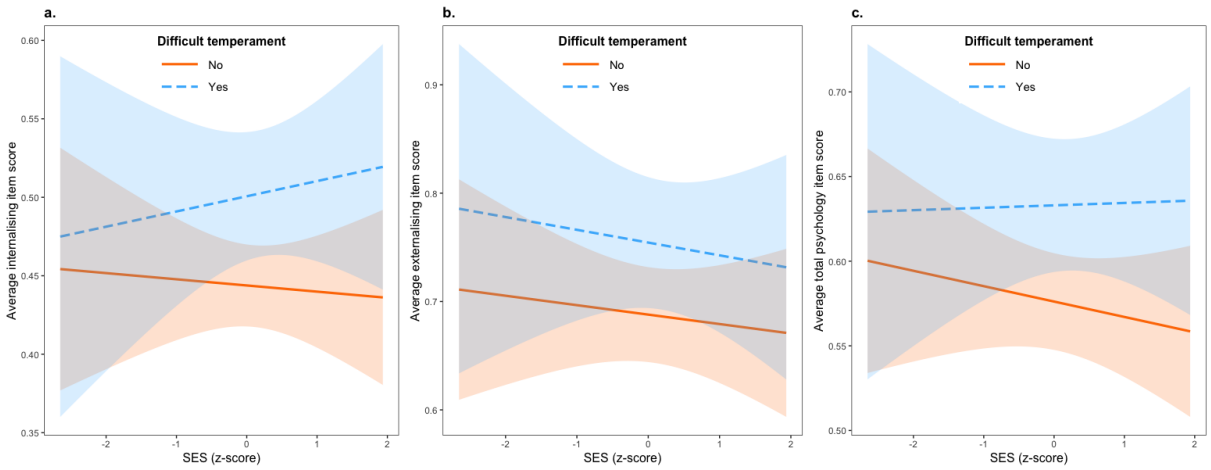


Figure 5.6: **Potential temperament x environment interactions in predicting childhood behaviour.** a) Difficult temperament children had worse internalising behaviour than non-difficult children for all levels of SES. The model was not a significant fit, which undermines any further interpretation of this result. b) Externalising behaviour appeared to diminish with higher SES for children of difficult temperament but remained stable for c) total psychology scores. Across all behaviours, children without a difficult temperament had moderately better behaviour as SES increased.

short allele of 5-HTTLPR, additional copies of which appeared to increase average item score for all three behaviour subscales (Figure 5.7). No noticeable effect of the 7R allele of *DRD4* was seen (Figure 5.8).

For modelling purposes, participants were dichotomised according to either presence or absence of a plasticity allele per genotype (S allele for 5-HTTLPR and the 7R allele for *DRD4*). This approach assumes the plasticity allele is at least co-dominant (rather than recessive) and was adopted for three main reasons. Firstly, a similar approach has been used by other authors (e.g. Morgan et al., 2017). Secondly, the number of individuals homozygous for a plasticity allele was inadequately low. Lastly, linear modelling with three genotypic categories requires careful reparameterisation of the regression equation to avoid biased results (Aliev, Latendresse, Bacanu, Neale, and Dick, 2014).

Following the exhaustive selection algorithm, fit statistics only favoured the inclusion of 5-HTTLPR, sex, birth weight and maternal education in order to predict behaviour. *DRD4* genotype (specifically the presence of the 7R allele) had no significant predictive power, in accordance with box plot observations (Figure 5.8). Possession of at least one S allele predicted significant increases in average behaviour item scores for all three subscales (Table 5.13). All models were of a significant fit, but of small effect size.

Case-wise diagnostics revealed just one case, in the internalising model, with a significantly large residual after Bonferroni correction. For all three models, there were no issues with VIF, tolerance or autocorrelation according to the Durbin-Watson test.

Table 5.13: Genotypic effects on behaviour

	Dependent variable:		
	Internalising	Externalising	Total psychology
	B (95% confidence intervals)		
Females	0.005	−0.076***	−0.031***
	(−0.022, 0.032)	(−0.112, −0.040)	(−0.054, −0.008)
Birth weight	−0.019	−0.024	−0.014
	(−0.045, 0.007)	(−0.058, 0.011)	(−0.037, 0.008)
Maternal education	−0.012*	−0.017*	−0.014**
	(−0.026, 0.002)	(−0.036, 0.001)	(−0.026, −0.002)
5-HTTLPR S allele	0.049***	0.048**	0.040***
	(0.021, 0.076)	(0.011, 0.085)	(0.016, 0.064)
Constant	0.550***	0.830***	0.685***
	(0.453, 0.648)	(0.700, 0.960)	(0.601, 0.768)
Observations	963	964	964
R^2	0.018	0.028	0.024
Adjusted R^2	0.014	0.024	0.020
Residual Std. Error	0.211 (df = 958)	0.282 (df = 959)	0.181 (df = 959)
F Statistic	4.410*** (df = 4; 958)	6.840*** (df = 4; 959)	6.002*** (df = 4; 959)
Note:			*p<0.1; **p<0.05; ***p<0.01

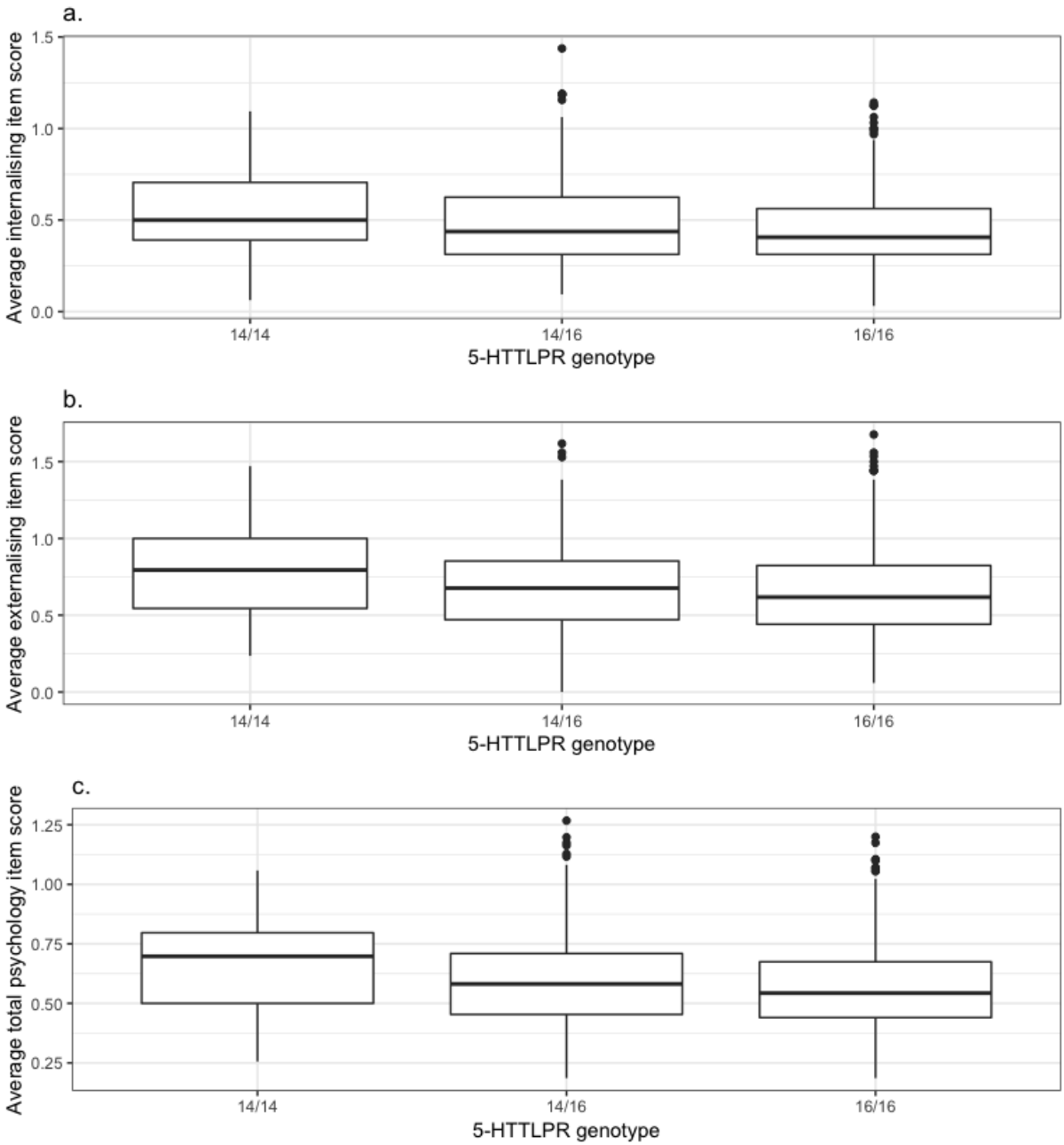


Figure 5.7: **Box plots showing average behaviour scores per 5-HTTLPR genotype.** With each additional copy of the 14-repeat S allele, average behaviour scores increased, suggesting more problematic behaviour.

5.3.6.3.2 Interaction effects

Interaction effects between the short allele and SES did not achieve significance (Figure 5.14), nor did simple slopes analysis reveal any significant slopes. Plots of the interaction models revealed suggestive patterns in line with diathesis-stress theorising (the projected intersection point was near the uppermost value for SES, Figure 1.8d) for internalising and total psychology scores, but not for externalising scores (Figure 5.9). Specifically, there was a general decline in behavioural problems with increasing SES, most noticeably in the case of internalising behaviour.

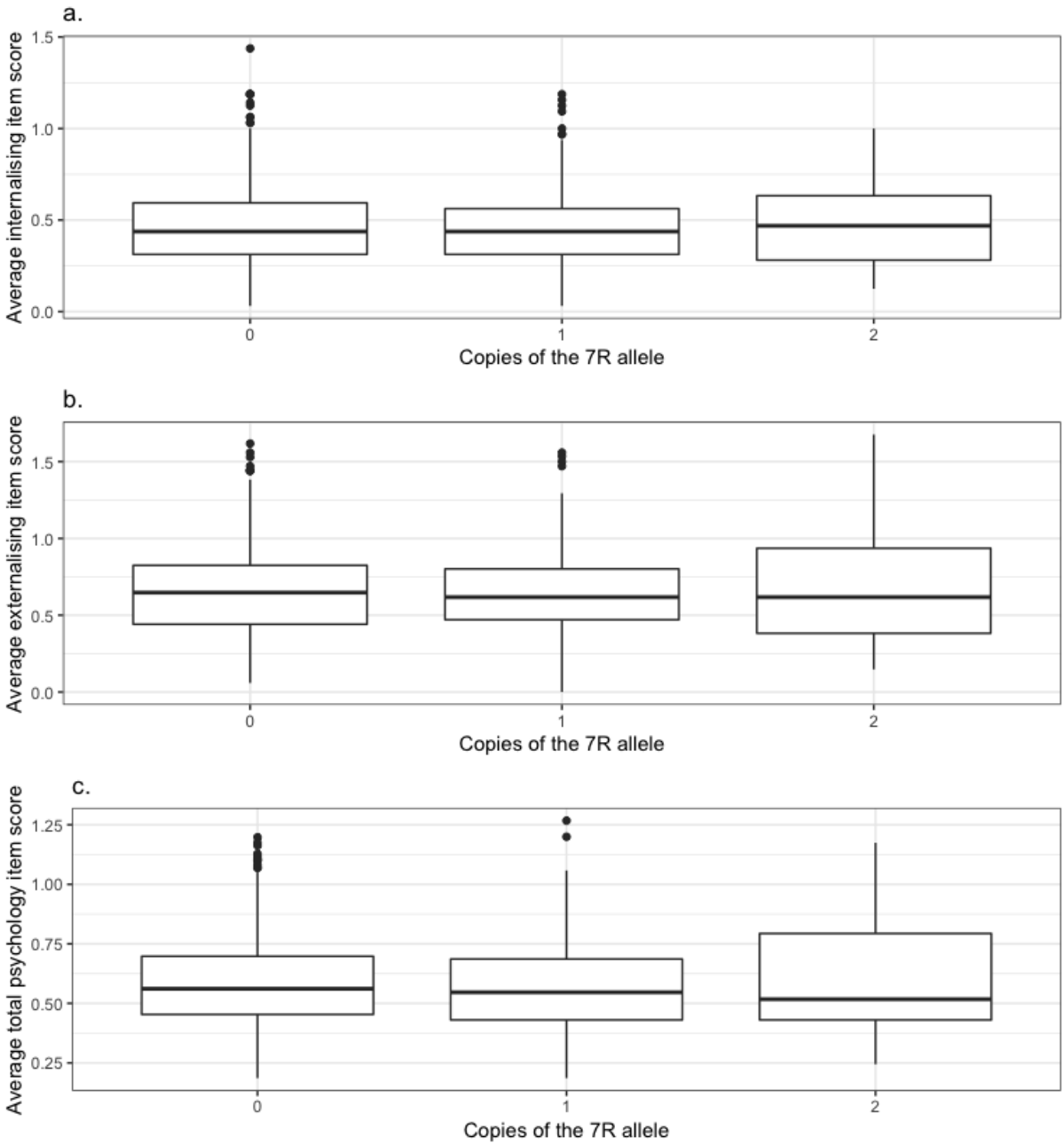


Figure 5.8: **Box plots showing average behaviour scores per *DRD4* genotype.** Average item scores per genotypic category did not differ substantially, suggesting no apparent influence of the 7R allele

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Although the 7R allele of *DRD4* had no main effects, its potential interaction with SES was still examined (Table 5.15). For internalising behaviour, the interaction model did not fit significantly. However, in the case of externalising behaviour, the model fit was highly significant ($p < .001$) and the interaction plot was suggestive of a differential susceptibility effect (although the interaction itself was not significant; $p = .26$). As with the result for birth weight, the slope of the model for 7R allele carriers was opposite to expectations. Carriers appeared to have worsening behaviour as SES improved.

Table 5.14: 5-HTTLPR x environment effects on behaviour

	Dependent variable:		
	Internalising	Externalising	Total psychology
	B (95% confidence intervals)		
Females	0.006	−0.075***	−0.030**
	(−0.021, 0.033)	(−0.111, −0.039)	(−0.053, −0.007)
Birth weight	−0.010	−0.012	−0.007
	(−0.023, 0.004)	(−0.030, 0.006)	(−0.019, 0.004)
Maternal education	−0.012	−0.021**	−0.016**
	(−0.027, 0.004)	(−0.042, −0.0001)	(−0.029, −0.002)
SES	0.003	0.010	0.006
	(−0.014, 0.020)	(−0.013, 0.032)	(−0.009, 0.020)
5-HTTLPR S allele	0.051***	0.049**	0.041***
	(0.023, 0.079)	(0.011, 0.086)	(0.017, 0.065)
SES:S allele	−0.018	−0.006	−0.010
	(−0.046, 0.010)	(−0.043, 0.032)	(−0.034, 0.014)
Constant	0.441***	0.682***	0.579***
	(0.419, 0.462)	(0.653, 0.711)	(0.561, 0.598)
Observations	963	964	964
R^2	0.020	0.029	0.025
Adjusted R^2	0.014	0.022	0.019
Residual Std. Error	0.211 (df = 956)	0.282 (df = 957)	0.181 (df = 957)
F Statistic	3.257*** (df = 6; 956)	4.685*** (df = 6; 957)	4.136*** (df = 6; 957)
Note:			*p<0.1; **p<0.05; ***p<0.01

Table 5.15: *DRD4* x environment effects on behaviour

	Dependent variable:		
	Internalising	Externalising	Total psychology
	B (95% confidence intervals)		
Females	0.005	−0.073***	−0.029**
	(−0.022, 0.033)	(−0.109, −0.037)	(−0.053, −0.006)
Birth weight	−0.010	−0.012	−0.007
	(−0.023, 0.004)	(−0.030, 0.006)	(−0.019, 0.004)
Maternal Education	−0.012	−0.022**	−0.016**
	(−0.027, 0.004)	(−0.043, −0.001)	(−0.030, −0.003)
SES	−0.011	0.0003	−0.001
	(−0.027, 0.006)	(−0.022, 0.022)	(−0.016, 0.013)
DRD4 7R carrier	−0.010	−0.014	−0.008
	(−0.039, 0.019)	(−0.052, 0.025)	(−0.034, 0.017)
SES:7R carrier	0.026*	0.023	0.012
	(−0.004, 0.055)	(−0.016, 0.062)	(−0.014, 0.037)
Constant	0.462***	0.701***	0.596***
	(0.440, 0.484)	(0.673, 0.730)	(0.577, 0.614)
Observations	955	956	956
R^2	0.010	0.024	0.015
Adjusted R^2	0.003	0.018	0.009
Residual Std. Error	0.213 (df = 948)	0.282 (df = 949)	0.182 (df = 949)
F Statistic	1.553 (df = 6; 948)	3.839*** (df = 6; 949)	2.441** (df = 6; 949)
Note:			*p<0.1; **p<0.05; ***p<0.01

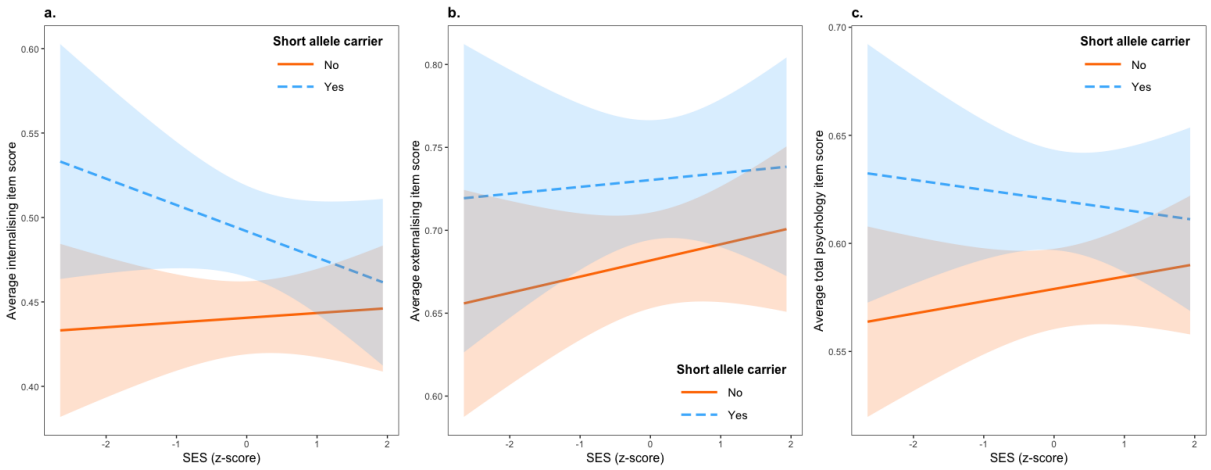


Figure 5.9: **Potential 5-HTTLPR x environment interactions in predicting childhood behaviour.** a) S allele carriers had decreasing internalising issues with improved SES levels. The projected interaction point is near the uppermost value for SES, which supports diathesis stress reasoning, with potential for a differential susceptibility effect in samples with more diverse SES. b) S allele carriers had worse externalising behavioural issues for all values of SES, compared to L allele homozygotes. c) Results for total psychology scores appropriately reflected a combination of internalising and externalising results.

5.3.6.4 Sensory processing sensitivity as a predictor

5.3.6.4.1 Main effects

As with temperament scores, continuous HSPS scores were not noticeably informative, but dichotomisation of the sample into non-sensitive and highly sensitive persons revealed clearer effects. Regression models revealed that being an HS person predicted significantly increased internalising and total psychology scores, but not externalising scores (Figure 5.16). Although a significant predictor for externalising and total psychology scores, sex was an uninformative predictor in the internalising regression model, suggesting that sex differences were already captured elsewhere, possibly by SPS levels and/or birth weight. All models fit significantly, but effect sizes were small.

5.3.6.4.2 Interaction effects

The interaction between HS person and SES trended towards significance at the 10% level in the internalising interaction model (p = .11), and simple slopes analysis also revealed a significant slope for HS persons at the 10% level, but otherwise interactive effects and slopes were not significant (Table 5.17). However, interaction plots across behavioural subscales were consistently suggestive of a diathesis-stress model, with HS persons demonstrating improved outcomes with increasing SES (Figure 5.11). Non-sensitive persons did not appear to be influenced by SES.

Table 5.16: SPS effects on behaviour

	Dependent variable:		
	Internalising	Externalising	Total psychology
	B (95% confidence intervals)		
Females		-0.074^{***}	-0.030^{**}
		$(-0.116, -0.031)$	$(-0.057, -0.002)$
Birth weight	-0.028^{*}	-0.027	-0.018
	$(-0.057, 0.002)$	$(-0.067, 0.013)$	$(-0.043, 0.008)$
Maternal education	-0.010	-0.024^{**}	-0.017^{**}
	$(-0.026, 0.007)$	$(-0.047, -0.001)$	$(-0.031, -0.002)$
HS Person	0.043^{**}	0.041	0.037^{**}
	(0.005, 0.082)	$(-0.012, 0.094)$	(0.003, 0.071)
Constant	0.590^{***}	0.893^{***}	0.724^{***}
	(0.480, 0.699)	(0.739, 1.046)	(0.626, 0.822)
Observations	692	692	692
R^2	0.016	0.026	0.022
Adjusted R^2	0.012	0.020	0.016
Residual Std. Error	0.204 (df = 688)	0.278 (df = 687)	0.177 (df = 687)
F Statistic	3.746^{**} (df = 3; 688)	4.544^{***} (df = 4; 687)	3.859^{***} (df = 4; 687)
Note:			*p<0.1; **p<0.05; ***p<0.01

Table 5.17: SPS x environment effects on behaviour

	Dependent variable:		
	Internalising	Externalising	Total psychology
	B (95% confidence intervals)		
Females		−0.073*** (−0.116, −0.030)	−0.029** (−0.056, −0.002)
Birth weight	−0.017** (−0.031, −0.002)	−0.014 (−0.035, 0.006)	−0.010 (−0.023, 0.003)
Maternal education	−0.005 (−0.023, 0.014)	−0.025* (−0.051, 0.0002)	−0.017** (−0.034, −0.001)
SES	−0.00000 (−0.018, 0.018)	0.002 (−0.023, 0.026)	0.002 (−0.014, 0.018)
HS person	0.054*** (0.015, 0.093)	0.044 (−0.010, 0.098)	0.041** (0.006, 0.075)
zSES:HS person	−0.034 (−0.074, 0.007)	−0.017 (−0.072, 0.039)	−0.019 (−0.054, 0.016)
Constant	0.461*** (0.444, 0.478)	0.706*** (0.674, 0.738)	0.597*** (0.577, 0.618)
Observations	689	692	692
R^2	0.022	0.026	0.024
Adjusted R^2	0.015	0.018	0.015
Residual Std. Error	0.201 (df = 683)	0.279 (df = 685)	0.177 (df = 685)
F Statistic	3.102*** (df = 5; 683)	3.082*** (df = 6; 685)	2.770** (df = 6; 685)
Note:			*p<0.1; **p<0.05; ***p<0.01

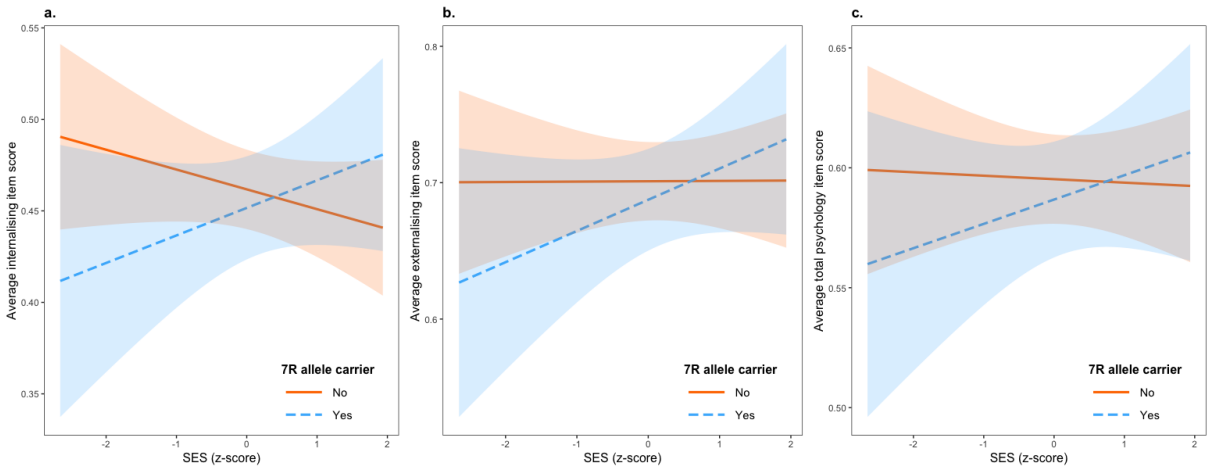


Figure 5.10: **Potential *DRD4* x environment interactions in predicting childhood behaviour.** a) The model for internalising behaviour as a function of SES for different *DRD4* genotypes did fit significantly, so no further interpretation was warranted. b) 7R carriers had worsening externalising behaviour and c) total psychology scores with increased SES, whilst individuals lacking a 7R allele showed no substantive change in behaviour as a function of environmental context. The plots resemble a differential susceptibility effect, although the slope of the model for 7R carriers is opposite to theoretical predictions.

5.3.6.5 SPS as an outcome variable

Across different datasets, the relationship of SPS to other available variables was examined. As described above, HS persons had significantly lower birth weight (p = .03), but gestational age proved the best predictor of SPS level. Longer gestation period predicted lower average item HSPS scores (B = -.03) at the 10% level (p = .07) with sex and birth weight as covariates (Figure 5.12). The model fit was significant ($p < .001$), with small effect size (Adjusted R^2 = .06).

5.3.7 Correlations between sensitivity markers

Chi-square testing was used to examine if any of the dichotomised sensitivity markers were meaningfully associated (except for those associations already noted above e.g. low birth weight and SPS). However, no associations were found, suggesting that HS persons were not more likely to carry a particular genotype, nor were they more likely to have a difficult temperament. Similarly, the latent classes of respondents to the HSPS (orchids, dandelions and tulips) showed no association to genotype or temperament. Temperament was also not significantly associated to genotype.

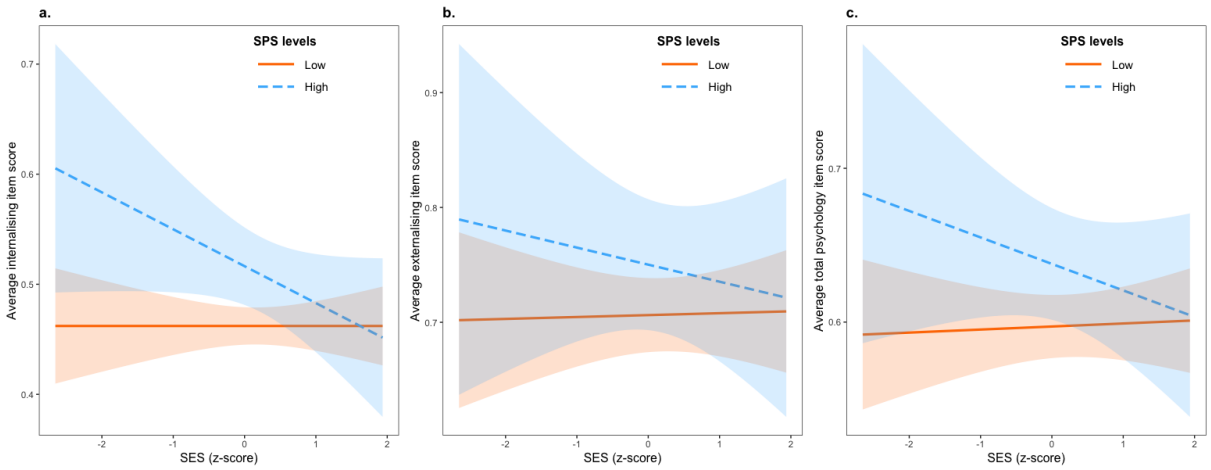


Figure 5.11: **Potential SPS x environment interactions in predicting childhood behaviour.** a) With improving SES, HS persons had lower childhood internalising behavioural problems. This was the most robust of the interaction findings, which neared significance at the 10% level. Although a diathesis stress model is supported, a differential susceptibility effect may be evident when sampling a wider range of environments. A similar, but weaker effect was observed for b) externalising and c) total psychology scores.

5.4 Discussion

This study was the first attempt to examine BTT+ cohort variables within a framework of Environmental Sensitivity (Pluess, 2015). Collectively, cohort members represent a highly diverse cultural and ethnolinguistic sample, raised in a mostly impoverished former township undergoing dramatic sociopolitical transformation. As outlined previously, data capture and completeness for the cohort has been consistently challenging (Section 5.1), and variables chosen for this study had large temporal distances between them. Taken together, these issues suggest that results from this sample should not be generalised to larger populations, but should rather be appreciated in an exploratory light. Although several significant main effects for sensitivity markers were detected, no marker x environment interaction was significant. Nevertheless, the patterns of these interactions were of interest, and their implications are tentatively discussed below.

5.4.1 Neonatal variables

Birth weight had significant main effects on externalising and total psychology scores, but not internalising scores. Previous literature has consistently identified later problematic behaviour in LBW infants, although effect size estimates have been small (Pettersson et al., 2019). BTT+ cohort results clearly align with this trend, given that regression models were also of small effect size (Adjusted R^2 = 0.02). LBW infants are at risk of poorer brain development (de Kieviet, Zoetebier, van Elburg, Vermeulen, and Oosterlaan, 2012) that might manifest in subsequent behavioural difficulties, especially when the post-natal environment remains stressful and adverse.

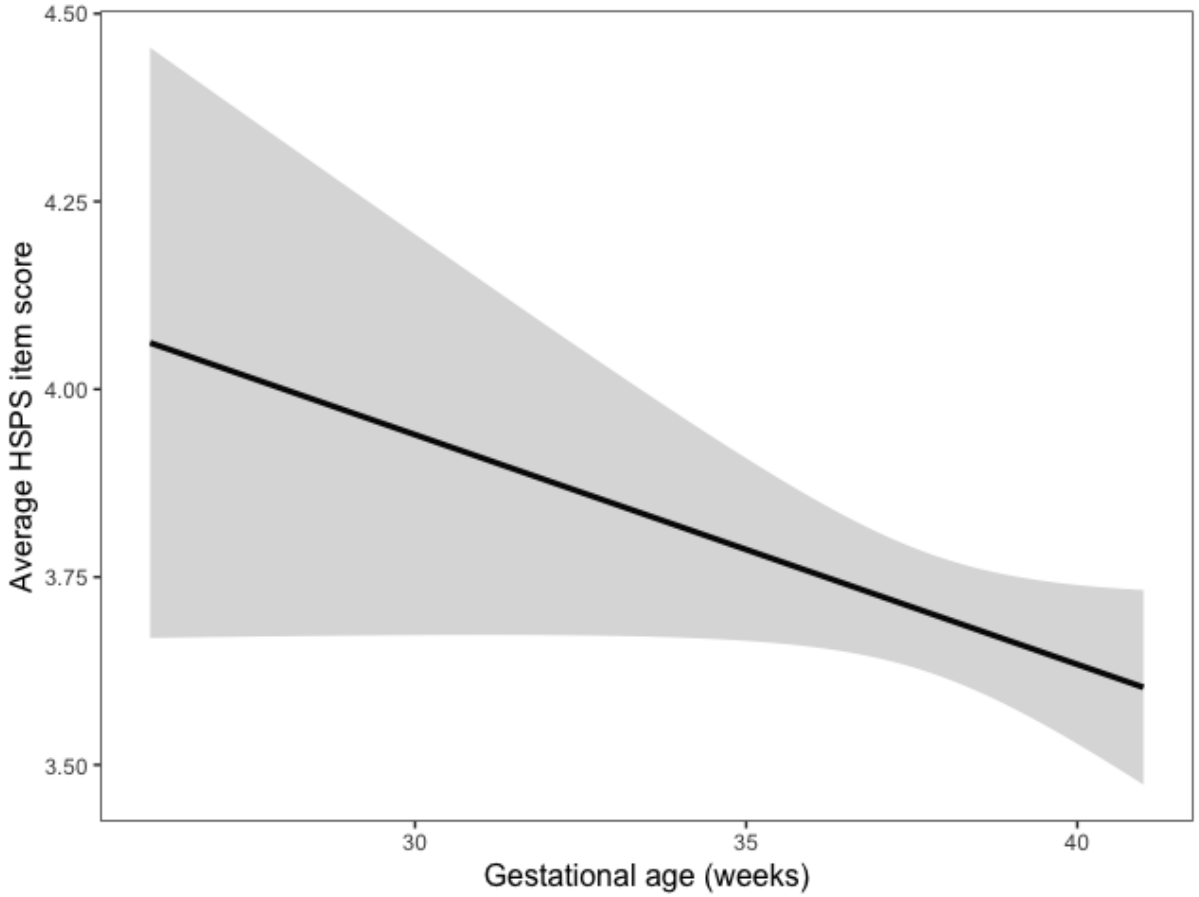


Figure 5.12: **Predicted HSPS average item score as a function of gestational age.** When controlling for sex and birth weight, longer gestational age significantly predicted lower HSPS scores (at age 28) at the 10% level. The shaded area reflects the 95% confidence interval.

Given the general living conditions of Soweto (Barbarin and Richter, 2001b), low birth weight infants, without adequate intervention, are clearly at risk for problematic childhood behaviour.

Interaction analysis suggested that LBW children had greater variance in behavioural problems as a function of SES. Specifically, scores tended to increase with increasing SES for LBW infants, but not for NBW infants. This pattern of results resembles a crossover interaction of the type seen for DS (e.g. Figure 1.8a), however, the direction of the slope for LBW infants is contrary to theoretical predictions - higher SES should have afforded *improved* behavioural outcomes for children of LBW. Some considerations are necessary before interpreting this finding. Firstly, the proportion of low birth weight infants (11%, n = 293) and their high variance in behaviour scores did not afford narrow confidence intervals. Secondly, the SES measure is separated from the behavioural outcome by seven years. Controlling for SES in the intervening years may have provided more accurate results, especially given the speculation that neuroplasticity levels are still under calibration during early childhood (Pluess et al., 2011, Figure 1.4). Lastly, Jaekel and colleagues (2015) were also unable to identify differential susceptibility effects in low and very low birth weight individuals, possibly undermining the assumption that low birth weight adheres to DS theorising. Nevertheless, should these study results still hold true despite the above issues, there is one possible interpretation that warrants mention. If diffi-

cult, problematic behaviour is a potential means for young children to interrogate their parents about the environment (Section 1.5.1), a tentative postulation is that LBW children, with low SES, have less reason to scrutinise the consistently poor quality of their context. Conversely, LBW children in a high SES context have received mixed signals regarding environmental quality and may use their problematic behaviour as a means of further hypothesis testing (Figure 1.4).

5.4.2 Temperament as a predictor

In line with previous literature, children with a more difficult temperament at 6-12 months were likely to have more problematic behaviour at 7 years of age. This was particularly true of externalising behaviour (and total psychology in which externalising behavioural items were nested). Higher SES predicted lower problematic behaviour regardless of temperamental style.

The limited findings for temperament are likely due to measurement and sample size issues. Firstly, only eight items, out of an available 90, were used to try gauge difficult temperament. This was a necessary abbreviation of the CITQ, given that many items posed translational difficulties and that mothers were kept busy with multiple other activities and assessments during each BTT+ data collection wave (L. Richter, personal communication; Barbarin and Richter, 2001b). Secondly, a major criticism of the CITQ is that it tends to measure the characteristics of the respondent care-giver rather than the child in question (Braithwaite et al., 2013; Vaughn and Taraldson, 1981). Vaughn and Taraldson (1981) found, in their sample, that children rated difficult almost always belonged to highly anxious mothers. Prenatal surveys confirmed that this anxiety was present even before the child's birth, and thus not a consequence of having a child with a difficult temperament. Lastly, temperament measurements were only available for a small subset of cohort members - a number not conducive to interaction modelling.

5.4.3 Genotype as a predictor

Prior to discussion on the main and interactive effects of genotype on behaviour, it is important to emphasise that neither of the genotypes correlated with other predictors, especially SES (i.e. no rGE correlation; Bakermans-Kranenburg and van IJzendoorn, 2015). A correlation between genotype and environment undermines investigations into GxE effects, because any identified interaction is then either a result of actual interactive effects between gene and environment, or simply the product of particular alleles being overrepresented in certain environments (Bakermans-Kranenburg and van IJzendoorn, 2015). Hence, the findings suggested by this study may reflect actual gene x environment interactions because alleles were not biased in their frequency at different socioeconomic levels.

The S allele of 5-HTTLPR had significant main effects on all three measured outcomes confirming that carriers are more prone to behavioural issues. These results are in full agreement with previously published observations. As emphasised earlier (section 1.5.1.3.1), the S allele has well-documented associations with internalising issues such as anxiety and depression. The allele has also been linked to shyness (Battaglia et al., 2005) and inhibited behaviour (Fox, Henderson, Marshall, Nichols, and Ghera, 2005) in children. Regarding externalising behaviour, low serotonin levels are known to heighten aggression, emotional outbursts and suicidal behaviour (Homberg et al., 2016; Moore and Depue, 2016). Moreover, the S allele has documented associations with changes in brain anatomy, including reduced gray matter volume in regions critically involved in negative emotion processing, particularly the perigenual anterior cingulate cortex and the amygdala (Åslund et al., 2013; Pezawas et al., 2005). These two brain regions have a tightly coupled role in the extinction of negative affect (Pezawas et al., 2005), thus their reduced volume might explain why S allele carriers struggle to disconnect from, and are subsequently more affected by, negative stimuli. Morphofunctional changes to brain anatomy may thus be key contributors to sensory and other processing differences in S allele carriers, which facilitate observable behavioural differences compared to L/L homozygotes (Homberg et al., 2016).

When including SES as part of an interaction term, S allele carriers demonstrated fewer internalising issues with increasing SES (although not significantly so). Previous studies have noted that S allele carriers are more sensitive to the effects of low SES (Way and Gurbaxani, 2008), resulting in displays of more delinquent, problematic behaviour (Åslund et al., 2013). The S allele has also been implicated in numerous diathesis-stress (e.g. Caspi et al., 2003) and differential susceptibility (e.g. Keers and Pluess, 2017) effects (section 1.5.1.3.1), often pertaining to internalising behaviour. Findings in the BTT+ cohort support a diathesis-stress effect for the S allele, especially for internalising behaviour. However, the range of the SES variable is notably restricted, given the generally low SES of Soweto, which may have masked a differential susceptibility effect. Recall that previous findings in the literature that have supported a diathesis-stress model (including GxE studies) have been criticised for their narrow sampling of the environment (section 1.5.1), with the vast majority of studies focusing on harsh, adverse environments (Belsky et al., 2009). True differential susceptibility effects can only be revealed when participants from both harsh *and* supportive contexts are sampled (Belsky et al., 2009; Pluess, 2015). Future studies to extend the work presented here should thus seek to examine Black African individuals developing in both high and low SES surroundings.

Interestingly, a small meta-analysis of the 5-HTTLPR S allele as a differential susceptibility marker revealed possible ethnic discrepancies (van IJzendoorn and Bakermans-Kranenburg, 2012). Specifically, in ethnically admixed individuals, the S allele more consistently adhered to a diathesis-stress model, whereas in European-ancestry individuals, the S allele more commonly afforded outcomes in line with differential susceptibility. The results seen in this study may further support these meta-analytic observations, given the apparent lack of DS effects for

BTT+ S carriers. Assuming this is a true effect, and not the product of poor study designs and/or disproportionate research focus on Caucasians, it suggests the S allele may have accrued further diversifying variants with migration out of Africa (Nakamura, Ueno, Sano, and Tanabe, 2000). In testament to these speculations, it has been noted that the S/S genotype, in African Americans, has been associated with *higher* cerebrospinal fluid levels of 5-hydroxyindoleacetic acid (the major metabolite of serotonin), but *lower* levels in individuals of European-ancestry (van IJzendoorn and Bakermans-Kranenburg, 2012; Williams et al., 2003), supporting functional differences of the S allele in Caucasians versus populations of African descent. These differences may have augmented environmental sensitivity to positive environments for Caucasians, allowing more opportunity for DS effects to operate. However, such speculations will need to be rigorously tested, and further motivate for a shift towards African-centric genetic research (Ramsay et al., 2011).

No main effects for *DRD4* on behaviour were detected. However, in interaction models, there was some evidence to suggest that behaviour in 7R carriers was modified by the environment, although opposite to hypothesised expectations (e.g. Figure 1.8a). The 7R allele has been mostly linked to novelty seeking (Auerbach et al., 1999; Benjamin et al., 1996) and externalising behavioural outcomes (Bakermans-Kranenburg et al., 2008; section 1.5.1.3.2). Possibly, children carrying the 7R allele were afforded more opportunities to seek novelty (expressed through greater externalising behaviour) with greater SES. Indeed, delinquent, externalising behaviour has been previously shown to bear a U-shaped relationship to SES, with the highest levels of delinquency seen in high and low SES adolescents, but average levels amongst teens with medium SES (Åslund et al., 2013). Similar to discussions previously regarding the birth weight results (and in section 1.5.2), novelty seeking might serve as a behavioural mechanism for interrogating the post-natal environment before calibrating neurosensitivity levels. BTT+ children carrying a 7R allele may have had more reason to conduct environmental investigations with higher SES, perhaps because it conflicted with the lower average SES of the surrounding Soweto neighbourhood (Barbarin and Richter, 2001). Alternatively, *DRD4* genotype may produce clearer DS effects in response to social rather than economic context. For example, Zohsel and colleagues (2014) found that children carrying at least one 7R allele showed more conduct disorder and/or oppositional defiance disorder at 8-15 years of age if their mothers' had high prenatal stress. Individuals homozygous for the 4R allele showed no such sensitivity to prenatal stress levels. In this study, as an additional investigation along this line of thought, an interaction between *DRD4* genotype and maternal education (a more socially-relevant variable) was tested for, but did not produce models of significant fit (data not shown). Lastly, *DRD4* genotypes could have been grouped differently and retested, but these different grouping strategies rest on tenuous theoretical support. Moreover, this would have put the research at higher risk of multiple testing errors (Munafò, Zammit, and Flint, 2014).

Note, also, that conflicting/contrasting results have been previously found when examining the *DRD4* 7R allele. Recall the study by Eisenberg and colleagues (2008) that examined

one pastoral and one nomadic sample of Kenyan Ariaal individuals (section 1.6). Pastoral 7R carriers were the most undernourished of the sample, yet nomadic 7R carriers were the most well-nourished. This result suggests the existence of important intraethnic differences in gene functioning as a product of lifestyle and environment. The "for better and for worse" formula of differential susceptibility may not always be as straightforward as theory would dictate - an issue that is perhaps symbolised by the unanticipated worsening of behaviour with improving SES seen for 7R-carrying BTT+ cohort members. Future investigations might consider, for example, comparing 7R carriers living urban versus rural lifestyles, rather than focusing on SES indicators. Indeed, these sorts of complexities might also bear relevance to the aforementioned discrepancies in DS versus diathesis-stress effects in S allele carriers of different ethnicities. Perhaps these discrepancies also occur intraethnically, but there has not been sufficient research to properly outline this possibility.

The lack of Hardy-Weinberg equilibrium for *DRD4* genotypes may have also influenced study findings. When genotypes are not in equilibrium, the consequent effect is a loss of statistical power, but no apparent change in the risk of Type I error (Fardo, Becker, Bertram, Tanzi, and Lange, 2009; Zou and Donner, 2006). The primary culprit in this scenario is genotyping error. Two independent researchers called all genotypes for this study, and samples with discordant calls were either re-run or re-amplified until consensus was reached in an effort to mitigate calling errors. Admittedly, sequencing a subset of samples (e.g. 10%) to confirm PCR results would have been a better validation strategy. Although genotyping error cannot be ruled out, others (e.g. Belsky et al., 2015) have also generated *DRD4* VNTR genotypes that failed equilibrium testing, even with sequencing validation of a smaller subset of samples. That the *DRD4* VNTR has a wide range of alleles, most of which have rare frequencies (i.e. $<$ five chromosomal observations even in large samples) possibly undermines statistical testing for equilibrium, resulting in Type I errors. Alternatively, the lack of equilibrium is the result of evolutionary forces (admixture, migration, selection, mating pattern, genetic drift; Mayo, 2008). Soweto is an eclectic mix of local and migrant populations, and its unique context likely imposes similarly unique and/or diverse selection pressures. Combined with the stochastic nature of genetic drift, there is ample reason to suspect that *DRD4* VNTR genotypes in this sample are imbalanced for evolutionary reasons, rather than laboratory error.

There was also no apparent effect of having both S and 7R alleles. Combining genotypes into a basic polygenic susceptibility score (PSS) did not unveil any novel insights, but this strategy has been informative in other examinations of African-ancestry individuals. For example, in African American youths, Simons et al. (2011) found evidence of DS when examining aggressive behaviour. Individuals with an S allele *and* a *DRD4* 7R (or longer) allele evinced the highest levels of aggressive behaviour in adverse environments, but the lowest levels in supportive environments.

Notably, the frequency of the S and 7R alleles is low in Africa, but both appear to increase

in occurrence with migratory distance from Africa (Chang et al., 1996; Murdoch et al., 2013, section 1.6). This observation suggests both alleles may have been important for acknowledging and adjusting to novel environmental contexts, which has aided human migration and expansion out of Africa. Indeed, the S allele variant of 5-HTTLPR has only been found, outside of humans, in four species of macaques (Dobson and Brent, 2013), which also show widespread distribution and thus the ability to adapt to different environments (Bakermans-Kranenburg and van IJzendoorn, 2015). Together, macaques and humans are considered "weed" species, because of their global spread. Meanwhile, the *DRD4* VNTR locus is polymorphic in all primate species, but the human repeat sequence appears unique suggesting a possible role in human evolution and migration (Chang et al., 1996). Possibly, the harsher living conditions on the African continent have favoured selection of more resilient phenotypes, thus limiting the increased spread of DS alleles. However, there has been no credible evidence of selective pressures acting on either the *SERT* or *DRD4* loci in Africa, although the number of studies is currently minimal (Murdoch et al., 2013). Here again, the need for further African-specific genetic research is highlighted, both in terms of Environmental Sensitivity and more broadly.

Previous studies of plasticity alleles have sometimes revealed sex-specific effects, but no such effects were evident in this study. As described in section 5.1, both Chhangur et al. (2017) and Belsky and Beaver (2011) noted DS effects for boys with selected plasticity alleles, but not for girls. All interaction results for this study were split by sex (data not shown), but no noteworthy consequences were observed. Entering sex as part of a three-way interaction with SES and the relevant sensitivity marker also failed to reveal sex-specific interactions (although sample sizes were not exactly amenable to three-way interaction analysis; Åslund and Nilsson, 2018). Other studies have also failed to identify sex-specific effects (e.g. Munafò, Clark, and Flint, 2004), suggesting that further research is required to resolve possible sex discrepancies in DS effects (Bakermans-Kranenburg and van IJzendoorn, 2015).

5.4.4 SPS as a predictor

HS persons (age 28) had significantly higher internalising and total psychology scores at age 7. These findings further support the vulnerability of HS persons to behavioural problems, especially of an internalising nature (section 1.4.2). Commensurate to theory, however, this association was seemingly moderated by SES. Although this moderation mostly supported diathesis-stress reasoning (e.g. Figure 1.8d) in the study sample, a true differential susceptibility effect is not ruled out because of the limited range of the SES variable. Interestingly, the results for the S allele and for SPS were notably similar, aligning with the speculation that the S allele may strongly predispose carriers to high levels of SPS (Homberg et al., 2016; Licht et al., 2011). However, there was no significant overlap between HSPs and S carrier cohort members to support this supposition.

That SPS offered the most robust predictive effects in interaction modelling is potentially encouraging for two main reasons. Firstly, it supports notions that SPS is (currently) the clearest indicator of meaningful neurosensitivity differences between individuals (Pluess et al., 2018). This would ring especially true if independent studies can confirm that measurements of SPS in adulthood still have reasonable retrospective predictive power for childhood outcomes, as observed in this study. Secondly, it strengthens the utility of the HSPS, which could serve as a useful tool in both research and clinical settings. Based on the similarity of psychometric results between the student and BTT+ cohort members, the HSPS appears to retain validity across cultures.

5.4.4.1 Psychometric results

Encouragingly, psychometric results for the HSPS closely mirrored those seen amongst students (Study 2). BTT+ cohort members were up to a decade older than student participants, and had far greater variation in English language comprehension and educational background. That these differences did not appear to undermine the general performance and reliability of the HSPS possibly speaks to the robust nature of the scale and the evolutionary-grounded theory on which it is based (Aron et al., 2012). As described previously, the scale has been translated (without apparent issue) to several different languages, and has also been adapted for assessment in children (Greven et al., 2019). There has even been an instrument designed to gauge SPS in dogs (Braem et al., 2017), further strengthening the evolutionary underpinnings of the trait. Findings in this study should thus provide further impetus for using the HSPS more extensively in cross-cultural contexts.

5.4.5 SPS as an outcome variable

On average, HS persons were significantly lighter at birth. Assuming low birth weight is an indicator of stressful *in utero* conditions, and that a plastic strategy is favoured following signals of consistent adversity (section 1.5.2), it is plausible that LBW infants are more predisposed to develop high levels of SPS as adults. When controlling for birth weight and sex, gestational age emerged as a potential predictor of adult SPS levels. Low gestational age is strongly correlated with lower birth weight, and so both these findings would seem to augment each other.

An alternative explanation is that the HSPS is also capturing individuals with pathological sensory issues (section 1.4.2.6). Pre-term birth is well known to compromise overall brain development (Damus, 2008), leading to various sensory and behavioural issues. These individuals are also likely to score high on the HSPS, even though they might not be accurately representative of the neutral, non-pathological SPS trait. The fact that psychometric results were similar to healthy student samples, and that remaining BTT+ cohort members are all functional adults sug-

gests study results were not severely contaminated by confounding pathological sensory issues. However, if this is not the case, it suggests an important limitation to the HSPS. Future use of the instrument might require investigators to carefully control for sensory-related pathologies.

5.4.6 Correlations between sensitivity markers

There was no strong evidence to suggest meaningful correlations between sensitivity markers in this study. Given the general malleability of children and the idea that they undergo a period of experimentation and programming/calibration (Section 1.5.2) before settling on a final threshold of neurosensitivity, it seems reasonable to anticipate low correlations between birth weight, temperament, SPS and genotype (5-HTTLPR and *DRD4*). Moreover, neurosensitivity is highly multifactorial, meaning that the presence of one marker of heightened neurosensitivity does not automatically imply the co-occurence of other markers. Each highly reactive individual will likely have a mixed assortment, and number, of these indicators. It is understandable, then, that examining markers one at time will extract different subsets of sensitive people from the population/sample at hand. Nevertheless, as described in section 1.5.3, co-occurence of neurosensitivity markers has been documented, likely resulting in a synergistic effect that increases the odds of a sensitive disposition (but does not guarantee it).

A unique aspect of this research is the temporal distance between sensitivity markers. Whilst genotype is fixed throughout life, and thus participant age at DNA extraction is of little concern (disregarding fluctuating epigenetic modification), birth weight, temperament and SPS levels are time-sensitive. That birth weight and gestational age were informative in predicting high levels of SPS suggests some consistency in neurosensitivity level over time, aligning with the notion that sensory processing ability displays developmental plasticity, not activational plasticity (section 1.2). However, this speculation would have been better supported if temperament and genotype were also correlated with SPS. The question of if, and how, environmental sensitivity fluctuates over time has not been adequately explored (Greven et al., 2019), and results thus far have been conflicting. For example, Berry and colleagues (2013) found environmental sensitivity to heighten in the period from pre-school to fifth grade, but Belsky and Pluess (2013a) and Windhorst (2014) noted declines in sensitivity over developmental time.

5.4.7 Implications

On balance, these study results suggest that individuals in possession of markers of high neurosensitivity are more malleable to their environmental context, although replication of these results in better powered studies is required. Low birth weight, the 5-HTTLPR S allele, the *DRD4* 7R allele and high levels of SPS all exhibited variable associations with childhood behaviour as a function of SES. Only SPS and S allele results aligned with hypothesised expectations (im-

proved outcomes in a high SES environment, but worse outcomes in a low SES environment), whilst results for birth weight and *DRD4* were less immediately interpretable. Although none of the interaction analyses achieved significance at the 5% level, statistical significance has come under increasing scrutiny as the sole benchmark for "valid" research findings (Amrhein and Greenland, 2018; Benjamin et al., 2018). Indeed, the American Statistical Association released a statement in 2016 (Wasserstein and Lazar, 2016, p. 132), addressing the shortcomings of narrowly focussing on p-values, and instead concluded that

> [g]ood statistical practice, as an essential component of good scientific practice, emphasizes principles of good study design and conduct, a variety of numerical and graphical summaries of data, understanding of the phenomenon under study, interpretation of results in context, complete reporting and proper logical and quantitative understanding of what data summaries mean. No single index should substitute for scientific reasoning.

In keeping with the spirit of this statement, the preceding results and discussions have thus considered general patterns of results (p-values, graphical summaries, effect sizes etc.) and their overall consistency, in accordance with the exploratory nature of the investigation.

Implicit in these findings is that a subset of individuals (regardless of ethnicity) would benefit from improvements to their environmental context, whilst the remaining individuals would likely not. The speculated value of diathesis-stress/differential susceptibility theory lies in its potential to accurately identify highly neurosensitive individuals so as to earmark them for possible intervention efforts (Belsky and van IJzendoorn, 2015). For example, Nocentini and colleagues (2018) conducted a large randomised control trial to examine the efficacy of an anti-bullying intervention amongst Grade 4-6 students (n = 2024). Across the entire sample, the intervention appeared to significantly lower bullying and victimisation. However, when subdividing participants in the intervention condition by neurosensitivity levels, it was the children high in SPS (especially boys) that primarily accounted for this finding. Low sensitivity children demonstrated no significant reduction in bullying or victimisation. Similarly, Morgan and colleagues (2017) re-analysed the effectiveness of a mother-infant attachment intervention conducted in Khayelitsha, South Africa. Originally, infants (n = 220) in the intervention group were found to have significantly improved odds of a secure attachment to their mothers (odds ratio = 1.7, p = .03) of modest effect (d = .29). However, when partitioning infants by their 5-HTTLPR genotype, S allele carriers were discovered to be the clear drivers of this finding, given their dramatically improved odds of secure attachment (odds ratio = 3.86, p $<$ .01) with notable effect size (d = .75). In contrast, L allele homozygous infants appeared to be largely indifferent to intervention efforts (odds ratio = .95, p = .86, d = .03). With relevance to the current study, although not intervention-based, higher socioeconomic status similarly served to improve internalising and externalising behavioural outcomes in BTT+ members, specifically those high in SPS and/or carrying an S allele. This finding suggests that targeted intervention efforts might

also yield greater success amongst neurosensitive Sowetan (and other Black African) children. A similar claim was made for a cohort of European-ancestry children whose psychological distress was studied as a function of their childhood material environment (Keers and Pluess, 2017). Identifying and intervening against internalising and externalising behavioural problems at an early age is particularly important. These behavioural issues can not only hamper individual growth well into adulthood (Albert, Belsky, Crowley, Bates, et al., 2015), but they also impose significant public costs to the health and criminal justice sectors (Albert, Belsky, Crowley, Latendresse, et al., 2015; Buchanan-Pascall et al., 2018). Understanding the source of childhood behavioural issues, and their considerable variance is thus necessary to structure effective interventions (Albert, Belsky, Crowley, Bates, et al., 2015), which are especially needed in historically impoverished contexts, like Soweto. This study provides potentially meaningful information on neurosensitivity markers that could be leveraged in future intervention studies. However, as discussed in the following chapter (section 6.4), the application of differential susceptibility theorising to interventions raises challenging, but important ethical issues that need to be carefully addressed.

Although a promising start, more robust replications of the identified trends seen here are required. In addition to limited statistical significance, the effect sizes in all linear models in this study were small. There are many environmental factors that dilute the effects of a single trait or genotype (Way and Gurbaxani, 2008), many of which could not be accounted for in this study. Indeed, this is the exact complication that necessitates careful delineation between *sensitivity* and *responsivity* (section 1.2) - the behaviour of individuals is determined by more than just their innate predispositions. Broader, more comprehensive studies into the young field of neurosensitivity (especially in developing contexts like South Africa) are thus well warranted.

5.4.8 Limitations

A number of study limitations must be accounted for. As alluded to previously, given the generally impoverished conditions of Soweto (especially in the early 1990s), there was an understandable range restriction on the SES measure used in this study. At it's highest level, the SES measure describes mothers with only a basic set of household durables and amenities that are otherwise standard for middle-class families. The average SES of mothers fell below this modest standard (notably, no mother was more than 1.9 standard deviations above the average SES for the cohort). More concerningly, the SES measure was a simple index of durables that ignored a wealth of other pertinent factors. The metric was based on just a handful of assets, which were not scored in any weighted manner that reflected their value (e.g. ownership of a washing machine would have increased the SES score by one point, as would ownership of a car, despite a car being a far more expensive asset). These assets were self-reported by mothers/caregivers, which raises questions about a possible social desirability bias (Tourangeau et al., 2009), especially since the distribution of the SES variable was skewed towards higher

scores (skew = -.59). No acknowledgement was made regarding household size, the average income of the household and how many earners contributed to the family income, amongst others. All considered, the SES variable was a relatively weak and indirect proxy measurement. A further issue is that data on the SES variable were collected over the first two post-natal years for each cohort member, but the outcome variable studied here was behaviour at age 7. Whilst SES during early infancy was the key focus of this study, given infancy's importance in Environmental Sensitivity theorising (section 1.5.2), it might have been preferable to control for SES when cohort members were 7 years old as well (e.g. Keers and Pluess, 2017). However, the SES level of cohort members remained relatively stable over the duration of the BTT+ study (L. Richter, personal communication), so any further steps taken to control for variation in SES might not have substantially altered statistical outcomes.

Similar to SES, the maternal education variable was unfortunately limited in scope. As a basic six point scale, responses on which were self-reported by mothers, the maternal education variable was also a relatively weak and indirect proxy assessment of each mother's educational competence and capability. Inferring that this metric had significant effects on child-rearing and development would be tenuous, especially given the lack of other, potentially more important factors such as maternal depression, maternal caregiving skill, maternal stress, and overall family unity, *inter alia*. That SES and maternal education were measured with high levels of error, whereas birth weight, gestational age and genotype were recorded with high accuracy speaks to a commonly raised concern regarding observational studies (Bakermans-Kranenburg and van IJzendoorn, 2015). Such discrepancies in error variance pose threats to statistical accuracy by lowering power and increasing the likelihood of Type I and Type II errors (Bakermans-Kranenburg and van IJzendoorn, 2015).

Regarding other predictor variables, birth weight is normally corrected for gestational age by incorporating a measure of gestational age as a covariate in regression modelling. However, in all study models (except when predicting SPS levels), gestational age only served to worsen model fit without changing the overall interpretation of the model (data not shown). This is possibly a consequence of the modest correlation between the two variables (r = .41), which would have rendered their combined use in regression models somewhat redundant. Notably, others (Jaekel et al., 2015) have encountered similar issues when trying to correct birth weight for gestational age and other covariates (e.g. birth order).

Due to a low number of S/S homozygote individuals, heterozygous S/L and homozygous S/S individuals were coded together as one group. This approach is not generally recommended (Aliev et al., 2014) because of the loss of information inherent in dichotomising an otherwise three level genotype. It also carries the assumption that the S allele acts in a dominant, or at least codominant, manner which has yet to be clarified and thus treating S/S and S/L homozygotes as similar is dubious at best (Alexander et al., 2012; Bakermans-Kranenburg and van IJzendoorn, 2015; Bradley et al., 2005). Reanalysis using a different genetic model for the S allele (e.g. re-

cessive; additive) may have produced different results. For example, Alexander and colleagues (2012) noted inconsistencies in the literature examining the effects of the S allele on amygdala reactivity, which have hindered conclusions about whether the amygdala activation pattern is best described by a tonic or phasic model. One potential reason for these inconsistencies was that studies had used different inheritance models for the S allele, which influenced the way in which study participants were partitioned and, in turn, perceived differences in resting state amygdala activation versus elevated amygdala reactivity. Nevertheless, grouping S/S and S/L individuals together is a widely practiced strategy (e.g. Morgan et al., 2017), resulting in a consistent pattern of outcomes that supports the S allele as a marker of differential susceptibility, according to meta-analysis (van IJzendoorn et al., 2012).

Since this was a retrospective study, the selection of predictor variables was largely based on what variables, of adequate sample size, were available for the BTT cohort. Results would have been stronger if predictor selection had been premised on relevant theory, and participants were recruited based on genotype and/or pertinent environmental exposure (Caspi et al., 2010). As alluded to previously, there are likely a host of covariates (e.g. birth order, maternal parenting skill) that would have strengthened analyses had suitable measures been available. Nevertheless, the predictor variables included here are highly similar to other studies that have explored differential susceptibility (e.g. Belsky et al., 2015).

Regarding the outcome variables, several drawbacks require acknowledgement. Firstly, as with SES and maternal education, behaviour scores were caregiver-rated, and thus prone to social desirability bias (Tourangeau et al., 2009). Issues with non-replication of findings in this field of research have mostly been blamed on self-report instruments, since interview-based studies have suffered fewer non-replicated findings (Caspi et al., 2010). Secondly, externalising behaviour may have been more accurately reported because of its greater visibility compared to internalising behaviour, which manifests through more subtle and difficult to interpret non-verbal cues (Bornstein, Hahn, and Suwalsky, 2013). Lastly, as indicated above, when using the CITQ, children rated difficult almost always belong to anxious mothers. Along similar lines, anxious mothers may have overestimated their child's behaviour ratings, further skewing results. Where possible, future studies should augment subjective self-report results with other, corroborating variables (e.g. biological markers; interviews etc.).

There are a number of general limitations to gene x environment studies (and interaction studies more broadly) that apply to the present study (Munafò et al., 2014). GxE research requires significant sample sizes in order to be suitably powered (Caspi et al., 2010; Duncan and Keller, 2011). A sample size of 600 is the suggested point at which large GxE effects will be evident, thus detecting smaller effects will require proportionately larger samples (Duncan and Keller, 2011). Many previously published GxE findings have only incorporated several hundred (< 1000) participants (Munafò et al., 2014). Sample sizes in this study, although mostly above the recommended minimum of 600, were constrained by data availability - there was

no possible way to better power the statistical analysis because of the retrospective design of the study. Furthermore, in most GxE studies, both the environmental and genotype variables are skewed in distribution. As highlighted previously, the SES variable in this study was negatively skewed, rather than normally distributed. Sample sizes per genotypic category were uneven, which prompted the grouping together of categories (S carrier vs L/L homozygote; 7R present vs 7R absent) to mitigate skewing of the genotype variable (Bakermans-Kranenburg and van IJzendoorn, 2015). The main threat of these skewed distributions is that they lower statistical power, reducing the chances of detecting true GxE effects (Bakermans-Kranenburg and van IJzendoorn, 2015). This might further encourage the recruitment of larger sample sizes, but unfortunately, the larger the sample size, the more afflicted data are by poor measurement issues (Caspi et al., 2010) which would undermine any increases to power that a larger sample size may have afforded. To escape this dilemma, many have suggested a shift towards experimental, rather than observational, studies where the environment can be tightly regulated (Bakermans-Kranenburg and van IJzendoorn, 2015; Munafò et al., 2014). Experimental manipulation greatly improves study power, and may require as little as one thirteenth of the sample size needed for a similar observational study (Bakermans-Kranenburg and van IJzendoorn, 2015). However, the scope for experimental study designs is rather narrow, especially when human participants are involved, given the important ethical considerations and constraints.

To have still found evidence suggestive of environmental sensitivity (especially for 5-HTTLPR and SPS) against the backdrop of these numerous limitations is an encouraging sign. This would suggest that far clearer effects might be evident in future studies that are specifically tailored to address differential susceptibility research questions in an African setting.

5.4.9 Future directions

In addition to tighter study designs that address aforementioned limitations, future investigations should consider examining variation in the *SERT* gene in more detail. Firstly, given the irregularity of the repeat unit (20-23 bp), and the existence of single base substitution events that can differentiate otherwise identical repeat units, the VNTR architecture of the 5-HTTLPR is highly complex (see Nakamura et al., 2000). Although each S allele is comprised of 14 repeats (and each L allele, 16 repeats), the composition of repeat units can differ. Nakamura et al. (2000) found four different types of S allele, and six different types of L allele in a sample of Japanese and European-ancestry individuals. What functional differences these sequence variants have, and whether further variation is present in other ethnicities, remains to be determined. As the most ancestral and genetically diverse extant population, examination of the 5-HTTLPR sequence diversity in Africans could prove highly informative. Secondly, unaccounted for here and in other early investigations of the 5-HTTLPR (van IJzendoorn et al., 2012) was a single nucleotide polymorphism (rs25531), 5' of the promoter VNTR, that has been found to bear important functional effects (Murdoch et al., 2013). The minor G allele (ancestral allele: A)

renders the L allele functionally similar to an S allele, meaning that S/L_G and L_G/L_G genotypes are equivalent to S/S (these three genotypes are sometimes denoted together as S'/S'; Alexander et al., 2009). In other words, an L_G allele is transcribed less efficiently, producing the same number of mRNA transcripts (and subsequent serotonin transporter molecules) as a short allele (see Figure 1.2). This modified functionality of the 5-HTTLPR L allele is thought to account for much of the inconsistency marring previous research findings, inspiring more careful efforts to address this issue in more recent research (Murdoch et al., 2013). Notably, the frequency of the G allele of rs25531 is slightly higher in African populations (Hemmings et al., 2018; Murdoch et al., 2013; Odgerel, Talati, Hamilton, Levinson, and Weissman, 2013), but this SNP has rarely been been included in research on African participants (Odgerel et al., 2013). Thirdly, there exists a second VNTR in intron 2 (labelled as "STin2" in genetic terminology) of the *SERT* gene (Murdoch et al., 2013; Way and Gurbaxani, 2008). This intronic VNTR has a repeat unit size of 16-17 bp, with two common alleles of 10- (lower expression) and 12-repeats (higher expression; Murdoch et al., 2013). In turn, these two alleles may also modify the interpretation of the 5-HTTLPR alleles, with S allele + 12-repeat allele carriers having increased expression over L allele + 10-repeat carriers (Kremer et al., 2005)[3]. In a Black South African sample, the 12-repeat allele (STin2) was found to be associated with increased aggressive behaviour (Hemmings et al., 2018), which may have relevance given that anger proneness has been previously suggested as a marker of DS (Kochanska, Aksan, and Carlson, 2005). Lastly, an additional SNP just 3' of rs25531 (rs25532) also has know effects on the expression levels of *SERT*. The minor T allele lowers transporter expression compared to the more common C allele (Murdoch et al., 2013). The above are just some examples of the extensive known variation found within the *SERT* gene (Way and Gurbaxani, 2008), which is anticipated to be even higher in African populations given that linkage disequilibrium across the gene is more fragmented (Murdoch et al., 2013) compared to other ethnicities.

The *DRD4* gene is similarly complex in structure, warranting further investigation (Chang et al., 1996). The 48 bp repeat unit forming the exon III VNTR is also imperfect in sequence, with at least 19 (alpha to zeta) known variations (Chang et al., 1996). Here again, because these repeat units can be arranged in a variety of ways, the 7R allele is not necessarily equivalent in different individuals. Indeed, Chang et al. (1996) found that the 7R allele in European communities is not the same as the allele observed in African populations, and this inconsistency may be a further reason behind the unanticipated *DRD4* findings in this study. There are also several additional, but less frequently investigated functional polymorphisms that might

[3]To elaborate, when the STin2 intronic VNTR consists of only 10 repeat units, the rate of mRNA transcription for the serotonin transporter (*SERT*) gene is lower than the rate of transcription for a *SERT* gene in which the intronic VNTR has 12 repeats. This is similar to the transcription rate differences seen between S (lower expression) and L (higher expression) alleles for the 5-HTTLPR VNTR which occurs upstream of the *SERT* gene. To better determine the *overall* transcription rate of a *SERT* gene, both the upstream VNTR and the intronic VNTR need to be considered. Examined in isolation, an S allele is considered to result in *less* gene expression than an L allele, but the combination of an S allele (5-HTTLPR) and a 12-repeat allele (STin2) results in an *SERT* gene that is transcribed *more* frequently than a gene comprising an L allele combined with a 10-repeat allele (Kremer et al., 2005).

modify the effect of the receptor protein (Online Mendelian Inheritance in Man, 2012). Lastly, some researchers have dichotomised *DRD4* genotypes into categories of short (2-5 repeats) and long (6-11 repeats) alleles (e.g. Bakermans-Kranenburg and van IJzendoorn, 2015; Chen et al., 1999). Whilst this may present a different dichotomisation strategy for future studies, it was not attempted here because the functional significance of rare alleles (e.g. 3, 10 and 11-repeat) has not been clarified, and so enforcing this particular type of dichotomisation makes doubtful assumptions regarding the effect of shorter versus longer *DRD4* VNTR alleles.

To best address these complexities in genetic variation, future studies should consider more comprehensive genotyping methods such as whole genome or whole exome sequencing (Choudhury et al., 2017). The genetic literature is increasingly characterised by studies involving these next generation sequencing (NGS) methods, especially as associated costs continue to decline (Levy and Myers, 2016; Mardis, 2008; Metzker, 2010). Sequencing with high coverage and high read depth will provide a clearer picture of genotypic differences between individuals (especially of African-ancestry) and how these might associate with phenotypes such as observable behaviour. However, there are significant challenges that currently limit NGS research in Africa (**Mulder2017**). The main issue is that NGS platforms remain unaffordable for most African laboratories. Although costs are declining to more feasible levels, taking full advantage of a next-generation sequencer requires excellent infrastructure in terms of computational power, data storage and high speed network transfer - all of which are severely limited in Africa (**Mulder2017**). Nevertheless, solutions to these challenges must be urgently prioritised to reduce inequality and ensure African science is able to keep apace with international trends, including new research areas such as Environmental Sensitivity (Need and Goldstein, 2009; Ramsay, 2012; Ramsay et al., 2011).

5.4.10 Conclusion

Examining behavioural and/or developmental outcomes as a function of social-environmental context has always yielded a "noisy" array of observations (Boyce, 2015), as has been evident in the BTT+ cohort. Researchers from all disciplines have long sought to identify robust patterns of environmental influence amidst this noise, but even with the tightest study design and statistical control of covariates in place, substantive variability in outcomes persists (Boyce, 2015). The question, then, of whether a particular environmental indicator is a good predictor of a selected outcome should be superseded by the question of why there is so much variability in outcomes as a consequence of context (Boyce, 2015)? Environmental Sensitivity theory makes at least some progress into answering this question. As findings from this study seem to suggest, individual differences in neurosensitivity are an important and practical consideration (Pluess, 2015). Although several results from this study support the diathesis-stress model, given the range restriction of the SES variable, the message remains that cohort members with markers of environmental sensitivity had behavioural outcomes that were proportionate to the quality

of their context. Admittedly, studies of this nature, which are only modestly powered, cross-sectional, rely on a handful of candidate genes, and reveal small effect sizes that might prove challenging to replicate, continue to fall out of favour in the scientific literature (van IJzendoorn and Bakermans-Kranenburg, 2012). However, such exploratory studies remain the early, foundational paving stones on a much longer path (Belsky et al., 2015; Belsky and Pluess, 2013a); a path which is still in its early phase of construction on the African continent.

Chapter 6

General Discussion

Total knowledge is annihilation
Of the desire to see, to touch, to feel
The world sensed only through senses
And immune to the knowledge without feeling.
- Dejan Stojanovic

6.1 Overview

The final chapter of this thesis serves two functions. Firstly, results of the multi-phase doctoral study are considered as a whole and various implications and future directions are discussed. Secondly, with results already discussed in detail per study, this chapter offers an opportunity to revisit and further explore the literature at large and summarise the current status of, and remaining gaps in SPS and environmental sensitivity research.

6.2 Summary discussion

This doctoral research has sought to provide a robust initial examination of sensory processing sensitivity (SPS) and its possible relevance to the South African context. The project entailed four different studies - a brief pilot study (Study 1); an in-depth psychometric assessment of the HSPS (Study 2); investigation of the association between highly sensitive students and adjustment to university life (Study 3); and an exploration of SPS and other markers of neurosensitivity as predictors of childhood behavioural outcomes in South Africa's largest longitudinal cohort (Study 4). On balance, these studies have augmented and further contributed to the

existing knowledge-base regarding Environmental Sensitivity (ES).

Across all studies, the HSPS performed with high levels of reliability (albeit with some language and phrasing hurdles - Study 1) and appeared to meaningfully partition participants by their neurosensitivity levels. Although a unique five factor solution was encountered following factor analysis (Study 2), arguably, the solution aligned better with SPS theory than previously published factor structures, augmenting speculation that examination of the instrument in culturally diverse samples would prove informative (Pluess et al., 2018; Şengül-İnal and Sümer, 2017). Latent class analysis results (Study 2 and 4) continued to identify three broad categories of neurosensitivity (dandelions, tulips and orchids). Zero-order correlations between SPS and the five-factor model of personality (Study 3) were all in agreement with a recent meta-analysis (Lionetti et al., 2019). Taken together, these findings suggest the HSPS, in its current form, is a robust instrument that remains sufficiently reliable and valid across diverse samples of respondents. Given the convenient brevity of the HSPS, its consistent performance in culturally diverse samples, and its ease of administration, the instrument certainly deserves more consideration as a research tool in South Africa.

Behavioural outcomes for highly sensitive persons were examined in Studies 3 and 4. In both studies, individuals with high SPS demonstrated poorer outcomes - either more difficulty in adjusting to university (Study 3) or more childhood behavioural problems (Study 4). Although these results importantly acknowledge the vulnerabilities of HSPs, and further motivate for the use of the HSPS as a means of identifying at-risk individuals, it is important to recall that negative outcomes seem driven only by select facets of the SPS trait (Study 3), particularly neural sensitivity and predisposition towards negative affect. The problem-focused nature of research (Belsky and Pluess, 2009b) draws attention towards these inherent weaknesses of HS persons (for practical reasons), but the counterbalancing strengths deserve equal recognition. HSPs are careful processors of the environment, which appeared to serve them well in the process of university adjustment (Study 3). Their aesthetic sensitivity has also been linked to positive outcomes (Bridges and Schendan, 2019; Evers et al., 2008; Liss et al., 2008), and HSPs are known to demonstrate high levels of interpersonal empathy and sensitivity (Acevedo et al., 2018). These features may endow HSPs with the ability to form closer friendships, identify appropriate romantic partners and more thoughtfully rear children - all of which further gene dispersal (Acevedo et al., 2018). Indeed, given the right amount of nurturing, HSPs may become notably gifted members of society (Lo, 2018; Mendaglio, 2003). Such issues were not explored in the course of this doctoral study, but should be prioritised agenda items for future research.

What differed between HS persons in Studies 3 and 4 was their response to the chosen environmental moderator. In Study 3, HS students were unexpectedly resilient towards the level of parental care they had received. Rather, it was non-sensitive students whose university adjustment improved with more nurturant parenting. In contrast, highly sensitive BTT+ cohort members were malleable to their early socioeconomic status in a manner anticipated by

diathesis stress (and potentially differential susceptibility) reasoning (i.e. improved outcomes with improving SES). These contrasting results speak to an existing uncertainty expressed in the literature, specifically, whether SPS (and human sensitivity more generally) manifests in a domain-general or domain-specific fashion (Belsky and Pluess, 2009c, 2013a; Pluess and Belsky, 2010, section 1.6). Evolutionary reasoning (Aron et al., 2012) and simulation modelling (Wolf et al., 2008) suggest that plasticity is domain-general, meaning that plastic individuals demonstrate malleability to all environmental influence. If environmental sensitivity is indeed an example of developmental plasticity (rather than activational plasticity; Section 1.2), then it should be set early in life and afford a wide array of non-specific sensitivities across the life course. That SPS (at age 28) evinced meaningful relationships to birth weight and gestational age (Study 4) is pertinent here, supporting acknowledgement of SPS as a trait-based construct (developmental plasticity), rather than a state-based, context dependent feature (activational plasticity). However, the varied but inconsistent findings of current environmental sensitivity research (which mostly examines a single domain at a time) undermine this supposition, keeping open the possibility that sensitivity sometimes operates under the influence of specific or situational environmental factors, that might differ from person to person (i.e. possibly more akin to activational plasticity). In other words, perhaps only a subset of plastic individuals are sensitive to parenting, whilst others are more heavily swayed by peers (for example; Belsky and Pluess, 2013a), or put conversely, plastic individuals might demonstrate resilience to selected components of their milieu, but not others. The findings of this doctoral research seem to have further highlighted this dilemma. Whether such inconsistencies are the result of various study limitations and single domain designs or reflect genuine domain-specific sensitivities requires substantially more research.

In Study 4, interaction effects were clearest (i.e. closest to statistical significance) for SPS compared to other sensitivity markers, despite the 21+ year difference between measurements of the predictor (SPS), outcome (childhood behaviour) and environmental moderator (SES). This finding may support current acknowledgement of SPS as the most proximal indicator of neurosensitivity levels (Pluess et al., 2018). Findings, to date, for temperament, reactive physiology and genetic variation (especially the 5-HTTLPR S allele) in an ES framework have been persuasive (section 1.5.2), but these markers are still distal proxies of complex neurosensitivity (Pluess et al., 2018). With its much shorter research history, SPS (and the HSPS) has enjoyed far less attention than temperament, physiology and GxE effects, but there exists clear potential that SPS will afford more accurate insights if it is included as a phenotype in future biopsychosocial research.

Regarding other markers of sensitivity, findings in Study 4 for the 5-HTTLPR S allele were the most consistent with previous literature. Following early issues with non-replication (Risch et al., 2009), the effects of the S allele and its interactions with the environment are now understood in more robust terms. Instead of exclusively serving to heighten vulnerability to adversity, the S allele mediates the influence of environment on behaviour (Homberg and Lesch, 2011;

Homberg et al., 2016; Way and Taylor, 2010a). Accordingly, amongst BTT+ members, the allele was a significant risk factor for internalising behavioural issues, and showed sensitivity to low SES in a diathesis-stress manner. However, as SES improved, behavioural issues for S allele carriers decreased which may have eventually resulted in a differential susceptibility effect had the SES variable not been so narrow in scope, or if other functionally important variation in the 5-HTTLPR and *SERT* gene had been accounted for. Given the apparent ethnic differences in the serotonergic system (Williams et al., 2003), and the fact that the S allele seems to offer more pronounced DS effects in Caucasians than non-Caucasians (van IJzendoorn et al., 2012), much more research into this locus in African individuals is warranted.

Less consistent with the previous literature were findings for temperament, *DRD4* and birth weight. Difficult temperament BTT+ infants did have more problematic behaviour compared to non-difficult infants, but there was no convincing evidence of diathesis-stress or differential susceptibility effects. However, this might have been due to various study limitations, rather than the absence of true effects, and so temperament deserves continued investigation in future ES research. Results for both *DRD4* and birth weight resembled crossover interactions, but instead of improved behaviour with improving contextual quality, 7R carriers and LBW infants scored higher on behavioural problems as SES increased. Several speculations for these findings were previously offered, but some additional considerations warrant mention.

Firstly, as alluded to earlier, highly reactive/sensitive phenotypes typically develop in contexts of both unusually stressful and unusually supportive environments, creating a U-shaped curve (Boyce, 2015) that has been confirmed in a number of investigations (Ellis, Essex, and Boyce, 2005; Engert et al., 2010; Gunnar, Frenn, Wewerka, and Van Ryzin, 2009; Lorber, Erlanger, and Slep, 2013; Seery, Holman, and Silver, 2010). Linear modelling with environmental variables that are skewed or otherwise restricted in range may miss these curvilinear trends, producing spurious results that only add background noise to an otherwise clear parabolic relationship (Li, 2018). Investigation of the models in this doctoral study using LOESS curves (e.g. Study 3 and diagnostic plots in Appendix) did reveal slight tendencies toward U-shaped distributions of behavioural outcomes in relation to the sensitivity marker x environmental moderator term. However, either the fitted linear models still amply overlapped LOESS curves, or the addition of second-order terms did not noticeably improve model fit. Nevertheless, findings for *DRD4* and birth weight in Study 4 might serve to highlight the pitfalls of applying linear models to a curvilinear relationship (Li, 2018) between neurosensitivity and environment. In studies with a broader environmental variable, curvilinear relationships will be important to consider.

Secondly, dichotomisation of study samples by ES markers (birth weight, genotype, SPS, temperament) was a central strategy in this doctoral study, and afforded insights that were not apparent when markers were left as continuous variables. Nevertheless, converting a continuously distributed phenotype into discrete categories has notable drawbacks (Aliev et al., 2014).

The primary issue is that highly similar individuals, clustered around the reference point for dichotomising a variable (e.g. 2.5 kg for separating low and normal birth weight infants), are suddenly treated as being categorically different. Another issue is that the sample size per category can be small and/or unbalanced. These issues are problematic for statistical testing, and can result in erroneous findings. However, dichotomisation directs the emphasis towards extreme examples of the spectrum, which can better power the discovery of individual differences. Nonetheless, it remains important to acknowledge that individual neurosensitivity itself is a continuum (Belsky and van IJzendoorn, 2017), with categorical labels of "fixed", "plastic", "orchid", "tulip" and "dandelion" used only as convenient shorthand to broadly class individuals.

A third explanation for the inconsistent findings seen in this set of doctoral studies lies in the potential shortfalls of SPS and ES theorising, to which attention now turns.

6.3 Critiques of SPS and Environmental Sensitivity

Heretofore, study limitations have been primarily blamed for weakly, or non-significant, findings, along with those that did not agree with trends in the extant literature (Studies 3 and 4 in particular). Unaddressed has been the possibility that such findings falsify (or otherwise weaken) the claims made by SPS, and the larger ES metaframework. This oversight is mostly attributed to the current paucity of critiques against these theories, which are still relatively young by research standards. However, this can be a problem in and of itself, warranting scepticism for a number of reasons. Here, these issues are acknowledged and discussed in more detail.

SPS theory arose from a need to address the previously muddled and poorly emphasised role of individual differences in human nervous system functioning (section 1.3.4, Aron, 2004). Recall that this historical confusion dates back over 100 years, to the time of Jung and Freud (Aron, 2004; Aron and Aron, 1997, section 1.3.1). In a comparatively shorter 22 year history, SPS has not yet been subject to rigorous assessment and review. A Scopus (https://www.scopus.com/) search revealed that Aron and Aron's (1997) initial article had been cited 247 times by October 2019. To the best of the author's knowledge, not one of these citations stemmed from an article or book chapter devoted to a critical appraisal of SPS theory. Rather, these subsequent citations have mostly spoken to two major issues. The first is the HSP Scale and its inconsistent psychometric findings, as discussed in Chapter 3. Although the scale continues to perform adequately, there are plans to develop a new or revised instrument that takes heed of contemporaneous research findings (M. Pluess, personal communication). The second issue is the confusing similarity between SPS and sensory-related issues in the field of occupational therapy (section 1.4.2.6). This problem has yet to be directly tackled (Greven et al., 2019), but may never be fully resolved given the broad scope of the term "sensitive". Similarly, the article

to first assemble the ES metaframework (Pluess, 2015) had been cited 79 times by October 2019 according to a Scopus search. None of these citations appeared to directly challenge the viability of the framework. Thus, since SPS and ES are, themselves, recent critiques against long standing research traditions (e.g. diathesis-stress theorising; bias towards adverse environments; overemphasis on observable behaviour at the expense of cognitive mechanisms; bias towards negative/pathological outcomes), there seems to have been insufficient time and/or evidence, thus far, to meaningfully contend SPS/ES theory.

However, as a consequence of its relative youth, there are two major criticisms that can be levelled against ES theorising. Firstly, the theory is currently promoted and advanced by just a handful of researchers, who frequently cross-reference each other in their various publications. This practice could unfairly inflate the apparent validity of the ES framework, at least until a more diverse set of research groups publish ES studies. Secondly, although popularity and scope for SPS/ES are rapidly expanding (see below, section 6.4), this can not yet be construed as support for theoretical validity, and might actually imply a high level of questionable findings instead. Ioannidis (2005) goes so far as to argue that most published research findings are incorrect. The probability of erroneous findings is, he claims, particularly high for "hot" topics (Ioannidis, 2005). Based on Scopus citation metrics, ES belongs to a topic of research with a prominence percentile score of 84 (October 2019), suggesting that the topic currently enjoys a high degree of research momentum and popularity. Moreover, the citation benchmark of the Pluess (2015) article is in the 99th percentile compared to other developmental psychology articles. But these promising metrics might only confirm that ES research findings, to date, are largely driven by short-sighted popularity rather than high scientific rigour, and thus should be treated with appropriate caution. Indeed, much of ES theorising was advanced on the basis of statistical practices that have subsequently needed substantial revision and improvement (Roisman et al., 2012; Widaman et al., 2012).

A rarely acknowledged, but potentially concerning critique of ES is its lack of falsifiability (Bakermans-Kranenburg and van IJzendoorn, 2015). The underpinning motivation behind the differential susceptibility hypothesis (Belsky et al., 1991) was to provide a counterpoint to the diathesis-stress model (Figure 1.1; Figure 1.5). However, the combination of these two models now covers such a wide spectrum of developmental outcomes that almost no room remains for alternative explanations. Wherever differential susceptibility modelling fails, a case of diathesis-stress is proclaimed instead and vice versa (e.g. Beaver, Hartman, and Belsky, 2015). Belsky, Pluess, and Widaman (2013) even provide a set of four reparameterised regression equations that afford the identification of strong versus weak differential susceptibility and strong versus weak diathesis-stress effects. Thus, a statistical model is available for nearly every developmental scenario, further protecting ES theorising from critical scrutiny. Indeed, this watertight defense may explain the currently conspicuous lack of critiques against ES. With minimal scope for falsification, ES runs the risk of becoming unscientific (Bakermans-Kranenburg and van IJzendoorn, 2015). That is, there might be no appropriate study design

that can ever prove ES false, which many consider to be an important prerequisite for scientific inquiry (Popper, 1979). If replicated elsewhere, some of the findings from this doctoral research (e.g. the limited effect of parental quality on HS students, the worsening behaviour of 7R allele carriers with improving SES) may place some needed strain on the ES framework. Ultimately, additional investigations are required that turn a more critical lens on ES theory and research. A wealth of unanswered questions remain, a number of which are explored in the proceeding section.

6.4 Unanswered questions and future directions

As a mostly exploratory investigation, this doctoral study sought to scrutinise existing knowledge on SPS and ES using a novel setting, rather than trying to meaningfully expand on these concepts. Further development of this field of research will require inventive studies that can enhance our understanding of human sensitivity. Notably, the popularity of SPS/ES amongst the media and public has grown exponentially since the release of Elaine Aron's first book on the topic (Aron, 1999). A range of other authors have contributed books of their own (e.g. Boyce, 2019; Lo, 2018; Sand, 2016; Zeff, 2004), two films have been made (Sensitive the Movie, 2015), dedicated conferences have been planned (HSP World, 2019) and numerous support programmes and training courses are now on offer. Even within the scientific community, SPS is being referenced in increasingly diverse contexts like epidemiology (Goldberg et al., 2018), anthropology (Rappaport and Corbally, 2018) and business (Harms, Hatak, and Chang, 2019). However, biological research (both basic and applied) aimed at understanding the mechanisms of SPS (and even environmental sensitivity more broadly) is still in its infancy (Greven et al., 2019). Moving forward, to avoid potential misinterpretations and misinformation, it will be important for scientific research on SPS and ES to keep apace with public interest (Greven et al., 2019).

An early priority on the research agenda is improving knowledge of the mechanistic coupling between different layers at which sensitivity operates (genome, epigenome, physiology, personality, cognition, and behaviour etc.; Boyce, 2015; Greven et al., 2019). Rodent (mouse/rat) models are providing some clues in this regard, given that 5-HTT knockout rodents (rodents whose serotonin transporter gene has been removed) have behavioural parallels to people with high levels of SPS (Greven et al., 2019; Homberg et al., 2016). Interestingly, these 5-HTT knockout rodents have slower neuronal maturation because of reduced expression of a potassium chloride co-transporter protein (known as KCC2; Miceli et al., 2017). This neuronal immaturity is speculated to increase the plasticity of the rodents (Castreń, 2013), possibly explaining why they also display outcomes in agreement with differential susceptibility (Kästner et al., 2015). If this speculation proves correct, a potential link between genotype, neuronal physiology and subsequent behaviour will have been outlined, which could then be further ex-

plored in humans.

Another point of interest is what exactly affords the reversal in outcomes as a function of the environment for neurosensitive individuals (Alexander et al., 2009; Way and Gurbaxani, 2008). One possibility resides in attentional processes. Fox and colleagues (2011) found that S allele carriers were more heavily biased towards both negative and positive emotional stimuli during a laboratory procedure. Similarly, Beevers, Ellis, Wells, and McGeary (2010) found that S allele homozygotes were more likely to direct their focus towards positive stimuli when presented with a collage of emotionally evocative images. The authors postulate that this behaviour may manifest from a concerted effort to avoid negative images, and thus recommend future research on how S allele attentional biases manifest under different cognitive loads. When stressed and overwhelmed, S allele carriers may struggle to prioritise positive stimuli over negative, explaining a propensity for poor outcomes in poor conditions and vice versa. In contrast, L allele homozygotes did not demonstrate a bias towards images of a particular valence. These sorts of attentional biases are similarly characteristic of HSPs as well, suggesting that social and environmental context ultimately determines which attentional bias is strengthened in neurosensitive individuals. A second possibility resides in the stress response system (Albert, Belsky, Crowley, Bates, et al., 2015; Tafet and Nemeroff, 2016). There are well known links between stress and plasticity markers like temperament, SPS and genotype which have been previously described (sections 1.5.1.3.1, 1.5.3). Indeed, the stress response system (specifically the HPA axis) seems to be the central endophenotype that connects all of the currently documented sensitivity markers. After SPS, stress response markers might serve as particularly accurate makers of neurosensitivity. Moreover, the differential stress response of neurosensitive individuals to supportive and adversive contexts may help to explain their for better and for worse outcomes.

Further investigations at the genotypic level will also be beneficial. Firstly, future studies should aim for a more comprehensive polygenic risk/susceptibility score (Belsky, Moffitt, and Caspi, 2013). Where genetic susceptibility has been tallied across multiple loci, far clearer GxE effects have been detected (Boyce, 2015) than when studies have relied on just a single genetic proxy. Secondly, epigenetic research may be particularly insightful (Alexander et al., 2014). Epigenetic mechanisms are at the interface between genetic and environmental interactions. Consequently, epigenetic marks can serve as signatures of environmental context. Because such marks are heritable, they form a sort of cellular/organismic memory that can help prepare future generations for environmental challenges. As a promising example, Beach et al., (2014) found that the 5-HTTLPR S allele and levels of socioeconomic adversity interacted to predict promoter methylation in over 200 genes linked to depression. Specifically, disadvantaged African American youths carrying an S allele had both the highest and lowest levels of promoter methylation in proportion to poverty-related stress levels. Teh and colleagues (2014) examined regions of variable methylation within the genomes of neonates. Genotype alone only accounted for 25% of the variance within these regions, but adding prenatal environmental and other factors (maternal smoking, depression, body mass index and infant birth weight,

gestational age and birth order) improved the amount of variance accounted for to 75%. Essex et al. (2013) found methylation differences in 15 year old adolescents that correlated with parent-reported environmental adversity during their child's infant and pre-school years. Differential methylation profiles have also helped explain PTSD susceptibility and resilience (Boyce, 2015; Sipahi et al., 2014). Lastly, Alexander et al. (2014) found that the 5-HTTLPR genotype and *SLC6A4* gene methylation status significantly interacted to predict cortisol stress reactivity. On average, it has been noted that S alleles are more methylated than L alleles (Homberg and Lesch, 2011), but a highly methylated L allele might be more functionally similar to an S allele (van IJzendoorn, Caspers, Bakermans-Kranenburg, Beach, and Philibert, 2010).

Epigenetic changes should not only be studied in relation to social, economic and emotional stressors, but also to the physical environment (Boyce, 2015). Methylation of DNA is readily altered by pollutants and toxins which might discourage environmental sensitivity, especially during early development. Olden, Lin, Gruber, and Sonawane (2014) note that epigenetic changes over time, as a consequence of chemical and non-chemical stressors, could potentially establish health disparities and differential susceptibility to disease. With this in mind, studying previously disadvantaged communities and informal townships like Soweto is of even greater importance, given not only the social and economic stressors, but also the potentially disproportionate exposure to harmful pollutants and toxins (Boyce, 2015; Kristensen and Olsen, 2006). Together, the above findings suggest that environmental experience (especially adversity and trauma) can leave residues on genetic-makeup. Such modifications could ultimately constrain or facilitate heightened neurosensitivity (i.e they "calibrate" the final level of neurosensitivity), particularly early in fetal development.

Perhaps the most promising avenue for future research lies in gene x intervention (GxI) studies (Albert, Belsky, Crowley, Latendresse, et al., 2015; Belsky, Moffitt, and Caspi, 2013; Belsky and van IJzendoorn, 2015). An unfortunate majority of psychosocial interventions have battled to obtain effect sizes larger than $d = .20$ (Albert, Belsky, Crowley, Latendresse, et al., 2015; Belsky and van IJzendoorn, 2015). Due to the controlled, experimental manipulation of GxI studies, they require one thirteenth of the sample size of observational GxE studies to achieve the same power, and are less prone to an omitted variable bias (Albert, Belsky, Crowley, Bates, et al., 2015; Bakermans-Kranenburg and van IJzendoorn, 2015; Belsky, Moffitt, and Caspi, 2013; Belsky and van IJzendoorn, 2017). For example, recall the earlier discussion (section 5.4.7) on the the study by Morgan et al. (2017) that demonstrated the improved effects of a mother-infant attachment intervention on S allele carriers, but not L allele homozygotes. Similarly, in a 2015 study, Cicchetti and associates (Cicchetti, Toth, and Handley, 2015) found that African American women with a particular plasticity-increasing haplotype (a set of linked genetic markers, on the same chromosomal segment, that are often inherited together from a single parent) had the most symptoms of depression in the absence of intervention, but the lowest levels of depression when part of an intervention group undergoing interpersonal psychotherapy. Such findings are part of a larger field of research known as therapy genetics (Andersson et al., 2013), which has

also found differential effects of cognitive behavioural therapy based on 5-HTTLPR genotype (Andersson et al., 2013; Eley et al., 2012; Eley et al., 2004). Albert and colleagues (2015) found that carriers (both children and adults) of an A allele (rs10482672) in *NR3C1* (the gene encoding the glucocorticoid receptor, which plays a prominent role in physiological reactivity) had the lowest levels of externalising behaviour if assigned to the intervention arm of the Fast Track program, but the highest levels when part of the control arm (Albert, Belsky, Crowley, Bates, et al., 2015; Albert, Belsky, Crowley, Latendresse, et al., 2015).

The drawback to GxI studies is that they stratify participants on the grounds of genetic differences, which at a public policy level is fraught with ethical concerns (Albert, Belsky, Crowley, Bates, et al., 2015; Albert, Belsky, Crowley, Latendresse, et al., 2015; Belsky and van IJzendoorn, 2015). Genetic differences can become the the source of stigma and discrimination (Belsky and van IJzendoorn, 2015), especially when such differences are mistakenly considered as deterministic without fuller appreciation for the complexity of gene x gene and gene x environment interactions (Albert, Belsky, Crowley, Latendresse, et al., 2015). Past GxI studies have relied on only one or a handful of genetic markers to tenuously infer neurosensitivity, which is surely a far more extensively complex and polygenic trait (Albert, Belsky, Crowley, Latendresse, et al., 2015). Whilst more markers could provide more accuracy, comprehensive genotyping efforts come attached with greater costs, which may be unwanted in large-scale interventions. Other neurosensitivity markers, like physiological markers (e.g. cortisol) and SPS, provide inexpensive alternatives to delineate levels of sensitivity, and thus their value in intervention research also needs further exploration. Early findings in this regard have shown great promise - recall the anti-bullying intervention studied by Nocentini and associates (2018) that was only of significant effect for highly sensitive children. Likewise, Pluess and Boniwell (2015) found that, amongst girls attending a disadvantaged school in London, those with high levels of SPS showed substantively decreased levels of depression that were still evident 6-12 months after a depression-based intervention, but no noticeable change in girls low on SPS. The advantage of physiological and psychological markers of neurosensitivity is that they might be more socially acceptable than genetic ones, overcoming at least one drawback of GxI studies.

Regardless of the neurosensitivity marker used, knowledge of the differential susceptibility of individuals toward intervention still raises an ethically difficult question - should interventions only be targeted towards those who will most likely benefit (i.e. neurosensitive, orchid individuals)? On one hand, targeting interventions in this manner would greatly improve efficacy and cost-effectiveness (Belsky and van IJzendoorn, 2015), which are highly desirable properties especially in low resource settings. On the other hand, passing judgement on an individual's appropriateness for intervention based on their neurosensitivity creates worrisome problems for equity of access (Belsky and van IJzendoorn, 2015). A possible compromise might be to use the knowledge of ES theory to identify neurosensitive intervention participants who could then be offered more intensive, or prolonged intervention efforts than would be necessary for more fixed/resilient participants. In this way, neurosensitivity classifications are not

used to exclude anyone from intervention, but to better structure how the intervention is offered. However, others (Albert, Belsky, Crowley, Bates, et al., 2015) have wondered if it might be best to restrict the use of differential susceptibility to informing theories on childhood development (Albert, Belsky, Crowley, Bates, et al., 2015), rather than intervention. Although an uncomfortable dilemma, policy makers will need to grapple with these issues especially given the movement of modern medicine towards personalised therapies and treatments that account for individual differences in genetics, environment and lifestyle (i.e. precision medicine; Ashley, 2016; Collins and Varmus, 2015).

Lastly, to what extent can plasticity be "hard-wired" and/or "programmable"? Is a sufficiently persuasive genetic predisposition enough to force an individual toward one or other sensitivity strategy (fixed or plastic)? Just how much power can environmental factors exert in altering the course of neurosensitivity? Although hypotheses have been offered (Pluess and Belsky, 2011), these are particularly complex questions that will require extensive multidisciplinary investigations.

6.5 Conclusion

The importance of sensory processing and sensitivity in humans has, until recently, not been appreciated because of the confusion that abounds personality research (Murphy and Davidshofer, 2005; Revelle, 1995). Understandably, historical research has been negatively biased and parochial, placing emphasis on only observable characteristics (e.g. sociability; Aron and Aron, 1997; Revelle, 1995) and their relationship to maladaption and ill-health. But with the aid of improving technology and study design, focus is shifting towards less observable cognitive, neurochemical, physiological and genetic characteristics. What is increasingly apparent from this attentional shift, as supported by this doctoral study, is that sensitivity and insensitivity to environmental context is a fundamental categorisation of organismic behaviour (Aron et al., 2012; Boyce, 2015), evidence for which can be found across biological layers (pheno-, endopheno- and genotype) and species, throughout evolutionary time (Wolf et al., 2008). Currently at the forefront of neurosensitivity research is the personality trait of sensory processing sensitivity (Greven et al., 2019). Already supported by evidence from numerous disciplines, including psychology, genetics and neuroimaging, this doctoral research has taken further steps in supporting the cross-cultural applicability of SPS and the HSPS.

As Boyce (2015) argues, *"[r]ecognition and protection of the most vulnerable and sensitive children result[s] in greater protection for all"*. Much like African individuals outline all possible human genetic variation (Ramsay et al., 2011), plastic individuals help to outline the extremes of various health and behavioural spectra. A greater appreciation of their biological functioning will provide insights that are beneficial to all individuals across these spectra. Continued examination of SPS and the wider Environmental Sensitivity theory will, therefore, be

of critical importance for the African context. SPS theory, and the HSPS, show tremendous potential for research, clinical and other practical applications - a potential that should continue to be explored with high priority.

Chapter 7

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Appendix A

Ethics clearance

Research Office

HUMAN RESEARCH ETHICS COMMITTEE (NON-MEDICAL)
R14/49 May

CLEARANCE CERTIFICATE	**PROTOCOL NUMBER: H15/08/30**
PROJECT TITLE	Sensory processing sensitivity revaluated in a South African context
INVESTIGATOR(S)	Mr A May
SCHOOL/DEPARTMENT	Human and Community Development/
DATE CONSIDERED	21 August 2015
DECISION OF THE COMMITTEE	Approved unconditionally
EXPIRY DATE	02 September 2018

DATE 03 September 2015 **CHAIRPERSON** _____
(Professor J Knight)

cc: Supervisor : Dr M Pitman

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10005, 10th Floor, Senate House, University.

I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to completion of a yearly progress report.**

_____ _____/_____/_____
Signature **Date**

PLEASE QUOTE THE PROTOCOL NUMBER ON ALL ENQUIRIES

Research Office

HUMAN RESEARCH ETHICS COMMITTEE (NON-MEDICAL)
R14/49 May

CLEARANCE CERTIFICATE	**PROTOCOL NUMBER: H16/05/34**
PROJECT TITLE	Exploring the psychology and genetics of sensory processing sensitivity in multicultural South Africa
INVESTIGATOR(S)	Mr A May
SCHOOL/DEPARTMENT	Human and Community Development/
DATE CONSIDERED	20 May 2016
DECISION OF THE COMMITTEE	Approved unconditionally
EXPIRY DATE	29 July 2019

DATE 30 July 2016 **CHAIRPERSON** J. Knight
(Professor J Knight)

cc: Supervisor : Dr M Pitman

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10005, 10th Floor, Senate House, University.

I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to completion of a yearly progress report.**

_____ _____/_____/_____
Signature **Date**

PLEASE QUOTE THE PROTOCOL NUMBER ON ALL ENQUIRIES

R14/49 Mr Andrew May

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M160232

NAME: (Principal Investigator)	Mr Andrew May
DEPARTMENT:	Human Genetics National Health Laboratory Services
PROJECT TITLE:	Exploring the Genetics and Psychology of Sensory Processing Sensitivity in Multicultural South Africa
DATE CONSIDERED:	26/02/2016
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr Michael Pitman and Dr Zane Lombard
APPROVED BY:	Professor P. Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL:	13/07/2016

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary in Room 10004,10th floor, Senate House/2nd floor, Phillip Tobias Building, Parktown, University of the Witwatersrand. I/We fully understand the the conditions under which I am/we are authorised to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated,from the research protocol as approved, I/we undertake to resubmit to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. in this case, the study was initially review in February and will therefore be due in the month February each year.

Principal Investigator Signature Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

27 February 2017

Mr Andrew May
Medical Scientist
Division of Human Genetics
Faculty of Health Sciences
University of the Witwatersrand
National Health Laboratory Service

Sent by email to: andrew.may@nhls.ac.za

Dear Mr May

Re: **Protocol Ref No: M160232**
Protocol Title: Exploring the Genetics and Psychology of Sensory Processing Sensitivity in Multicultural South Africa
Principal Investigator: Mr Andrew May
Protocol Amendments

- **Administration of HPS to Members of the Twenty Cohort**
- **Access to Historical Birth to Twenty Data**
- **Genotyping of Cohort Members at the *5-HTTLPR* and *DRD4 Loci***

This letter serves to confirm that the Chairman of the Human Research Ethics Committee (Medical) has approved the protocol amendments for the abovementioned protocol, as detailed in your letter dated 03 November 2016.

The following documents were received:

- Summary Letter 03 November 2016.
- Permission Letter 05 February 2017.

Thank you for keeping us informed and updated.

Yours Sincerely,

L.moeng

Mr Lebohang Moeng
Administrative Officer
Human Research Ethics Committee (Medical)

UNIVERSITY OF THE WITWATERSRAND
OFFICE OF THE DEPUTY VICE CHANCELLOR RESEARCH
27 FEB 2017
RESEARCH OFFICE HREC (Medical)
JOHANNESBURG

Research Office Secretariat: Faculty of Health Sciences, Phillip Tobias Building, 3rd Floor, Office 302, Corner York Road and 29 Princess of Wales Terrace, Parktown, 2193 Private Bag 3, Wits 2050 I **T**+27 (0)11-717-1234/2656/2700/1252 **E**: Lebo.Moeng@wits.ac.za I **Office E** HREC-Medical.ResearchOffice@wits.ac.za IWebsite: www.wits.ac.za/research/about-our-research/ethics-and-research-integrity/

Appendix B

The Highly Sensitive Person Scale

QUESTIONNAIRE (HSP Scale)

INSTRUCTIONS: This questionnaire is completely anonymous and confidential. Answer each question according to the way you personally feel, using the following scale:

1	2	3	4	5	6	7
Not at All			**Moderately**			**Extremely**

____ 1. Are you easily overwhelmed by strong sensory input?

____ 2. Do you seem to be aware of subtleties in your environment?

____ 3. Do other people's moods affect you?

____ 4. Do you tend to be more sensitive to pain?

____ 5. Do you find yourself needing to withdraw during busy days, into bed or into a darkened room or any place where you can have some privacy and relief from stimulation?

____ 6. Are you particularly sensitive to the effects of caffeine?

____ 7. Are you easily overwhelmed by things like bright lights, strong smells, coarse fabrics, or sirens close by?

____ 8. Do you have a rich, complex inner life?

____ 9. Are you made uncomfortable by loud noises?

___ 10. Are you deeply moved by the arts or music?

___ 11. Does your nervous system sometimes feel so frazzled that you just have to go off by yourself?

___ 12. Are you conscientious?

___ 13. Do you startle easily?

___ 14. Do you get rattled when you have a lot to do in a short amount of time?

___ 15. When people are uncomfortable in a physical environment do you tend to know what needs to be done to make it more comfortable (like changing the lighting or the seating)?

___ 16. Are you annoyed when people try to get you to do too many things at once?

___ 17. Do you try hard to avoid making mistakes or forgetting things?

___ 18. Do you make a point to avoid violent movies and TV shows?

___ 19. Do you become unpleasantly aroused when a lot is going on around you?

___ 20. Does being very hungry create a strong reaction in you, disrupting your concentration or mood?

___ 21. Do changes in your life shake you up?

___ 22. Do you notice and enjoy delicate or fine scents, tastes, sounds, works of art?

___ 23. Do you find it unpleasant to have a lot going on at once?

___ 24. Do you make it a high priority to arrange your life to avoid upsetting or overwhelming situations?

___ 25. Are you bothered by intense stimuli, like loud noises or chaotic scenes?

___ 26. When you must compete or be observed while performing a task, do you become so nervous or shaky that you do much worse than you would otherwise?

___ 27. When you were a child, did parents or teachers seem to see you as sensitive or shy?

HSP Scale © 1997 E. Aron (For additional information see Aron & Aron, *JPSP*, 1997 or email aron@ic.sunysb.edu)

Appendix C

Study instruments

Below, the study instruments used in this doctoral research are reproduced in their original format in the following order:

1. The Parental Bonding Instrument
2. The Measure of Parental Style
3. The Student Adaptation to College Questionnaire - Modified
4. The Big Five Inventory
5. The Resistance to Peer Influence Scale
6. The South African Child Assessment Schedule
7. Carey Infant Temperament Questionnaire items used in the BTT+ cohort study

PARENTAL BONDING INSTRUMENT (PBI)



Authors
Gordon Parker, Hilary Tupling and L.B. Brown

Variables measured
Two scales termed 'care' and 'overprotection' or 'control', measure fundamental parental styles as perceived by the child. The measure is 'retrospective', meaning that adults (over 16 years) complete the measure for how they remember their parents during their first 16 years. The measure is to be completed for both mothers and fathers separately. There are 25 item questions, including 12 'care' items and 13 'overprotection' items.

Scoring instructions
Unlike the Intimate Bond Measure (IBM), not all items are scored in the same direction.

Care	
Items: 1, 5, 6, 11, 12, 17:	Very like = 3 Moderately like = 2 Moderately unlike = 1 Very unlike = 0
Items: 2, 4, 14, 16, 18, 24	Very unlike = 3 Moderately unlike = 2 Moderately like = 1 Very like = 0
Overprotection	
Items: 8, 9, 10, 13, 19, 20, 23	Very like = 3 Moderately like = 2 Moderately unlike = 1 Very unlike = 0
Items: 3, 7, 15, 21, 22, 25	Very unlike = 3 Moderately unlike = 2 Moderately like = 1 Very like = 0

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Parental bonding quadrants In addition to generating care and protection scores for each scale, parents can be effectively "assigned" to one of four quadrants:	
"affectionate constraint" = high care and high protection	"affectionless control" = high protection and low care
"optimal parenting" = high care and low protection	"neglectful parenting" = low care and low protection
Assignment to "high" or "low" categories is based on the following cut-off scores:	
• For **mothers**, a *care* score of 27.0 and a *protection* score of 13.5. • For **fathers**, a *care* score of 24.0 and a *protection* score of 12.5.	

Populations measured
Original data [1] were generated from 150 subjects including students and nurses and 500 general practice attenders. Numerous other populations have been studied subsequently.

Reliability and validity
The PBI has been found to have good reliability and validity based on several studies.

In the original study [1] the PBI possessed good internal consistency and re-test reliability. Further reassuring data have been derived by examining the test-retest reliability of the PBI over extended periods, and we will shortly be publishing data for a 20-year interval. The PBI has been shown to have satisfactory construct and convergent validity and to be independent of mood effects [see 2].

Availability
A copy of the full 25-item forms for scoring mothers and fathers is attached below. Please follow the scoring instructions. The standard application asks subjects to score their biological parents (one for each form) as the subject remembers them in their first sixteen years. In some studies, other "parent figures" have and can clearly be rated.

A modified version of the PBI (the MOPS or Measure of Parenting Style) was developed in 1997 for two purposes. It overcame one of the PBI limitations in having some 'double negative' items, and which can cause some confusion. Thus, all items are constructed in a direct way. Secondly, while preserving the 'care' and 'control' scales, they are considerably reduced in terms of the numbers of items. Thirdly, there is an 'abuse' scale. Thus, the MOPS is described after the PBI measure.

The PBI is not held under copyright. Therefore, clinicians and researchers are free to use the measure without obtaining permission.

References
[1] Parker, G., Tupling, H., and Brown, L.B. (1979) A Parental Bonding Instrument. British Journal of Medical Psychology, 1979, 52, 1-10.

[2] Parker, G. (1983) Parental Overprotection: A Risk Factor in Psychosocial Development, Grune & Stratton, New York. [A monograph describing the development of the PBI and its application across a wide range of psychiatric conditions and other disorders, as well as validity studies]

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MOTHER FORM

This questionnaire lists various attitudes and behaviours of parents. As you remember your MOTHER in your first 16 years would you place a tick in the most appropriate box next to each question.

	Very like	Moderately like	Moderately unlike	Very unlike
1. Spoke to me in a warm and friendly voice	☐	☐	☐	☐
2. Did not help me as much as I needed	☐	☐	☐	☐
3. Let me do those things I liked doing	☐	☐	☐	☐
4. Seemed emotionally cold to me	☐	☐	☐	☐
5. Appeared to understand my problems and worries	☐	☐	☐	☐
6. Was affectionate to me	☐	☐	☐	☐
7. Liked me to make my own decisions	☐	☐	☐	☐
8. Did not want me to grow up	☐	☐	☐	☐
9. Tried to control everything I did	☐	☐	☐	☐
10. Invaded my privacy	☐	☐	☐	☐
11. Enjoyed talking things over with me	☐	☐	☐	☐
12. Frequently smiled at me	☐	☐	☐	☐
13. Tended to baby me	☐	☐	☐	☐
14. Did not seem to understand what I needed or wanted	☐	☐	☐	☐
15. Let me decide things for myself	☐	☐	☐	☐
16. Made me feel I wasn't wanted	☐	☐	☐	☐
17. Could make me feel better when I was upset	☐	☐	☐	☐
18. Did not talk with me very much	☐	☐	☐	☐
19. Tried to make me feel dependent on her/him	☐	☐	☐	☐
20. Felt I could not look after myself unless she/he was around	☐	☐	☐	☐
21. Gave me as much freedom as I wanted	☐	☐	☐	☐
22. Let me go out as often as I wanted	☐	☐	☐	☐
23. Was overprotective of me	☐	☐	☐	☐
24. Did not praise me	☐	☐	☐	☐
25. Let me dress in any way I pleased	☐	☐	☐	☐

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FATHER FORM

This questionnaire lists various attitudes and behaviours of parents. As you remember your FATHER in your first 16 years would you place a tick in the most appropriate box next to each question.

	Very like	Moderately like	Moderately unlike	Very unlike
1. Spoke to me in a warm and friendly voice	☐	☐	☐	☐
2. Did not help me as much as I needed	☐	☐	☐	☐
3. Let me do those things I liked doing	☐	☐	☐	☐
4. Seemed emotionally cold to me	☐	☐	☐	☐
5. Appeared to understand my problems and worries	☐	☐	☐	☐
6. Was affectionate to me	☐	☐	☐	☐
7. Liked me to make my own decisions	☐	☐	☐	☐
8. Did not want me to grow up	☐	☐	☐	☐
9. Tried to control everything I did	☐	☐	☐	☐
10. Invaded my privacy	☐	☐	☐	☐
11. Enjoyed talking things over with me	☐	☐	☐	☐
12. Frequently smiled at me	☐	☐	☐	☐
13. Tended to baby me	☐	☐	☐	☐
14. Did not seem to understand what I needed or wanted	☐	☐	☐	☐
15. Let me decide things for myself	☐	☐	☐	☐
16. Made me feel I wasn't wanted	☐	☐	☐	☐
17. Could make me feel better when I was upset	☐	☐	☐	☐
18. Did not talk with me very much	☐	☐	☐	☐
19. Tried to make me feel dependent of her/him	☐	☐	☐	☐
20. Felt I could not look after myself unless she/he was around	☐	☐	☐	☐
21. Gave me as much freedom as I wanted	☐	☐	☐	☐
22. Let me go out as often as I wanted	☐	☐	☐	☐
23. Was overprotective of me	☐	☐	☐	☐
24.Did not praise me	☐	☐	☐	☐
25. Let me dress in any way I pleased	☐	☐	☐	☐

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MEASURE OF PARENTAL STYLE (MOPS)

The Measure of Parental Style (MOPS) was developed to overcome some shortcomings in the Parental Bond Instrument.

The MOPS is a self-assessment tool used to measure perceived parenting styles across the following three measures:

- Indifference
- Abuse
- Overcontrol.

Scoring instructions:

Items 5, 8, 10, 11, 12, 13 relate to the 'Indifference' measure

Items 2, 7, 9, 14, 15 relate to the 'Abuse' measure

Items 1, 3, 4, 6 relate to the 'Overcontrol' measure.

Sum the scores of the responses to items in each of the three categories to produce a total score for each category.

There is no cut-off score; the total score for each category provides a dimensional measure showing the degree to which that parental style was experienced by an individual.

Reference:

Parker, G., Roussos, J., Hadzi-Pavlovic, D., Mitchell, P., Wilhelm, K. and Austin, M-P. (1997) The development of a refined measure of dysfunctional parenting and assessment of its relevance in patients with affective disorders. Psychological Medicine, 1997, 27, 1193-1203.

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Black Dog Institute – Measure of Parental Style (MOPS)
www.blackdoginstitute.org.au

During your first 16 years how 'true' are the following statements about your MOTHER's behaviour towards you

Rate each statement either as:

0 - not true at all
1 - slightly true
2 - moderately true
3 - extremely true

1. Overprotective of me ☐
2. Verbally abusive of me ☐
3. Over controlling of me ☐
4. Sought to make me feel guilty ☐
5. Ignored me ☐
6. Critical of me ☐
7. Unpredictable towards me ☐
8. Uncaring of me ☐
9. Physically violent or abusive of me ☐
10. Rejecting of me ☐
11. Left me on my own a lot ☐
12. Would forget about me ☐
13. Was uninterested in me ☐
14. Made me feel in danger ☐
15. Made me feel unsafe ☐

During your first 16 years how 'true' are the following statements about your FATHER's behaviour towards you

Rate each statement either as:

0 - not true at all
1 - slightly true
2 - moderately true
3 - extremely true

1. Overprotective of me ☐
2. Verbally abusive of me ☐
3. Over controlling of me ☐
4. Sought to make me feel guilty ☐
5. Ignored me ☐
6. Critical of me ☐
7. Unpredictable towards me ☐
8. Uncaring of me ☐
9. Physically violent or abusive of me ☐
10. Rejecting of me ☐
11. Left me on my own a lot ☐
12. Would forget about me ☐
13. Was uninterested in me ☐
14. Made me feel in danger ☐
15. Made me feel unsafe ☐

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PsycTESTS

Student Adaptation to College Questionnaire--Modified
Version Attached: Full Test

Note: Test name created by PsycTESTS

PsycTESTS Citation:
LaBrie, J. W., Ehret, P. J., Hummer, J. F., & Prenovost, K. (2012). Student Adaptation to College Questionnaire--Modified [Database record]. Retrieved from PsycTESTS. doi: http://dx.doi.org/10.1037/t32673-000

Test Format:
This 55-item measure employs a 9-point Likert scale ranging from1 (Doesn't apply to me at all) to 9 (Applies very closely to me).

Source:
LaBrie, Joseph W., Ehret, Phillip J., Hummer, Justin F., & Prenovost, Katherine. (2012). Poor adjustment to college life mediates the relationship between drinking motives and alcohol consequences: A look at college adjustment, drinking motives, and drinking outcomes. Addictive Behaviors, Vol 37(4), 379-386. doi: 10.1016/j.addbeh.2011.11.018. © 2012 by Elsevier. Reproduced by Permission of Elsevier.

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doi: http://dx.doi.org/10.1037/t32673-000

Student Adaptation to College Questionnaire--Modified SACQ

Items

Positve college adjustment items	Negative college adjustment items
I feel that I fit in well as part of the college environment.	I haven't been able to control my emotions very well lately.
I have been keeping up to date on my academic work.	I am finding academic work at college difficult.
I am meeting as many people, and making as many friends as I would like at college.	I feel I am very different from other students at college in ways that I don't like.
I know why I am in college and what I want out of it.	I have felt tired much of the time lately.
I am very involved with social activities in college.	Lately I have been feeling blue and moody a lot.
I am adjusting well to college.	I'm not working as hard as I should at my coursework.
I am satisfied with the level at which I am performing academically.	Lately I have been giving a lot of thought to transferring to another college.
I have had informal, personal contact with college professors.	I am having difficulty feeling at ease with other people at college.
I am pleased now about my decision to go to college.	I have been having lots of headaches lately.
I am pleased now about my decision to attend this college in particular.	I am having a lot of trouble getting started on homework assignments.
I am satisfied with the extent to which I am participating in social activities at college.	I'm not really smart enough for the academic work I am expected to be doing right now.
My academic goals and purposes are well defined.	I worry a lot about my college expenses.
Getting a college degree is important to me.	I have been feeling tense of nervous lately.
My appetite has been good lately.	I wish I were at another college or university.

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doi: http://dx.doi.org/10.1037/t32673-000

Student Adaptation to College Questionnaire--Modified SACQ

Items

Positve college adjustment items	Negative college adjustment items
I am satisfied with the extracurricular activities available at college.	Recently I have had trouble concentrating when I try to study.
I feel I have enough social skills to get along well in the college setting.	I'm not doing well enough academically for the amount of work I put in.
I am attending classes regularly.	I've put on (or lost) too much weight recently.
I have several close social ties at college.	I haven't been sleeping very well.
I am enjoying my academic work at college.	I have been getting angry easily lately.
I feel I have good control over my life situation at college.	I really haven't had much motivation for studying
I have been feeling in good health lately.	Sometimes my thinking gets muddled up too easily.
I have some good friends of acquaintances at college with whom I can talk about any problems I may have.	Most of the things I am interested in are not related to any of my course work at college.
I am quite satisfied with my social life at college.	I have been feeling lonely a lot at college lately.
I am quite satisfied with my academic situation at college.	I haven't been very efficient in the use of study time lately.
I feel confident that I will be able to deal in a satisfactory manner with future challengers here at college.	I have given a lot of thought lately to whether I should ask for help from the Psychological/Counseling Services Center of from a psychotherapist outside of college.
	Being on my own, taking responsibility for myself, has not been easy.
	Lately I have been having doubts regarding the value of a college education.

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doi: http://dx.doi.org/10.1037/t32673-000

Student Adaptation to College Questionnaire--Modified SACQ

Items

Positve college adjustment items	Negative college adjustment items
	Lately I have been giving a lot of thought to dropping out of college altogether and for good.
	I find myself giving considerable thought to taking time off from college and finishing later.
	I am experiencing a lot of difficulty coping with the stresses imposed upon me in college

Note . This 55-item measure employs a 9-point Likert scale ranging from 1 (*Doesn't apply to me at all*) to 9 (*Applies very closely to me*).

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BIG FIVE INVENTORY (BFI)

Reference

John, O. P., & Srivastava, S. (1999). The Big-Five trait taxonomy: History, measurement, and theoretical perspectives. In L. A. Pervin & O. P. John (Eds.), *Handbook of personality: Theory and research* (Vol. 2, pp. 102–138). New York: Guilford Press.

Description of Measure:

44-item inventory that measures an individual on the Big Five Factors (dimensions) of personality (Goldberg, 1993). Each of the factors is then further divided into personality facets.

The Big Five Factors are (chart recreated from John & Srivastava, 1999):

Big Five Dimensions	**Facet (and correlated trait adjective)**
Extraversion vs. introversion	Gregariousness (sociable) Assertiveness (forceful) Activity (energetic) Excitement-seeking (adventurous) Positive emotions (enthusiastic) Warmth (outgoing)
Agreeableness vs. antagonism	Trust (forgiving) Straightforwardness (not demanding) Altruism (warm) Compliance (not stubborn) Modesty (not show-off) Tender-mindedness (sympathetic)
Conscientiousness vs. lack of direction	Competence (efficient) Order (organized) Dutifulness (not careless) Achievement striving (thorough) Self-discipline (not lazy) Deliberation (not impulsive)
Neuroticism vs. emotional stability	Anxiety (tense) Angry hostility (irritable) Depression (not contented) Self-consciousness (shy) Impulsiveness (moody) Vulnerability (not self-confident)
Openness vs. closedness to experience	Ideas (curious) Fantasy (imaginative) Aesthetics (artistic) Actions (wide interests) Feelings (excitable) Values (unconventional)

For more information about the Big Five, visit this website:
http://www.uoregon.edu/~sanjay/bigfive.html#where

Abstracts of Selected Related Articles:

Bouchard, T. J. & McGue, M. (2003). Genetic and environmental influences on human psychological differences. *Journal of Neurobiology*, *54*, 4-45.

> Psychological researchers typically distinguish five major domains of individual differences in human behavior: cognitive abilities, personality, social attitudes, psychological interests, and psychopathology (Lubinski, 2000). In this article we: discuss a number of methodological errors commonly found in research on human individual differences; introduce a broad framework for interpreting findings from contemporary behavioral genetic studies; briefly outline the basic quantitative methods used in human behavioral genetic research; review the major criticisms of behavior genetic designs, with particular emphasis on the twin and adoption methods; describe the major or dominant theoretical scheme in each domain; and review behavioral genetic findings in all five domains. We conclude that there is now strong evidence that virtually all individual psychological differences, when reliably measured, are moderately to substantially heritable.

Tkach, C., & Lyubomirsky, S. (2006). How do people pursue happiness?: Relating personality, happiness-increasing strategies, and well-being. *Journal of Happiness Studies, 7*, 183-225.

> Five hundred ethnically diverse undergraduates reported their happiness strategies – that is, activities undertaken to maintain or increase happiness. Factor analysis extracted eight general strategies: Affiliation, Partying, Mental Control, Goal Pursuit, Passive Leisure, Active Leisure, Religion, and Direct Attempts at happiness. According to multiple regression analyses, these strategies accounted for 52% of the variance in self-reported happiness and 16% over and above the variance accounted for by the Big Five personality traits. The strongest unique predictors of current happiness were Mental Control (inversely related), Direct Attempts, Affiliation, Religion, Partying, and Active Leisure. Gender differences suggest that men prefer to engage in Active Leisure and Mental Control, whereas women favor Affiliation, Goal Pursuit, Passive Leisure, and Religion. Relative to Asian and Chicano(a) students, White students preferred using high arousal strategies. Finally, mediation analyses revealed that many associations between individuals' personality and happiness levels are to some extent mediated by the strategies they use to increase their happiness – particularly, by Affiliation, Mental Control, and Direct Attempts.

Shiota, M.N., Keltner, D., & John, O. P. (2006). Positive emotion dispositions differentially associated with Big Five personality and attachment style. *The Journal of Positive Psychology, 1*, 61-71.

> Although theorists have proposed the existence of multiple distinct varieties of positive emotion, dispositional positive affect is typically treated as a unidimensional variable in personality research. We present data elaborating conceptual and empirical differences among seven positive emotion dispositions in their relationships with two core personality constructs, the "Big Five" and adult attachment style. We found that the positive emotion dispositions were differentially associated with self- and peer-rated Extraversion, Conscientiousness, Agreeableness, Openness to Experience, and Neuroticism. We also found that different adult attachment styles were associated with different kinds of emotional rewards. Findings support the theoretical utility of differentiating among several dispositional positive emotion constructs in personality research.

Scale:

The Big Five Inventory (BFI)

Here are a number of characteristics that may or may not apply to you. For example, do you agree that you are someone who likes to spend time with others? Please write a number next to each statement to indicate the extent to which you agree or disagree with that statement.

Disagree strongly	Disagree a little	Neither agree nor disagree	Agree a little	Agree Strongly
1	2	3	4	5

I see Myself as Someone Who...

____1. Is talkative

____2. Tends to find fault with others

____3. Does a thorough job

____4. Is depressed, blue

____5. Is original, comes up with new ideas

____6. Is reserved

____7. Is helpful and unselfish with others

____8. Can be somewhat careless

____9. Is relaxed, handles stress well

____10. Is curious about many different things

____11. Is full of energy

____12. Starts quarrels with others

____13. Is a reliable worker

____14. Can be tense

____15. Is ingenious, a deep thinker

____16. Generates a lot of enthusiasm

____17. Has a forgiving nature

____18. Tends to be disorganized

____19. Worries a lot

____23. Tends to be lazy

____24. Is emotionally stable, not easily upset

____25. Is inventive

____26. Has an assertive personality

____27. Can be cold and aloof

____28. Perseveres until the task is finished

____29. Can be moody

____30. Values artistic, aesthetic experiences

____31. Is sometimes shy, inhibited

____32. Is considerate and kind to almost everyone

____33. Does things efficiently

____34. Remains calm in tense situations

____35. Prefers work that is routine

____36. Is outgoing, sociable

____37. Is sometimes rude to others

____38. Makes plans and follows through with them

____39. Gets nervous easily

____40. Likes to reflect, play with ideas

____41. Has few artistic interests

____20. Has an active imagination

____21. Tends to be quiet

____22. Is generally trusting

____42. Likes to cooperate with others

____43. Is easily distracted

____44. Is sophisticated in art, music, or literature

Scoring:

BFI scale scoring ("R" denotes reverse-scored items):

Extraversion: 1, 6R, 11, 16, 21R, 26, 31R, 36
Agreeableness: 2R, 7, 12R, 17, 22, 27R, 32, 37R, 42
Conscientiousness: 3, 8R, 13, 18R, 23R, 28, 33, 38, 43R
Neuroticism: 4, 9R, 14, 19, 24R, 29, 34R, 39
Openness: 5, 10, 15, 20, 25, 30, 35R, 40, 41R, 44

Appendix

Resistance to Peer Influence Scale

For each question, decide which sort of person you are most like — the one described on the right or the one described on the left. Then decide if that is "sort of true" or "really true" for you, and mark that choice. For each line mark only ONE of the four choices.

Really True for Me	Sort of True for Me				Sort of True for Me	Really True for Me
❑	❑	Some people go along with their friends just to keep their friends happy.	BUT	Other people refuse to go along with their friends want to do, even though they know it will make their friends unhappy.	❑	❑
❑	❑	Some people think it's more important to be an individual than to fit in with the crowd.	BUT	Other people think it is more important to fit in with the crowd than to stand out as an individual.	❑	❑
❑	❑	For some people, it's pretty easy for their friends to get them to change their mind.	BUT	For other people, it's pretty hard for their friends to get them to change their mind.	❑	❑
❑	❑	Some people would do something that they knew was wrong just to stay on their friends' good side.	BUT	Other people would not do something they knew was wrong just to stay on their friends' good side.	❑	❑
❑	❑	Some people hide their true opinion from their friends if they think their friends will make fun of them because of it.	BUT	Other people will say their true opinion in front of their friends, even if they know their friends will make fun of them because of it.	❑	❑
❑	❑	Some people will not break the law just because their friends say that they would.	BUT	Other people would break the law if their friends said that they would break it.	❑	❑
❑	❑	Some people change the way they act so much when they are with their friends that they wonder who they "really are".	BUT	Other people act the same way when they are alone as they do when they are with their friends.	❑	❑
❑	❑	Some people take more risks when they are with their friends than they do when they are alone.	BUT	Other people act just as risky when they are alone as when they are with their friends.	❑	❑
❑	❑	Some people say things they don't really believe because they think it will make their friends respect them more.	BUT	Other people would not say things they didn't really believe just to get their friends to respect them more.	❑	❑
❑	❑	Some people think it's better to be an individual even if people will be angry at you for going against the crowd.	BUT	Other people think it's better to go along with the crowd than to make people angry at you.	❑	❑

Scoring instructions: Score each item from 1 to 4 (reading left to right on the instrument). Reverse-score items 2, 6, and 10. Sum the scores for valid responses and divide by the number of valid items. It is recommended that at least 7 items have valid responses.

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Revision received July 12, 2007
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BIRTH TO TEN: 1997
SOUTH AFRICAN CHILD ASSESSMENT SCHEDULE (SACAS)

Today's Date | | | | | | | 1 | 9 | 9 | 7 |

BTT ID | | | | | | | |

CHILD'S NAME: _____
SURNAME: _____
INTERVIEWER: _____
WHO PROVIDED THE INFORMATION: _____
WHAT IS THE RELATIONSHIP OF THE INFORMANT TO THE CHILD? _____

I have some question I would like to ask you about problems and skills some children have. I would like you to tell me the extent to which it is true that your child has these. In responding tell me whether it is……

0 = NOT TRUE; 1 = SOMETIMES TRUE; 2 = OFTEN TRUE

0	1	2	1.	Does (CHILD) seem fragile or cry when an adult just looks at him/her?
0	1	2	2.	Does (CHILD) accept and listen to criticism calmly?
0	1	2	3.	Does (CHILD) accept restrictions from adults?
0	1	2	4.	Does (CHILD) act too young for His/Her age?
0	1	2	5.	Does (CHILD) adjust well to changes in the classroom routine?
0	1	2	6.	Is (CHILD) affectionate to others?
0	1	2	7.	Is (CHILD) an angry child?
0	1	2	8.	Does (CHILD) approach new experiences confidently, without fear?
0	1	2	9.	Does (CHILD) argue?
0	1	2	10.	Does (CHILD) avoid activities which S/He is not good at?
0	1	2	11.	Does (CHILD) brag or boast?
0	1	2	12.	Does (CHILD) bully or is S/He mean to others?
0	1	2	13.	Is (CHILD) unable to concentrate, pay attention for long?
0	1	2	14.	Is (CHILD) unable to get His/Her mind off certain thoughts?
0	1	2	15.	Is (CHILD) unable to sit still, does (CHILD) squirm?
0	1	2	16.	Can (CHILD) accept things not going His/Her way?
0	1	2	17.	Does (CHILD) carry out requests and directions responsibly?
0	1	2	18.	Does (CHILD) cling to adults, is (CHILD) too dependant?
0	1	2	19.	IS (CHILD) co-operative?

0	1	2	20.	Does (CHILD) complain of aches or pains in arms or legs?
0	1	2	21.	Does (CHILD) complain of dizziness?
0	1	2	22.	Does (CHIL) complain of headaches?
0	1	2	23.	Does (CHILD) complain of loneliness?
0	1	2	24.	Does (CHILD) complain of nausea of feeling sick?
0	1	2	25.	Does (CHILD) complain of stomach aches or cramps?
0	1	2	26.	Does (CHILD) complete homework?
0	1	2	27.	Is (CHILD) confused, in a fog (Does not keep up with others.)?
0	1	2	28.	Does (CHILD) cry without good reason?
0	1	2	29.	Is (CHILD) curious or enthusiastic about new activities?
0	1	2	30.	Does (CHILD) day dream or get lost in His/Her thoughts?
0	1	2	31.	Does (CHILD) defy authority or break rules?
0	1	2	32.	Does (CHILD) deliberately destroy things that belong to others?
0	1	2	33.	Does (CHILD) demand attention?
0	1	2	34.	Does (CHILD) destroy His/Her own things?
0	1	2	35.	Is (CHILD) disobedient at home?
0	1	2	36.	Is (CHILD) disobedient at school?
0	1	2	37.	Does (CHILD) do unusual original, creative work?
0	1	2	38.	Does (CHILD) eat poorly?
0	1	2	39.	Is (CHILD) easily jealous?
0	1	2	40.	Does (CHILD) express needs and feelings appropriately?
0	1	2	41.	Does (CHILD) face the pressures of competition well?
0	1	2	42.	Does (CHILD) have specific fears?
0	1	2	43.	Does (CHILD) fear H/She might do something bad?
0	1	2	44.	Does (CHILD) feel good about Him/Herself?
0	1	2	45.	Does (CHILD) feel S/He has to be perfect?
0	1	2	46.	Does (CHILD) feel too guilty?
0	1	2	47.	Does (CHILD) feel worthless or inferior?
0	1	2	48.	Does (CHILD) feel or complain that no one loves Him/Her?
0	1	2	49.	Does (CHILD) follow rules and directions?
0	1	2	50.	Does (CHILD) function well even with distractions?
0	1	2	51.	Is (CHILD) generally relaxed?
0	1	2	52.	Does (CHILD) get teased by other children?

0	1	2	53.	Is (CHILD) good at counting (MATHS)?
0	1	2	54.	Is (CHILD) happy?
0	1	2	55.	Is it too hard to understand what (CHILD) is saying?
0	1	2	56.	Does (CHILD) have a good sense of humor, smile a lot?
0	1	2	57.	Does (CHILD) have many friends?
0	1	2	58.	Does (CHILD) have strange ideas – if true Describe : _____
0	1	2	59.	Does (CHILD) hear things that aren't there? If true Describe : _____
0	1	2	60.	Does (CHILD) hesitate to try new things?
0	1	2	61.	Is (CHILD) impulsive or does (CHILD) act without thinking?
0	1	2	62.	Is (CHILD) independent, does (CHILD) like to do things without help?
0	1	2	63.	Is (CHILD) interested in school work?
0	1	2	64.	Is (CHILD) irritable?
0	1	2	65.	Is (CHILD) a good reader for His/Her Grade?
0	1	2	66.	Does (CHILD) know His/Her strengths and weaknesses?
0	1	2	67.	Does (CHILD) look unhappy without good reason?
0	1	2	68.	Is (CHILD) Loud, Noisy?
0	1	2	69.	Is (CHILD) loving, shows affection to others?
0	1	2	70.	Is (CHILDS) mood even and stable?
0	1	2	71.	Does (CHILD) make nervous movements or twitch?
0	1	2	72.	Is (CHILD) nervous, high strung or tense?
0	1	2	73.	Is (CHILD) able to take turns and share?
0	1	2	74.	Is (CHILD) not liked by other children?
0	1	2	75.	Is (CHILD) overactive, restless, unable to sit still?
0	1	2	76.	Is (CHILD) overtired, sleepy during the day?
0	1	2	77.	Is (CHILD) overweight?
0	1	2	78.	Does (CHILD) physically attack people?
0	1	2	79.	Does (CHILD) plat enthusiastically?
0	1	2	80.	Is (CHILD) polite and courteous?
0	1	2	81.	Does (CHILD) do poor work at school?
0	1	2	82.	Is (CHILD) poorly co-ordinated or clumsy?
0	1	2	83.	Does (CHILD) prefer playing with younger children?

0	1	2	84.	Does (CHILD) prefer to be alone?
0	1	2	85.	Does (CHILD) have problems with eyes, not corrected by glasses?
0	1	2	86.	Does (CHILD) require restrictions to control Him/Herself?
0	1	2	87.	Doe (CHILD) have rashes or other skin problems?
0	1	2	88.	Does (CHILD) refuse to talk in certain situations?
0	1	2	89.	Does (CHILD) repeat certain acts over and over?
0	1	2	90.	Doe (CHILD) resolve peer problems on His/Her own?
0	1	2	91.	Is (CHILD) sad or depressed?
0	1	2	92.	Doe (CHILD) scream?
0	1	2	93.	Is (CHILD) secretive, does (CHILD) keep things to Him/Herself?
0	1	2	94.	Does (CHILD) seem to think that others are out to get Him/Her?
0	1	2	95.	Does (CHILD) see things that are not really there?
0	1	2	96.	Is (CHILD) self-conscious or easily embarrassed?
0	1	2	97.	IS (CHILD) a self-starter, begins without waiting for adults?
0	1	2	98.	Does (CHILD) share things with others?
0	1	2	99.	Does (CHILD) show interest in people around Him/Her?
0	1	2	100.	Does (CHILD) Show off or Clown?
0	1	2	101.	Is (CHILD) shy or timid?
0	1	2	102.	Does (CHILD) stare blankly?
0	1	2	103.	Does (CHILD) stare into space or seem preoccupied?
0	1	2	104.	Does (CHILD) start fights?
0	1	2	105.	Does (CHILD) have strange behavior? Describe? _____
0	1	2	106.	Is (CHILD) stubborn, sullen or irritable?
0	1	2	107.	Does (CHILD) have sudden changes in mood or feelings?
0	1	2	108.	Does (CHILD) pull a face, sulk or pout?
0	1	2	109.	Is (CHILD) suspicious of others?
0	1	2	110.	Does (CHILD) talk too much?
0	1	2	111.	Does (CHILD) tease other kids?
0	1	2	112.	Does (CHILD) have temper tantrums or hot temper?
0	1	2	113.	Does (CHILD) threaten people?
0	1	2	114.	Is (CHILD) too fearful or anxious?
0	1	2	115.	Does (CHILD) try to help others?

0	1	2	116.	Is (CHILD) trustworthy?
0	1	2	117.	Is (CHILD) under active, slow-moving or lacks energy?
0	1	2	118.	Doe (CHILD) vomit, throw up?
0	1	2	119.	Is (CHILD) well liked by other children His/Her age?
0	1	2	120.	Is (CHILD) well behaved in school?
0	1	2	121.	Is (CHILD) withdrawn, doesn't get involved with others?
0	1	2	122.	Does (CHILD) work up to potential?
0	1	2	123.	Does (CHILD) work well with out adult support?
0	1	2	124.	Does (CHILD) suck His/Her thumb?
0	1	2	125.	Does (CHILD) do things to hurt Him/Herself (e.g. Bang head on wall)?
0	1	2	126.	Does (CHILD) worry?

B. Compared to other children His/Her age, how well does _____
(Childs Name)

127. . . Get along with children His/Her own age?

1	Worse than others	2	About the same	3	Better than other

128. . . Get along with His/Her brothers and sisters?

1	Worse than others	2	About the same	3	Better than other

Selected Carey Infant Temperament Questionnaire items for the Birth to Twenty Cohort.

I'm going to read you some descriptions of a baby of the same age as Your child. I'd like you to tell me if the description is a lot like your child, Not really like your child, or very different from your child.

32. From the beginning, my baby has been fussy and cried a lot.
    1. Very like 2. Not really
    3. Very unlike/different

33. If my baby fusses, I can generally tell what's bothering him/her.
    1. Very like 2. Not really
    3. Very unlike/different

34. My baby usually smiles and laughs during his/her bath
1. Very like 2. Not really
    3. Very unlike/different

35. My baby is very easily upset, starts to cry very easily.
1. Very like 2. Not really
    3. Very unlike/different

36. My baby's initial reaction to most new people is friendly.
    1. Very like 2. Not really
    3. Very unlike/different

37. When my baby gets cross he/she shows anger very strongly.
    1. Very like 2. Not really
    3. Very unlike/different

38. My baby is very cooperative and easy while being dressed.
1. Very like 2. Not really
    3. Very unlike/different

39. I generally find my baby's personality very difficult to deal with.
    1. Very like 2. Not really
    3. Very unlike/different

Appendix D

List of manufacturers

Table D.1: List of manufacturers

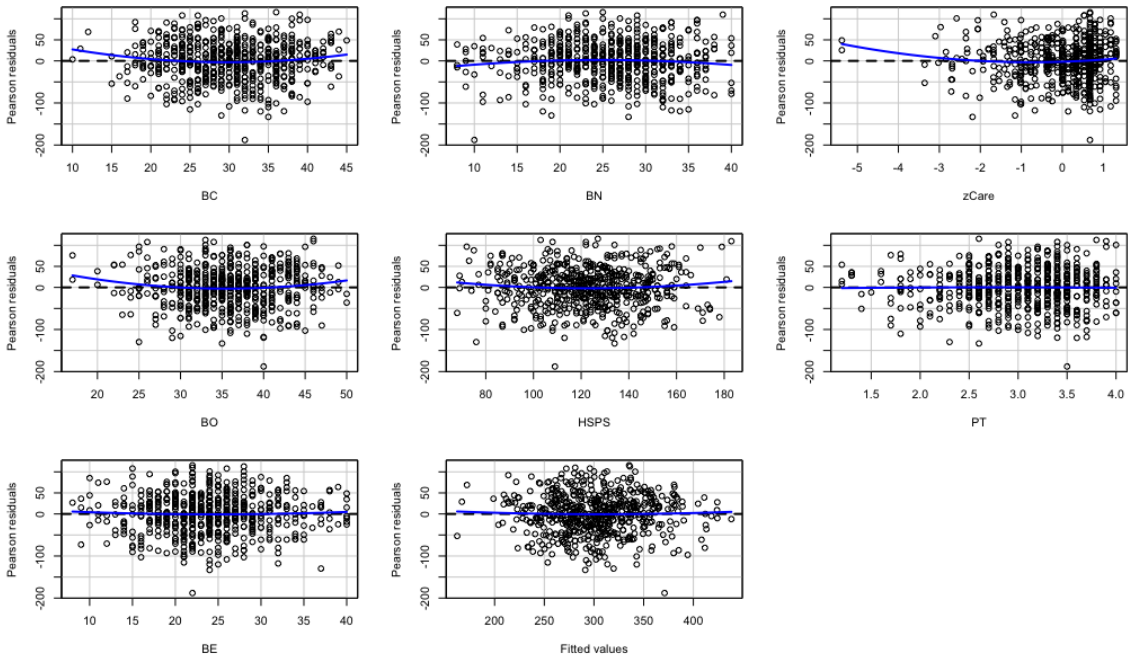
Equipment	Manufacturer	Manufacturer location
T100 thermocycler	Bio-Rad	California, USA
NanoDrop 1000 spectrophotometer	Thermo Fisher Scientific	Massachusetts, USA
Omega Fluor gel documentation system	aplegen	California, USA
Gel electrophoresis tanks (30 cm)	Cleaver Scientific	Warwickshire, UK
Powerpro-300 power pack	Cleaver Scientific	Warwickshire, UK
Reagent	**Manufacturer**	**Manufacturer location**
Accuprime GC-rich polymerase	Invitrogen	California, USA
50 bp DNA ladder	Invitrogen	California, USA
SeaKem LE Agarose	Lonza	Maine, USA
Ethidium Bromide	Sigma-Aldrich	Steinheim, Germany

Appendix E

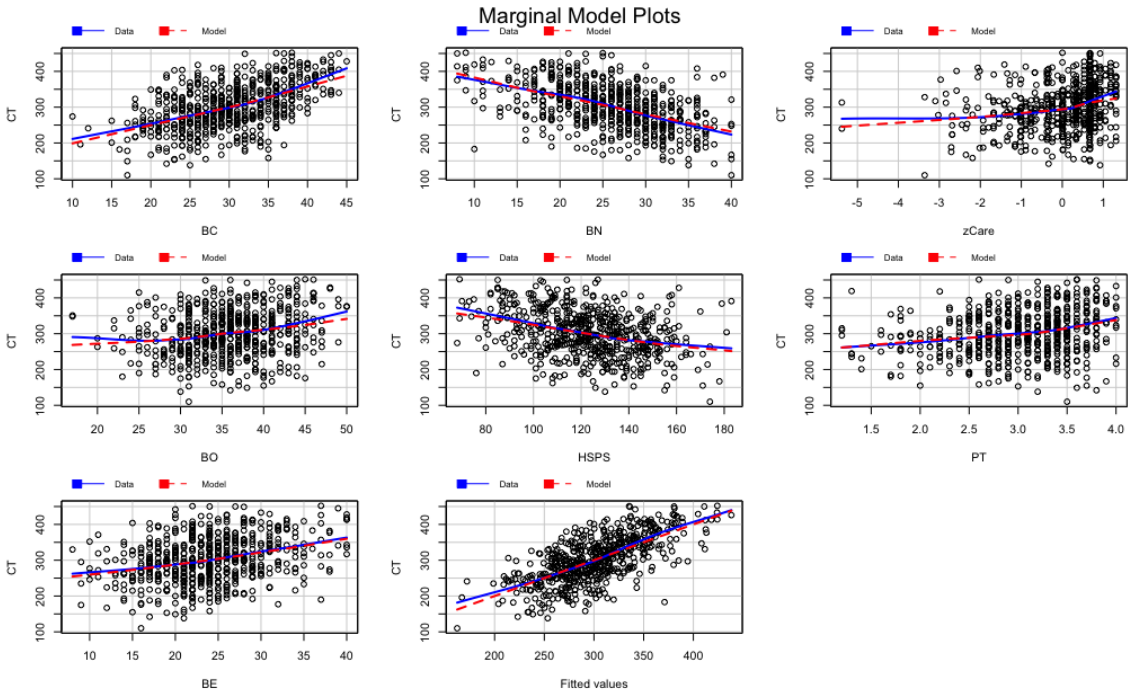
Model diagnostics - Study 3

In the two figures below, diagnostics for the university adjustment model (Study 3, Table 4.7) are shown. In Figure E.1, panel a) shows the Pearson residual values based on each predictor variable in the model. Dotted lines reflect ideal trends in well-fitted models. Blue lines are the trends of the constructed model. Panel b) shows the marginal model plots, which indicate the relationship between each predictor and the outcome variable while ignoring other predictors. The solid blue line represents the LOESS line, while the red dotted line reflects the regression model.

In Figure E.2, panel a) shows the quantile-quantile (QQ) plot. Panel b) displays the added-variable plots, where the regression line of each predictor is plotted, whilst holding other predictors constant. Panel c) shows the case-wise diagnostic plots. The Cook's distances, studentised residuals, Bonferroni-adjusted p-values following outlier assessment and hat-values are plotted per case.

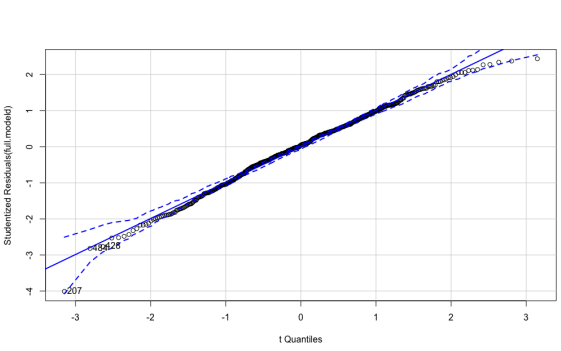


(a)

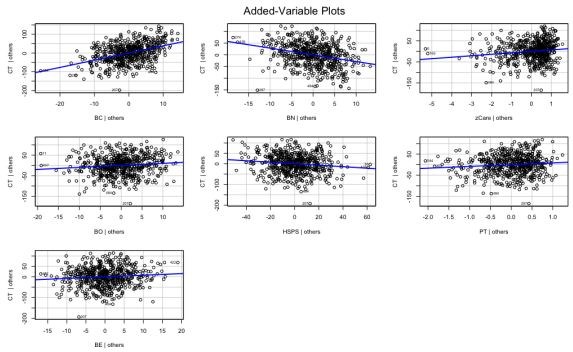


(b)

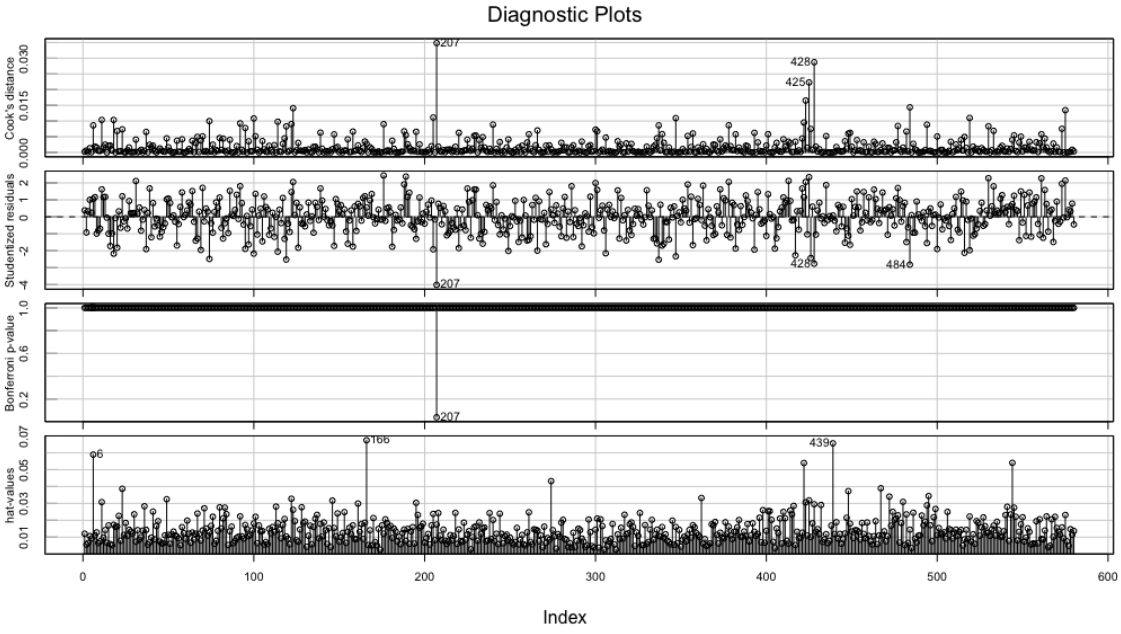
Figure E.1: **Diagnostic plots for the university adjustment model (Study 3)**



(a)



(b)



(c)

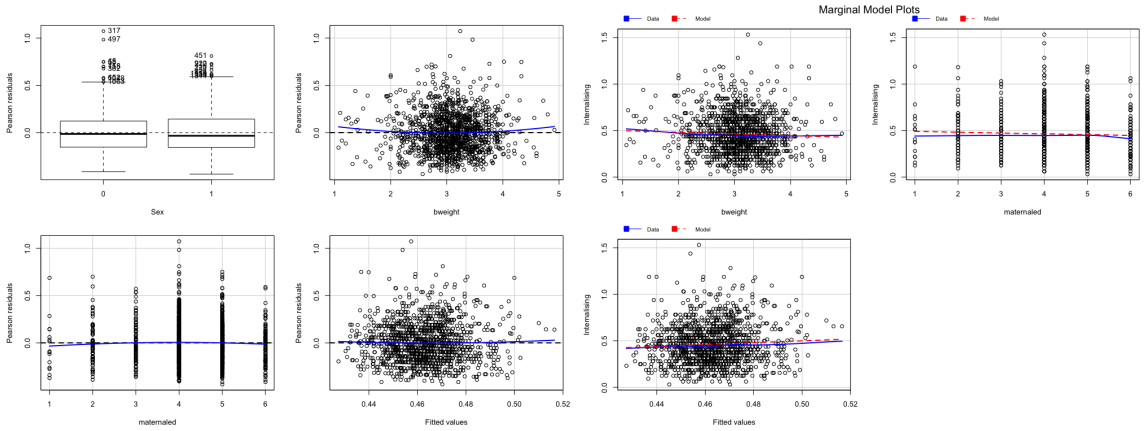
Figure E.2: **Diagnostic plots for the university adjustment model (Study 3) continued**

Appendix F

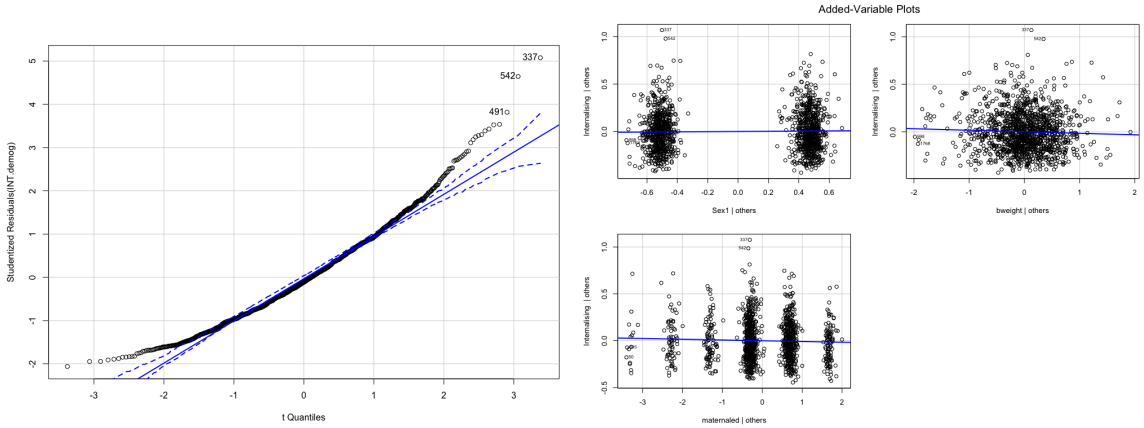
Model diagnostics - Study 4

Following below, diagnostic plots are shown for each of the main effect linear models described in Study 4. In each plot, particularly unusual cases are labelled with their row number. The plots are arranged as follows:
a) Plots of the Pearson's residual values
b) Marginal model plots
c) Quantile-quantile plot
d) Added variable plots
e) Case-wise diagnostic plots.

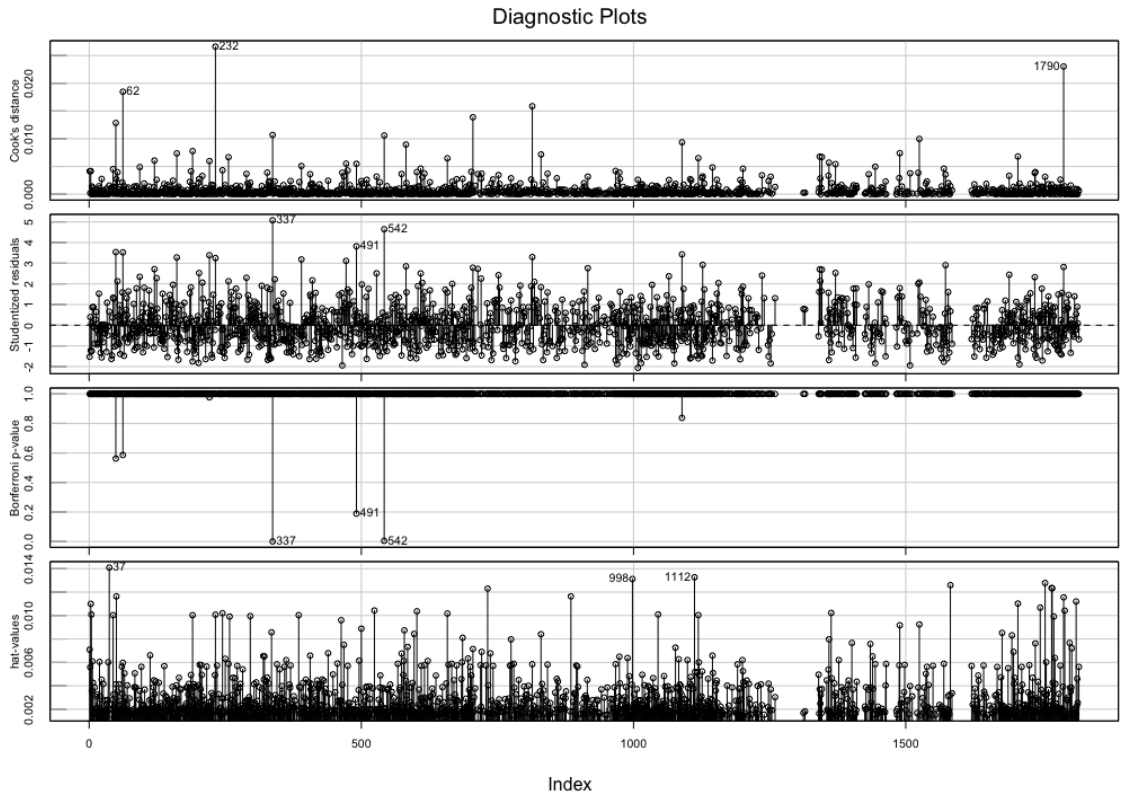
All study models had good fits, without any substantive issues in residual distribution, Cook's distances or hat values. In rare circumstances, cases were removed because their residual values remained significantly outlying even after Bonferroni correction.



(a) (b)

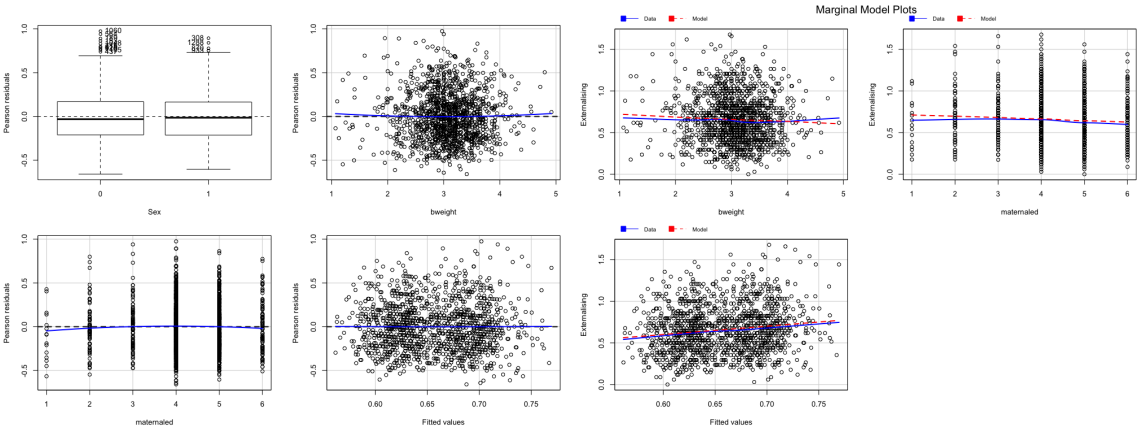


(c) (d)

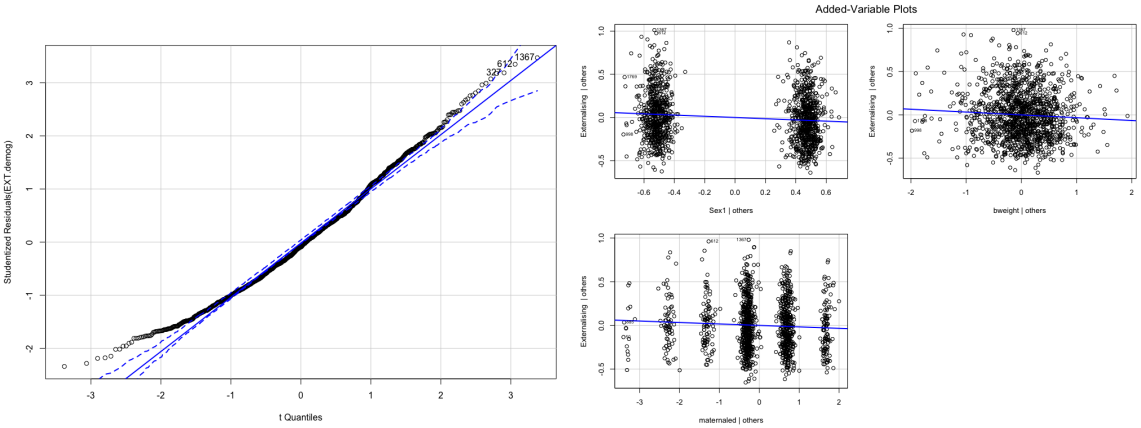


(e)

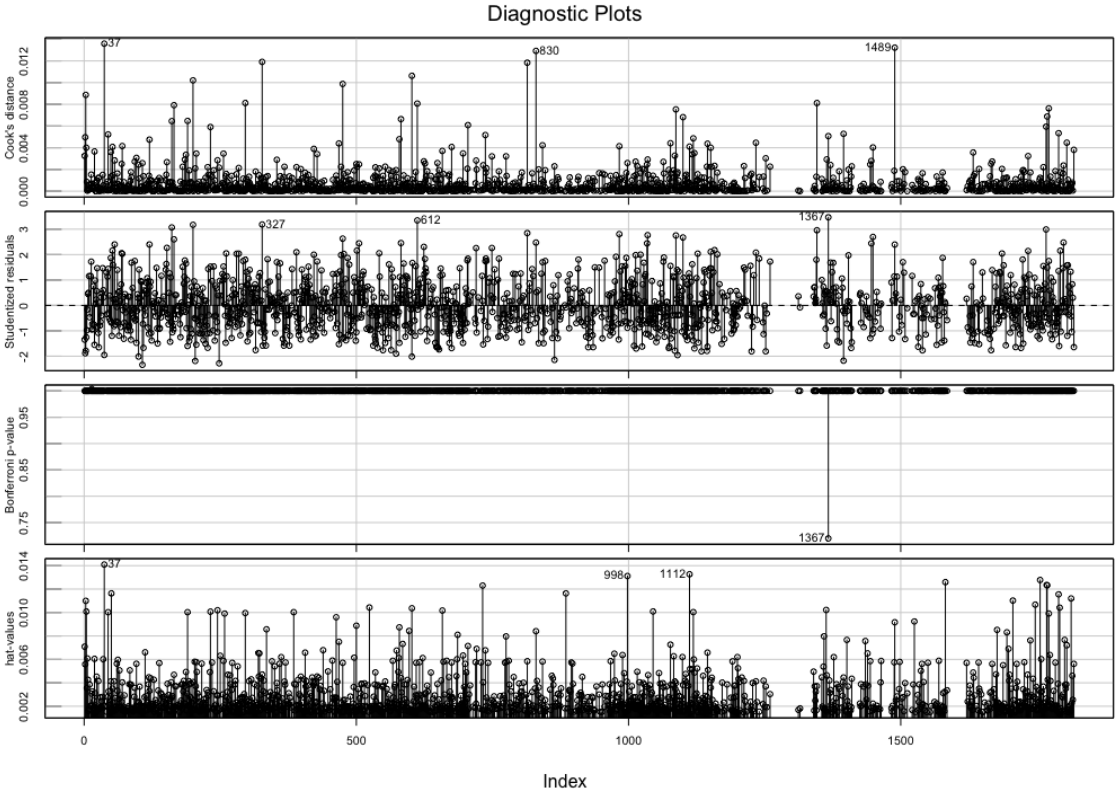
Figure F.1: **Internalising behaviour predicted by neonatal variables**



(a) (b)

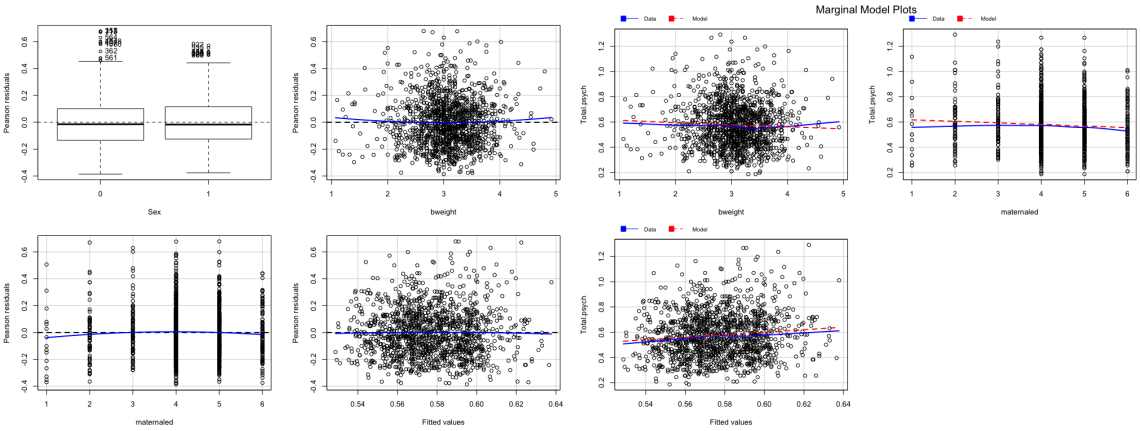


(c) (d)



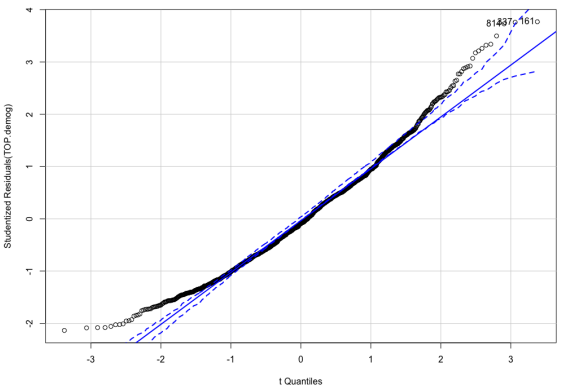
(e)

Figure F.2: **Externalising behaviour predicted by neonatal variables**

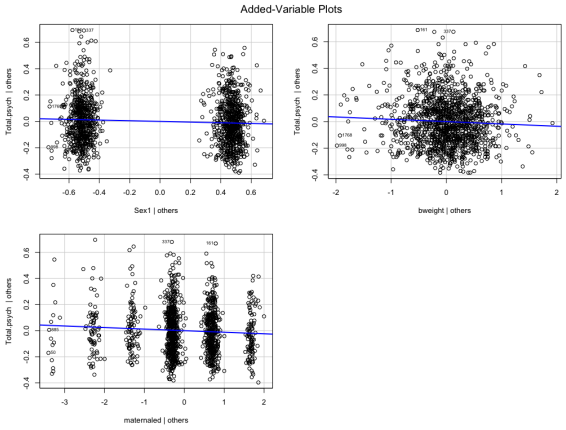


(a)

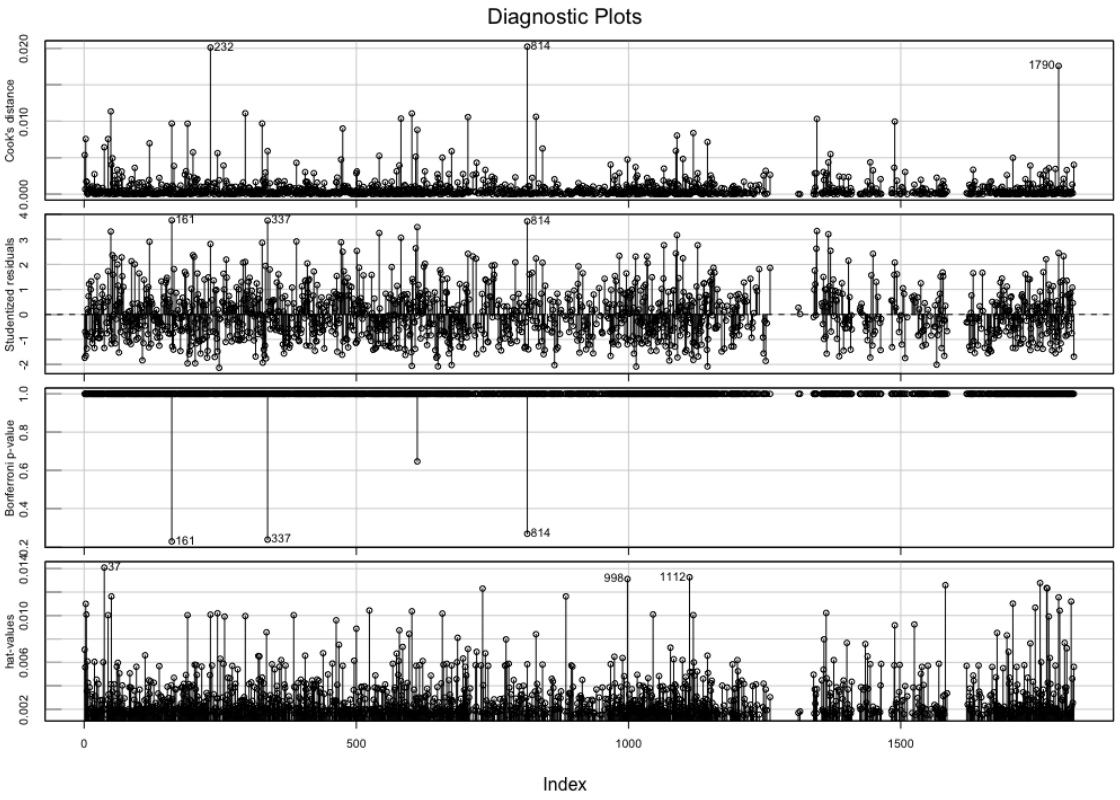
(b)



(c)

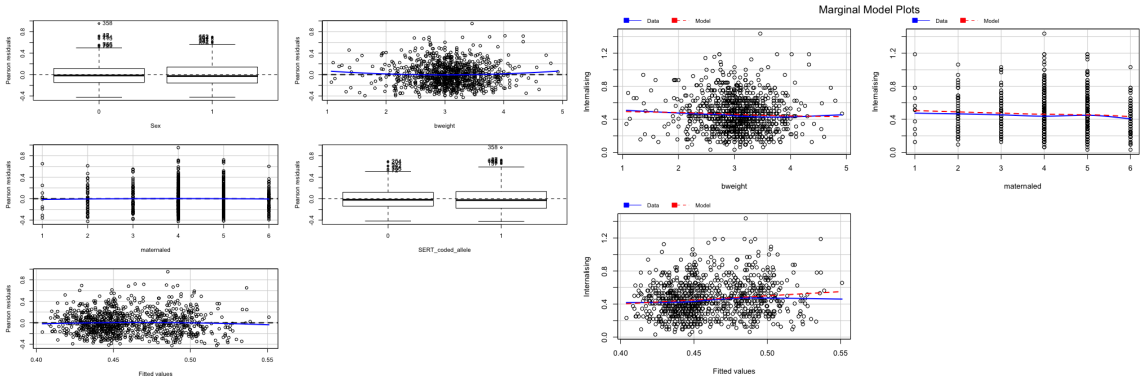


(d)



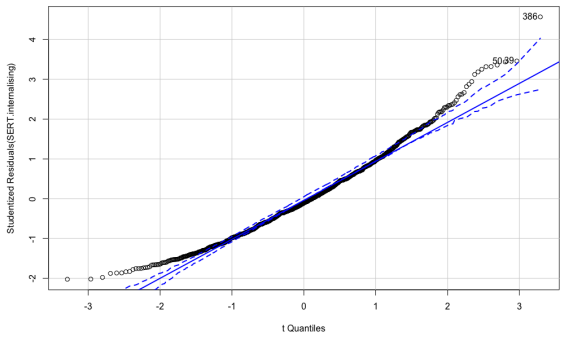
(e)

Figure F.3: **Total psychology scores predicted by neonatal variables**

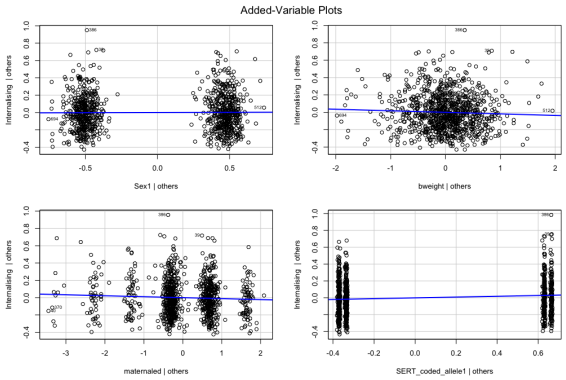


(a)

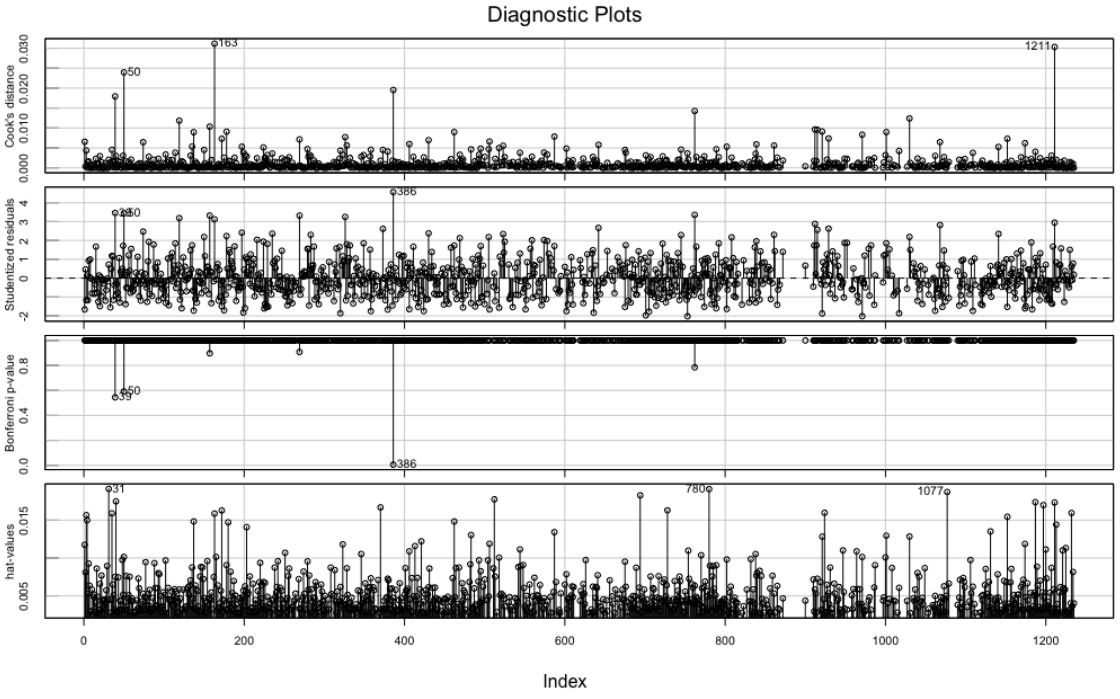
(b)



(c)

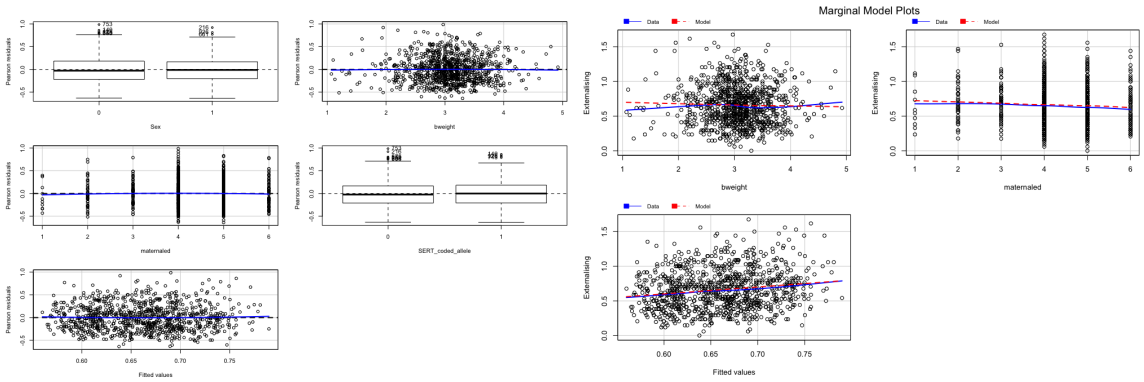


(d)

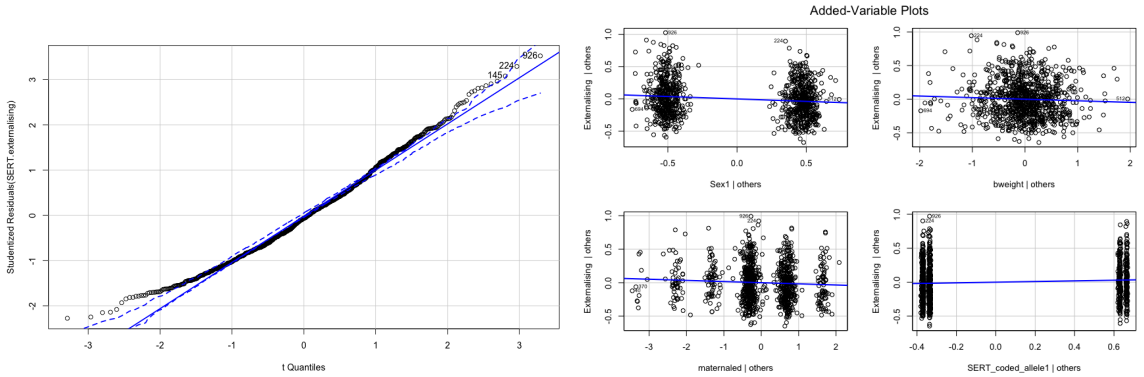


(e)

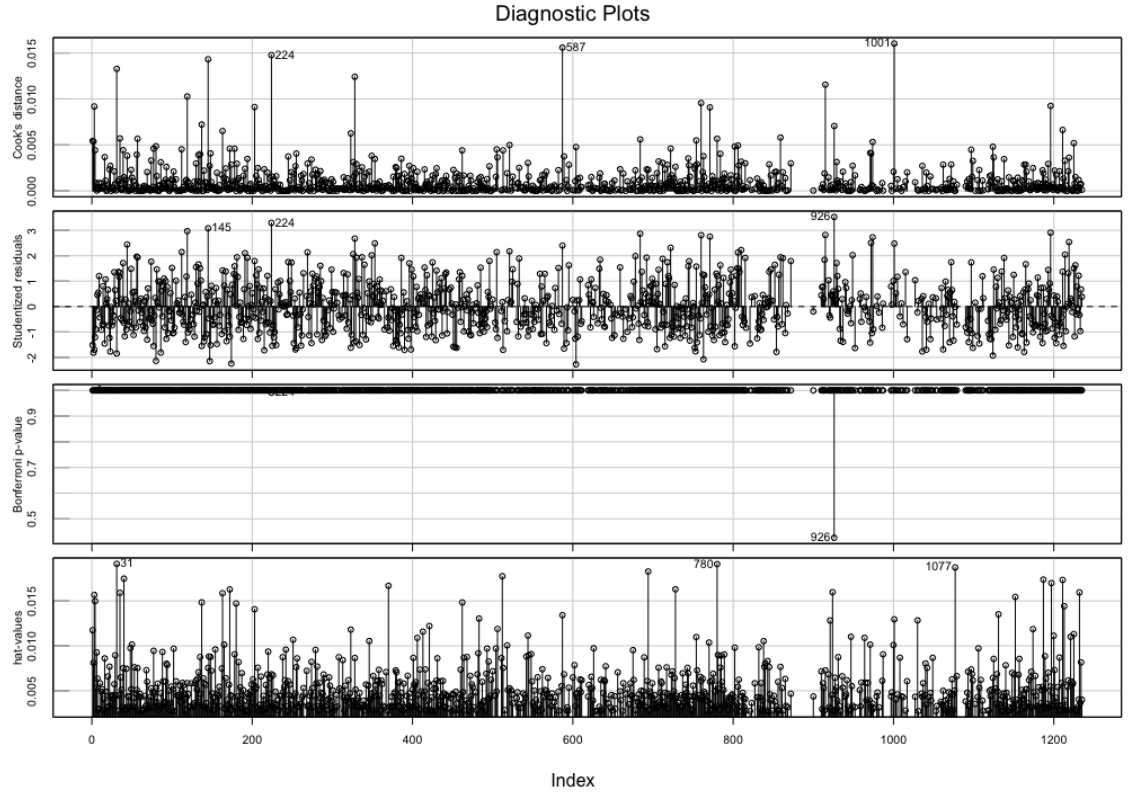
Figure F.4: **Internalising scores predicted by genotype**



(a) (b)

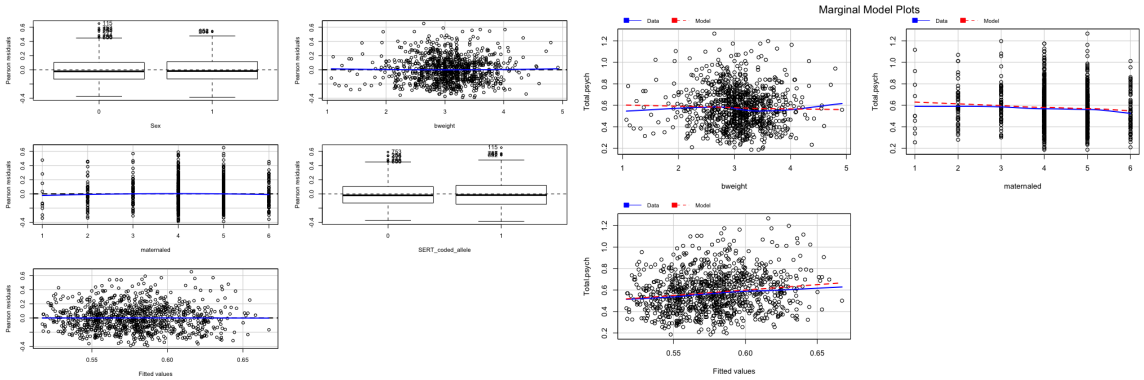


(c) (d)



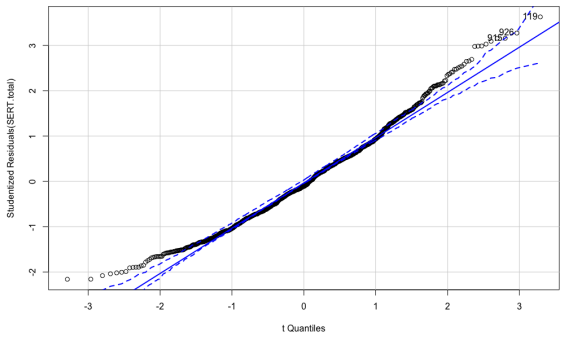
(e)

Figure F.5: **Externalising scores predicted by genotype**

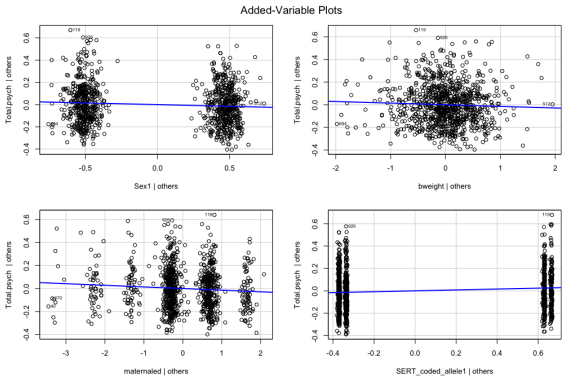


(a)

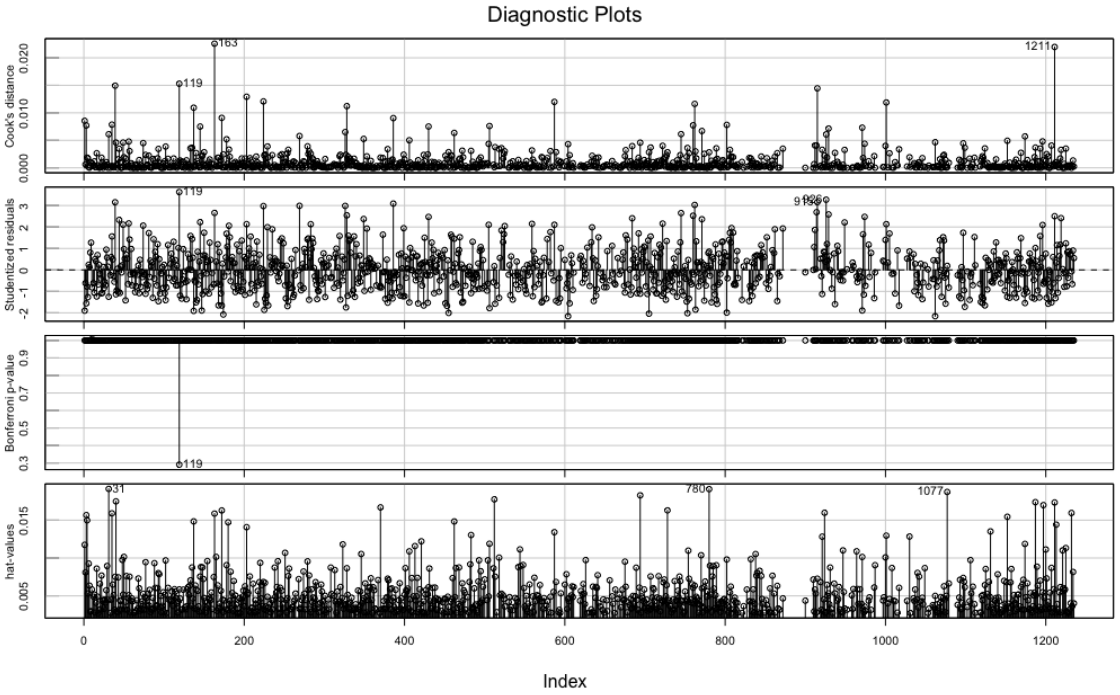
(b)



(c)

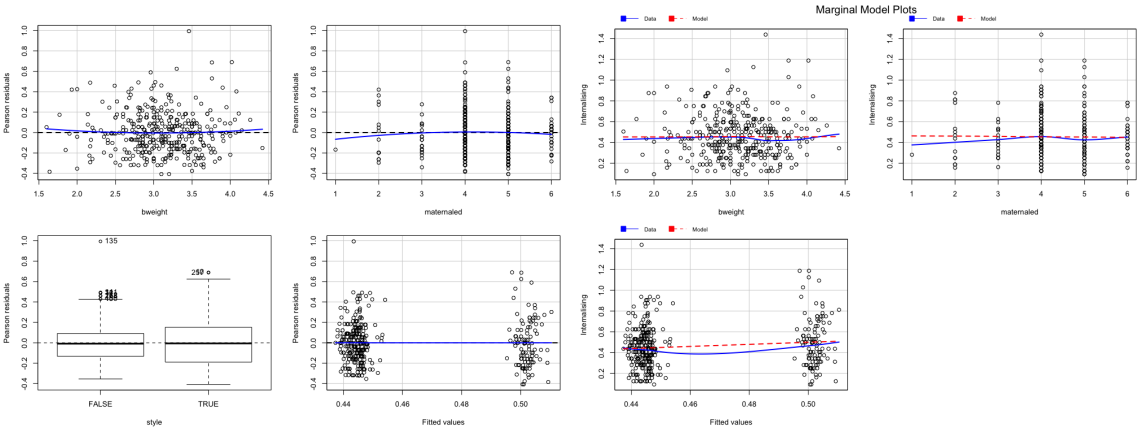


(d)

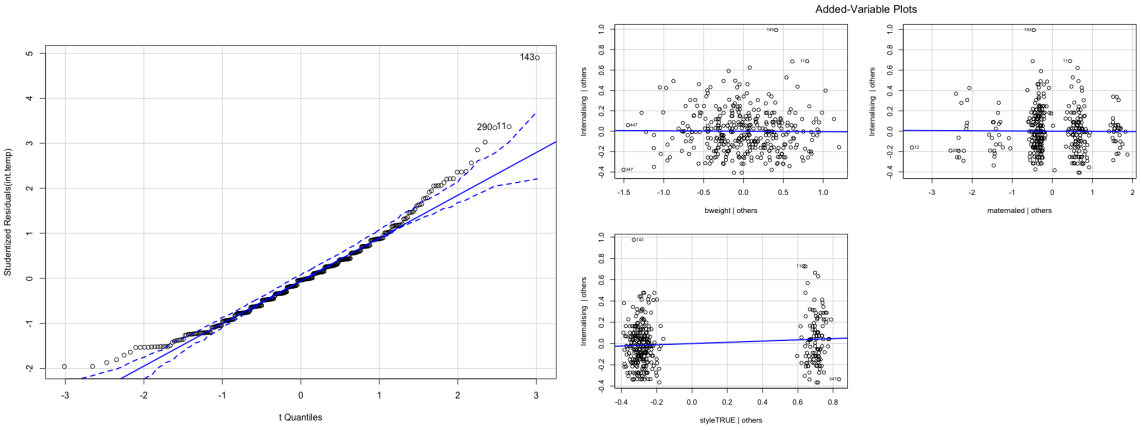


(e)

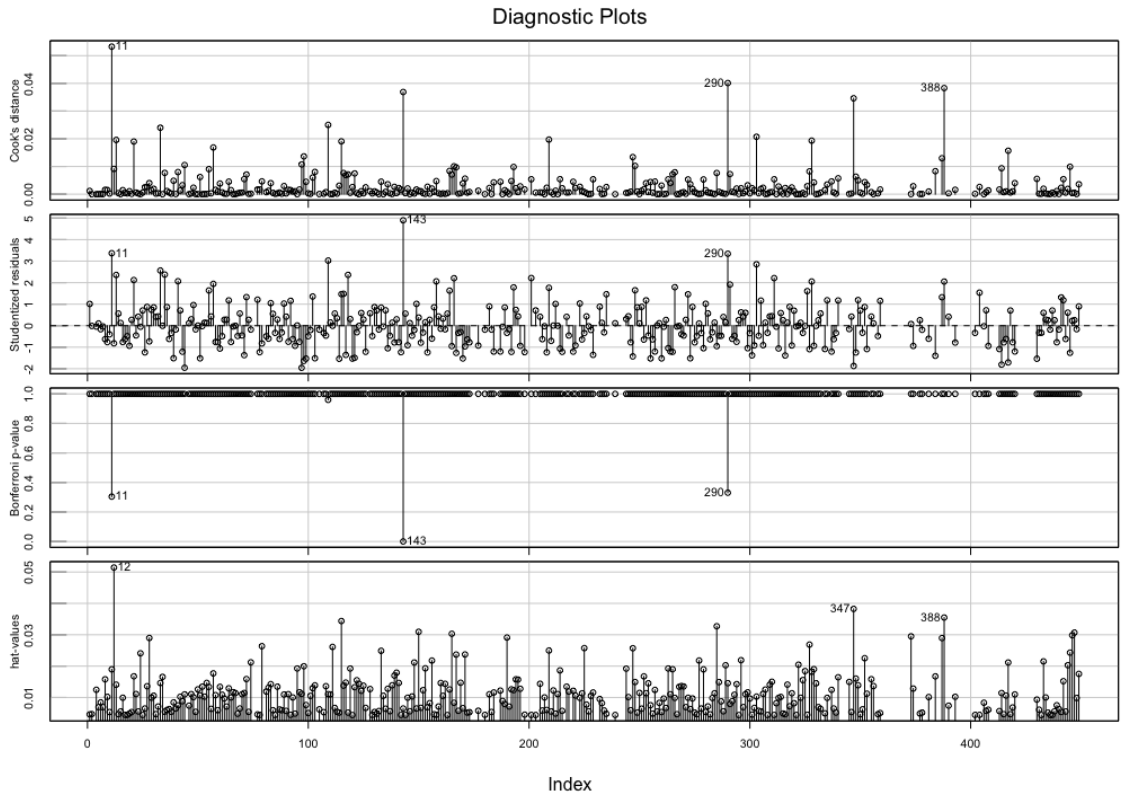
Figure F.6: **Total psychology scores predicted by genotype**



(a) (b)

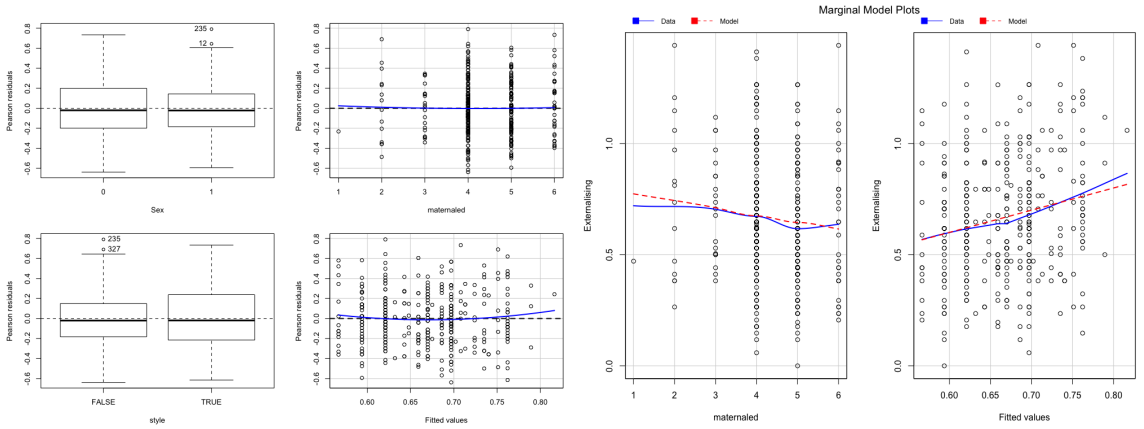


(c) (d)



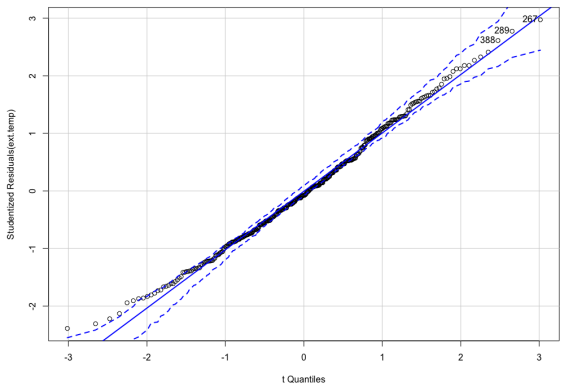
(e)

Figure F.7: **Internalising scores predicted by temperament**

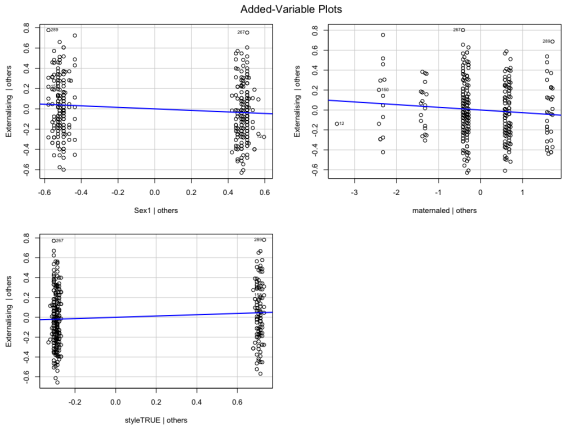


(a)

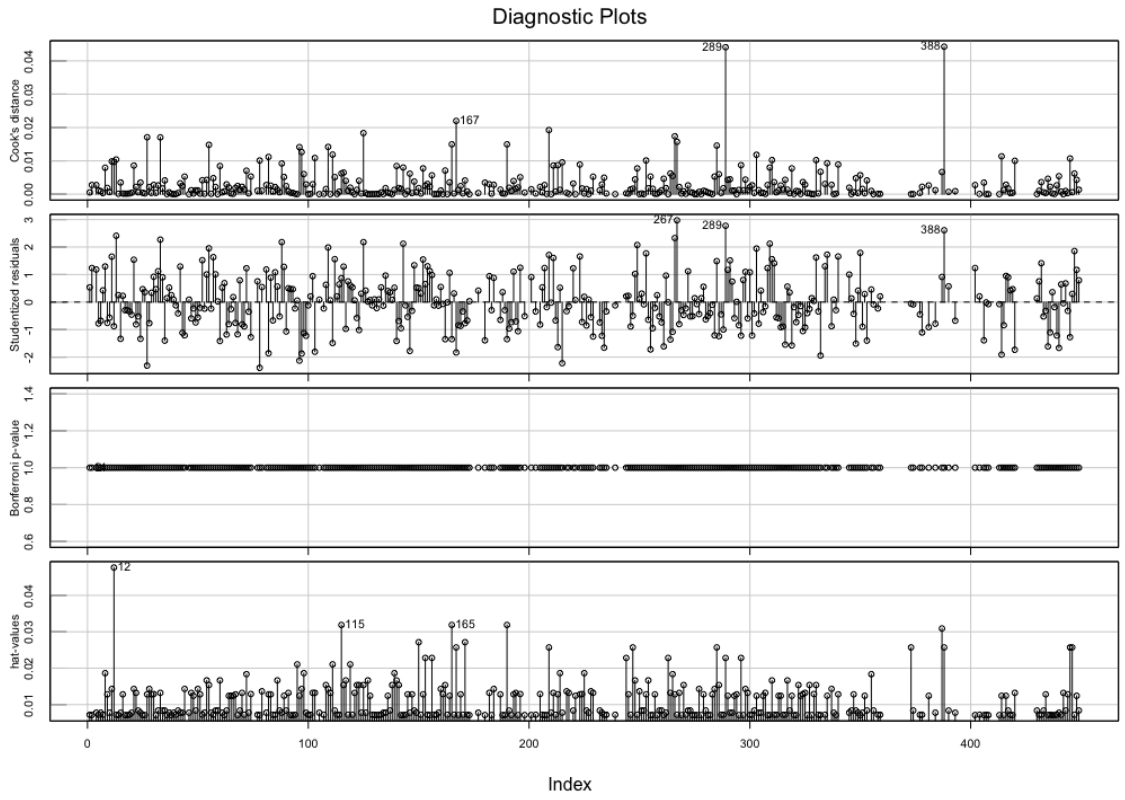
(b)



(c)

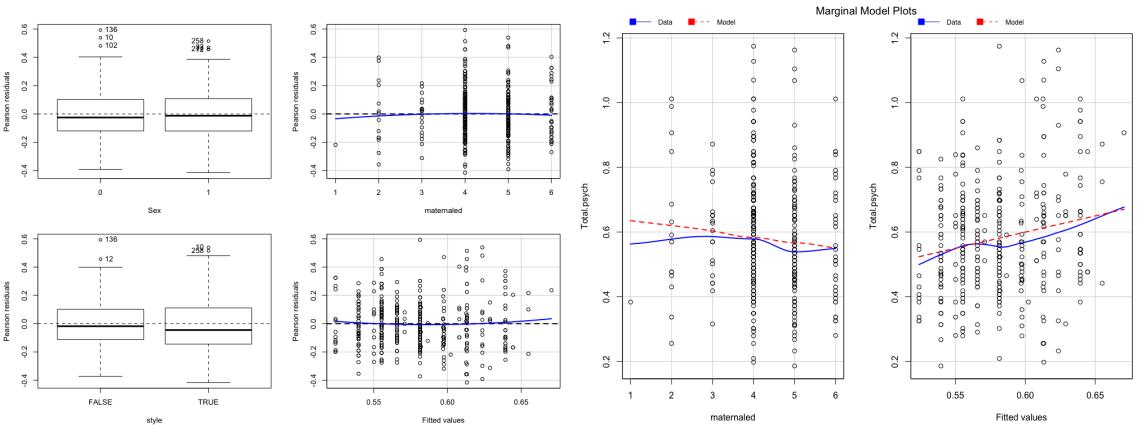


(d)



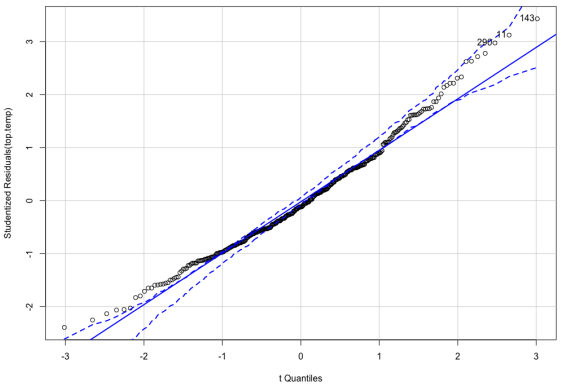
(e)

Figure F.8: **Externalising scores predicted by temperament**

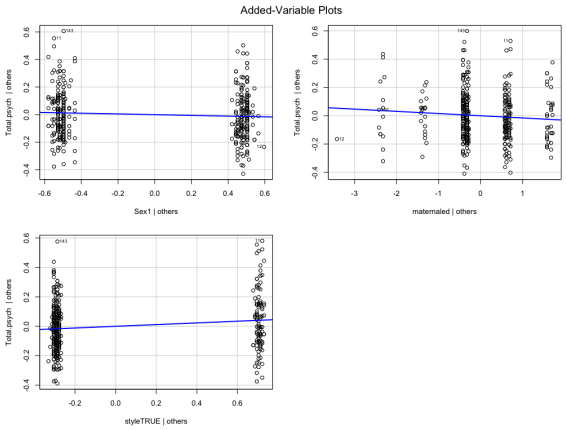


(a)

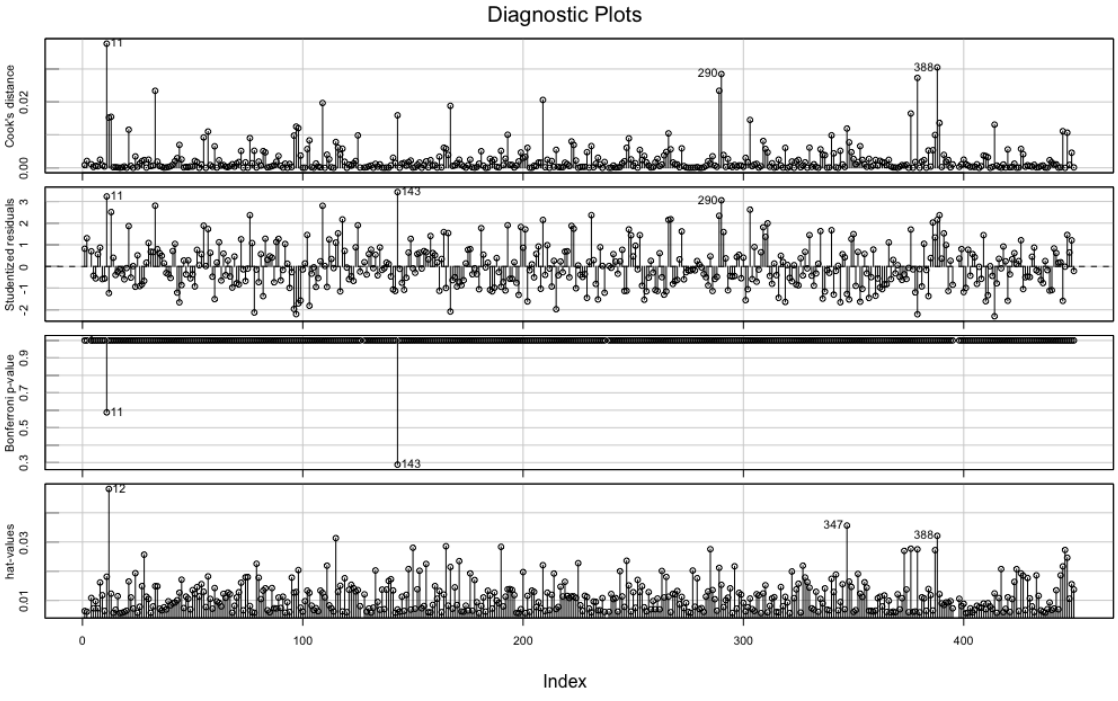
(b)



(c)

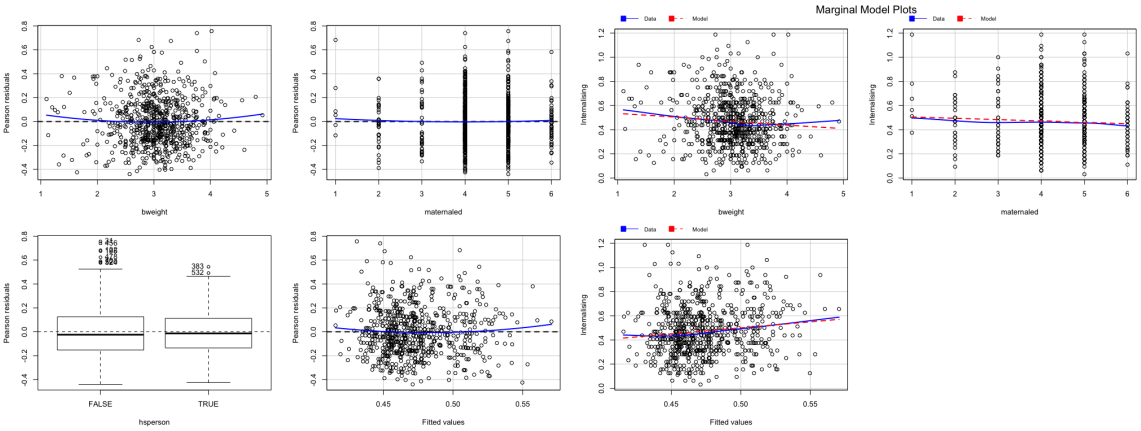


(d)

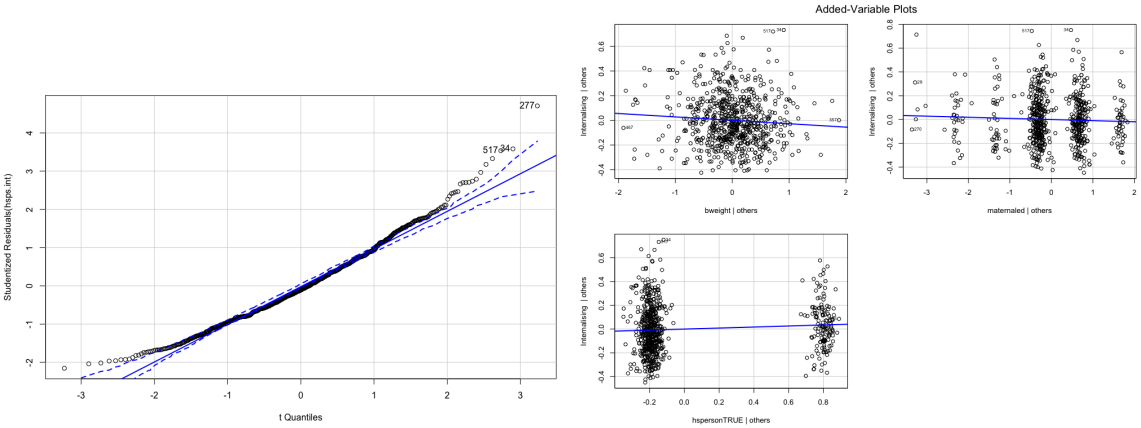


(e)

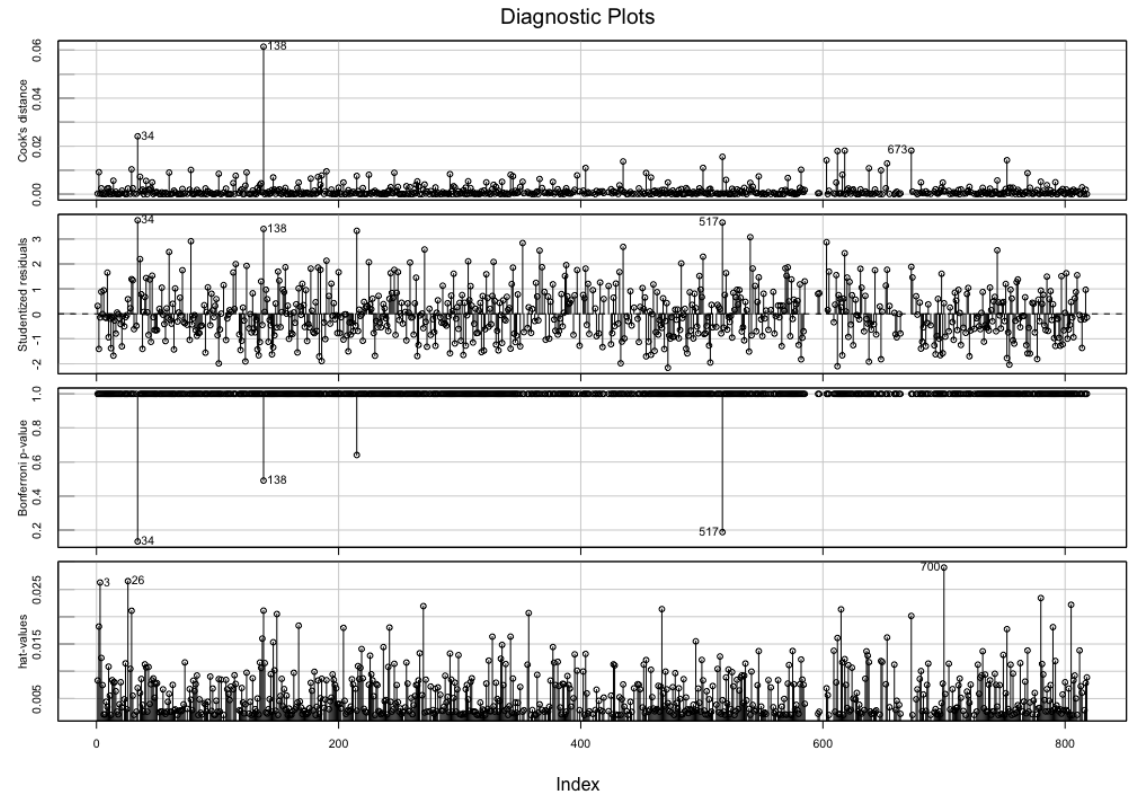
Figure F.9: **Total psychology scores predicted by temperament**



(a) (b)

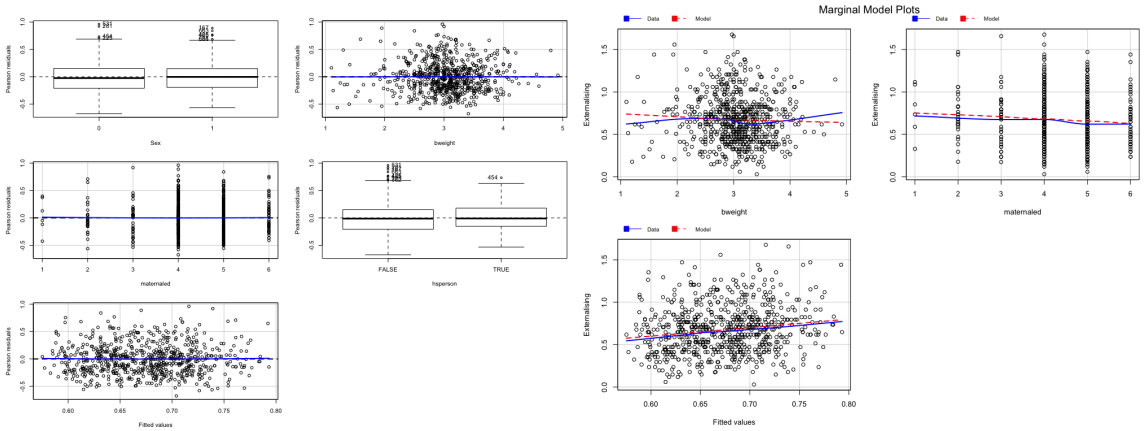


(c) (d)



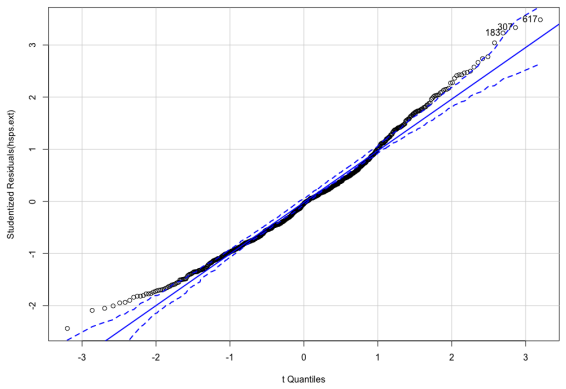
(e)

Figure F.10: **Internalising scores predicted by SPS**

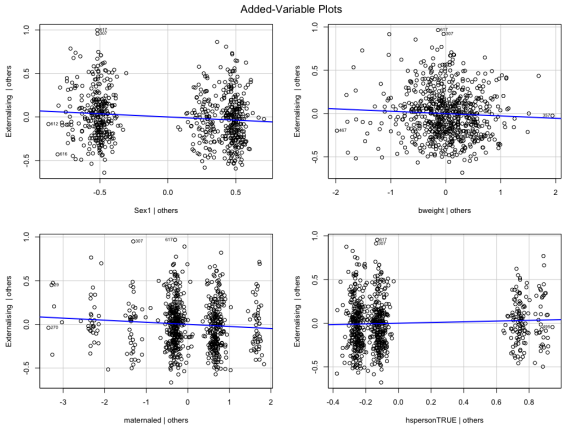


(a)

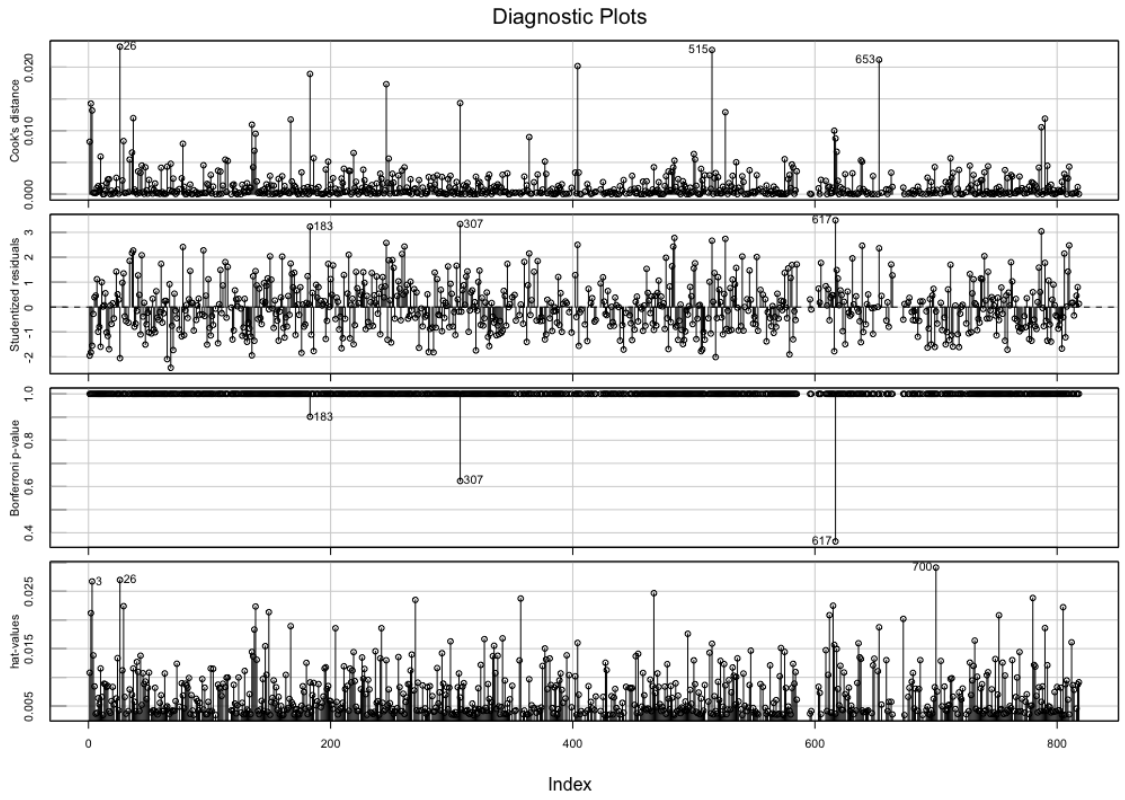
(b)



(c)

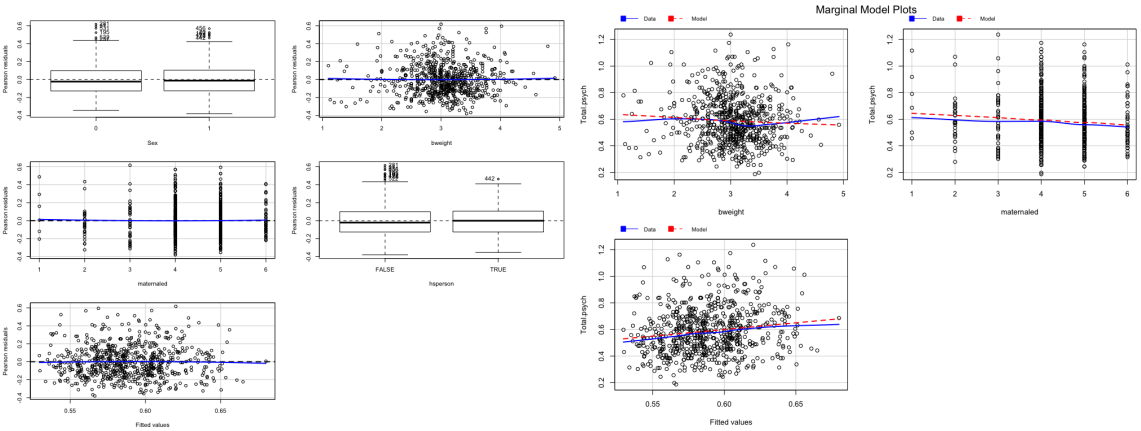


(d)



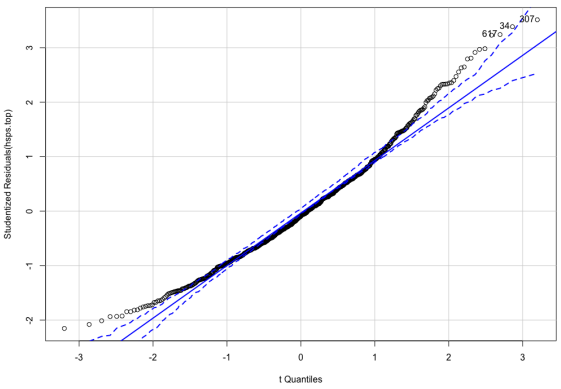
(e)

Figure F.11: **Externalising scores predicted by SPS**

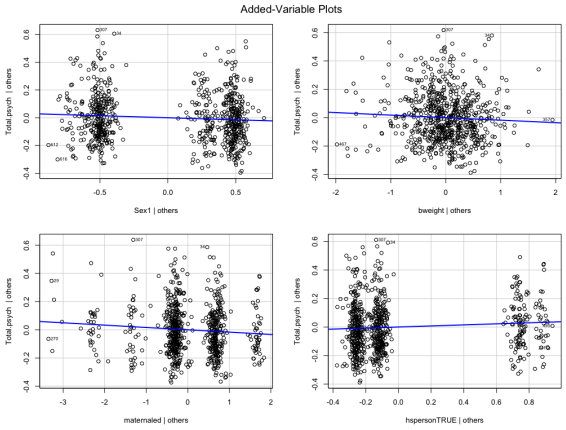


(a)

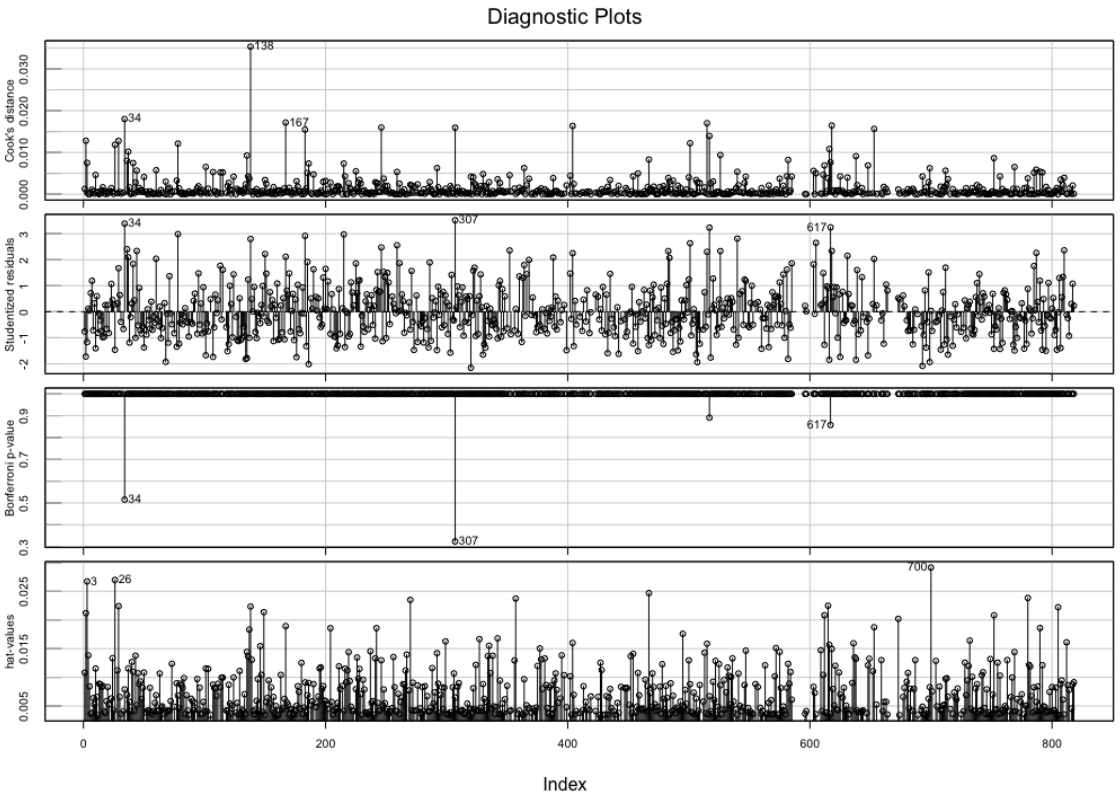
(b)



(c)



(d)



(e)

Figure F.12: **Total psychology scores predicted by SPS**