# The Effect of Conscious Sedation on Verbal Working Memory

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## Declaration

This research project is submitted in partial fulfilment of the requirements for the degree of MA Research Psychology, by coursework and research report in the Faculty of Humanities at University of the Witwatersrand, Johannesburg.

I declare that this research report is my own work. It has not been submitted before for any other degree or examination at Wits or any other university.

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Sharlene Richard Date

## Research Investigators

In addition to the author of this research report, three more researchers participated in a larger study titled: “Is there a true psychological (cognitive functioning and mood) effect of conscious sedation during endoscopic procedures?” The overall research project was compiled by all four researchers (including data collection). As the different researchers focused on their specific constructs from the overall project, data analysis was conducted individually. Below is a list of the researchers and their corresponding projects.

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## Abstract

Findings of past studies are inconsistent regarding the effects of anaesthetic drugs on working memory. Some studies suggest that the drugs decrease the immediate functioning of working memory while others propose no significant effects. This study looked at the effects of propofol and midazolam on verbal working memory functioning of 32 endoscopic patients; by means of a pre- and post-test design. The test battery used to measure verbal working memory consisted of the following subtests: Letter Number Sequencing and Digits Backwards of the WAIS-III, and the D-KEFS Colour- Word Interference conditions 3 and 4. Uncorrected and total errors made in condition 3 of the D-KEFS Colour- Word Interference test significantly increased, while completion time in condition 4 decreased significantly during post-testing. The completion time and corrected errors in D-KEFS Colour- Word Interference condition 3; corrected, uncorrected and total errors in D-KEFS Colour- Word Interference condition 4; and the WAIS-III Letter Number Sequencing and Digits Backwards subtests yielded no significant change. These results demonstrate partial effect of conscious sedation on verbal working memory. This study furthermore found that none of the subtests were subjected to practice effects, which holds value for future research aiming to use the same neuropsychological tests for pre- and post-test designs.

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# Chapter One: Introduction

Anaesthetic drugs administrated to patients during stressful medical procedures to deliberately inhibit episodic memory, eliminate the recollection of painful procedures and also the associated trauma (Gupta et al., 2012). When patients are relaxed by the anaesthetic drugs, medical practitioners are able to better focus at their task at hand (Veselis, 2006). Sedation (the administration of anaesthetics) is beneficial for (i) patients by making painful medical experiences more endurable; and (ii) medical practitioners by permitting optimal technical success (Daneshmend, Bell, & Logan, 1991; Rex, 2012). Sedation and natural sleep both affect the same neural pathways in the thalamus and cortical regions, and similarly induce a state of unawareness (Franks, 2008; Hutt, 2009). Similar to general anaesthesia, conscious sedative drugs are administered at lower dosages, for endoscopic procedures (colonoscopies and gastroscopies) when patients need to retain a level of consciousness in order for surgeons to give instructions (Daneshmend et al., 1991; Veselis, 2006). The most advocated anaesthetics used for endoscopic procedures are midazolam and propofol, due to their compatible pharmacological elements (Gupta et al., 2012).

Although conscious sedation specifically targets episodic memory, it is a complex cognitive system, relying on short-term and working memory to encode information. Based on the interconnected processing of working memory and episodic memory, and its shared brain regions of functioning; theory and fMRI studies suggest that working memory may also be affected by sedative drugs (Cabeza, Locantore, & Anderson, 2003; Ranganath, Cohen, & Brozinsky, 2005; Tsukiura et al., 2001; Voss & Sleigh, 2007). Working memory is crucial for day to day cognitive functioning as it enables us to manipulate information for further processing and/ or long term storage (Baddeley, 2004; Chun & Wolfe, 2005). Owing to working memory,

we can accomplish higher cognitive tasks such as reading, studying, and comprehension (amongst many others) (Baddeley, 2004). The effective functioning of working memory relies strongly on adequate sleep (Walker, 2008). Given that sedation affects neural pathways similarly to sleep, it is suggested that various cognitive functions, like working memory, are affected accordingly (Franks, 2008).

A literature review based on previous studies that looked at the effects of conscious sedation on working memory, is analysed in terms of its contradictive outcomes. Some studies found that midazolam and propofol decreased working memory functioning, respectively (Fisher, Hirshman, Henthorn, Arndt, & Passannante, 2006; Lianga, Manelisb, Liub, Aizensteinc, Gyulaid, & Quinland, 2012; Veselis et al., 1992). On the other hand, studies that looked at the combined effects of propofol and midazolam found less significant effect of the sedative drugs on working memory (Hsu, et al., 2012; Veselis et al., 2009).

This current study looks at the combined effects of midazolam (less than 1 mg) and propofol (between 180 mg and 310 mg) on verbal working memory in a group of endoscopic patients. The aim of the study is to test whether midazolam and propofol have any significant effects on working memory functioning. Baddeley's (2004) model is the theoretical framework used to explain working memory. The research design is a pre- and post-test, within subjects design (Stagnor, 2011). Prior to their endoscopic procedures, patients were assessed on a battery of verbal working memory tasks, and again when they woke up after their procedures. Paired samples t-tests and Wilcoxon Signed Rank tests are used to compare pre-and post-test results of verbal working memory. Effect sizes are used to evaluate the impact of statistically significant results. These results are then examined and discussed in relation to the literature and previous studies. Lastly the limitations of this study and recommendations for future research are reported.

# Chapter Two: Literature Review

## A Brief Theoretical Review of Working Memory

Throughout daily tasks such as making conversation, reading and problem solving the human brain depends on the efficacious functioning of working memory. Working memory structures enable a network of connections between perception, attention and long term memory (Baddeley, 2000). By its key mediating role between stimuli and long term memory, working memory essentially allows us to process, memorise, recall and manipulate relevant information for brief periods of time before it is encoded into long-term memory (Baddeley, 2004; Chun & Wolfe, 2005). Episodic memory is a type of long term memory that represents specific events of specific time periods (Ranganath et al., 2005). Given its key role in long term memory processing, working memory has an inevitable role in episodic memory. Short term memory, working memory and episodic memory systems all operate in the pre-frontal cortex (Cabeza et al., 2003; Tsukiura et al., 2001). Regarding neural activity, working memory can be understood as prolonged synaptic activity (Voss & Sleigh, 2007).

Baddeley and Hitch's (1974) model of working memory is presented as a theoretical backdrop to this study because of its influence in cognitive- and neuropsychology, and its impact on working memory tests like the ones used in this study. Their initial working memory model comprised of three independent parts: the central executive, the visuospatial sketchpad and the phonological loop. Later, Baddeley (2000) identified an additional component namely the episodic buffer. These four segments work together to achieve overall working memory functioning, however, each of these components has a distinctive role (Baddeley, 2004). Identified as the attentional model, the central executive controls the remaining three components from the top down (Baddeley & Hitch, 1974). Rosazza and Minati (2011)

summarised in a review on functional magnetic resonance imaging (fMRI), that the central executive is in the following brain regions: medial frontal gyrus, superior frontal gyrus, and anterior cingulate cortex.

Subsequent to the central executive, the phonological loop and visuospatial sketchpad are responsible to process distinctive aspects of working memory (Baddeley & Hitch, 1974). Auditory and speech-based information is processed by the phonological loop, which enables both speech comprehension and production (Baddeley, 2004). The phonological loop, also understood as verbal working memory, plays a key role in learning languages. Speech comprehension is managed by the phonological store that holds information long enough for it to be processed by the articulatory rehearsal component which in turn enables speech production (Baddeley, 2004). The phonological store is located in the Wernicke's area (cerebral cortex) and the rehearsal component in the Broca's area (left frontal lobe) as indicated by fMRI studies (Baddeley, 2000). The accuracy of the phonological loop processing is influenced by the type of sounds and length of words (Baddeley, 2004). Baddeley (2003) points out that, for example, it is easier to recall letters that have dissimilar sounds to one another like *F, K, V, Y, R, X;* as opposed to letters of similar sounds like *B, G, V, T, C, D.* Furthermore, shorter words are easier to remember than longer ones.

Parallel, but separate to the phonological loop, the visuospatial sketchpad processes both visual and verbal information. The visuospatial sketchpad is predominantly responsible for processing visual information through its distinct visual and spatial components, thus allowing us to process the colour, shape, location and speed of objects (Baddeley, 2004). The visual and spatial components have passive storage systems, holding information long enough to be processed by the active manipulation section (Repovs & Baddeley, 2006). The visuospatial

sketchpad furthermore allows for spatial and geographical awareness. Object recognition is supported by a ventral stream which spreads from the occipital to the temporal cortex, while spatial operations are enabled by a dorsal stream that links the occipital and parietal cortices (Müller & Knight, 2006).

Baddeley (2003) explains the distinct functioning of the phonological loop and the visuospatial sketchpad by the ability to track the movement of a light on a board without it interfering with the efficient functioning of the phonological loop. Yet, it is important for the phonological loop and the visuospatial sketchpad to correspond as allowed for by the episodic buffer, the fourth component proposed by Baddeley (2000). This component is responsible for integrating verbal, visual and spatial information into representable sequences (Baddeley, 2004). The episodic buffer furthermore has a significant role in assisting the central executive by acting as a storage component (Baddeley, 2004). Different to the other component of the working memory model, brain regions representative of the episodic buffer are more challenging to pinpoint. In line with Baddeley's initial hypothesis, evidence shows that the left anterior hippocampus is involved. However, further research is needed to identify other brain regions involved (Berlingeri et al, 2008). Figure 1, on the next page, is a visual representation of Baddeley's (2004) model.

Figure 1. Baddeley's working memory model.

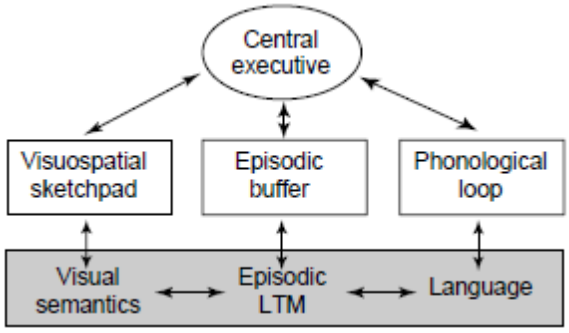


*Figure 1*. Baddeley's three-component model of working memory. From "Working Memory and Language: an Overview," by A. Baddeley, 2003, *Journal of Communication Disorders, 36,* p. 196. Copyright 2003 by Elsevier Science Inc.

## Working Memory and Sleep

Adequate quality sleep is an essential behavioural state for our overall wellbeing: proper functioning of the immune system and effective cognitive performance (Colrain, 2011). Sleep enables neural activities that integrate knowledge and consolidate memories (Hutt, 2009). In terms of working memory, the ability to focus on and process information is adjusted by the amount and quality of sleep (Walker, 2008). Several studies have supported the importance of sleep, compared to sleep deprivation, for proper working memory functioning (Chee & Choo, 2004; Chee et al., 2005; Fenn & Hambrick, 2011; Mu et al. 2005; Turner, Drummond, Salamat, & Brown, 2007).

Fenn and Hambrick (2011) suggested that sleep improved working memory performance in a group of 255 undergraduate university students (mean age: 19), compared to their peers who were not allowed to sleep. Students were assessed before and after either sleep (12 hours in

which students followed their normal sleep pattern) or wake (12 hours awake) experimental conditions. The working memory assessment instruments entailed cued recall and operational span tasks. An analysis of variance (ANOVA) showed that students from the sleep condition improved significantly ($p<.01$, $d = 1.97$) in their post-test results compared to the wake condition ($p = .08$).

Mu et al. (2005) obtained similar results with added neuroimaging support. Magnetic resonance images (MRIs) of 30 healthy male participants (mean age: 28) were analysed after adequate sleep and again after 30 hours of sleep deprivation. During both imaging trials the participants completed the Sternberg verbal working memory task. The results of the first images (after sufficient sleep), showed prominent activity in the following brain regions: left dorsolateral prefrontal cortex, Broca's area, supplementary motor area, right ventrolateral prefrontal cortex, and the bilateral posterior parietal cortices. After 30 hours sleep deprivation the MRIs indicated significant activity decline in the aforementioned brain regions, particularly in the bilateral posterior parietal cortices. Evidently the participants' performances on the Sternberg verbal working memory task also worsened.

In a more comprehensive study involving 14 healthy participants (mean age: 23), Chee and Choo (2004) found that working memory performance after sleep deprivation was determined by the task at hand. Two working memory tasks were completed before and after sleep deprivation, both entailing letter tasks. In the first, simpler task, participants had to match upper and lower case letters, but the stimuli were interrupted by time delay and distractors. The second, more difficult task required participants to manipulate the letters presented to them by thinking of the subsequent alphabetical letter, and memorise the manipulated information for the next task. Performance on higher cognitive task, which required advanced manipulation of

information were better preserved compared to preceding simpler task. MRIs indicated that prefrontal and thalamic activity compensated for the sleep deprivation during the more complex working memory tasks (Chee & Choo, 2004).

In a later study, Chee et al. (2005) suggested that the preserved performance of more complex tasks seen in their previous study is expected to be subjective to individual difference. Chee et al. (2005) assessed 26 healthy adults (19 – 25 years) on the same working memory tasks explained in their previous study (Chee et al., 2004). There were three experimental conditions for the same group of participants: right after adequate sleep; 24 hours after sleep deprivation; and 35 hours after sleep deprivation. Brain activity was measured by MRI during each condition. No significant MRI differences were found between the 24 – and 35 hours sleep deprivation conditions. Chee et al. (2005) suggested that neural activity in the left frontal and left parietal regions right after sleep correlated positively with effective working memory performance after 24 hours sleep deprivation; showing that some individuals were better able to preserve complex working memory task completion after sleep deprivation. However, these MRI results were not consistent for all participants, indicating individual differences as some participants were able to preserve complex working memory functioning, but not the entire sample.

Turner et al. (2007) found results that confirm the effect of individual difference in verbal working memory on task performance after sleep deprivation. Forty healthy participants (aged 19-39) completed pre-and post- testing on attention, verbal working memory and episodic memory before and after a 42 hour sleep deprivation. Of the three constructs assessed, verbal working memory tasks most significantly declined after sleep deprivation; as illustrated by a matched pairs t-test ($p<.05$). Working memory tasks entailed memorising nonsense words which they had to later recognise. These tasks were interfered by a few seconds delay and other stimuli.

Although the overall results indicated a decline in verbal working memory functioning after sleep deprivation, on closer investigation the researchers found that some participants (N = 5) were more resilient to the effects of sleep deprivation, indicating preserved performance.

In the studies by Turner et al. (2007) and Chee et al. (2005) individual differences between participants revealed inconsistent results, however, the overall results for all the studies in this section consistently indicated that sleep deprivation significantly decreases the effective functioning of verbal working memory. These studies support the theory that sufficient sleep is necessary for proper cognitive functioning. Individual differences, as pointed out by some of these studies, should be considered in similar research of cognitive functioning as these may well impact the overall outcome of results.

## Conscious Sedation

During anaesthetic sedation, changes in the brain stem, cortex and thalamus due to drugs overlap with changes during sleep. However, the drug effects are not the same in comparison to sleep, especially in the event of conscious sedation (Voss & Sleigh, 2007). Under conscious sedation patients remain at an altered level of consciousness, compared to the more severe general anaesthesia where patients are unresponsive (Daneshmend et al., 1991). Both conscious sedation and general anaesthesia mostly entail intravenous administration of anaesthetic drugs. The same drugs used for general anaesthesia is administered during conscious sedation, at lower dosages to achieve a decreased effect (Stamatakis, Adapa, Absalom, & Menon, 2010).

For procedures such as endoscopies, medical practitioners rely on a level of awareness to communicate important instructions to patients. The administration of conscious sedation is an optimal solution as it allows communication without leaving patients with traumatic memories of the procedure (Veselis, 2006). Conscious sedation promotes pain relief which subsequently

increases patients' tolerance of painful and intrusive procedures. It furthermore permits continuous independent functioning of the patients' airways (Daneshmend et al., 1991). The overall outcome is more comfortable and more technically successful procedures (Daneshmend et al., 1991; Rex, 2012). Conscious sedation has become a common global practice in preparation of painful procedures such as endoscopies as the benefits outweigh the risks when done under proper medical conditions (British Society of Gastroenterology, n.d.; Bannert et al., 2012; Daneshmend et al, 1991). During conscious sedation, drug levels are properly monitored to ensure a successful procedure without patient interference, promoting limited patient distress (Gupta et al., 2012).

Essentially, conscious sedation depresses the central nervous system, although not as extensive as general anaesthesia (Gupta et al., 2012; Stamatakis et al., 2010). The anaesthetic drugs used for conscious sedation result in anterograde amnesia, thus preventing the patients of remembering the procedure. More specifically, anaesthetic drugs inhibit episodic memory: memory that represents specific events at specific times. While under sedation, patients can thus not remember their experiences during the procedure because external stimuli are not reconciled into episodic memory (Veselis et al., 2009). Due to its effects on the central nervous system, and especially on memory system, conscious sedation has gained its relevance in the field of cognitive functioning (Stamatakis et al., 2010).

There is a variety of sedative drugs used for conscious sedation, mostly administered in a combination of two or more drugs. Propofol and midazolam are well known for their combined effects during conscious sedation (Padmanabhan, Leslie, Eer, Maruff, & Silbert, 2009; Veselis, 2006). The combination of midazolam and propofol is recommended due to its compatible pharmacological attributes (Gupta et al., 2012). For the purposes of this research the effects of

midazolam and propofol are reviewed as these were the drugs administered to the endoscopy patients that formed part of the study.

Midazolam is a type of benzodiazepine. Benzodiazepines, such as midazolam act by binding to the receptor cells responsible for gamma-Aminobutyric acid (GABA) release (Gupta et al., 2012). The effect of GABA, an inhibitory neurotransmitter, is thus enhanced; which leads to analgesia (the inability to feel pain) (Vasileiou, et al., 2009). Due to this enhanced effect of GABA, neural activity in cortical regions decreases. The benzodiazepine thus directly affects cortical regions, but also indirectly via the endogenous brain stem and hypothalamic arousal system. Stimuli are therefore cut off at the cortex (Voss & Sleigh, 2007). Referring back to the section on the background theory of working memory; recall that both working memory and episodic memory processes are carried out in subcortical regions. The question arises as to whether sedative drugs affect all cortical regions (including short-term memory and working memory).

Benzodiazepines are known for their anterograde amnesiac effects especially during the encoding stage of episodic memory. Midazolam generally offers 30 to 40 minutes of total amnesia (Gupta et al., 2012; Raaijmakers & Shiffrin, 1981). Although consciousness is required to attend and remember information, it does not support episodic memory encoding (Voss & Sleigh, 2007). Consciousness in itself is not sufficient for encoding (Fisher et al., 2006).

Based on its interference during encoding, researchers became interested in whether midazolam also affects short-term and working memory. Fisher et al. (2006) did a study on 32 healthy participants (aged 18 to 35) and found that midazolam negatively affected both short-term memory and working memory. The ANOVA results were significant [$F(1, 31) = 4.57$, $p < .04$, $MSE = 4.63$]. The effects of midazolam were reported as less extensive on short-term- and

working memory in comparison to its effects on episodic memory. The researchers only used one working memory task (digits backwards task) and recommended that further studies use a wider range of tests.

A similar pre-test/ post-test study with nine healthy participants also indicated that midazolam decreased their ability of backwards recall (Lianga et al., 2012). In a study with 30 colonoscopy patients, midazolam significantly decreased psychomotor speed and attention in comparison to a control group. However, working memory did not show the same significant difference. Hsu et al. (2012) found that when patients were assessed 120 minutes after sedation, no traces of cognitive decline (attention and psychomotor speed) were left.

Propofol is a sedative/ hypnotic anaesthetic drug with similar outcomes to midazolam, and also increases GABBA performance (Stamatakis et al., 2010). Propofol is different to midazolam in that memories seem to be encoded but not able to be recalled at later stage, thus inhibiting memory reconciliation (Veselis, 2006). Propofol blocks the neural pathways that enable sensory information to reach high-order networks. This prevents information from being integrated, thus impacting various cognitive processes such as long-term memory (Liu et al., 2012). Under mild sedative conditions (conscious sedation) propofol inhibits explicit memory, especially episodic memory (Quan et al., 2013). Propofol was also found to reduce short term memory, impair recall and decrease recognition (Veselis et al., 1992).

The half-life (active duration) of anaesthetics is a significant variable when investigating its cognitive effects. There are two types of half-life: distribution and elimination. Distribution half-life is the time that anaesthetics take to fully distribute throughout patients' systems. Elimination half-life is the time that the anaesthetics take to become fully metabolised. Midazolam has a distribution half-life of 6 to 30 minutes and an elimination half-life of 1 to 4

hours. Propofol's distribution half-life is 2 to 4 minutes and has an elimination half-life of 30 to 60 minutes (Gupta et al., 2012). From this it becomes clear that the different sedative drugs affect memory systems at different time periods. Furthermore, individual metabolic rates will evidently impact the time span of the half-life of the different drugs (Stamatakis et al., 2010).

Consistent with the recommended combined use of midazolam and propofol, researchers have investigated the effects of thereof. In a study with 55 healthy participants, Veselis et al. (2009) suggested that working memory was not significantly affected by a combination of midazolam and propofol. Working memory was assessed by one task only: a picture recognition task. Participants successfully recognised pictures when the visual information was still in working memory; compared to limited recognition when information has been already stored in long term memory ($p = .002$)(Veselis et al, 2009).

Padmanabhan et al. (2009) did a large study on 200 colonoscopy patients. Patients were divided into one of the following three sedative conditions: propofol, propofol plus midazolam, or propofol plus fentanyl. Attention and working memory tasks were completed before and after the administration of sedative drugs. There was no significant difference in cognitive performance between the three groups, but significant differences between pre- and post-testing (Padmanabhan et al., 2009). The researchers did not give much detail on the type of assessment instruments used, or instructions related to task completion (whether time limits were introduced, etc.).

## Sleep and Sedation

The complex neural underpinnings and interconnectedness of both sleep and sedation are not yet fully comprehended by research (Franks, 2008; Hutt, 2009). Although two different phenomena, a key common ground between sedation and sleep is that they both reduce

consciousness (Franks, 2008). Not only do both sleep and sedation work through the same neural pathways (in the cortex and thalamus), they also perform similarly in these pathways (Hutt, 2009). There is thus value in research that extend our understanding of the effects of sedation, which act similarly to sleep, on cognitive functioning. During both natural sleep and sedation the thalamus becomes largely deactivated, leading to cortical inhibition (Franks, 2008). Cortical inhibition entails a vast amount of cognitive activity, in which working memory plays an important role (Baddeley, 2000). As Franks (2008) advocate, more research is needed to understand the extent of cortical inhibition, and thus critical cognitive functioning like verbal working memory during sedation.

## Rationale

Conscious sedatives are administrated to patients during endoscopic procedures to intentionally induce anterograde episodic memory amnesia. The inability for patients to recall painful and stressful procedures makes it less traumatising (Gupta et al., 2012). Relaxed patients enable medical practitioners to work with better accuracy (Veselis, 2006). Patients need to remain at a level of consciousness in order for surgeons to communicate important instructions (Veselis, 2006). The most advocated anaesthetics used for endoscopic procedures are midazolam and propofol, due to their compatible pharmacological elements (Gupta et al., 2012).

Because memory entails complex and integrated cognitive systems, conscious sedation affects more than just episodic memory (Padmanabhan et al., 2009; Veselis et al., 1992). In association with attention and short term memory, working memory enables information to be encoded into long term memory (Baddeley, 2000). Working memory enables day to day cognitive functioning by manipulating information for further processing and/ or long term storage (Baddeley, 2004; Chun & Wolfe, 2005). Based on the interconnected processing of

working memory and long term memory, and its shared brain regions of functioning, theory and fMRI studies suggest that working memory may also be implicated by sedative drugs (Cabeza et al., 2003; Ranganath et al., 2005; Tsukiura et al., 2001; Voss & Sleigh, 2007).

Similar to sleep, sedation affects the thalamus and cortical brain regions, especially in terms of neural connectivity (Franks, 2008). Sleep is essential for proper working memory functioning, amongst other cognitive processes (Walker, 2008). Franks (2008) advises that there is still much research to be done on the similarities of sleep and sedation on the various cognitive processes associated with the cortical regions, leading to questions such as the comparable effects of sedation and sleep on working memory processing.

Previous research studies have conflicting results regarding the effects of conscious sedation on working memory. Results from studies by Fisher et al. (2006) and Lianga et al. (2012) suggested that midazolam significantly decreased the effective functioning of working memory. Similarly, Veselis et al. (1992) suggested that propofol significantly decreased the effective functioning of working memory and short term memory. Padmanabhan et al. (2009) tested whether different combinations of sedatives had unique effects on working memory and found no significant differences, but did suggest that sedatives decrease in working memory functioning.

Contrary to the decreased working memory results, Hsu et al. (2012) found that midazolam significantly affected psychomotor speed and attention, but not working memory. A combined administration of propofol and midazolam resulted in no changes of working memory functioning (Veselis et al, 2009).

Overall, these studies relied on single task tests for working memory. More consistent results may arise from studies that opt for a battery of tests. Another implication for the different

results from sedation could be the half-life of the drugs. Both the distribution and elimination half-life of the different drugs vary. Midazolam has a longer distribution (6 to 30 minutes) and elimination half-life (1 to 4 hours), compared to propofol's distribution (2 to 4 minutes) and elimination half-life (30 to 60 minutes) (Gupta et al., 2012). Different sedative drugs affect memory systems at different levels and time periods. Furthermore, individual metabolic rates will evidently impact the time span of the half-life of the different drugs (Stamatakis et al., 2010). The time between drug administration and working memory tests can thus also account for discrepancies in the literature.

More research is needed to investigate the effect of midazolam and propofol on verbal working memory functioning; comprising of a battery of tests to measure verbal working memory performance. Understanding the effects of sedative drugs on verbal working memory may add to the overall literature that guides regulations involving the time patients get discharged after their procedures. Furthermore, research in this field may improve overall patient satisfaction if they know what side effects to expect.

## Research Question

Is there a statistically significant difference between pre- and post-test results for verbal working memory for a group of patients undergoing conscious sedation (midazolam and propofol) prior to endoscopic procedures?

# Chapter Three: Method

## Research Aim

To determine if verbal working memory is significantly affected by conscious sedation that is administered to patients undergoing endoscopic procedures.

## Variable System

### Independent Variable

#### Conscious sedation.

##### *Theoretical definition.*

Conscious sedation produce a state in patients in which they can better endure unpleasant medical procedures. The sedatives used for this technique can be with or without numbing effects, but does not disturb cardiorespiratory functioning and stability (Daneshmend et al., 1991; Rex, 2012).

##### *Operational definition.*

Low dose sedation protocol: Prior to the endoscopic procedure the following anaesthetic drugs were administered to the patients: midazolam in a single dose of less than 1mg (regulated by patients' bodyweight per kilogram); and propofol, based on the anaesthetist's judgement (between 180 and 310 mg).

## Dependent Variables

### Verbal working memory.

#### *Theoretical definition.*

Working memory enables relevant information to be processed, memorised, recalled and manipulated for brief periods of time for the task at hand. Working memory is distinctively subdivided into verbal and visual working memory. Verbal working memory entails the work of the phonological loop, which manages speech comprehension and production (Baddeley, 2004).

#### *Operational definitions.*

Raw scores from the following tests were used to measure verbal working memory:

- Letter Number Sequence subtest from the Wechsler Adult Intelligence Scale III (WAIS III);
- Digit Span Backwards from the Digits Span subtest from the Wechsler Adult Intelligence Scale III (WAIS III);
- Delis Kaplan Executive Function System (D-KEFS) Colour- Word Interference test (Conditions 3 and 4).

## Extraneous Variables

### Variables that were controlled for.

- There is a causal relationship between level of education and cognitive ability (Scarmeas & Stern, 2003). Level of education were controlled for by only including participants with at least a matric level of education, including a minimum of five years of formal high school English teaching;

- No participants suffering from severe headaches, hypertension and/ or nausea after the endoscopic procedures were assessed on the post-test battery as these symptoms may have affected test-taking;
- All participants using medication for neurological or psychiatric illnesses were excluded because of its influences on cognitive performance (Medalia, & Lim, 2004). Furthermore, patients who took mood stabilizing drugs, antidepressants, benzodiazepines or chronic opioids were excluded as the chronic use thereof can likely affect cognitive performance (Dassanayake, Michie, Carter, & Jones, 2011);
- Participants who abused alcohol and/ or who took any illegal drug(s) were excluded as this affects cognitive abilities (Dregan & Gulliford, 2012);
- Based on the neuropsychological nature of this study, participants with any history of traumatic brain injury, dementia, and/ or central nervous system injury were excluded (Schinka & Vanderploeg, 2011);
- Both depression and anxiety negatively affects working memory (Landrø, Stiles, & Sletvold, 2001). The Hamilton Rating Scales for Depression (HAM –D) and Anxiety (HAM – A) were therefore used to measure depression and anxiety, respectively, as part of the bigger project. Participants with high scores on depression and/ or anxiety were excluded.

**Variables that were not controlled for.**

- As this study formed part of a bigger project, different researchers assessed the participants. Individual differences may have influenced the test-taking experience of the participants, especially as the nature of the assessments was very interactive

(Weiner, 2003). All the assessors were well trained on the tests to abide by the standardisation process;

- Neuropsychological tests should be performed in a room with limited noise and other distractions (Hebben & Milberg, 2009). Due to the nature of assessing patients, assessments were conducted in the general day ward in which noise levels and other distractions were not as controlled for;
- Patients react differently to sedative drugs based on their metabolism speeds and how their bodies react to the anaesthetics (Mistraletti, Donatelli, & Carli, 2005). The time interval between the pre-and post-test battery thus varied for participants, depending on how fast they recovered from sedation and the endoscopic procedure;
- Cognitive functioning is known to decrease with age (Salthouse, 2004). The age range of participants varied significantly between 29 and 78 years, with a mean age of 55 years. Endoscopic patients generally are older adults (Amornyotin, Leelakusolvong, Chalayonnawin, & Kongphlay, 2012). This meant that due to the nature of this study, age could not be controlled for;
- The medical reasons that determined the patients' endoscopic procedures did not form part of the sample selection criteria. Patients suffering from illnesses or diseases prior to or during the research may have had affected their cognitive functioning (Kaplan & Saccuzzo, 2013). However, the researchers could not control for any of these if the participants did not inform the researchers either through the demographic questionnaire or verbally;
- Given South Africa's multi-linguistic context, most of the participants were at least bilingual. Participants with English as a second language were included if they had at

least five years of formal high school English education. Although it was important for the participants to be fluent in English due the nature of the assessments, proficiency was never formally controlled for. Language, in particular bi/multilingualism, has a strong influence on working memory (Bialystok, Craik, & Luk, 2008);

- Although the Johannesburg hospital is a private institution, higher socio-economic status (SES) could not be assumed as some patients might have been funded (by employers for example). Private healthcare was thus not used to ascertain SES (Lehohla, 2012);
- Previous exposure to neuropsychological tests was not controlled for, Experience in testing likely results in higher test-wiseness and refined strategies during test taking, especially in terms of practice-effects (McCaffrey, Ortega, Orsillo, Nelles, & Haase, 1992);
- Participants who are motivated to do their best during assessments have been found to perform better than those who are unmotivated (Chan, Schmitt, DeShon, Clause, & Delbridge, 1997). However, motivation levels were not measured and thus not controlled for.

**Research Design**

There was no control group as the test batteries were administered to the same participants before and after the sedation procedure. Furthermore, the researchers had no control over the sedation procedure and it was not manipulated. Overall, the best suited research design was a pre-experimental, repeated measured, within subjects design (Stagnor, 2011).

## Sample and Sampling

Based on the cognitive effects of the specific combination of sedative drugs that the researchers intended to study, a convenient sample was sourced (Stagnor, 2011). Therefore, patients who were scheduled for endoscopic (gastroscopy and/ or colonoscopy) procedures at a private Johannesburg hospital were invited to voluntarily participate, subject to the list of *variables that were controlled* for outlined earlier (Stagnor, 2011). In addition to those variables there was also a medical exclusion criterion list, employed by the medical team that applied to any patient:

- Who was admitted with a bleeding pathology under emergency conditions;
- Whose gastroscopy or colonoscopy procedure involved any interference to control bleeding;
- Whose sedation was changed to a general anaesthetic;
- Who underwent general anaesthesia due to cardiorespiratory disease;
- With an unprotected airway during sedation, that could have jeopardised the patient's general condition.

Data collection took place during four months in 2014, concluding with a sample size of 42 participants of which six could not complete the post-test battery. Reasons for incompletion mainly included patients feeling sick or fatigued after their procedure. Furthermore, the researchers had to exclude the data of another four participants after realising that these patients were taking antidepressants. An overall sample of 32 participants was used to analyse the difference of verbal working memory between pre-and post-testing.

Table 1 presents a descriptive summary of the sample based on the demographic and medical information that was collected by the Demographic Questionnaire (Appendix A). The

age range was extremely broad with 49 years difference between the youngest (29 years) and oldest participant (78 years). As indicated by a histogram, the sample was normally distributed in terms of age. The sample was mostly represented by an older age group with a mean of 55 years (SD 11 years). Males and females were almost equally representative with only two more females that participated. Participants who only spoke one language formed 16% of the sample. Half of the sample spoke two languages, followed by 34% who spoke three or more languages. English was by far the most common home language (80%), and all participants were fluent in English even if it was not their first language. The entire sample had at least a matric level of education. Additionally, more than half (51.6%) of the sample had at least one degree.

Although the majority of the sample (almost 60%) was hospitalised previously for various reasons, only two of the cases were for endoscopic procedures. The majority of the participants (65.6%) reported anecdotal attention/ and or memory problems. The type of endoscopic procedure (colonoscopy, or gastroscopy, or both) was not consistently recorded. The available data shows that most patients (28%) went for both colonoscopies and gastroscopies. All patients received less than 1 mg of midazolam. The average propofol dosage administered to the group of patients was 245.5 mg (SD 39.6 mg).

Table 1

*Sample Descriptive Statistics*

| Descriptor | |
|---|---|
| Age | |
| Mean | 54.8 years |
| Standard Deviation | 11.2 years |
| Maximum | 78 years |
| Minimum | 29 years |
| Gender | |
| Male | 15 (46.8%) |
| Female | 17 (53.1%) |
| Number of Languages | |
| 1 | 5 (15.6%) |
| 2 | 16 (50%) |
| >3 | 10 (34.4%) |
| Home Language | |
| English | 26 (80.1%) |
| Other | 6 (19.9%) |
| Education Level | |
| Matric | 9 (29%) |
| Diploma | 6 (19.4%) |
| Degree | 8 (25.8%) |
| Post Graduate | 8 (25.8%) |

Table 1. *Sample Descriptive Statistics* (*continued*)

| Descriptor | |
|---|---|
| Complaints of attention/ memory difficulties | |
| Yes | 21 (65.6%) |
| No | 11 (34.4%) |
| History of gastroscopy | 7 (12.3%) |
| History of colonoscopy | 11 (19.3%) |
| History of gastroscopy and colonoscopy | 16 (28.1%) |
| Sedatives | |
| Midazolam | All<1mg |
| Propofol | |
| Mean | 245.5 mg |
| Standard Deviation | 39.6 mg |
| Range | 180-310 mg |

## Instruments

Verbal working memory was assessed by a test battery comprising of the following subtests.

### The Letter Number Sequence Subtest (WAIS III)

In the Letter Number Sequence subtest the assessors read out a combination of numbers and letters in mixed order to the participants. The participants had to respond with numbers in ascending order first, followed by the letters in alphabetical order. Participants were allowed a

practice trial before starting with the first item. The subtest comprised of seven items, each with three trials. The first item had one number and letter in each trial. When a participant had at least one correct trial he/ she progressed to the next item. Three incorrect trials in one item discontinued the subtest. An extra number and letter were added as participants progressed to the next item. One point was assigned to each correct trial that were added up for an overall score. The highest possible overall score was 21 points. Higher scores indicated stronger verbal working memory performance (Wechsler, 1997).

The United States norming sample consisted of 2232 participants. The split-half method was used to determine the reliability of the Letter Number Sequencing subtest, and presented with a suitable Cronbach's alpha score of .82. Exploratory factor analysis confirmed that the Letter Number Sequence subtest (amongst the others that measure working memory) does measure the construct of working memory, showing that it is a valid measure (Wechsler, 1997).

The WAIS III has been adapted for, and widely used in the South African context (Claassen, Krynauw, Paterson, Wa Ga Mathe, 2001). The South African norming sample with 277 participants presented with a lower Cronbach's alpha of .72 for the Letter Number Sequencing subtest (Claassen et al., 2001). Reasons for the lower reliability scores likely relates to sampling, in that the South African adapted WAIS III is related to level of education (Shuttleworth-Edwards, Gaylard, & Radloff, 2013). Level of education did not, however, pose a threat to this study as all participants had at least a matric level of education.

**The Digit Span Subtest (WAIS III) (Digit Span Backwards)**

For the Digit Span Backwards subtest, the assessors read out a series of numbers which the participants had to repeat in the reversed order. Participants were allowed a practice example before proceeding to the items. Altogether there were seven items each with two trials.

Participants advanced to the next item if they had at least one correct trial in the previous item. Two consecutive incorrect trials concluded the subtest. As participants progressed, an extra number was added to each item, requiring participants to recall progressively more numbers in backwards order. One point was assigned to each correct trial, which were added up for an overall score. The maximum possible score was 14 points. Higher scores indicated stronger verbal working memory performance (Wechsler, 1997).

The split-half method was also used to assess the reliability for the Digit Span subtest and presented with a high Cronbach's alpha of .9, in a USA sample. As discussed under the previous section, factor analysis indicated that this subtest is valid in measuring working memory (Wechsler, 1997). In a South African sample, the Cronbach's alpha came out lower at .81 (Claassen et al., 2001). The same argument raised for the Letter Number Sequencing subtest applies for these reliability inconsistencies.

**The Delis Kaplan Executive Function System (D-KEFS) Colour- Word Interference (Conditions 3 and 4)**

All conditions of the D-KEFS Colour- Word Interference test were timed, which required participants to complete each task as fast as they could. Conditions 3 and 4 followed the preceding conditions 1 and 2 in which participants were primed to name colours and read black printed colour names respectively, without any switching/ inhibition. In both condition 3and 4 participants had to name the colour of the ink in which colour names was printed. However, the ink colour did not correspond with the typed colour name. This condition required participants to inhibit their instincts to read words when they were required to name the ink colours (Delis, Kaplan, & Kramer, 2001).

As in condition 3, participants had to name the ink colour and not read the contradicting colour name. In condition 4, an extra task was added as some colour names were printed in a block. The participants had to read the colour names printed in the blocks, then switch to naming the colours of the words not printed in blocks. Participants were allowed to correct themselves in all conditions, but corrections were regarded as errors. Corrected errors and uncorrected errors were added up to total errors. In this case higher scores indicated difficulty to inhibit the impulse to read out the words, and to switch between tasks in condition 4. Higher scores thus meant poorer verbal working memory performance (Delis et al., 2001).

The Internal Consistency reliability for ages 16 to 89 ranged between .75 and .77, which is acceptable. The test-tests reliability scores for conditions 3 and 4 were high at .9 and .8 respectively. This test has been standardised in the United States of America population, but participants' results were not compared to norms for any of the verbal working memory subtests (Delis et al., 2001).

## Procedure

### Preparation

Medical ethical clearance was obtained from the Human Research Ethics Committee (Medical) at the University of the Witwatersrand on the 9th of May 2014 (Appendix B). The hospital in Johannesburg (Appendix C) granted permission to conduct the research among its endoscopic patients. Meetings were scheduled with the relevant hospital staff that assisted in the research procedures, during which the researchers explained their aims and requests. A shortened version of the Information Letter (Appendix D) was made available to all patients that were scheduled for endoscopic procedures, beforehand.

**Pre-Testing**

On the day of their endoscopic procedures, interested patients were briefed by the researchers and provided with a more detailed information sheet (Appendix E) and a consent form (Appendix F). Briefing and assessment took place in the general ward where the patients waited to be taken into theatre. As part of the larger research project, all participants completed a series of mood and cognitive assessments. Once consent was obtained, the researchers proceeded with the following pre-test battery, which took 45 minutes on average to complete:

1. Demographic questionnaire;
2. Hamilton Rating Scale for Depression (HAM-D);
3. Hamilton Rating Scale for Anxiety (HAM-A);
4. Profile of Mood States (POMS);
5. Letter Number Sequence subtest (WAIS III);
6. Digit Span subtest (WAIS III);
7. D-KEFS Colour- Word Interference test;
8. Mental Control subtest (WMS IV).

**Sedation**

The researchers were in no way involved in the sedation or endoscopic procedures. Each patient was evaluated by an anaesthesiologist to confirm suitability of conscious sedation prior to the endoscopic procedure. The anaesthesiologist explained the sedation and endoscopic procedures after which they obtained medical consent from the patients.

The patients were fully monitored by the American Society of Anesthesiology standards. Additional oxygen was administered according to each patient's medical condition. Before sedation a local anaesthetic (Lignocaine: 0,1ml 1% solution) was sprayed into the back of the

patient's throat. Patients had to lie on their left sides in line with a biting block that was used to provide a safe passage through their mouths, thus protecting their teeth and the endoscopy equipment. Thereafter patients were given the following combination of anaesthetics:

- Midazolam in a single dose of less than 1mg;
- Propofol, based on the anaesthetist's judgement (between 180mg and 310 mg).

During the sedation the anaesthesiologist consistently monitored patients' vital readings (saturations, pulse and ECG) and any changes was managed accordingly. The anaesthesiologist also monitored the anaesthetic levels which were guided by the type of endoscopic procedure and the patient's anticipated pain threshold. As the purpose of sedation is to relieve painful experiences, the anaesthesiologist ensured to obtain clinical procedural amnesia and analgesia. After the endoscopic procedures all patients were attended to, and monitored at a post anaesthetic care unit (PACU) by trained nurses until discharge.

**Post-Testing**

As soon as the patients woke up from the anaesthetics (within an hour after the endoscopic procedures), they were administered the following post-test battery:

1. Letter Number Sequence subtest (WAIS III);
2. Digit Span subtest (WAIS III);
3. D-KEFS Colour- Word Interference test;
4. Mental Control subtest (WMS IV).

Post- testing took 15 minutes on average.

## Ethical considerations

According to the National Health Act (Act No. 61 of 2003) of South Africa this research project is classified as 'health research' because it aimed to contribute to the biological and

psychological understanding of human beings. Therefore this research got ethical clearance from the Human Research Ethics Committee (Medical) of the University of the Witwatersrand, Johannesburg on the 9th of May 2014; clearance certificate number M140302 (Appendix B). In addition, and subject to this ethical approval, a letter from a Johannesburg hospital (appendix C) granted permission for this research study. Furthermore, this study adhered to the *General Ethical Guidelines for Health Researchers* as published by the Health Professions Council of South Africa (HPCSA) (HPCSA, 2008). These guidelines, as listed below, ensured responsible health research that was ethically, scientifically and legally sound. Throughout the research process the participants were treated according to what is right and proper and their rights were protected as prescribed by the following guidelines (HPCSA, 2008).

- Participation in this study was completely voluntary. The patients had the right to autonomy granting them a choice of whether they wanted to participate in the study or not, without any negative outcomes for choosing not to participate. All interested patients received an information sheet containing a full disclosure of the research aims (appendix E). Participants were required to sign their own consent form; given that no one under the age of 18 years requiring parental consent was invited to participate (appendix F). Furthermore, according to the right of autonomy, participants had the right to withdraw from this study without any explanation needed or negative consequences.
- All the demographic information and assessment results were kept confidential, and are securely locked away in the Psychology department of the University of the Witwatersrand. All of the electronically captured information and data, along with the analysis records were saved on a password protected computer and backed up on a disc that is kept with the paper records. Confidential information was not, and will not be

shared with anyone other than members on the research team and was only used for the research purposes stipulated in the information sheet. The research team had no access to any patient hospital records. Participants only received feedback on their endoscopies from the medical team after the assessment batteries were completed, to avoid interference with neuropsychological test performance. Because the researchers met patients face to face, participation was not completely anonymous. To protect the identity of participants a two digit number was assigned to assessment papers instead of using their names. Individual feedback was not possible because of the participant numbers that were used, but participants have access to the overall research results.

- To ensure that no loss or damage were caused to the participants and/ or the community, the following was taken into consideration in line with the non-maleficence principle:
    - All the assessors involved were thoroughly trained on the assessment tools by the supervising registered clinical psychologist, Ms Aline Ferreira Correia.
    - Contact information for the South African Depression and Anxiety Group and Life Line were in the information sheet for any participant that required psychological support, especially since the overall project examined mood (anxiety and depression).
    - All neuropsychological tests were non-invasive. Based on the participants' level of education (minimum matric), they all had a sufficient level of test-wiseness which limits the pressure of test performance anxiety. All tests were administered by pen and paper which participants, given their education, were all familiar with.

# Chapter Four: Results

All statistical analyses were conducted by means of the IBM® SPSS® Statistic 22 software programme. First, descriptive statistics including the means, standard deviations, minima, maxima and medians were calculated for both the pre- and post-test verbal working memory batteries (Tables 2 and 3).

Thereafter the normality of the datasets were analysed by the Shapiro-Wilk test, which determined whether further analysis had to be parametric or non-parametric testing. In cases where assumptions for normality were met, matched paired samples t-tests were run. Where normality assumptions were not met, the Wilcoxon Signed Rank tests were used for analysis (Elliott & Woodward, 2007).

## Descriptive Statistics

Tables 2 and 3 presents the descriptive statistics of the verbal working memory subtests according to the pre- and post-test intervals respectively.

From table 2, the mean score for the Letter Number Sequence subtest from the WAIS III was almost 10 out of a possible score of 21. The minimum score is low at 4, but no participant had a score of 0. The maximum score of 14 indicates that there were no perfect scores. For the Digits Backwards subtest, participants had a mean score of at least 6 correct item responses out of a possible score of 14. Again, no participants scored 0, nor did anyone have a perfect score of 14. The mean completion times between conditions 3 and 4 of the D-KEFS Colour- Word Interference test were very similar, with less than one second's difference between the two. In condition 3, participants made more corrected than uncorrected errors. Condition 4 results were inversed to condition 3, as uncorrected error scores were higher than corrected error scores.

The post-test scores from table 3 reveal similar patterns to the results observed from table 2, especially the mean scores for both the Letter Number Sequence and the Digit Span Backwards subtests. However, there is a slight increase in both these subtests' maximum scores, but also a decrease in the minimum scores. The D-KEFS Colour- Word Interference post-test completion times for conditions 3 and 4 again only varied by less than a second. The uncorrected errors made in both conditions 3 and 4 were more, compared to the corresponding corrected errors.

Table 2

*Descriptive Statistics*

| Pre – Tests | Mean | SD | Minimum | Maximum | Median |
|---|---|---|---|---|---|
| WAIS III | | | | | |
| Letter Number Sequence | 9.90 | 2.30 | 4.00 | 14.00 | 10.00 |
| Digit Span Backwards | 6.48 | 2.03 | 3.00 | 10.00 | 7.00 |
| D-KEFS Colour- Word Interference | | | | | |
| Condition 3 completion time (seconds) | 66.74 | 25.75 | 40.73 | 152.00 | 61.00 |
| Condition 3 corrected errors | .97 | 1.35 | .00 | 5.00 | .00 |
| Condition 3 uncorrected errors | .71 | 1.47 | .00 | 7.00 | .00 |
| Condition 3 total errors | 1.68 | 2.53 | .00 | 12.00 | 1.00 |
| Condition 4 completion time (seconds) | 67.83 | 21.48 | 40.00 | 160.00 | 62.00 |
| Condition 4 corrected errors | .94 | 1.10 | .00 | 4.00 | 1.00 |
| Condition 4 uncorrected errors | 1.81 | 2.77 | .00 | 14.00 | 1.00 |
| Condition 4 total errors | 2.74 | 2.76 | .00 | 14.00 | 2.00 |

Table 3

*Descriptive Statistics*

| Post – Tests | Mean | SD | Minimum | Maximum | Median |
|---|---|---|---|---|---|
| WAIS III | | | | | |
| Letter Number Sequence | 9.66 | 2.88 | 3.00 | 15.00 | 10.00 |
| Digit Span Backwards | 6.39 | 2.55 | 2.00 | 13.00 | 6.00 |
| D-KEFS Colour- Word Interference | | | | | |
| Condition 3 completion time (seconds) | 61.99 | 26.68 | 30.00 | 180.00 | 56.00 |
| Condition 3 corrected errors | 1.52 | 1.69 | .00 | 6.00 | 1.00 |
| Condition 3 uncorrected errors | 1.74 | 2.13 | .00 | 7.00 | 1.00 |
| Condition 3 total errors | 3.26 | 3.37 | .00 | 12.00 | 2.00 |
| Condition 4 completion time (seconds) | 62.81 | 26.93 | 38.00 | 180.00 | 57.00 |
| Condition 4 corrected errors | 1.13 | 1.24 | .00 | 4.00 | 1.00 |
| Condition 4 uncorrected errors | 1.81 | 2.12 | .00 | 9.00 | 1.00 |
| Condition 4 total errors | 2.61 | 2.20 | .00 | 8.00 | 2.00 |

## Comparisons

### Normality of the Data

Prior to inferential analysis the normality of the neuropsychological test data was analysed. Based on the sample size (N = 32), the best suited test for normality was the Shapiro-Wilk test as it is more sensitive to samples of less than 50 cases (Ghasemi & Zahediasl, 2012). The Shapiro-Wilk test results are presented in table 4.

Based on the findings of the Shapiro-Wilk test, only the Letter Number Sequence and Digit Span Backwards subtests from the WAIS III were normally distributed. For this reason matched paired samples t-tests were used to analyse the Letter Number Sequence and Digit Span Backwards subtests (Elliott & Woodward, 2007). Because neither condition 3 nor 4 of the D-KEFS Colour- Word Interference test was normally distributed, Wilcoxon Signed Rank tests were used for analysis (Elliott & Woodward, 2007).

Table 4

*Results of the Shapiro-Wilk Tests of Normality*

| Test | Pre-test | | Post-test | |
|---|---|---|---|---|
| | Test Statistic *W* | p-Value | Test Statistic *W* | p-Value |
| WAIS III | | | | |
| Letter Number Sequence | .953 | .076 | .959 | .270 |
| Digit Span Backwards | .939 | .188 | . 966 | .426 |
| D-KEFS Colour- Word Interference | | . | | |
| Condition 3 completion time (seconds) | .765 | .000* | .683 | .000* |
| Condition 3 corrected errors | .749 | .000* | .812 | .000* |
| Condition 3 uncorrected errors | .542 | .000* | .804 | .000* |
| Condition 3 total errors | .669 | .000* | .827 | .000* |
| Condition 4 completion time (seconds) | .758 | .000* | .689 | .000* |
| Condition 4 corrected errors | .807 | .000* | .862 | .000* |
| Condition 4 uncorrected errors | .646 | .000* | .772 | .000* |
| Condition 4 total errors | .772 | .000* | .900 | .007* |

*Note.* *p < .05

**Comparisons of the verbal working memory pre- and post-tests.**

The research aim was to see whether there is a significant difference in verbal working memory performance before and after conscious sedation administered to endoscopy patients. The results of the matched paired samples t-tests and the Wilcoxon signed rank tests, that were used to analyse the difference between pre- and post- testing, are all presented in table 5.

Table 5

*Results of the Paired Samples t-Tests, and Wilcoxon Signed Rank Tests*

| Test | Test | | Statistic | p-Value |
|---|---|---|---|---|
| WAIS III | | | | |
| Letter Number Sequence | Paired Samples t- | t | .17 | .866 |
| Digit Span Backwards | Test | | .32 | .751 |
| D-KEFS Colour- Word Interference | | | | |
| Condition 3 completion time (seconds) | Wilcoxon Signed | Z | -1.77 | .076 |
| Condition 3 corrected errors | Rank Test | | -1.93 | .054 |
| Condition 3 uncorrected errors | | | -2.66 | .008* |
| Condition 3 total errors | | | -2.81 | .005* |
| Condition 4 completion time (seconds) | | | -2.98 | .003* |
| Condition 4 corrected errors | | | -1.36 | .173 |
| Condition 4 uncorrected errors | | | -.112 | .908 |
| Condition 4 total errors | | | -1.04 | .298 |

*Note. *p < .05*

From the WAIS III subtests neither the Letter number Sequence subtest (t = .17, p = .886) nor the Digit Span Backwards (t = .32, p = .751) subtest scores changed significantly between pre-and post-testing. For condition 3 of the D-KEFS Colour- Word Interference test, the completion time in seconds (Z = -1.77, p = .076) and the corrected errors (Z = -1.93, p = .054) yielded no significant difference between pre- and post-testing. The uncorrected (Z = -2.66, p = .008) and total errors (Z = -2.81, p = .005) for condition 3 of the D-KEFS Colour- Word

Interference test changed significantly between pre-and post-testing. The medians of the uncorrected errors in condition 3 for pre- and post-testing were 0 and 1 respectively. For total errors in condition 3 the medians were 2 and 1 for pre- and post-testing, respectively.

The completion time in seconds for condition 4 also showed a significant change between pre-and post-testing ($Z = -2.98$, $p = .003$). In the pre-test condition, the median for completion time in condition 3 was 62 seconds, compared to the median time in post-testing which was 57 seconds. None of the error scores, corrected ($Z = -1.36$, $p = .173$), uncorrected ($Z = -.112$, $p = .908$) and/ or total errors ($Z = -1.04$, $p = .298$) in condition 4 changed significantly between pre- and post-testing.

**Effect sizes.**

Effect sizes were calculated to interpret the practical impact of the significant results obtained from the Wilcoxon Signed Rank tests. The effect sizes were calculated using the following formula: $r = \frac{Z}{\sqrt{N}}$ ; where *Z* was the respective Wilcoxon signed rank scores and *N* the sample size (32) (Elliott & Woodward, 2007). All the effect sizes were moderate: $r = .47$ and $r = .49$ for uncorrected and total errors in D-KEFS Colour- Word Interference condition 3 respectively, and $r = .53$ for completion time in condition 4.

# Chapter Five: Discussion

By depressing the central nervous system, sedation deliberately interferes with episodic memory for the duration that the sedative drugs are active in patients' systems (Gupta et al., 2012). The effects of conscious sedation on episodic, and thus, long term memory are undebated and well recognized. However, the sedative effects on the underlying systems involved in long term memory, like working memory, are still to be recognised (Baddeley, 2004; Cabeza et al., 2003; Ranganath et al., 2005; Tsukiura et al., 2001; Voss & Sleigh, 2007).

Previous research studies show discrepancies regarding the effects of sedative drugs on working memory. Fisher et al. (2006) and Lianga et al. (2012) concluded that midazolam significantly decreased the effective functioning of working memory. Similarly, Veselis et al. (1992) suggested that propofol significantly decreased the effective functioning of working memory and short term memory. Incongruently, Hsu et al. (2012) suggested that midazolam significantly affected psychomotor speed and attention, but not working memory. A combined administration of propofol and midazolam resulted in no changes of working memory functioning (Veselis et al, 2009).

Supplementary research on the effects of conscious sedation on working memory is needed to reach more consistent conclusions. This current study assessed verbal working memory performance by using more than one test, on a sample of 32 participants. Although relatively small, the sample size is in accordance with clinical samples (see Aleksic et al., 2006; Deeprose, Andrade, Varma, & Edwards, 2004). Padmanabhan et al. (2009) researched a sample of 200 colonoscopy patients, but it is unusual as most endoscopy samples range from 14 to 50 participants (sse Fisher et al., 2006; Hsu et al., 2012; Lianga et al., 2012; Veselis, 2006). Both genders were fairly equally representative (female 53%), and also similar to previous endoscopic

research studies (Aleksic et al., 2006; Amornyotin et al., 2012; Deeprose et al., 2004; Salthouse, 2004).

The mean age of 55 years was expected, given that endoscopic procedures are typically done for older adults (Amornyotin et al., 2012). The age range was, however, very large between 29 and 78 years. Age is a typically considered variable in neuropsychological and/ or cognitive testing as there is a significant causal relationship between age and cognitive performance. As age increases, cognitive ability decreases (Salthouse, 2004). In this study, the higher age group therefore likely decreased the overall scores of cognitive performance. However, because there was a baseline score for each participant, age had less of an impact on the overall analysis of sedative effects than it would have had if only post-testing were conducted.

All the participants were fluent in English, as measured by the demographic questionnaire (Appendix A). The specific breakdown of languages is presented in Table 1 on page 32: the majority (80%) of the sample spoke English as their first language, and an even larger number (84%) spoke two or more languages. Because the assessments were in English, it required that all the participants could speak and understand it fluently.

Important to this study, language in terms of monolinguals or bi/multilingualism, affects working memory functioning. Bilinguals perform worse in verbal working memory tasks, compared to monolinguals, placing them at a disadvantage (Luo, Craik, Moreno, & Bialystok, 2013). Luo et al. (2013) suggests that this disadvantage is likely because of a mild deficit in verbal processing in bilinguals. Even when the verbal working memory tasks were conducted in participants' first language, bilinguals still performed poorer in comparison to the monolinguals (Bialystok et al., 2008; Gollan, Montoya, Fennema-Notestine, & Morris, 2005). Thus, although the majority of the current study's sample spoke English as a first language, the fact that they

were bi/multilingual still affected their performance. The advantage of this study's pre- and post-test design is that baseline scores were obtained to compare the post-test results to.

All the participants completed formal education at a minimum level of matric. Formal education is positively correlated with test-wiseness, indicating that the participants were more likely to have been assured and confident in the assessment setting (Chan et al., 1997). Test-wiseness is important for internal validity to warrant that results were not influenced by inexperience to perform in a test environment (Chan et al., 1997).

Based on the outcome of the statistical results, the uncorrected and total errors of condition 3, and the completion time of condition 4 of the D-KEFS Colour- Word Interference test yielded significant results. Both the amount of uncorrected and total errors made in condition 3 significantly increased while the time in seconds significantly decreased in condition 4 during post-testing.

After sedation, in condition 3, participants had more difficulty to inhibit the impulse to read the words (as they were primed to do in preceding conditions 1 and 2), when supposed to name the ink colours. However, only the uncorrected and total errors made in condition 3 during post-testing were significantly more. In other words, participants made more errors that they were unaware of and consequently did not correct. Predictably, more uncorrected errors resulted in more total errors. The uncorrected and total errors made in condition 3 after sedation, were unlikely a result of rushed responses, as there were no significant time difference in seconds compared to pre-testing. Conversely, participants were able to complete condition 4 significantly quicker after sedation, but without making any significantly more errors.

The extent, to which the significant results indicated difference in performance between pre-and post-testing, is shown by the effect sizes (Sullivan & Feinn, 2012). For the uncorrected

and total errors made in condition 3 the effect sizes were r = .47 and r = .49 respectively, both moderate at almost r = .5. The moderate differences in uncorrected and total errors made in condition 3 after sedation suggests practical effects of sedation in these specific tasks. From the insignificant difference between completion times for condition 3, we can presume that the increased amount of uncorrected and total errors were not due to rushed responses. The effect size for completion time in condition 4 was also moderate (r = 0.53), suggesting an actual enhanced speed of verbal working memory processing in condition 4, after sedation. From the insignificant changes for all the errors in condition 4, we know that the faster response in this condition did not impede on performance.

In condition 3, participants made more uncorrected and total errors after sedation, and we know from Bialystok et al. (2008) that bi/ multilinguals perform worse at verbal working memory tasks. In other words, the challenge posed by language processing for bi/multilinguals could enhance the effects of the sedation during post-testing on this verbal working memory task. Similar decrease in verbal working memory functioning were not shown by the WAIS III subtests, as these yielded no significant change after sedation.

Inconsistent with the findings of D-KEFS Colour- Word Interference condition 3, no decreased performance appeared in condition 4 after conscious sedation. As stated by the design of the D-KEFS Colour- Word Interference test, condition 4 requires more inhibition as an additional distractor task is added which creates more switching/ inhibition (Delis et al., 2001). Based on this objective of the D-KEFS Colour- Word Interference test design, it was expected that the errors made in condition 4 presented with similar significant difference between pre-and post-testing. However, related to the results of this current study, Lippa and Davis (2010) found that their patients performed better in condition 4 compared to condition 3, during a clinical trial

with 119 outpatients. Their patients made significantly more total errors in condition 3 during post-testing as opposed to condition 4 that revealed no significant changes (Lippa & Davis, 2010).

Lippa and Davis (2010) suggested that because condition 4 presents with an additional distractor, the more difficult task results in enhanced executive control functioning. The added distractor in condition 4, compared to condition 3, likely elicits more executive control effort to complete the task successfully (Lippa & Davis, 2010). Accompanying this argument, bi/multilingual people perform better on executive control tasks as a consequence of having to successfully switch between languages (Morales, Calvo, & Bialystok, 2013).

Recall that bi/multilingual people perform worse on verbal working memory tasks in particular, on the one hand (Bialystok et al., 2008). On the other hand, bi/multilinguals have advanced executive functioning based on the brain's effort to switch languages (Morales et al., 2013). We thus know that condition 4 required more executive functioning, and that bi/multilinguals have better performance in such tasks (Morales et al., 2013). Because the participants knew from pre-testing that condition 4 required more processing, they were able to put more effort into the more difficult task. The enhanced executive ability of bi/multilingual participants could add to the non-significant effects of the sedatives on condition 4. The predetermined extra effort put into completing condition 4 may also explain why participants were able to complete it in significantly less time during post-testing.

The influence of practice effects caused concern, since the exact tests were used for pre- and post-testing in a short period of time (within the same day, hours apart). Basso, Carona and Axelrod, (2002) investigated the practice effects of the WAIS-III subtests on 51 participants and found that most of the subtest results increased significantly as a result of practice effects even

after three and six months waiting periods. However, they found that the working memory subtests yielded no significantly increased results, indicating that these subtests are not subjected to practice effects (Basso et al., 2002). In congruence with Basso et al. (2002), the WAIS-III verbal working memory subtests showed no practice effects in this current study; as it would have been revealed in significantly higher test scores during post-testing. However, the effects of the sedative drugs should be considered in line with the absence of practice effects. The sedative effects could have concealed possible improved performance due to practice effects. Under the condition of sedation, participants showed no practice effects, but this cannot be generalised across conditions without sedation.

In the afore-mentioned study on the D-KEFS Colour- Word Interference test done by Lippa and Davis (2010) no practice effects were found for conditions 3 and 4. Concurrent with Lippa and Davis (2010) this current study found a decrease in verbal working memory performance in the post-tests for uncorrected and total errors made in condition 3. Significant practice effects would have enhanced the post-test results as opposed to results either remaining the same or decreasing. Yet, the same argument regarding the sedation condition applies in that the effects of the sedatives could possibly conceal practice effects.

Another consideration regarding practice effects is the effect of emotional stress during baseline testing. Voss and Sleigh (2007) argued that the stress involved in medical procedures may impact memory consolidation at the working memory stage, thus influencing cognitive tasks. On the other hand, Fisher et al. (2006) used samples that were not scheduled for hospital procedures, but administered sedatives for research purposes. These participants were not exposed to the stress of hospital procedures, and their performance on working memory showed decreased working memory effects after sedation (Fisher et al., 2006). In the Fisher et al. (2006)

study, participants' baseline performance would not be affected by stress in the same way for patients undergoing medical procedures. It may be that in studies involving medical procedures, patients are so stressed during pre-testing that they do not perform as well as they would without the distraction of the approaching procedure, ultimately affecting baseline results. The effects of stress could conceal the effects of sedative drugs in that the baseline results are not as strong as it would be without the stress, ultimately concealing possible decline after sedation.

Although this study measured anxiety as part of the bigger research project, it looked at anxiety in general and not specifically at the stress that some patients may have experienced prior to their medical procedures. A large part of the sample (40%) were hospitalised for the first time when this study was conducted. For many, the unknown experience of hospitalisation in itself was stressful, let alone the endoscopic procedure ahead. Psychological stress does decrease the performance of working memory, specifically related to life events that lead to longitudinal stress exposure (Klein & Boals, 2001; Schoofs, Preuß, & Wolf, 2008). Stress could thus have influenced the overall outcome of the test-results but due to the nature of the study, could not be controlled for.

The half-life of the drugs is another extraneous variable that may have affected the results, especially as post-testing were conducted at least an hour after the sedatives were administered. Given that propofol has an elimination half-life of 30 to 60 minutes, and midazolam one to four hours, the effects of the sedatives would have likely started to wear off by the time that post-testing occurred (Gupta et al., 2012). Furthermore, different patients' metabolisms likely resulted in different levels of sedative drugs during post-testing.

Overall, the significantly more uncorrected and total errors made in condition 3 of the D-KEFS Colour- Word Interference test partly suggests that verbal working memory performance

decreased as a result of conscious sedation. However, this was inconsistent with the results from D-KEFS Colour- Word Interference condition 4, and the WIAS III Letter Number Sequence and Digits Backwards subtests. The advantage of using a test battery is that the different test results can be compared to get a better overall verification of verbal working memory performance. This enables the researcher to draw conclusions that are more systematic and validated (Flanagan, Ortiz, & Alfonso, 2007).

# Chapter Six: Limitations and Recommendations

The testing environment posed a challenge for this study. Assessments were conducted in the day ward due to logistical reasons. Ideally neuropsychological tests should be conducted in a separate room for each participant, free from noise and other distractions (Hebben & Milberg, 2009). Future research can arrange for a separate room in close proximity of the day ward where assessments can be conducted with fewer distractions.

Not all of the neuropsychological tests used in this study were developed and/ or adapted for the South African population, like the D-KEFS Colour- Word Interference test. However, the results of the participants were not used for diagnostic purposes nor compared to international norms. Future research could opt for an entire test battery that are adapted and standardised for the South African population. Furthermore, incorporating other tests will add to the literature in relation to whether the findings of this study were due to the instruments used, or the impact of sedatives on verbal working memory.

Throughout this study, assessments were conducted by four different assessors whose individual characteristics may have influenced the outcome of the assessment procedure. Assessment tools that require personal interaction with the participant, such as the tools used in this study, are more sensitive to the personal influence of the assessor (Weiner, 2003). In accordance to this study, future research studies should also adhere to standardised tests that require professional training; if more than one assessor is involved.

Sedative drugs affect individuals differently in terms of patients' different metabolism speed and effect on their nervous systems (Mistraletti et al., 2005). Some patients took longer to wake up which meant that the time period between sedation administrations and post-testing was not controlled for. The researchers could not control for the amount of sedative drugs and the

effect thereof during post-testing. Future research should obtain the schedule of the time that the sedation were administered for each patient. Researchers can then record the time that they start with the post-test battery to consider the duration that passed before the patient was ready for post-testing.

Specific sample characteristics were not representative of the South African population. All of the participants (100%) had at least a matric level of education as opposed to the South African population in which only 28.4% hold a matric level of education or higher (Stats SA, 2012).Furthermore, the majority of the sample spoke English as their home language. These factors affect the generalizability of the results to the South African population.

Bi/multilingualism has a major effect on verbal working memory in that monolinguals normally do better in verbal working memory tasks (Bialystok et al., 2008). In multilingual samples similar to this study, future research should assess the difference in working memory performance between mono- and bi/multi-linguals.

The sample size of this study was small (N = 32) as in the case of studies similar to this research, for example in Aleksic et al. (2006) (N = 33) and Deeprose et al. (2004) (N = 33). The pre- and post-test results did not yield consistently significant results, with only the uncorrected and total errors of condition 3, and the completion time in condition 4 of the D-KEFS Colour-Word Interference test showing significance. A smaller sample size likely contributes to these inconsistent findings (Redmond & Colton, 2001).

Both the sample bias and size influences the generalizability of this study to the South African population, and therefore also the external validity. Future research could enquire about the general demographical information of hospitals' patients prior to conducting research in order to choose a sample more representative of the South African population.

Because there was no control group, the statistical results could only account for pre-and post-comparisons under the sedation condition. Future studies should have a control group of participants not scheduled for endoscopies and thus not undergoing sedation. Statistical analysis can then be done to more accurately determine whether the tests yielded practice effects. And therefore also more reliably distinguish between practice, sedatives and psychological stress effects.

# Chapter Seven: Conclusion

This research investigated the effect of propofol and midazolam on verbal working memory. Health care policies are influenced by research investigating the cognitive effects of sedation in order to ascertain how long patients should be monitored before discharge. Only the uncorrected and total errors of condition 3, and the completion time in condition 4 of the D-KEFS Colour- Word Interference test yielded significant results. None of the other subtests yielded significant results, resulting in overall inconclusiveness of the effects of conscious sedation on verbal working memory. Language, practice effects and psychological stress may have influenced the outcome of the test results. Given the small sample size, the outcome of the results were not sufficient to make claims of whether conscious sedative affects verbal working memory functioning. Future research could aim for a larger sample by expanding the data collection period, and should also include a control group not scheduled for sedation. This research found that there were no practice effects on any of the tests. This is valuable for future research also wanting to use the same tests for pre- and post- testing.

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# Appendices

## Appendix A. Demographic Questionnaire

***TO BE COMPLETED BY MEDCAL TEAM ONLY:***
*PARTICIPANT NUMBER: _____*

*PLEASE TICK: A____ B____(sedation protocol after pre -test)*

*TO BE COMPLETED BY PARTICIPANT:*
Demographic information:

- How old are you? _____
- How many languages do you speak (please specify the languages)?
  _____
- Which one is your home language? _____
- How many years of formal education do you have? _____
- What is your highest level of education? _____

Health history:

- Are you taking any medication? | Yes | No |
  - If you answered 'yes' to the previous question, please specify
    _____
- Do you have any history of hospitalisation? | Yes | No |
  - If you answered 'yes' to the previous question please specify
    _____
- How many alcoholic beverages, on average, do you take in a week?

| None | 1-5 | 5-14 |
|---|---|---|

- Have you experienced any problems with attention and/ or memory in the past 6 months? (e.g. feeling distracted, forgetfulness, getting lost)

| Yes | No |
|---|---|

  - If you answered 'yes' to the previous question please specify your experience(s):
    _____

**If any of the following apply to you, please decline participation:**
History of: traumatic brain injury, dementia, central nervous system injury, and/ or illegal drug use.

**Appendix B. Ethical Clearance Certificate from the Human Research Ethics Committee (Medical) of the University of the Witwatersrand**

R14/49 Ms Sharlene Richard et al

## HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

## CLEARANCE CERTIFICATE NO. M140302

| | |
|---|---|
| **NAME: (Principal Investigator)** | Ms Sharlene Richard et al |
| **DEPARTMENT:** | Psychology<br>Netcare Rosebank |
| **PROJECT TITLE:** | Is there a True Psychological (Cognitve Functioning and Mood) Effect of Consious Sedation during the Endoscopic Procedure? |
| **DATE CONSIDERED:** | 28/03/2014 |
| **DECISION:** | Approved unconditionally |
| **CONDITIONS:** | |
| **SUPERVISOR:** | Ms Aline Ferreira Correia |
| **APPROVED BY:** | Professor P Cleaton-Jones, Chairperson, HREC (Medical) |
| **DATE OF APPROVAL:** | 09/05/2014 |

**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 Secretary in Room 10004, 10th floor, Senate House, University.
I/we fully understand the conditions under which I am/we are authorized 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 the application to the Committee. **I agree to submit a yearly progress report**.

Principal Investigator Signature Date 16 MAY 2014

**PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES**

## Appendix C. Letter from a Johannesburg Hospital

Netcare Rosebank Hospital

Tel: +27 (0) 11 328 0500
Fax: +27 (0) 11 328 0509
14 Sturdee Avenue, Rosebank, South Africa
PO Box 52230, Saxonwold, 2132, South Africa
www.netcare.co.za

**Date:** 1/4/2014

**To: University of .WITS. Ethics Committee**

**RESEARCH TO BE CONDUCTED IN NETCARE FACILITY**

The Management of Netcare Rosebank Hospital has taken note of the application for ethical approval by WITS Ethical Committee for the following research study to be conducted

IS THERE A TRUE PSYCHOLOGICAL EFFECT OF CONSCIOUS SEDATION DURING ENDOSCOPIC PROCEDURE ? (Title of research)

In principle the Netcare Hospital Management does not have any reservations for the abovementioned research to be conducted on its premises subject to unconditional ethics approval being granted.

We furthermore confirm that application will then be made to the Netcare Research Committee and that the research may not commence prior to receipt of FINAL APPROVAL from the Academic Board of Netcare (Research Committee).

Yours faithfully

**Signed by Hospital Management** — **Date** 01/04/2014

General manager.
**(Specify designation)**

## Appendix D. Invitation to Participate

Psychology
School of Human & Community Development
Private Bag 3, Wits 2050, South Africa. Telephone: +27 11-717-4500/2/3/4. Fax: +27-11-717-4559

Dear Sir/ Madam

Our names are Sharlene Richard, Tasneem Hassem, Melissa Vrachionidis and Rivkie Hadar. We are Psychology students at the University of the Witwatersrand, and will be doing research at [redacted] Hospital. The aim of our research is to investigate the effects of sedation associated with endoscopic procedures. Such effects include thinking and reasoning processes, and emotions.

You are scheduled for an endoscopic procedure with either Dr. Strimling or Dr. Wolowitz and are invited to take part in this research study tilted: *The psychological effect of conscious sedation administered for endoscopic procedures*. Participation will entail psychometric testing both before and after your endoscopic procedure. The pre-assessment battery will take about 45 minutes. The post battery will take about 30 minutes.

To date, there is very little known about this area. Your participation will thus enable us to contribute to the knowledge of such effects and will be much appreciated.

Please don't hesitate to contact Sharlene if you have any questions or queries, at richard.sharlene@gmail.com or 082 328 2704.

Kind Regards
Sharlene Richard, Tasneem Hassem, Melissa Vrachionidis and Rivkie Hadar.

## Appendix E. Participant Information Sheet



Psychology

School of Human & Community Development

Private Bag 3, Wits 2050, South Africa. Telephone: +27 11-717-4500/2/3/4. Fax: +27-11-717-4559

2014

Dear Partient

Our names are Sharlene Richard, Tasneem Hassem, Melissa Vrachionidis and Rivka Hadar. We are Psychology students (Masters in Psychology by Coursework and Research; and Honours) in the School of Human and Community Development, at the University of the Witwatersrand.

As part of our degree requirements, we need to complete a research study. The aim of our research is to investigate the cognitive and emotional implications of sedation associated with endoscope procedures. These possible implications have been known to be transitory. As a patient about to undergo an endoscope procedure, you are invited to take part in this research study titled: *The psychological effect of conscious sedation administered for endoscopic procedures*. To date, there is very little known about this area. Your participation will thus enable us to contribute to the knowledge of such cognitive effects.

Participation will require completing the following psychological assessment batteries both before and after your endoscope procedure:

- Questionnaire (only in the pre-test): A brief questionnaire will be used to collect demographic data (age, level of education, and home language) and health history (presence of any neurological or psychiatric illness, current medication, cognitive complaints, and use of illegal substances);
- Profile of Mood States (POMS): A self-rating scale consisting of adjectives describing your feelings of the last week as well as feelings experienced while filling out the questionnaire;
- Hamilton Rating Scale for Depression and for Anxiety (HAM-D & and HAM-A) (only in the pre-test): two 17 and 14 item self-rating scales respectively, designed to assess symptoms associated with depression and anxiety in adults;
- The following Neuropsychological tests will be used to assess attention and working memory: D-KEFS Colour Word Interference test; Letter Number Sequence and Digit Span Subtests (WAISIII); Mental Control and Spatial Addition Subtest (WMSIV). These tests will require you to remember information and solve mind-puzzle like problems.

The pre-test battery, before sedation, should take about 60 minutes to complete and the post-test, after discharge from the PACU unit, about 40 minutes.

Participation in this research study requires the completion of the entire assessment process as outlined above. The assessment process will take place in a private room at the [redacted] Hospital, in two sessions (pre- and post-testing). These sessions will be scheduled in accordance with your endoscope procedure. Should you agree to participate in this research study, you will be asked to sign the attached consent form. This form will be kept separately from the rest of the data for the purpose of anonymity and confidentiality. The consent

form will only be made available to the University authorities should it be required for a random audit process.

Please note that participation will not be compensated for, monetary or otherwise. Results of the assessments will be saved anonymously and therefore, the researchers will not be able to provide any feedback regarding assessment results. As the researchers of this study, we do not foresee any obvious risks in participating. However, the assessment process might reveal difficulties with certain activities and elicit sensitive personal information. We would therefore like to stress that your participation in this study is completely voluntary and you may withdraw from it at any point until results are saved. Because results will be saved anonymously, we will not be able to retract your results after this stage. You may also refrain from answering any particular questions with no negative consequences. If you experience any distress associated with the assessment process, please refer to the following free counselling services: The South African Depression and Anxiety Group at 011 262 6396/ 0800 20 50 26; and/ or Life Line at 011 728 1347.

Your identity as a participant will only be known to the medical team involved in the endoscope procedure and the four assessors/ researchers. All the assessment results will be saved anonymously and will be locked in a secured office for 5 years. The entire research process will be dealt with confidentially. The assessment results will not be published or used for purposes other than the research aim stated in the beginning.

The thesis resulting from this research will be available in the library of the University of the Witwatersrand, which offers access to material on the world-wide web. The findings will also potentially be published in scientific journals. If you wish to access the results, you may request so by contacting us.

This project has been approved by the Human Research Ethics Committee of the University of The Witwatersrand, Johannesburg. If you have any questions please do not hesitate to contact the committee.

Should any matters require further clarification please do not hesitate to contact:

- Sharlene Richard (082 328 2704 – richard.sharlene@gmail.com),
- Tasneem Hassem (082 494 9725- 361406@students.wits.ac.za ),
- Melissa Vrachionidis (071 371 3327 - melissav86@me.com);
- Rivka Hadar (072 988 2008 -Rivkiehadar@gmail.com ).

You may also contact our supervisor, Ms Aline Ferreira Correia (011 717 4527- Aline.FerreiraCorreia@wits.ac.za.).

**Many thanks for considering participating**.

Kind regards,

Sharlene Richard, Tasneem Hassem, Melissa Vrachionidis and Rivka Hadar

**Appendix F. Participant Consent Form**

Psychology

School of Human & Community Development

Private Bag 3, Wits 2050, South Africa. Telephone: +27 11-717-4500/2/3/4. Fax: +27-11-717-4559

Consent for research participation

I am an adult person above the age of 18 years and I confirm that I have read and understand the information provided in the information sheet in relation to the participation in *The psychological effect of conscious sedation administered during endoscopy procedures*. I have been informed about what the psychological assessments entail and what is required of me. I also understand that:

- My participation is completely voluntary;
- I may withdraw from the assessment at any time with no negative consequences for me;
- All the information I provide and my participation will be kept confidential;
- No rewards will be offered or provided for my participation;
- No feedback on the results will be provided to me;
- I have received the contact details of the researchers Sharlene Richard, Tasneem Hassem, Melissa Vrachionidis, Rivka Hadar; and the supervisor Aline Ferreira Correia;

- I have received contact details for free counselling services in case I experience any distress regarding the assessment activities.

Therefore, I agree to undergo the psychological assessment administered by the researchers.

Researcher's Name:

_____

Researcher's signature:

_____

Participant's name:

_____

Participant's signature:

_____

Date: _____