THE UNIVERSITY OF HULL

An Investigation into Implicit Emotional Memory with Concurrent Midazolam Amnesia Following Colonoscopy

being a Thesis submitted in partial fulfilment of
the requirements for the Degree of
Doctor of Clinical Psychology

In the University of Hull

By

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July 2003

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ACKNOWLEDGEMENTS

I would like to thank my academic supervisor, Professor Michael Wang, for his guidance and support. I would also like to acknowledge all the staff at the Hull University Clinical Psychology Department for their patience and support in general throughout my clinical training. I would like to offer a special thanks to Di Toseland, you provided so much support when my life got flipped upside down; I will never forget your kindness and encouragement.

My thanks also extend to all staff at the Endoscopy Department in Castle Hill Hospital: the surgeons, nurses, technicians and administration staff. In particular I would like to acknowledge Mr Graeme Duthie, Mr James Gunn, Mr Steve Pilinger and Sister Sally Wood for their support, patience and encouragement throughout the long hours of data collection.

I would also like to acknowledge my friends and family. To my very dear friends, Ash, Chez, Sophs, Laura and KT, I would like to say thanks for always being there, for the highs and the lows, and for getting me through some of the most difficult times of my life. I could say so much about how each of you have helped me, and how much you mean to me, but I hope you already know. I would also like to mention Dave and Paul who helped, often unwittingly, in their own inimitable way. I would like to thank Roger and Jennifer who, despite their own trauma, always made me feel thought of and cared for; I hope I can always be there for you to. Of course, I would like to thank my mum and dad. Mum, you have backed me all the way and your encouragement and support has never gone unnoticed or unappreciated, thank you. Dad, no one could have guessed

what this year has unfolded; I hope I have made you as proud of me as I am of you, keep fighting and never give up. I would also like to mention Jim and Joyce; thanks for your support and encouragement. Lastly, but by far not the least, thank you Tom; you are my rock when all around us crumbles away. We have been through more than we could ever predict and survived more than anyone could ever expect of us, the fact that we are still together and stronger than ever is testament to our feelings for each other. Before I am forever condemned for being verbose or sycophantic I just want to thank you for your patience and love. I hope you will always know how much I love and appreciate you.

I shall be ever indebted to you all; this is just as much your achievement as it is mine.

ABSTRACT

The aim of this study was to investigate whether implicit emotional memory could be demonstrated in patients undergoing a colonoscopy with midazolam sedation. It was hypothesised that the distress associated with a noxious non-surgical procedure would facilitate the conditioning of neologisms designed to readily associate with the negative experience of colonoscopy. It was further hypothesised that mood (in particular high levels of anxiety), personality (specifically introverted and neurotic patients) and objectively rated peri-operative behavioural distress (especially high ratings of distress) may increase the likelihood of implicit emotional memory formation.

The study design was a prospective randomised pre and post repeated measures double blind trial including comparison between three groups. Measurement took place at three different time points both pre- and post-surgical procedure (i.e. immediately before and after the colonoscopy and up to one week post procedure). Also the group that participants were allocated to was randomised and unknown to both the researcher and the participant. The measures used were the Hospital Anxiety and Depression Scale, the Eysenck Personality Inventory, the Behavioural Distress Scale, free recall as a measure of explicit memory for intra-operative events and skin conductance response change as a measure of implicit emotional memory for intra-operatively presented neologisms.

The investigation failed to find any statistically significant evidence for implicit memory of neologisms presented during colonoscopy, as detected by skin conductance response, or any differences between those participants presented with 'emotive' and

'neutral' neologisms. There was also no significant effect of mood, personality or behavioural distress on this hypothesised interaction.

A potentially unrepresentative and relatively small sample, plus some limitations of methodology, implementation and interpretation are discussed with reference to other research and literature related to the field of interest. Finally, some suggestions are made concerning the direction of future research.

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INTRODUCTION

Foreword

> It seems, then, that we owe to memory almost all that we either have or are; that our ideas and conceptions are its work, and that our everyday perception, thought, and movement is derived from this source. Memory collects the countless phenomena of our existence into a single whole; and, as our bodies would be scattered into the dust of their component atoms if they were not held together by the attraction of matter, so our consciousness would be broken up into as many fragments as we had lived seconds but for the binding and unifying force of memory.
>
> (Hering, 1870, pp.74-75)

The above quotation encapsulates the overarching rationale for this study as it highlights eloquently the importance of memory to human existence. The thread of this argument runs throughout the current thesis, applied specifically to the debate surrounding the use of amnestics in a non-surgical procedure known as colonoscopy. In brief, in order to introduce the purpose of the following literature review, a colonoscopy is an endoscopic procedure involving an examination of the colon using a fibre optic camera inserted into the large intestine via the anus. This procedure is becoming increasingly more prescribed, sometimes in conjunction with other investigations (e.g. barium meals, gastroscopy), to determine diagnoses for gastric disturbances. A contributory factor in the increase in demand for this procedure is the application of benzodiazepines to induce a state known as conscious sedation. Benzodiazepines are

used to reduce anxiety, sedate and prevent conscious recall of any painful and stressful intra-operative experiences in the absence of full general anaesthesia. Ultimately this increases the patient turnover by reducing the need for specialist staff (e.g. anaesthetists) and equipment, decreasing the risks of morbidity and mortality, reducing the length of hospital stay so that patients can be seen as outpatients (colonoscopies typically take 10-30 minutes and recovery from benzodiazepine sedation only 30-60 minutes), which in turn significantly decreases the risks of contracting hospital borne infections.

Therefore, in summary, the argument for amnestics, as opposed to general anaesthesia, in non-surgical procedures, is that they evidently reduce costs in respect to time, money and patient medical care, all whilst resulting in patients having no recall post-operatively of their experiences of pain and discomfort prevalent in such invasive and noxious medical procedures as colonoscopy. However, this medical innovation has proven controversial, firstly, in light of disturbing reports of the psychological pathology following episodes of awareness and 'wakefulness' during general anaesthesia; and secondly, in view of developments in memory theory furthering the idea of an implicit / explicit memory divide (defined primitively for the purpose of this brief prologue, as unconscious and conscious memory, respectively) and the likelihood that benzodiazepines may selectively impair only explicit memory.

Literature Review

Firstly, the literature on intra-operative awareness and memory under anaesthesia will be reviewed to illustrate where the interest in conscious sedation originated. This will also incorporate the growing literature on the psychological impact of wakefulness during procedures that require general anaesthesia or amnestic sedation. Then the

neurobiology of memory and the neuropharmacology of benzodiazepines will be examined to provide a theoretical framework for the amnesic action of these anxiolytic drugs. The development of memory theory, models and processes and the current understanding in this area will be reviewed; followed by an appraisal of the factors that affect memory formation, storage and retrieval. Lastly, a consideration of the factors and mechanisms by which benzodiazepines induced amnesia may be modulated will link in the previously discussed literature into my research rationale, aims and hypotheses.

Anaesthetic Awareness and Associated Psychological Distress

The History of Anaesthesia

In 1845, Horace Wells, an American dentist, conducted the first demonstration of surgical anaesthesia. Despite the patient reporting no awareness or memory of pain following the procedure, Wells' demonstration was deemed a failure because the patient screamed and struggled throughout the surgery (Kihlstrom, Couture, Schacter & Cork, 1998). By 1847, ether and chloroform were firmly established as general anaesthetics on both sides of the Atlantic with a great deal more success than the nitrous oxide used by Wells. Later, it was discovered that morphine lessened the amount of anaesthetic agent required; and in 1942, Griffith & Johnson administered curare to reduce motor responses to surgical incisions (and artificial respiration to maintain breathing), which also allowed less anaesthetic agent. This yielded the "balanced anaesthesia" procedure still in use today (with the use of more modern medications): a cocktail of drugs to reduce pre-operative anxiety, induce loss of consciousness, eliminate pain, and calm the operative area. A contemporary definition of general anaesthesia would include loss of

awareness, no post-operative recall of events, a lack of overt response to stimuli and the process should be reversible (Nunn, Utting & Brown, 1989).

Despite the advent of anaesthesia being one of single most important medical inventions its development has not gone smoothly from the days of Horace Wells. The use of sedatives, neuromuscular blockades and painkillers has allowed for anaesthetic lightening in an attempt to reduce intra-operative complications and increase patient survival and recovery following their administration. Unfortunately, this act of improving patient care has resulted in a group of silent sufferers.

Intra-Operative Awareness

The history of memory for events under anaesthesia is as old as the history of anaesthesia itself (Ghoneim & Block, 1992). By the turn of the century, it was becoming evident that although patients did now, at least, appear to be unconscious and insensible to the surgery, it was likely that part of them remained conscious. George Crile (1911) was one of first to document this concern; trying to conceive the horrors the conscious part of the brain must experience during surgery if unable to communicate their distress. Evans (1987, p186) reported the following account of a twenty-nine year old woman who experienced awareness during surgical anaesthesia, which illustrates the helplessness, pain and horror that insufficient depth of general anaesthesia causes.

> As soon as I was out of intensive care and able to feebly clutch a pencil, I scrawled down my experiences before it became distorted by memory, imagination and distance. I am confident that this account of surfacing during an operation is accurate because it is still etched upon my mind with terrifyingly

> vivid clarity. The consciousness was terrifying. PAIN. Christ, the pain! The desperate animal terror of trying to signal one's conscious state to someone, but being unable to twitch a bloody eyelash. This is a nightmare to end all nightmares, being horrifyingly unable to communicate anything because paralysed. Had as much vision as peeping through eyelashes when pretending to be asleep. Could see patent glazing of roof lights, huge circular lamps, recognised surgeon houseman and senior registrar. "Will you be playing golf this weekend, sir?" asked the senior registrar.

Historically, general anaesthesia has been conceptualised as a physical phenomenon, and the assumption before, and to some extent even after the introduction of neuromuscular blockade, was that physical signs reflected cognitive states. As the above quotation disturbingly demonstrates, this is not necessarily the case. Jones (1989) describes four stages of awareness that are entered consecutively as anaesthetic depth increases:

1. Conscious perception with explicit memory
2. Conscious perception without explicit memory
3. Subconscious perception with implicit memory
4. No perception and no implicit memory

Clearly, having full explicit recall of intra-operative events post-procedure presents itself as a major psychological trauma. However, a more problematic scenario exists when a level of awareness, referred to as wakefulness, occurs during the surgery but on recovery from the anaesthetic there is no conscious, explicit recollection of this event (Russell, 1985). Psychological disturbance may result but the patient may be initially

unable to connect this to the surgery and would thus have difficulties in resolving their problems. Fortunately, the incidence of explicit memory of awareness during surgical anaesthesia is low (estimated at well under one percent). However, people who experience conscious awareness during surgical anaesthesia without explicit memory of this event are less easily identified.

A disturbing study conducted by the medic Levinson, published in 1965, purported to demonstrate such an occurrence. He experimented with ten patients undergoing dental surgery with general anaesthesia. Shortly after induction, a mock crisis was staged. The anaesthetist called to the surgeon 'stop the operation; I don't like the patient's colour. His / her lips are turning too blue. I am going to give a little oxygen' at which point the surgeon did indeed stop. After a few moments, the anaesthetist indicated that all was now well, and the surgery could continue. Post-operatively no patient had spontaneous recall of the crisis. However, one month later, Levinson probed for evidence of assimilation of this crisis by inducing hypnosis, regressing the patient back to the time of the operation. Of the ten patients, four were able to quote the anaesthetist's words verbatim, and a further four showed evidence of having registered the crisis in the form of emotional distress. Levinson's study has been heavily criticised for the obvious methodological flaws, such as absence of a control group, non-random selection of subjects, absence of double blind study design, the possibility of the investigator asking leading questions under hypnosis and the subjective nature of the interpretation of responses, not to mention important ethical considerations. However, the insights that his findings have provided have prompted much serious thought about the potential effects of intra-operative auditory information.

Tunstall (1977) added further evidence for this stage of anaesthetic awareness with the introduction of the isolated forearm technique. This technique involves a tourniquet being placed on the contralateral arm to that used for drug administration and hence one limb is isolated from the effects of the neuromuscular blocking drugs. Whilst the tourniquet remains, the patient is able to communicate during surgical anaesthesia by moving the arm as requested. Estimates of affirmative responses to intra-operative commands ranges from around a 33 percent up to 72 percent of the sample tested, with no post-operative recall (Russell, 1989, 1993; Tunstall, 1977).

Psychological Consequences of Intra-Operative Wakefulness

Despite the literature on surgical perception and post-surgical memory being somewhat variable with respect to the results found and the conclusions drawn, it is unarguable that any form of memory, be it available to conscious awareness post surgery or not, has real potential to result in psychological disturbances.

When a patient does have full conscious recall of an episode of intra-operative awareness cognitive therapy can have a purposeful direction (Wang, 2000) and links between post traumatic stress disorder symptoms and the intra-operative awareness can be made. However, when this connection is unconscious, resolution of any resultant difficulties can be problematic. Bennett (1990) described a patient who had been treated for gunshot wounds to the abdomen but only amnestic drugs (midazolam and scopolamine) and no anaesthetic drugs had been administered. A few months later the patient returned to hospital for follow up surgery, but fled from the ward the night before the operation in panic. It was only when the same thing happened two weeks later that the possibility of intra-operative implicit memory was entertained and

discussed with the patient. Once this explanation had been given, the patient was able to go ahead with the much needed surgery. Tinnin (1994) reported a very similar case of a patient with an almost suicidal refusal to undergo surgery for inter-uterine cancer following an episode of implicitly remembered traumatic pain from a previous operation involving extensive orthopaedic repairs to her crushed legs.

The Great Amnestic Debate

The above reports are intriguing but are nonetheless anecdotal and therefore fall foul to numerous methodological limitations. However, with the balance between optimally safe anaesthetic depths and the potential for awareness with explicit and implicit memory formation being a fine one, there is urgent need to investigate these phenomena in a more standardised, and methodologically and ethically rigorous manner. Also, as the report from Bennett highlights, the increasing usage of amnestics (e.g. benzodiazepines) in the absence of balanced surgical anaesthesia for non-surgical yet noxious medical procedures (e.g. colonoscopy), is, as explained in the *Foreword*, ethically dubious. This is also paramount if when one considers that true informed consent is rarely possible due to the potential impact of telling the patient about to undergo surgical or noxious non-surgical procedures that they may be aware of considerable pain during the procedure but will be unlikely to recall this explicitly post-operatively. This opens the field for litigation and risks efficient patient care.

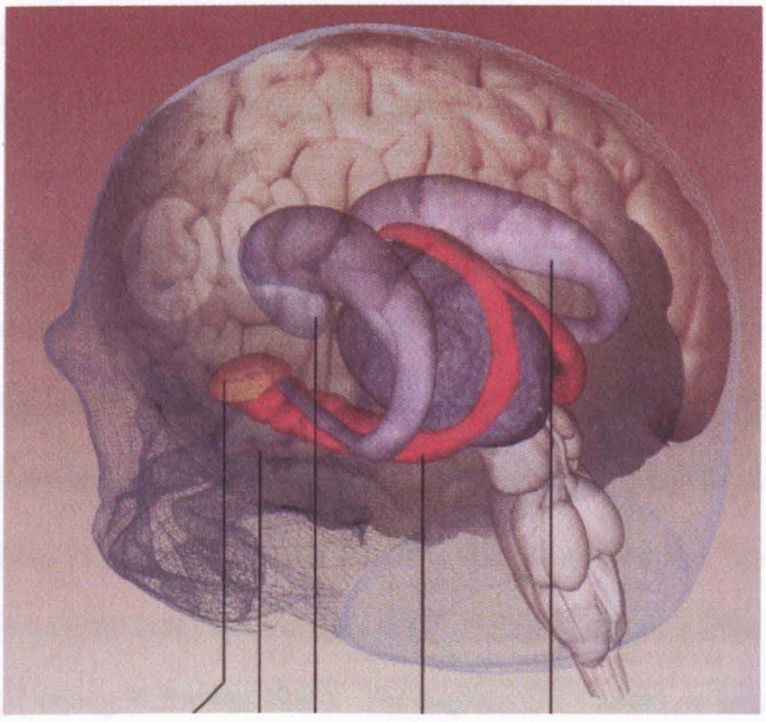
The Neurobiology of Memory and the Effects of Benzodiazepines

In light of the debate surrounding the possible effects of benzodiazepines on memory it will be helpful to delineate the underlying neurobiology of memory and the proposed

neuropharamacological effects of these drugs on such mechanisms. The structures currently thought to be involved in learning and memory are the cerebellum, hippocampus, amygdala, and cerebral cortex (Mishkin & Appenzeller, 1987; Thompson, 1986).

Figure 1 – The Human Memory System

(Carter, 2002, p. 264)



amygdala temporal lobe putamen hippocampus caudate nucleus

Learning and memory involve synaptic plasticity, i.e. changes in the structure or biochemistry of synapses that alter their effects on postsynaptic neurons (Carlson, 1998). Long-term potentiation (LTP) is a form of synaptic plasticity that has, since the early1980's, been investigated and proposed as a model for the storage of information in the brain. The phenomenon was first discovered in the hippocampal formation (Lømo, 1966); a specialised region of the limbic system located in the temporal lobe.

Lømo reported that intense electrical stimulation of axons leading from the entorhinal cortex to the dentate gyrus caused a long-term increase in the magnitude of excitatory postsynaptic potentials in the postsynaptic cells, thereby strengthening the connection. LTP has since been demonstrated in the prefrontal cortex, piriform cortex, motor cortex, visual cortex, thalamus and amygdala (e.g. Clugnet & LeDoux, 1990; Lynch, Larson, Staubli & Granger, 1991). Interestingly, many experiments have demonstrated that long-term potentiation in hippocampal slices can follow the Hebb rule. That is, when weak and strong synapses to a single neuron are stimulated at approximately the same time, the weak synapse becomes strengthened. This phenomenon is known as associative long-term potentiation (e.g. Kelso & Brown, 1986).

LTP requires some sort of additive effect, i.e. a series of pulses delivered at a high rate all in one burst rather than at a slow rate. In fact low-frequency stimulation can lead to the opposite phenomenon: long-term depression. The reason for this LTP phenomenon is that synaptic strengthening only occurs when molecules of a neurotransmitter bind with postsynaptic receptors located in a dendritic spine that is already depolarised, i.e. LTP requires two events: activation of synapses and depolarisation of the postsynaptic neuron (Kelso, Ganong & Brown, 1986). The explanation for this, at least in some parts of the brain, lies in the characteristics of a specialised ionotropic glutamate receptor called N-methyl-D-aspartate (NMDA). An important feature of the NMDA receptor is that it contains at least six different binding sites, four located on the exterior of the receptor and two located deep within the calcium ion channel it controls (Carlson, 1998). Normally the calcium channel in the NMDA receptor is blocked by magnesium ions, which prevent the calcium ions entering the cell, even when the receptor is stimulated by glutamate. However, if the postsynaptic membrane is depolarised whilst glutamate has bound to the receptor, the magnesium ions are ejected from the ion

channel, and the channel is free to admit calcium ions. It is generally agreed that the entry of calcium activates some special calcium-dependent enzymes known as protein kinases. When activated these enzymes add phosphate groups to particular protein molecules, causing some part of the protein to move, changing its properties, both biochemical and structural. These alterations provide one of the building blocks of a newly formed memory (Brown, Ganong, Kairiss, Keenan & Kelso, 1989).

Glutamate is the principle excitatory neurotransmitter in the brain and spinal cord, which stimulates and binds to a number of receptors; in particular NMDA with respect to memory formation. Gamma-aminobutyric acid (GABA), conversely, is the most important inhibitory transmitter substance in the brain and spinal cord (Haefely, Kulscar, Möhler, Pieri, Polc & Schaffner, 1975). Two GABA receptors have been identified: $GABA_A$ and $GABA_B$. The former is an ionotropic receptor that controls a chloride channel and the latter is a metabotropic receptor that controls a potassium channel. Due to the mass of neuronal interconnections in the brain, without the activity of inhibitory synapses most of the neurones in the brain would, very rapidly, be firing uncontrollably (as occurs during a seizure - a characteristic of the neurological disorder of epilepsy). $GABA_A$ receptors are of particular interest to this research, as they are found in their highest densities in the cortical and limbic structures where memory formation is thought to occur (Mishkin & Appenzeller, 1987; Thompson, 1986). GABA exerts its major effects by interacting with $GABA_A$ receptors, which triggers the gating of a channel for chloride ions. The intracellular flow of ions inhibits the ability of the neuron to conduct impulses. Like NMDA receptors, $GABA_A$ receptors are complex; they contain at least five different binding sites. The principle binding site is, of course, for GABA. However, one site on the $GABA_A$ receptor binds with a class of anxiolytic drugs called benzodiazepines. When benzodiazepines bind to the

corresponding receptor site the channel-gating process is modulated (Möhler & Okada, 1977; Squires & Braestrup, 1977). Benzodiazepines promote the activity of the $GABA_A$ receptor; thus, these drugs serve as agonists, i.e. they facilitate the effects of the neurotransmitter, GABA, on the postsynaptic cell. Therefore, if the postsynaptic neuron is inhibited it will not depolarise. The consequence of this is that regardless of whether glutamate has bound to neighbouring NMDA receptors, LTP cannot occur in the presence of $GABA_A$-benzodiazepine-receptor complex and as a result, making new memories should be, in theory, impossible.

Memory is inextricably linked with learning and is therefore worth considering also. Learning enables us to adapt to our environment and to respond to changes in it. In particular, it provides us with the ability to perform an appropriate behaviour in an appropriate situation. Situations can be as simple as the sound of a buzzer or as complex as the social interactions of a group of people. The initial component of learning, and the aspect with which this current project is most interested in, involves learning to perceive, i.e. learning about things, not what to do when they are present. Perceptual learning can be further sub-divided into simple perceptual learning, i.e. learning to recognise particular stimuli and categories of stimuli, and complex perceptual learning, i.e. learning sequences of events that have taken place at a particular time and place, often referred to as relational learning or an aspect of declarative memory (Carlson, 1998). Again, due to the vastness of this literature and the nature of the current research project, only simple perceptual learning of auditory stimuli will be examined. This will be illustrated with an example of an auditory stimulus that evokes a conditioned emotional response highlighting the effects of arousal on synaptic plasticity within the neocortex.

Simple perceptual learning appears to take place in appropriate regions of sensory association cortex, i.e. learning to recognise sounds takes place in the auditory association cortex. However, very simple perceptual learning has even been postulated as being accomplished subcortically by mechanisms we inherited from our remote ancestors, who lived before the evolution of the cerebral cortex. Interestingly, although we can learn to recognise stimuli even when nothing important happens, the occurrence of an important stimulus, i.e. one that motivates us to approach or escape from it, facilitates perceptual learning. That is, we are more likely to remember stimuli associated with events that affect us emotionally. This is due to the release of acetylcholine (ACh) that activates the cerebral cortex (Vanderwolf, 1992). ACh, unlike GABA and glutamate, is a neurotransmitter that modulates neural activity as opposed to being involved in the transmission of information. For example, secretion of ACh activates the cerebral cortex and facilitates learning, but the information that is learned and remembered is transmitted by neurons that secrete glutamate and GABA (Feldman, Meyer & Quenzer, 1997).

A series of studies by Weinberger and his colleagues using an auditory learning task illustrated that when an auditory stimulus (tone) was paired with an aversive stimulus changes could be seen in the responses of neurons in the auditory cortex when the tone was presented again. The tone had become a conditioned stimulus and elicits the same range of behavioural, autonomic, and hormonal responses, such as freezing, increased blood pressure and heart rate, secretion of stress hormones etc. as the aversive stimulus (Bakin & Weinberger, 1990; Edeline & Weinberger, 1991a; 1991b; 1992). The changes in the response characteristics of the cortical neurons appear to be triggered by activation of the central nucleus of the amygdala, a structure that plays an important role in emotional responses. These changes appear to be long lasting and have been found

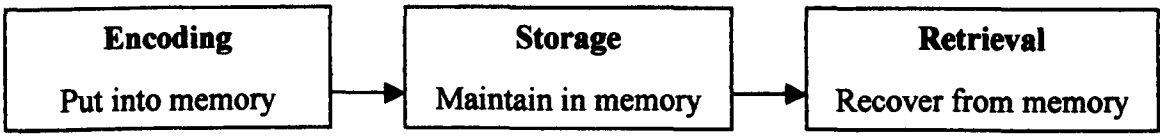
up to eight weeks later. Furthermore, the central nucleus then activates the nucleus basalis, which results in the release of acetylcholine in the cortex. This association may be strengthened through the action of the Hebb rule. It is important to note that the experiments conducted by Weinberger and colleagues used guinea pigs and generalisation to humans is therefore tentative. However, it is encouraging that other animal studies have found the same results (LeDoux, 1995; Sananes & Davies, 1992).

Memory Models and Processes

Having considered the underlying physical mechanisms of memory and learning and the pharmacological effects of benzodiazepines, it is both essential and pertinent to review current psychological theories of memory models and processes and how these may be affected by conscious sedation. There are three critical distinctions to memory. The first concerns the three stages of memory: encoding, storage and retrieval. The second distinction deals with different memories for storing information for short and long periods of time. The third distinction is about different memories being used to store different types of information.

Memory Processes

Figure 2– The Three Stages of Memory



To learn and be able to recall information at least three processes are required: encoding / acquisition, storage, and retrieval. The first stage of memory involves perceiving,

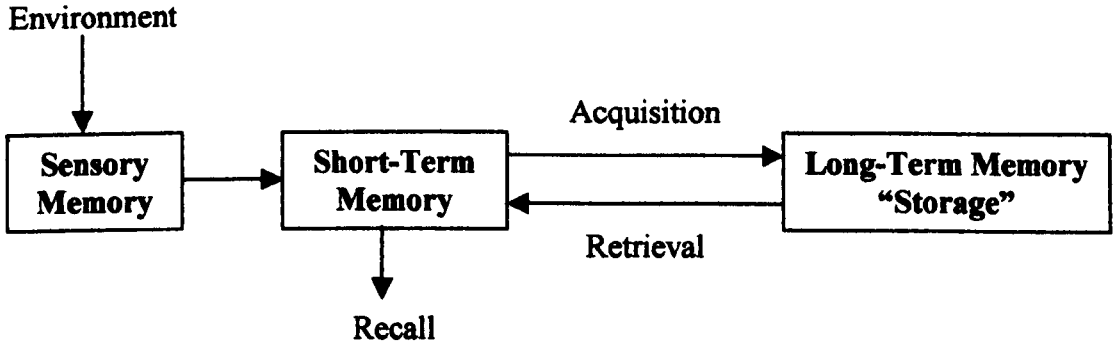
attending to and transforming the physical input (e.g. sound waves) into the kind of code that memory accepts, which are then "placed" into memory, i.e. the encoding stage. This process of forming a durable permanent memory trace is sometimes referred to as consolidation. Some encoding appears to occur automatically as in our knowledge of our location in time and space, while acquisition of other information typically requires conscious effort, as in the learning of a list of words (Hasher & Zacks, 1979). Second, is to retain, or store, the information for future use, i.e. the storage stage. Retention of information in memory involves not allowing it to decay, be replaced, or destroyed. Third, the relevant information from storage when the need arises, is recovered, i.e. the retrieval stage. Memory, then, can in theory fail at any of these three stages, which is the foundation of many theories of forgetting (Melton, 1963). Much of the current research on memory attempts to specify the mental operations that occur at each stage to help explain how they can go awry and result in memory failure. Furthermore, understanding where a chemical agent has its effect will enable more accurate predictions about how a patient's memory will be influenced, which may have an impact on treatment and recovery. For example, a drug that only disrupts acquisition processes would be expected to produce anterograde amnesia, and reduced learning of new information following treatment. It should not produce retrograde amnesia, i.e. loss of information learned prior to treatment.

Divisions of Memory

Research on human memory has a long history (Ebbinghaus, 1885) but has greatly intensified since cognitive psychology completed its separation from behaviourism in the 1960's (Anderson, 1995). The development of a theory of short-term memory was a very important event in cognitive psychology and highlighted that memory was not a

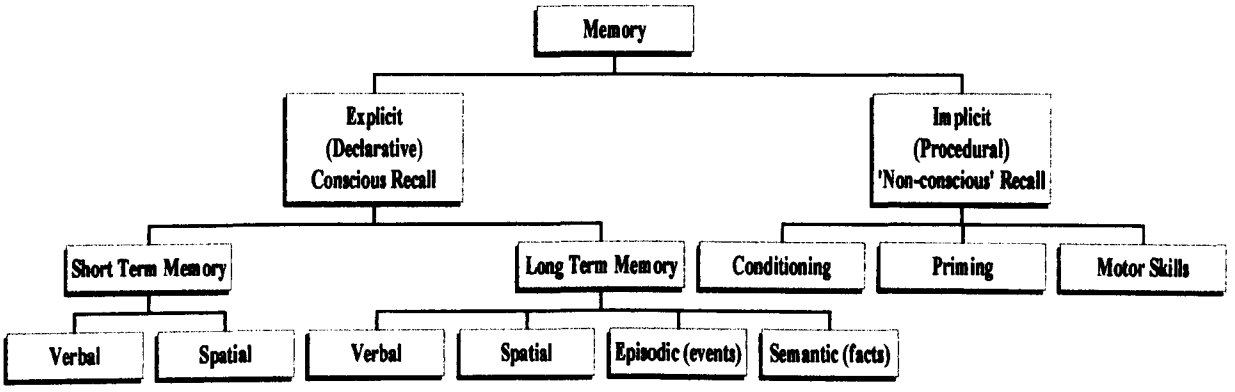
unitary process or entity (Atkinson & Shiffrin, 1968; Broadbent, 1958; Waugh & Norman, 1965). Ideas from this two-process theory continue to play a crucial role in some of the modern theories that will be described later and will therefore be included in this review. The theory of short-term memory proposed that information coming in from the environment would be held in transient sensory stores from which it is lost if not attended to. Each of the five sensory memory systems are considered to be passive in that they are activated by incoming stimuli and are not under conscious control. The attended information is then passed into an intermediate short-term memory store where it must be rehearsed or it will typically fade in about twenty seconds or less (Ghoneim & Mewaldt, 1990). The capacity of short-term memory is thought to be quite limited, estimated at around seven plus or minus two items (Miller, 1956). Short-term memory is considered an active store and is often equated to awareness, in that whatever the person is currently thinking about is in their short-term memory. If information here is rehearsed then it is thought more likely to pass into a relatively permanent long-term memory store. Information is thought to be stored in long-term memory indefinitely and without active effort. To recall this information it must be located and retrieved or brought back into conscious awareness (short-term memory) (Atkinson & Shiffrin, 1971).

Figure 3 – The Theoretical Relationship Between Three Memory Systems



Continuing research and analysis has led researchers to question the ability of a relatively simplistic model to account for, and fully explain, the complexities of human memory and learning. Based on work investigating the memory and learning capacities of various brain-damaged patients, researchers have proposed a more fundamental division of memory: explicit (declarative) and implicit (nondeclarative) memory (Graf & Schacter, 1985; Hodges, 1994).

Figure 4 – The Major Subdivisions of Memory



Explicit memory is what most people think of as memory and underlies a conscious recollection of something in the past, including the circumstances of the learning episode. Explicit memories include images, facts, and records of experiences that can be called to mind. Implicit memory underlies perceptual, motor and cognitive skills and is sometimes referred to as procedural memory. It is often expressed as change in some perceptual, motor or cognitive phenomenon without any conscious recollection of the experiences that led to the change. Implicit memory is demonstrated in acquired skills like riding a bike, throwing a ball, or touch-typing. To take the last example as an illustration, many accomplished typists cannot recall the arrangement of the keys, but show perfect knowledge when asked to type; their fingers seem to remember, but they have no conscious access to this information (Anderson, 1995). Implicit memory would

also include the results of prior classical conditioning such as a person salivating to the smell of bacon frying or other conditioning phenomena such as habituation and priming. Habituation refers to the reduction in strength of a response to a repeated stimulus. Priming refers to an enhancement of the processing of a stimulus as a function of prior experience (which may not be recalled explicitly).

Factors Which Affect Memory

Despite the expansion and delineation of memory classification there remains some difficulty in detecting, differentiating and measuring the different aspects of memory. Explicit learning (learning accompanied by conscious awareness of the information being learned and the circumstances of the learning episode) can lead to explicit memory (i.e. they can recall it, or when they encounter the information again, are able to recognise it) or implicit memory (i.e. is inferred from behavioural changes following, and attributable to, an encounter with that stimulus). Implicit learning (learning without conscious awareness of the information being learned or the circumstances of the learning episode) can only lead to implicit memory.

However, as we know from everyday experience, inattention and distraction while learning information can make it harder to recall or recognise that information on a subsequent occasion. Also, explicit memory can be influenced by the context in which it is learned i.e. state dependent learning. It can be easier to recall something if you return to the place in which it was learned (e.g. Godden & Baddeley, 1975) or to reinstate the mood you were in when you first encountered it (Eich, 1995) or even be under the same influence of a particular drug e.g. alcohol or marijuana (Atkinson, Atkinson, Smith, Bem & Nolen-Hoeksema, 1996). Furthermore, emotion can play a

significant role in what we remember and forget; we are much more likely to remember an emotionally charged stimulus as we tend to think and talk about it more than neutral ones. However, we may also forget extremely emotionally charged information if to do so protects us from its negative connotations (psychogenic amnesia or repression). Therefore, there are several reasons why someone may fail to recall information they learned explicitly. They may have not attended to it or processed too little to form an explicit memory, or they may have formed an explicit memory which cannot be retrieved because the current environment provides no cues to aid retrieval (Andrade, Stapleton, Harper, Englert & Edwards, 2000).

However, it has also been postulated that implicit memory, and in particular conditioning, can be affected by factors such as mood, personality and pain. As mentioned earlier an unconditioned stimulus can be conditioned to produce the same autonomic arousal as an aversive stimulus if paired together (Bakin & Weinberger, 1990; Edeline & Weinberger, 1991a; 1991b; 1992). This could mean one is more likely to learn a neutral stimulus implicitly if it is presented with an aversive or painful stimulus purely by association and the conditioning of fear or arousal (i.e. implicit emotional memory). Also, it seems logical that very neurotic and introverted personalities are more likely to experience negative emotions like anxiety and may be more sensitive to fear conditioning due to a pre-existing high level of arousal or sensitivity to stimuli.

While the usefulness of these distinctions in memory is still being investigated, it is much less meaningful to merely report that a drug impairs memory than to distinguish its effects on various aspects and processes of memory. In addition, the use of anaesthetics and benzodiazepines that are used, in part, to provide amnesia for the

procedures for which awareness, memory, or learning may have serious ramifications on physical recovery and future psychological health of the patients, highlights another reason for further research. This introduction so far has explained the reports and research that has lead to interest in anaesthetic drug effects on memory during surgery and how this is potentially increasing in relevance in the field of medicine due to the lightening of anaesthetics and the adoption of conscious sedation in some procedures for quicker and physically safer surgery; a review of the current thinking on how this may be neurobiologically possible; and a discussion of memory models and processes. It is now pertinent to review and evaluate the literature on the effects of benzodiazepines on memory and the factors that may modulate this, which will lead on to the rationale and aims of the current research project.

Mechanisms by Which Benzodiazepines Impair Memory

> I was on an overnight transatlantic flight and said to my colleague, "The dinner cart is one cabin ahead. I'm going to take a benzodiazepine so that I get a good night's sleep after dinner." The following morning I awoke and said, "That worked quickly, I was asleep before dinner," to which he replied, "No, you were not. You ate dinner and we talked all through the meal." To this day I have no recollection of that meal. Yet, I have no doubt that the memory exists somewhere in my subconscious (Sebel, 1995, p 668).

The profound anterograde amnesic effect that Sebel (1995) describes is one of the reasons why benzodiazepines, such as midazolam, are used when inducing conscious sedation, along with its sedative and anxiolytic effects. Midazolam-induced amnesia is of clinical importance to mitigate aversive experience that may arise during surgical

and/or medical procedures (Pain, Launoy & Oberling, 2000), which may have a negative effect on physical recovery or psychological health post-procedure.

Anterograde amnesia with benzodiazepines is a well-known phenomenon and is well described in the literature, but there remains debate over the completeness of this amnesia and whether this amnesia is a true impairment in memory or a bi-product of its sedative action. Curran (1986) reviewed studies published between 1973 and 1985, which investigated the effects of benzodiazepines. From this review she concluded that anterograde amnesia appears to be a common effect of all benzodiazepines, although its onset and duration varies with the particular benzodiazepine, its dose and route of administration. Memory impairments increase with task difficulty. She found evidence that partial tolerance to amnesic effects develops with repeated doses of diazepam, but research with other benzodiazepines was inconclusive. She concluded that amnesia was in part a by-product of the benzodiazepines general depressant reaction on the whole central nervous system, although these drugs may also have a specific effect of disrupting the consolidation of information in long-term memory (Ghoneim & Mewaldt, 1975). State-dependent effects are partial and relatively small. Finally, she highlighted methodological problems such as the lack of repeated dose studies, of studies with patient populations and with anxious volunteers. Lister (1985), in a similar review, summarised in addition to Curran (1986) that episodic long-term memory was the aspect of memory that was most affected by benzodiazepines. These drugs impaired the acquisition of new information, but did not impact retention, semantic memory and the acquisition of skills and may even facilitate retrieval of information learnt before medication. He also concluded that although state-dependent learning may be observed it was a small effect and could not account for most of the observed impairments. Lister (1985) suggested that benzodiazepines might provide the cognitive psychologist with a

useful tool to investigate the mechanism of normal memory as a reversible model of organic amnesia.

To aid a critique of these findings within this introduction, research literature has been divided under the headings of the debates they address.

Sedation vs. Amnesia

Benzodiazepines produce sedation and it is therefore pertinent to investigate whether impaired memory performance is a by-product of this sedation rather than a specific effect of the drugs. The increase in understanding of the neural organisation of memory (as described earlier) has mainly developed through the analysis of patterns of spared and impaired memory functions that are a consequence of discrete lesions of the central nervous system (Zola-Morgan, Squire & Amaral, 1986). The strength of this approach is that it provides a framework to link lesions of specific brain structures with specific cognitive deficits. Unfortunately, the strength of this approach is also one of its weaknesses, since the experimenter must rely on the results of pathological events or therapeutic surgical interventions. In either case, the nature and extent of the lesion cannot be known with certainty until after death of the participant. This makes interpretation of cognitive findings in terms of neuroanatomy problematic. Also, since many humans with cognitive impairment have multiple lesions, selection of an appropriate control group is difficult (Hommer, Weingartner & Breier, 1993).

A more recent parallel approach to studying memory is a neuropharmacological approach, which allows the study of reversible changes in cognitive functions with participants acting as their own controls. The limit of this approach to the study of

memory is determined primarily by the specificity of the drugs used as probes. In many ways, benzodiazepines are an ideal pharmacological probe of human cognition, the action of which is well known (Young & Kuhar, 1979), as described above. The syndrome produced by acute benzodiazepine administration in humans appears to resemble closely the amnesic syndrome observed in patients with damage limited to the medial temporal lobes, except that it also causes sedation and impairment of attention (Squire, 1987). On initial inspection the memory impairment and level of sedation are highly correlated, both of them increasing in a dose-dependent pattern (Hommer, Matsou & Wolkowitz, 1986), making it possible that the former are secondary to the latter. This would support the value of benzodiazepines as probes into the neurobiology of memory minimal.

There are, however, several reasons to suspect that benzodiazepine-induced memory impairment is not simply a bi-product of sedation. Firstly, correlation does not imply causation and therefore sedation may not cause amnesia just because they appear related. Also, during chronic benzodiazepine treatment tolerance develops to its sedative effects but not to the resultant memory impairments (File & Lister, 1982; Ghoneim, Mewaldt, Berie & Hinrichs, 1981; Lucki, Rickels & Geller, 1986). Furthermore, a specific benzodiazepine receptor antagonist, flumazenil, which reliably blocks the sedative effects of benzodiazepines, has been shown to produce dissociation between the sedative and amnesic effects of several benzodiazepines (Birch & Curran, 1990; Dunton, Schwam & Pitman, 1988; Ghoneim, Dembo & Block, 1989; O'Boyle, Lambe, Darragh, Taffe, Brick & Kenny, 1983). However, it is not yet clear whether higher doses are required to reverse benzodiazepine-induced amnesia than has been used in demonstrations of sedation reversal. Nor is it yet known the mechanisms by which flumazenil blocks the non-amnestic effects while failing to antagonise the

amnesia. One possibility is that the amnestic and non-amnestic effects of benzodiazepines are mediated through different classes of benzodiazepine receptors. Although there is evidence for multiple subtypes of benzodiazepine receptors in the human brain, as described earlier (Montaldo, Serra, Concas, Corda, Mele & Biggio, 1984), there is no evidence that flumazenil possesses differential affinity for them (Hantraye, Kaijima, Prenant, Guibert, Sastre, Crouzel, Naquet, Comar & Maziere, 1984).

Finally, it is important to reflect that the specificity and selectivity of the amnesia produced by benzodiazepines that will be discussed subsequently, add further evidence that these drugs do not simply depress the central nervous system. It would therefore seem unlikely that sedation explains all amnesic phenomena.

Acquisition vs. Retrieval

It is generally accepted that benzodiazepines impair acquisition or encoding of new information while having no disruptive effect upon either retention or retrieval of previously stored information. In Figure 3 (*see page 16*) the process disrupted is represented by the arrow indicating the transfer of information from short-term to long-term memory. Evidence for this process comes from numerous studies which have found that participants who were required to learn information (e.g. lists of words) prior to drug administration and then asked to recall the material during a period of drug action, showed no impairment in their recall relative to that of placebo participants, despite sedative effects. In contrast, recall of information learned following drug administration is greatly reduced (Brown, Lewis, Brown, Horn & Bowes, 1982; Ghoneim & Mewaldt, 1975). The recall of pre-drug material not being impaired whilst

the recall of post-drug material suggests that differences are due to lowered levels of learning in the drugged participants.

Other explanations include that the information may not have been stored explicitly after drug administration and maybe access to these memories can only be possible through memory tests that are sensitive to implicit memory. Also, just to say that it is a deficit in encoding does not highlight whether it was a problem with depth of processing, faster rates of forgetting, or rehearsal problems.

Episodic vs. Semantic Memories

The research literature also points to the fact that benzodiazepines seem to greatly impair episodic memory, whilst leaving semantic memory unaffected. If participants are asked to generate words that represent a particular semantic category, e.g. four-footed animals, types of music etc., their ability to do so will not be affected by the drugs, although it may be slowed (Ghoneim & Mewaldt, 1975; Preston, Broks, Traub, Ward, Poppleton & Stahl, 1988). Lister & File (1984) found that even though lorazepam prevented some participants from remembering that they had done the task previously (episodic memory), the drug did not impair their learning of a backward reading task (a task requiring both semantic and implicit memories).

Explicit vs. Implicit Memories

The last and most important deliberation in relation to the current study is the explicit verses implicit controversy. A study by Fang, Hinrichs & Ghoneim (1987) is the key study cited in testament to this debate. This is primarily due to the very small number

of studies that have been designed specifically to investigate this division in memory under the influence of benzodiazepines. The absence of empirical research is in part because of the belief that with the common absence of explicit memory for intra-operative events following conscious sedation there is no memory formed and therefore no adverse effects on psychological and physical recovery. In light of the increasing weight of evidence to the contrary under general anaesthesia there is a real need to investigate memory under conscious sedation, which by definition is not so much farther down the awareness continuum.

Fang et al (1987) investigated the effects of diazepam on several tests of memory in a double-blind study of twenty-four healthy paid volunteers. Following a single oral administration of diazepam or placebo, participants in the diazepam group showed marked impairment in immediate free recall of words as compared to placebo control participants. However, diazepam-treated participants demonstrated performance benefits from prior exposure to the same words on tests of memory priming using word completion and category-generation tasks. The two types of memory tests differ in their demands for conscious recollection. Tests of free recall have explicit memory demands whereas the priming tests place only implicit demands upon memory. Fang et al (1987) concluded that their results demonstrated that diazepam spares some forms of memory, as does amnesia induced by neurological impairment. However, it is important to consider that despite being experimentally double blind, it is unlikely that either the participants or the investigators could mistake the diazepam-treated participants compared to the placebo controls. Adding to this the fact that the participants were being paid and they had probably been informed that the researchers were investigating the effects of these benzodiazepines on memory, one has to bear in mind the impact of demand characteristics and the possibility for 'faking good'. Also, with so few

participants and without a repeated measures design, generalisability is limited; especially to the implicit memory of post-surgical psychopathology, which is qualitatively different and most likely based in classical conditioning learning paradigms rather than priming ones as discussed later. Despite these methodological queries this study undoubtedly highlights a need for more research to be undertaken in this area.

In summary, the literature confirms that benzodiazepines produce anterograde amnesia and postulates that it presents as a reversible form of amnesia characteristic of an organic impairment. More specifically, the supposition based on somewhat contentious research formulates that benzodiazepines result in a breakdown in the acquisition of explicit episodic memory, whilst preserving retrieval processes, and the formation of semantic and implicit memory.

Factors that may Affect Benzodiazepine-Induced Amnesia

As with most research into the effects of drugs there are many other variables, which mediate their action. It is important to understand the impact of these other variables to help explain some of the differences present in the results of different studies looking at the same, or similar areas of interest.

Drug, Dose, Tolerance and Route of Administration

There are distinct pharmacokinetic differences between the various benzodiazepines (Greenblatt, Shader, Divoll & Harmatz, 1981). They have different rates of absorption, distribution and elimination that result in different times of onset and offset for their

effects. The rate of distribution of the drug in and out of the brain is perhaps the most important determinant of the duration of the drug action after single doses. Lipid solubility of the drug also determines the rate of distribution. The highly lipid soluble members like diazepam and midazolam have rapid onset of action that is of relatively short duration compared with the less lipid soluble drugs like lorazepam and oxazepam that have a longer onset time and longer duration of action (Shader, Dreyfuss, Gerrein, Harmatz, Allison & Greenblatt, 1986).

Generally speaking, all benzodiazepines have similar pharmacodynamic profiles, appearing to have qualitatively similar effects on memory and performance. In spite of this, the degree and duration of memory impairments is not purely related to the pharmacokinetic properties of the drug but also the dose administered. However, reports have concluded that there is no study of dose-response function in relation to the effects these drugs have on memory, that do not suffer from faulty methods. Such methodological flaws include failure to use a placebo group or double-blind assignment of subjects, use of absolute rather than weight-relative doses and / or insensitive tests (e.g. Greg, Ryan & Levin, 1974; Kothary, Brown, Pandit, Samara & Pandit, 1981). Needless to say it is clear that the dosage of one benzodiazepine is not necessarily equipotent to another.

Another factor causing differences in research findings is the effects of repeated administrations. Repeated administrations of benzodiazepines like other central nervous system active drugs, results in tolerance to the drugs' effects. This includes a reduction in the effects on memory; however, complete tolerance does not develop (Lucki & Rickels, 1986; McLeod, Hoehn-Saric, Labib & Greenblatt, 1988). It is generally accepted that when a drug is given repeatedly, the plasma concentration

increases with each dose until a steady state is reached; and that this accumulation is proportional to the elimination half-life. Therefore, less accumulation and perhaps less drowsiness and performance impairment are expected with drugs with a short elimination half-life.

A fourth factor that affects benzodiazepine-induced amnesia is the route in which it is administered. The magnitude of memory impairment will be maximal at the time of peak concentration in the brain. The peak concentration of a benzodiazepine in the brain will be highest (and quickest) following intravenous administration and lowest (and slowest) following oral treatment, with intramuscular and subcutaneous routes intermediate. However, the same spectrum of effects follows all methods of administration and the rates of recovery are similar (Ghoneim, Mewaldt & Hinrichs, 1984).

Population Characteristics

Despite the general pattern of benzodiazepine effects, like all drugs, the individual characteristics of the person being administered the drug can mediate these outcomes and must be taken into account when comparing results of different studies.

- Aging

Considerable evidence exists to suggest that the elderly are more sensitive to the behavioural effects of benzodiazepines (Meyer, 1982), although the reason for this remains unclear. There appears to be no evidence of age-related changes in pharmacokinetics or pharmacodynamics. However, it may not be due to the synergistic

action of the drugs at all, but merely the lower baseline performance of the elderly (Pomara, Stanley, Block, Berchou, Stanley, Greenblatt, Newton & Gerson, 1985).

- Pain

The second relevant individual difference is pain. Human recognition of pain is largely contingent on the interplay between conscious and unconscious systems and the combination of cognitive, emotional and physiological responses that this generates. Although amnestics may reduce the cognitive components of pain perception, it cannot be assumed that patients' discomfort was negligible as pain perception can be associated with pain receptor activity alone (Schuster & Leonard, 1990). Despite this, one can still argue that the experience of pain in a sedated patient with no conscious recall may be qualitatively different to that which occurs in a state of full consciousness. In the absence of post-operative verbal reports of pain several physiological and behavioural indicators have been reported. Anand & Hickey (1987) identified changes in cardio-respiration and hormonal and metabolic stress responses. Mehlman, Kanoti & Orlowski (1994) identified tachycardia (rapid heart rate), mydriasis (dilated pupils), diaphoresis (profuse perspiration), wincing and even verbalisations.

- Anxiety

The third relevant individual difference is anxiety. Gastric problems are traditionally associated with anxiety, benzodiazepines are used to reduce anxiety, and anxiety has a profound impact on memory; therefore, anxiety is a factor of interest to the current study. O'Malley, Wang, Kroenke, Roy & Wong, (1998) investigated the prevalence of psychiatric disorders in 116 patients with gastro-intestinal complaints undergoing upper

endoscopy. Psychiatric disorders were detected in 70 of the patients with the most common diagnoses being somatoform, anxiety, and depressive disorders. In relation to performance, it is thought to vary with an individual's general arousal level along an inverted U curve (Yerkes & Dodson, 1908). Thus both low and high arousal is associated with poor performance. It can be argued from this that drugs acting as anxiolytics will impair performance of those suffering with a moderate level of anxiety but improve the performance of highly anxious individuals (Desai, Taylor-Davies & Barnett, 1983). However, it may be too simplistic to equate arousal with anxiety. Also, this effect may only be observed for single doses of drugs and the doses usually prescribed may be too large to detect improved performance (Angus & Romney, 1984).

- Depression

Fourthly, it is a well-documented phenomenon that depressed people often complain of poor memory. It is not clear whether the source of this is biological or due to a lack of drive and energy. Depressed patients are also prone to cognitive distortions, filtering out positive information and selectively attending to negative emotions, i.e. selective abstraction (Beck, 1976; Fennell & Teasdale, 1987). Therefore, depression predisposes surgical patients to attend to negative feelings, thoughts and experiences before, during and after the medical procedure and this may cause them to lay down strong memory traces. However, it remains difficult to draw parallels to what is known about how people behave in normal situations and how they may behave when undergoing painful and unpleasant medical procedures.

- Personality

Lastly, personality impacts on our thoughts, feelings and behaviours and is likely to play an important factor in the interaction of medication on memory formation. It has been discussed throughout this review that this interaction is not clear-cut, with different studies showing markedly varying results and many potential covariates acting on this predicted relationship. Wilson, Whiteoak, Dewey & Watson (1989) compared soldiers attending an endoscopy unit with soldiers from a standard medical ward and an alcohol treatment unit. The Eysenck Personality Inventory (Eysenck & Eysenck, 1964) was used to screen for differences in personality. They found that soldiers from the alcohol unit were the most neurotic, with soldiers from the endoscopy clinic coming a close second.

Sensitivity of Memory Tasks to the Benzodiazepines

The third issue to be discussed to aid understanding of the inconsistencies and continuing debates surrounding the effects of amnestics in noxious medical procedures and the mechanisms of memory, is the variation in tests utilised to measure what has been defined as, or is presumed to be, the same entity. When trying to detect implicit memory (as in this current study) it is important to consider the type of information to be remembered. It has been illustrated during this review that implicit memory is formed without awareness of the learning event. These memories include procedural and skill based memory, conditioning, priming and habituation and so the to-be-remembered information must have at least some of these characteristics. Also it is necessary to take into account the factors that we know affect memory formation, such as personal relevance, highly emotive stimulus, low distraction, motivation to remember

etc. Lastly, the actual way of detecting memories that are not accessible to conscious recall poses another potential difficulty. Improved performance on some tasks, word association tasks (known as priming tasks) and physiological responses have all been used in past studies.

Amygdala and Hippocampal Processing Systems

The final, and perhaps most crucial, issue to be discussed that may affect benzodiazepine-induced amnesia is the type of learning paradigm adopted to illustrate the possible sparing of implicit memory. Classical conditioning has been predicted to be robust enough to persist despite organic amnesia (Weiskrantz & Warrington, 1979) or inhalation of a subanaesthetic concentration of nitrous oxide (Block, Ghoneim, Fowles, Kumar & Pathak, 1987). Weinberger, Gold & Sternberg (1984) even succeeded in conditioning fear in rats deeply anaesthetised with pentobarbitone, but only by injecting adrenaline during training. If these findings could be extrapolated to humans, one might expect to observe conditioning during surgery, since this is a potent stressor associated with substantial catecholamine release (Bennett, 1985). However, Ghoneim, Block & Fowles (1992) were unable to establish a conditioned skin conductance response during anaesthesia, despite using a paradigm which elicited conditioning in non-anaesthetised participants. They went on to suggest that multiple (and therefore impracticable in humans) conditioning sessions may be needed to induce a conditioning response under anaesthesia. However, the crucial factor in the lack of findings of conditioning in humans under general anaesthesia is that although Ghoneim et al (1992) used a loud noise (which innately evokes an electrodermal response) to pair with the target word, the words themselves are neutral in affect and unconnected to the stress of surgery.

To clarify some of the variability of findings with respect to conditioning under sedation and general anaesthesia the neurobiological mechanisms of cognition and emotion (as mentioned earlier), need to be revisited and discussed in more depth. In 1937 Kluver and Bucy made one of the most important discoveries in the history of neurobiological studies of emotion. These researchers discovered that lesions to the amygdala resulted in the phenomenon they termed "psychic blindness", a neural disconnection of sensory processing areas from the affective system causing a loss of acknowledgement of the affective significance of sensory stimuli (Mishkin & Aggleton, 1981; Weiskrantz, 1956). Recordings of electrical activity indicate that some amygdaloid cells respond preferentially to the affective significance of sensory stimuli (Halgren, 1981); appear to be less sensitive to physical features of stimuli than to their affective significance (Sanghera, Rolls & Roper-Hall, 1979); respond better to novel than familiar stimuli and better to affective than neutral stimuli, some even respond differentially to positive and negative affective significance of stimuli (Nishijo, Ono & Nishino, 1988). Considerable work has focused on the question of how sensory stimuli normally activate the amygdala. Sensory information reaches the amygdala from the thalamus and the sensory association areas of the cortex. It has been found that when simple sensory cues are used as conditioned stimuli, the thalamo-amygdala projections are necessary and sufficient for conditioning of fear response and are best established for the auditory system. It was also discovered that cortico-amygdala projections are necessary when complex stimuli are processed (LeDoux, Sakaguchi, Iwata, & Reis, 1986).

What the amygdala is to emotional processing, it is thought that the hippocampus is to cognitive processing. It is known that the emotional and cognitive processing systems can be separated (as will be discussed below), however, there are neural connections between the amygdala and the hippocampus that facilitates some of the interactions

between these two systems. An example of how cognitive information may mediate affective processing involves stress-induced gastric pathology. Amygdala lesions greatly reduce the development of ulcers following stress, and ulcer formation may depend upon descending connections from the amygdala to the gut. In contrast, hippocampal lesions aggravate the development of stress-induced ulcer formation because in the absence of the hippocampus animals are less able to cope with stress (Henke, 1982).

However, the cognitive and emotional processing systems can also function independently. Lesions to the hippocampus do not produce emotional changes of the Kluver-Bucy syndrome (Weiskrantz, 1956), nor do they interfere with conditioned emotional responses (Rickert, Bennett, Lane & French, 1978), but do effect performance on a variety of cognitive tasks such as various long-term memory tasks (Squire & Zola-Morgan, 1983). Also the hippocampus, unlike the amygdala receives sensory information via a more convoluted route to allow for complete processing of the whole of the stimulus rather than specific features. It thus makes sense that affective processing can occur faster than, and independent of, cognitive processing (Zajonc, 1980). Further evidence of the potential independence of the cognitive and emotional processing system comes from Jacobs & Nadel (1985) who have proposed an intriguing explanation of infantile amnesia (i.e. having little or no conscious recall or the first two years of life despite it being a time when a tremendous amount of learning takes place). They argued that infantile amnesia is due to the hippocampus not being fully developed at birth, but taking about eighteen months to two years postpartum to mature. During this time, other early maturing systems (such as the amygdala) form memories in codes, which are indecipherable to the hippocampus when it finally matures, making these memories inaccessible to conscious explicit recall. Jacobs & Nadel (1985) also drew

parallels with their idea of infantile amnesia to fear and phobia learning in adults. When stressed, hormones are released that interfere with normal hippocampal function, resulting in implicit fear conditioning. Further evidence of this comes from the fact that stress hormones are known to interfere with the development of long-term potentiation (LTP) as mentioned earlier.

Therefore, one might predict that if the emotional amygdala-driven processing system is relatively unaffected by sedation and can act independently from the affected cognitive hippocampal-driven processing system, then implicit memory formation is only likely to be possible when a classical aversive conditioning paradigm that emotionally reflects the stress of the medical procedures is employed. This may be why Ghoneim et al (1992) failed to establish a conditioned skin conductance response during anaesthesia, despite using a paradigm, which elicited conditioning in non-anaesthetised participants.

Conclusions

Benzodiazepines and the state they induce (conscious sedation) have been shown to have great potential in investigating the divisions of memory and as a model of awareness during general anaesthesia. They are also commonly used in a popular noxious non-surgical procedure, colonoscopy. Therefore participants are more readily available than those with an organic explicit amnesia or those who have been aware during surgical anaesthesia. Another benefit of using benzodiazepines to investigate memory is the fact that it is reversible and so pre- and post-procedure measures can be taken and consciousness during the procedure is guaranteed. Also the use of benzodiazepines for noxious non-surgical procedures requires investigation in its own right.

It was decided that explicit memory for intra-operative events would be measured by free recall and implicit memory would be measured by change in skin conductance response to neologisms presented during the procedure compared to those that were not. To investigate whether implicit memory is modulated by emotion and in particular conditions to negative stimuli, the participants were divided into those who were presented a neologism with a negative association or a neutral association during the colonoscopy. As described earlier it was important to have data on self-rated pain, objectively measured behavioural intra-operative distress, personality, mood and drug dosages to evaluate their impact on the conditioning of neologisms.

Research Aims and Hypotheses

Research Aim:

To investigate whether implicit emotional memory can be demonstrated in patients undergoing a colonoscopy with benzodiazepine sedation.

Null Hypotheses

1. Participants will have no implicit memory for neologisms presented during colonoscopy, as detected by skin conductance response, following intravenous administration of midazolam.

2. There will be no significant difference in skin conductance response change from pre- to post-colonoscopy between intra-operatively presented neologisms designed to provoke an emotional association and 'neutral' neologisms.

3. There will be no significant effect of mood on implicit memory formation for neologisms presented during colonoscopy, as detected by skin conductance response, following intravenous administration of midazolam.

4. There will be no significant effect of personality on implicit memory formation for neologisms presented during colonoscopy, as detected by skin conductance response, following intravenous administration of midazolam.

5. There will be no significant effect of objectively rated behavioural distress on implicit memory formation for neologisms presented during colonoscopy, as detected by skin conductance response, following intravenous administration of midazolam.

Experimental Hypotheses

1. Participants will have implicit memory for neologisms presented during colonoscopy, as detected by skin conductance response, following intravenous administration of midazolam.

2. There will be a significant difference in skin conductance response change from pre- to post-colonoscopy between intra-operatively presented neologisms designed to provoke an emotional association and 'neutral' neologisms.

3. There will be a significant effect of mood on implicit memory formation for neologisms presented during colonoscopy, as detected by skin conductance response, following intravenous administration of midazolam.

4. There will be a significant effect of personality on implicit memory formation for neologisms presented during colonoscopy, as detected by skin conductance response, following intravenous administration of midazolam.

5. There will be a significant effect of objectively rated behavioural distress on implicit memory formation for neologisms presented during colonoscopy, as detected by skin conductance response, following intravenous administration of midazolam.

METHOD

Design

The design of this study is a prospective randomised pre and post repeated measures double blind trial including comparison between three groups. Measurement took place at three different time points both pre- and post-surgical procedure (i.e. immediately before and after the colonoscopy and up to one week post procedure). Also the group that participants were allocated to was randomised and unknown to both the researcher and the participant. The advantage of a prospective design is that it enabled measurement after the midazolam had been metabolised and enabled detection of change over time. The advantage of a repeated measures design was that the participants acted as their own control, which maximised the statistical power for a small group of participants. The obvious advantage of the pre and post aspect of the study's design is that it was possible to investigate causal relationships due to baseline and post intervention comparisons. A double blind design is often sought in empirical investigations to reduce biases resulting from participant or researcher expectation (known as demand characteristics and investigator bias respectively) as neither participant nor investigator are aware of the condition participants are allocated to. Random allocation to conditions or groups is also desirable where possible to help reduce the impact of random extraneous variables, which are uncontrolled in such field experiments.

Table 1 – Research Design

Group Number	Pre-colonoscopy (baseline)	Intra-operative	Post-operative 1 (immediately before discharge)	Post-operative 2 (follow-up within 1 week)
1	Stage 1 - SCRs to all 3 words (tapes 1-6)	Stage 2 – word A presented (tape A)	Stage 3 – checking for explicit memory, if any.	Stage 4 – SCRs to all three words (same tape as in pre-op).
2	Stage 1 - SCRs to all 3 words (tapes 1-6)	Stage 2 – word B presented (tape B)	Stage 3 – checking for explicit memory, if any.	Stage 4 – SCRs to all three words (same tape as in pre-op).
3	Stage 1 - SCRs to all 3 words (tapes 1-6)	Stage 2 – word C presented (tape C)	Stage 3 – checking for explicit memory, if any.	Stage 4 – SCRs to all three words (same tape as in pre-op).

The independent variables included the particular neologism presented during the colonoscopy. The dependent variable was the skin conductance response to the neologisms (see 'Procedure' section below) as measured on the Skin Conductance Response (SCR) monitor. Potential covariates include midazolam dose, anxiety and depression scores on the Hospital Anxiety and Depression Scale (HADS) and personality traits on the Eysenck Personality Inventory (EPI) and objectively rated behavioural distress on the Behavioural Distress Scale (BDS). These variables are not thought to cause a change in the dependent variable but may mediate the predicted relationship between the independent and dependent variables.

Participants

The study group consisted of consecutive outpatients, both male and female, aged 18 and above, which was attending the Castle Hill Hospital Endoscopy Department for a colonoscopy procedure on Monday (morning and afternoon) and Wednesday (afternoon only) within a nine-week period spanning April to June 2003. The exclusion criteria were as follows:

- Patients aged less than eighteen years of age.
- Outpatients attending for a diagnostic or therapeutic colonoscopy with entry into the colon not via the anus, but by some other route, such as a colostomy wound.
- Any patient who was an inpatient, due to the fact they often had other more serious or complicating medical conditions that may have impacted on the data collected.
- Patients who had other procedures planned at the same time as the colonoscopy, e.g. gastroscopy (i.e. an endoscopic examination of the upper digestive system from the oesophagus to the beginning of the small bowel).
- Patients who were not being given sedation for the procedure.
- Patients not fluent in the English language due to the potential inability to get informed consent and to complete questionnaires accurately.
- Patients who had significant hearing impairments due to inability to hear the neologisms through headphones.
- Patients who did not want to take part or were unable to attend for the follow-up appointment for the final measurement point at Castle Hill Hospital Endoscopy Department within one-week post procedure.
- Patients currently taking benzodiazepine medication for anxiety.

Out of the 151 consecutive patients that were asked to take part, 43 signed a consent form and 108 refused to participate. Those that consented were then randomly allocated to one of three groups using random number tables. The three groups differed in that a different neologism was presented to each one during the colonoscopy procedure. Only 28 completed all stages of the study and therefore were included in the data analysis.

Measures

- Skin Conductance Response (SCR)

Skin conductance was measured using aqueous gel filled electrodes applied to the abraded and cleaned medial phalanges of the index and forefinger on the right hand of the participant. The electrodes were then connected to the apparatus, which measured, processed and analysed the electrical conduction between the two fingers as a measure of psychophysiological response. The reason that SCR was chosen as a measure of autonomic arousal as a function of emotional reactions as opposed to other response paradigms (e.g. heart rate and blood pressure) was that most people produce skin conductance responses. Therefore, it was logically the most sensitive measure to detect any evidence of emotional reaction that the participant may be only partially aware of, if at all. The difference between the mean baseline skin conductance level and the mean skin conductance response amplitude will be used as the value for analysis assuming no correlation between the two variables (see *Statistical Analysis* section for details).

- Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith,1983)

(See Appendix I)

This fourteen-item scale was developed to provide a brief state measure of anxiety and depression in a medical out patient clinic. Although the HADS does not allow one to make definite diagnoses, it can be used to detect the presence of these clinical syndromes and to give an indication of their severity. Furthermore, the scale is not contaminated by reports of physical symptomatology.

The scale consists of seven items to measure anxiety and seven items to measure depression. Each item is scored from zero to three and thus the total range of scores is from zero to twenty-one for both depression and anxiety respectively. The higher the score obtained, the more severe the anxiety or depression. The scale is self-administered and takes between five and ten minutes to complete and approximately one minute to score, making it a popular choice with both participants and researchers. In terms of its psychometric status, Moorey, Greer, Watson, Gorman, Rowden, Tunmore, Robertson & Bliss (1991) assessed its internal consistency and found that Cronbach's Alpha was 0.93 for anxiety and 0.90 for depression. It has good face validity and has been found to have good concurrent validity (Zigmond & Snaith, 1983). Furthermore, Moorey et al (1991) confirms that the HADS has good construct validity as a scale measuring two separate factors. Discriminant validity between the two factors has since been questioned due to the high correlations between the two subscales found in most patient groups. However, a review by Herrman (1997) argued that this is more likely to be due to a genuine coincidence of anxious and depressed symptoms in patient groups than caused solely by inadequacies in the scale itself.

As stated earlier the HADS is not designed to generate definitive diagnoses of clinical anxiety or depression as it gives a dimensional rather than categorical representation of mood. Although there is no single, generally accepted cut off score for the HADS, Zigmond & Snaith's (1983) original study recommended cut off scores of 7-8 for "possible" anxiety or depression and 10-11 for "probable" anxiety or depression. However, later experience with the HADS has established that it may be used as a measure of severity of the two mood states. The four ranges can be classified 'normal' (0-7), 'mild' (8-10), 'moderate' (11-14) and 'severe' (15-21) (Zigmond & Snaith, 1983).

- Eysenck Personality Inventory (EPI) (Eysenck & Eysenck, 1964)

(*See Appendix II*)

The EPI measures personality along two orthogonal dimensions: extraversion / introversion and neuroticism / emotional stability, with participants' scores generating personality types. The inventory also includes a lie scale in order to monitor participants' tendencies to produce socially desirable but potentially misleading answers.

With regard to its psychometric status, the EPI has been found to have good test re-test reliability. Form B has generated a reliability coefficient of 0.83 for the extroversion scale and 0.86 for the neuroticism scale when testing nine months apart. The inventory also has good internal consistency. Although figures are not available for Form B, split half reliability coefficients for the EPI as a whole have been calculated (see *Table 2*).

Table 2 - Split Half Reliability Coefficients for the EPI

	Normals	Neurotics	Psychotics
Ea vs Eb	0.757	0.750	0.741
Na vs Nb	0.811	0.873	0.906

With regard to validity, personality scales are notoriously difficult, as the notion of "agreement with a criterion" clearly does not apply here. However, S. B. G. Eysenck (1962) and Eysenck & Eysenck (1963) have demonstrated that the scales correlate well with independent judges' assessments of participants' introversion and extroversion.

As personality is assumed to be fairly stable over time, the participants only completed the EPI once. The inventory was included in the current study as the participants' basic personality could influence how likely they are to condition to emotionally challenging experiences and therefore the EPI scores could be a potential covariate.

- Behavioural Distress Scale

(*See Appendix III*)

The study investigated whether participants would classically condition a very unpleasant and often painful experience (unconditioned stimulus) with highly associable neologisms (conditioned stimulus). Therefore, it was essential that some objective measure of how distressing the experience was found to be by the participant should be included when interpreting the results. The degree to which someone manifests their distress behaviourally will depend on sensitivity to the disinhibiting effect of sedation

and personality. The Behavioural Distress Scale was first conceptualised by Bohin (1999) for gastroscopy patients and further modified by Woodruff (in preparation) specifically for colonoscopy patients. Despite having not been standardised and its validity and reliability has not been examined, in the absence of a more suitable measure it was thought an appropriate choice and has been found useful to both previous researchers.

The scale used to monitor behavioural distress during each minute of the ten minutes the tape was played. Instantaneous heart rate was also recorded at one minute intervals. A behavioural stress composite score was obtained by converting the behavioural ratings into standard z-scores and these were combined with the range of heart rate scores (which was also converted to a z-score for each participant). These two factors contribute equally to the behavioural distress composite score.

- Pre-Colonoscopy Questionnaire

(*See Appendix IV*)

This questionnaire was designed by the researcher to screen participants for the major exclusion criteria that were not obvious from medical notes such as hearing impairments. It also provided basic demographic data like sex and age, as well as information on current medication and health status, previous history of colonoscopy and participants' perceptions of why they were having a colonoscopy on this occasion. The questionnaire also asked for a subjective rating of state anxiety on a ten point Likert Scale.

- Post-Colonoscopy Questionnaire

(See Appendix V)

This questionnaire was designed by the researcher to obtain a qualitative indication of the participants' explicit memory of the procedure (if any) and the neologism that had been presented during the colonoscopy, by free recall. It attempted to identify the last memory before any amnesic period and the first clear memory after any amnesic period. It also asked participants for a subjective rating of pain during the procedure and state anxiety, both on a ten point Likert Scale. The latter could be compared to the pre-colonoscopy rating. The reason this was completed on the follow-up appointment up to a week after the colonoscopy as well as immediately after the procedure was to see if the presence or absence of midazolam had any impact on this questionnaire.

Apparatus

- Skin Conductance Response (SCR) Monitor

The skin response was measured using apparatus for psychophysiology research from Contact Precision Instruments (Psylab interface) via a unit known as the SC4 Skin Conductance Amplifier. This unit is a self-balancing electrodermal activity coupler (*see Appendix VI for details of the module specifications*). Beckman silver-silver chloride disk electrodes attached to the medial phalanges of the first and second fingers of the right hand recorded skin conductance and sent this information to the SC4 unit. The

electrodes were attached to the fingers using adhesive rings, which exposed 1 cm^2 of skin to the conducting medium contained in the electrode cups. The electrolyte used was K-Y medical lubricating jelly as recommended by Lader (1975). The output was fed into a Compaq 386SX computer and processed with the Psylab set of programmes. A programme was written to analyse the skin conductance record in relation to the ten-second interval that followed the neologisms presented on the tapes being played at the same time as recording. The purpose of this was to detect any significant changes in response to each word.

- Tapes

Stage One and Four Tapes

For the pre and post colonoscopy SCR measurements the participants were played a tape with four neologisms. Two of them were designed to be readily associated with the experience of the non-surgical procedure than by chance alone, thus being more readily emotionally learnt: *pote* being like poke and *scrate* being like scrape. These words had been proposed on and initial study design, but were substituted with neologisms as a result of concern expressed by the Local Research Ethics Committee. The other two were designed to be neutral neologisms not readily associated to anything negative, positive or to the colonoscopy: *moof* and *brust*. All the tapes began with the word brust (in order to orientate the participant to the word stimuli) and then at ten second intervals the three remaining words were presented twice. The six alternative combinations were used with participants in balanced order as illustrated in *Table 3* overleaf.

Table 3 – Tape Combinations for Stage One and Four

	Participant 1	Participant 2	Participant 3	Participant 4	Participant 5	Participant 6*
1st word	Brust	Brust	Brust	Brust	Brust	Brust
2nd word	Pote	Scrate	Pote	Moof	Moof	Scrate
3rd word	Scrate	Pote	Moof	Scrate	Pote	Moof
4th word	Moof	Moof	Scrate	Pote	Scrate	Pote
5th word	Pote	Scrate	Pote	Moof	Moof	Scrate
6th word	Scrate	Pote	Moof	Scrate	Pote	Moof
7th word	Moof	Moof	Scrate	Pote	Scrate	Pote

* Combinations were repeated for subsequent participants.

Stage Two Tapes

During the colonoscopy the participants were played a tape with one neologism: pote, moof or scrate, once every ten seconds for ten minutes. Each of the three tapes were coded A, B or C respectively. The word that was on these three tapes was unknown to both researcher and participant until all data were collected and ready for analysis.

- Endoscopy Department Consulting Room

The endoscopy department was a surgical ward in a NHS hospital. It comprised a reception area, four consulting rooms, four theatres, a recovery ward and various offices and endoscope preparation rooms. The four consulting rooms were basically the same: they had one door and no windows, lockable cupboard of some description containing

basic medical supplies and information leaflets, at least two chairs, and some work surface (e.g. a table or a reachable cupboard top).

- Endoscopy Department Theatres

The four theatres were also basically the same containing: a controlled drugs cabinet, a fridge, a stretcher, an endoscopy unit (comprising an endoscope, a waste collection unit, a printer and two video screens), a pulse oximeter (comprising a finger clip and LCD unit), an oxygen unit with nasal tube, a computer for the surgeon to input data from the patient and procedure, and numerous stools for staff. There were no windows but all had well used air conditioning units. There was one entrance for patients and one other door that led to the endoscopy preparation rooms.

- Endoscopy Department Recovery Room

The recovery ward was comprised of ten cubicles divided by curtains. In each cubicle there was space for a stretcher (the patient was pushed out of the theatres on their own stretcher and remained on it until they recovered) and on the back wall were various medical units such as oxygen tubes. Also present in the recovery ward was one movable unit to measure blood pressure, heart rate and blood oxygen saturation. There was also a small waiting area with several high backed armchairs, where the nurses could make hot and cold drinks for the recovering patients.

Procedure

Ethical approval was obtained from the Hull and East Riding Local Research Ethics Committee for this study before data collection began.

There were four stages to the research procedure, which began with the arrival of a patient for a colonoscopy procedure on Monday morning and afternoon and Wednesday afternoon outpatient appointments. The patient had already taken the prescribed purgative preparation and had not eaten for at least four hours before their arrival. Once in the endoscopy department they confirmed their arrival with the secretary and took a seat in the waiting room. When the nursing staff were ready to prepare the patient for the procedure they called them from the waiting room. The "prep" nurse then took the patient to one of four consulting rooms, where they explained what would happen in the procedure, obtained a brief medical history and current health status, asked the patient to get undressed from the waist down and to put on a surgical gown with the opening at the back, took a baseline measure of blood pressure and heart rate, and inserted a cannula in the back of their right hand if possible. This final stage sometimes proved problematic in which case the needle was placed elsewhere in the arm by a surgeon or other nurse.

After the patient had been prepared the surgeon performing the colonoscopy answered any queries the patient may have had and obtained consent for the procedure. At this point, if the patient was eligible to partake in the research, the surgeon briefly explained that a trainee clinical psychologist was undertaking some research in the department. The research was investigating the effects of the medication that they would be given during the colonoscopy (which had already been explained to them by the "prep" nurse)

on memory. They also explain that taking part would involve answering a few questions about their health and how they felt about the procedure, listening to some words through headphones before and during the colonoscopy and coming back to the department within the next week to listen to some more words and complete some questionnaires. The patients were then asked if they might be willing to take part in the research and be introduced to the researcher who would explain the research in more depth before they made any agreement to participate. If the patient was willing the surgeon introduced the researcher and they entered stage one of the study procedure as described below.

In general, consecutive eligible patients were approached to take part in the research unless the researcher was already in theatre with another participant at the time the surgeon obtained consent from the patient. If the researcher was still in stage one, two or three with any previous participant the next eligible patient when the researcher became available was approached to partake in the project.

- Stage One

After being introduced to the researcher the patients were provided with the Participants Information Sheet (*see Appendix VII*) and once they had been offered a chance to ask any questions the researcher asked them to read and sign a Consent Form (*see Appendix VIII*), which was then countersigned by the researcher and the surgeon. Having agreed to take part the surgeon left the consulting room, and the door closed to reduce any sound that may disturb the participant during the skin conductance measurement. The researcher assigned an individual code that indicated the number of the participant and the tapes they would be played. The researcher then asked the participant the questions

on the Pre-Colonoscopy Questionnaire (*see Appendix IV*). The researcher recorded the answers given verbatim in the spaces provided on the questionnaire sheet.

The participant was then asked to present their upturned right hand and it was explained that the middle section of the forefinger and index finger would be abraded using regular emery board and wiped with an alcohol wipe to improve the electrode conduction for the SCR machine to detect their skin conductance or finger sweating. Once this was done the researcher attached the two prepared electrodes (see *Measures* section above for full explanation) to the two abraded areas and connected these to the SCR monitor, which was turned slightly out of the participants sight. The researcher then explained that she would place the headphones on the participant's head through which he/she would hear some nonsense words. As mentioned in the *Apparatus* section, there were six tapes, identified by a number from one to six, which could be played for the baseline measurements in order to vary the six possible order combinations of the neologisms. The tape was selected on a sequential basis, i.e. the first participant listened to tape one, the fifth participant listened to tape five, the twelfth participant listened to tape six etc. The researcher and the participant were unaware of the order of the neologisms. The participant was told that he/she must simply listen to the tape, which would last only eighty seconds. The SCR recording programme was initiated to record skin conductance at the exact same time as the tape was started and has stopped eighty seconds later when the tape's material had finished. Once this was done the electrodes and headphones were removed and the participant was provided with a tissue to wipe the aqueous gel from the electrodes from their fingers.

The researcher reminded the participant that they would have some headphones placed on their ears in the theatre before the colonoscopy began and a tape would be played,

the contents of which they were to try to remember. The researcher explained that she would remain in the theatre, monitor the participant's heart rate and observe them until the tape finished. The participants were also reminded that the researcher would come and ask the participant some quick questions about the colonoscopy and what they remembered when they had recovered and were ready to leave, at which point a follow-up appointment would be arranged.

- Stage Two

After stage one was completed the researcher informed the "prep" nurse caring for the patient that they were ready for the procedure and the nurse then led them into one of four theatres. Once in the room the patient was asked by the nurse to lie on the stretcher on their left hand side with their knees bent up. The nurse then placed a sheet over them, placed a clip on one finger to measure blood oxygen saturation and pulse, and an oxygen tube placed under the nose to provide a steady flow of oxygen whilst under sedation. At this point the researcher placed the headphones of the personal stereo on the patient and positioned herself so she could see the patients face and the pulse oximeter (the machine that reads the data from the finger clip) clearly. The surgeon then prepared the medication (midazolam – a sedating anxiolytic and fentanyl – an opioid analgesic) and some saline rinse and injected the desired amount into the patient's cannula, which the researcher noted down (dose and time). The surgeon then raised the stretcher to the appropriate height; smoothed aqueous gel onto the fibre optic camera tube and the patient's anus and informed them that they were about to begin the procedure. Once the camera was placed into the anus (usually between one to two minutes after the medication had been administered) the researcher began the tape and pressed 'start' on a stopwatch.

As described in the *Apparatus* section there were three different tapes that could be played during stage two and each one had a different neologism on it which was presented once every ten seconds for ten minutes. The participant was assigned a tape by the use of a random number table. The tapes were coded A, B and C and the researcher and participant were unaware of which neologism they would be played. Once the tape was begun the researcher monitored the behavioural distress of the patient during each of the ten, one-minute intervals and recorded the data on the Behavioural Distress Scale (*see Appendix III*) along with heart rate on the minute for the ten minutes of the tape. Had the surgeon provided the patient with any further medication, asked them to role onto their front or back, or taken biopsies or removed polyps the researcher recorded all this. After ten minutes the tape was stopped and when the procedure was completed the headphones were removed and the nurse wheeled the patient into recovery on their stretcher trolley. The researcher attached the Post-Colonoscopy Questionnaire (*see Appendix V*) to the patient's clipboard that the nurses used to record the details of the procedure, the medication used and the patient's recovery. This indicated to nurses in the recovery ward that the patient was involved in the research project and was not to be discharged before the researcher had seen them.

- Stage Three

The patient was then left usually between half an hour to an hour to recover from the procedure and come round from the sedation. Once they had recovered the patient was then asked to sit in a small waiting area where they could have a drink and some biscuits and a nurse could remove the cannula. At this point the researcher had the opportunity to ask the questions on the Post-Colonoscopy Questionnaire (*see Appendix V*) and wrote down their responses verbatim in the spaces provided on the sheet. This

questionnaire (as mentioned in the *Measures* section above) included, among other things, questions checking for any explicit memory of the procedure.

The researcher then arranged an appointment for the patient to come back to the endoscopy department to complete stage four of the study and their phone number was recorded should the patient need to be contacted. A nurse then saw the patient to discuss what had been done in the procedure, what they had found (obviously results from biopsies and polyp removals cannot be provided at this point), and to arrange an outpatient appointment to meet the surgeon. The patient was then discharged to go home with someone who would supervise them for the following twenty-four hours until the sedation had been metabolised.

- Stage Four

This was the follow-up stage of the project and occurred up to one-week later. The participant was called from the endoscopy department waiting room and taken by the researcher to one of the four consulting rooms. The door was again shut to reduce any sounds that could have disturbed the participants during skin conductance monitoring. They were then reminded that this stage of the research was the final one and would involve answering a few short questions about what they remembered about the procedure and how they felt about it; that they would be linked up to the SCR monitor and would hear another tape with nonsense words on it, and lastly would complete a couple of questionnaires.

The participant was then asked the same questions from the Post-Colonoscopy Questionnaire (*see Appendix V*) and their responses were recorded verbatim. The

patient was then connected to the SCR monitor and was played the same tape in exactly the same way as in stage one. The participant was then asked to complete two standardised questionnaires: the Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1983) (*see Appendix I*) and the Eysenck Personality Inventory (Eysenck & Eysenck, 1964) (*see Appendix II*). Before the patient left they were asked if they had any questions and comments about the research, the latter of which, was noted by the researcher. The participant was then thanked again for their participation.

Statistical Analysis

The data were cleaned of all those who failed to complete all stages of the research. The raw data were then transferred, by the researcher, into the Statistical Package for the Social Sciences (SPSS) for Windows, version 10.0.

Initially, the mean baseline skin conductance level was analysed for a correlation with the mean skin conductance response amplitude. This was required due to the Law of Initial Values, which states that the true response of a variable to a stimulus decreases as the true pre-stimulus level increase i.e., change has a negative correlation with initial level (Wilder, 1950). The general notion is that there is some optimal level for a variable (i.e. skin conductance). Therefore, if the pre-stimulus level is above the optimal level, the absolute size of response is limited by a ceiling effect. If this law holds then the effects of the correlation can be partialled out of the analyses by regarding the baseline level as a covariate. As no correlation was found ($r = 0.007$; p

(two-tailed Pearson Correlation) = 0.88) the researcher next calculated the descriptive statistics for all independent variables, dependent variables and potential covariates.

Lastly, inferential statistics were employed to test the five hypotheses delineated at the end of the *Introduction* section. Hypotheses 1 and 2 were tested using a Repeated Measures Analysis of Variance (ANOVA) (Group X Neologism Presented). Within-subject effects were used to test hypothesis$_1$ and within-subjects quadratic contrasts were used to test hypothesis$_2$. Hypotheses 3-5 were tested using Repeated Measures Analysis of Covariance (ANCOVA).

RESULTS

Sample Characteristics

- Gender

Figure 5 – Gender Distribution

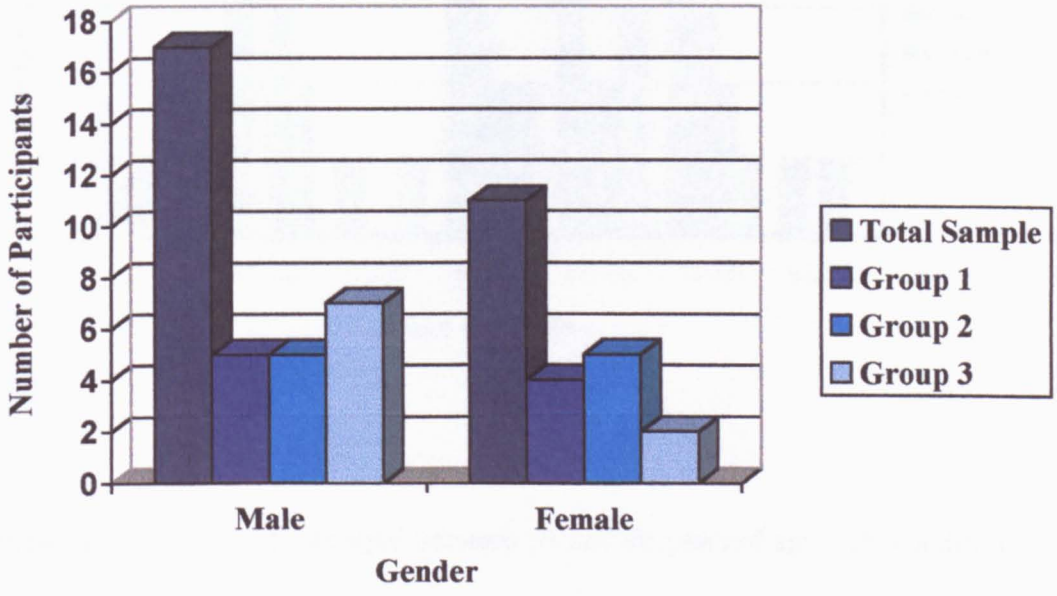
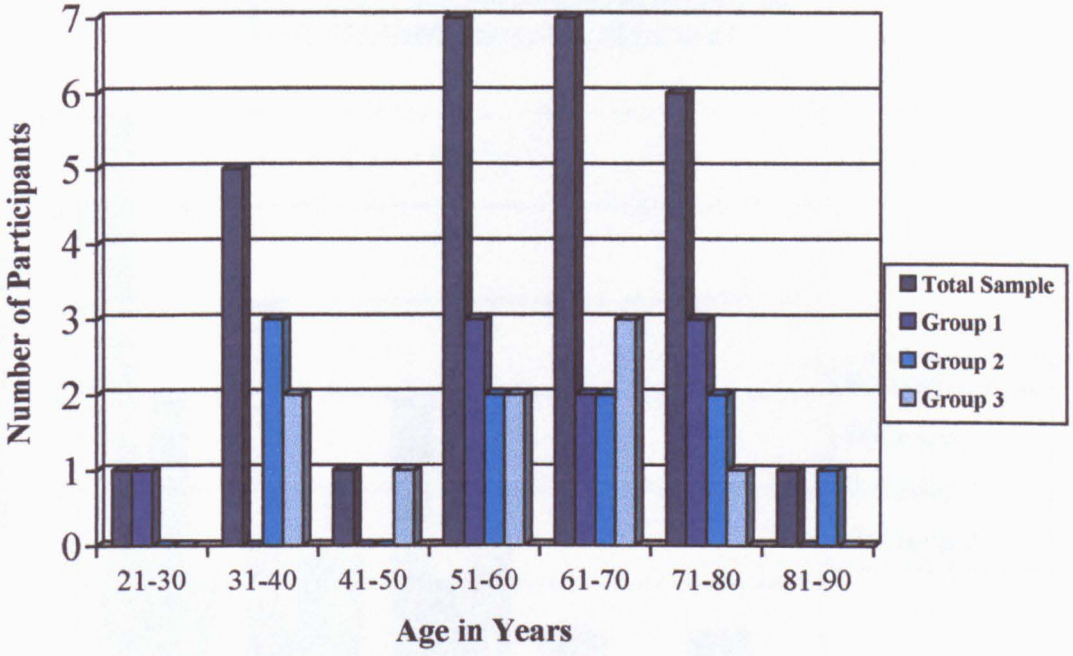


Figure 5 illustrates that overall, there was an even spread of males and females except in Group 3 who had just over three times the number of males compared to the number of females. Although this group has a fairly skewed distribution, it is fairly representative of the actual distribution of the sexes having colonoscopies.

- Age

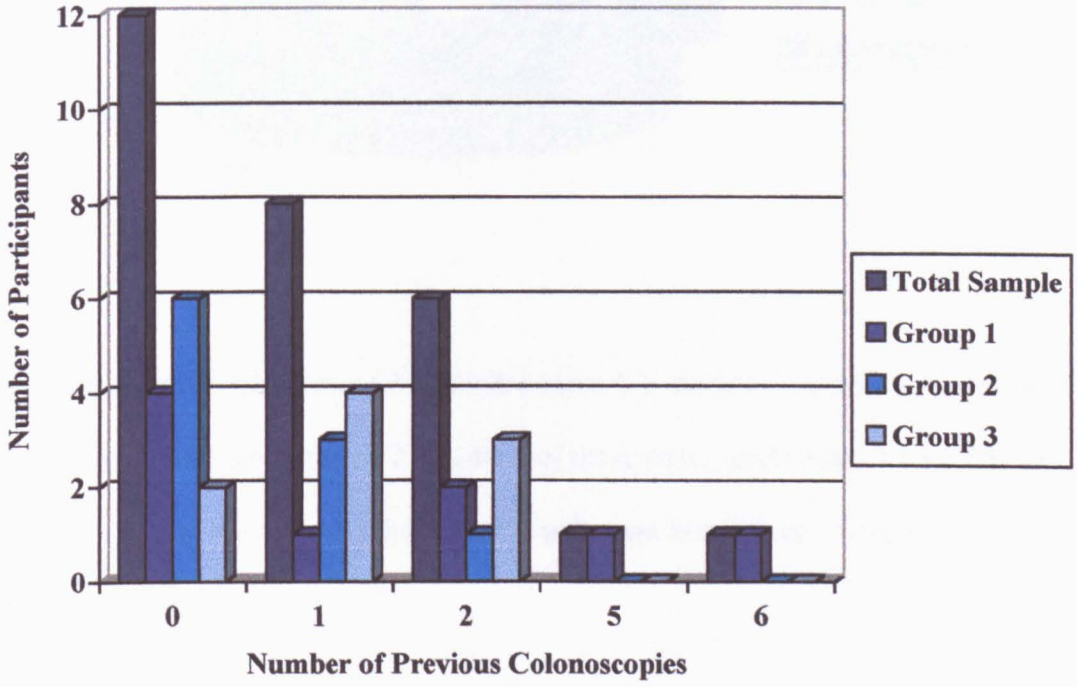
Figure 6 – Age Distribution



The majority of the sample was aged between 51 and 80 years of age. This distribution again seems skewed but is very much representative of the actual population of people having colonoscopies. The few younger people sampled aged 21 to 40 years of age were generally being seen due a family history of colon cancers having had their first experiences of bleeding or sudden and noticeable changes in bowel movements. The older aged participants were predominantly being seen for polypectomies or investigative yearly follow-ups to check for re-growths of both benign and malignant tumours. The three groups were fairly evenly matched.

- Previous Experience of Colonoscopy

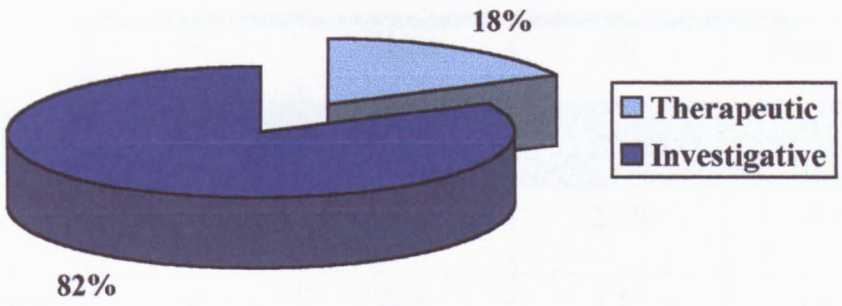
Figure 7 – Distribution of Participants with Previous Experience of Colonoscopy



Just less than half of all the participants had never experienced a colonoscopy procedure before. Group 3 had slightly more people who had had a colonoscopy before compared to Group 1 and Group 2. The effect of previous experience is unknown and was not a factor directly investigated by this study.

- **Type of Colonoscopy**

Figure 8 – Distribution of Participants Having Therapeutic or Investigative Colonoscopy



With regard to the distribution of therapeutic cases (i.e. polyps removed) between the 3 groups: Group 1 had none; Group 2 had 40% of these cases; and Group 3 had 60% of these cases. Again, the effect of this factor is unknown and was not directly investigated in this study.

- Midazolam and Fentanyl Dosages

Table 4 – Mean Doses of Midazolam and Fentanyl (2dp)

	Total Sample	Group 1	Group 2	Group 3
Midazolam (milligrams)	4.04	3.89	3.9	4.32
Fentanyl (micrograms)	91.07	94.44	82.5	97.22

The three groups are evenly matched in respect to the midazolam dosages. They would also be evenly matched in respect to the fentanyl dosages had it not been for one participant in Group 2 having had no pain relief.

Dependent Variable Analysis

- Descriptive Statistics

Table 5 – Descriptive Statistics for Group 1

		N	Mean	SD	Skewness
SCR difference score	**Pote**	9	0.27	0.95	2.96
	Moof	9	-1.12	2.38	-1.52
	Scrate	9	-0.50	3.13	-0.35

Key: • Highlighted text refers to the neologism that this group was presented with during the colonoscopy.

Group 1 showed an increase in SCR scores from pre- to post-colonoscopy only to the word they were presented during the procedure. This follows the pattern predicted by Experimental Hypothesis$_1$ and is the only group to have experienced this effect.

Table 6 – Descriptive Statistics for Group 2

		N	Mean	SD	Skewness
SCR difference score	**Pote**	10	1.44	2.12	0.39
	Moof	10	1.14	2.78	-0.11
	Scrate	10	1.66	1.38	1.85

Key: • Highlighted text refers to the neologism that this group was presented with during the colonoscopy.

Group 2 (as illustrated in *Table 6* on the previous page) showed the largest increase in SCR, from pre- to post-colonoscopy, to the neologisms deemed emotive and less so to the neologism deemed neutral that they were actually presented during the procedure.

Table 7 – Descriptive Statistics for Group 3

		N	Mean	SD	Skewness
SCR difference score	**Pote**	9	-1.28	2.33	-0.23
	Moof	9	-1.18	2.87	-0.21
	Scrate	9	-1.23	3.57	-1.32

Key: • Highlighted text refers to the neologism that this group was presented with during the colonoscopy.

This group showed no increase in SCR from pre- to post-procedure on any of the three neologisms.

NB: - A constant of 10 was added to all the SCR change scores converting them to positive scores which enabled the standard deviation value to be calculated.

For a full Descriptive Statistics (including total sample statistics) SPSS output see *Appendix X.*

- Inferential Statistical Analysis of the Hypotheses 1 & 2

Null Hypothesis$_1$

- Participants will have no implicit memory for neologisms presented during colonoscopy, as detected by skin conductance response, following intravenous administration of midazolam.

Experimental Hypothesis$_1$

- Participants will have implicit memory for neologisms presented during colonoscopy, as detected by skin conductance response, following intravenous administration of midazolam.

Figure 9 – Profile Plot A - Illustrating the Relationship Between the Neologism Presented and the Group Membership According to the SCR Difference Scores

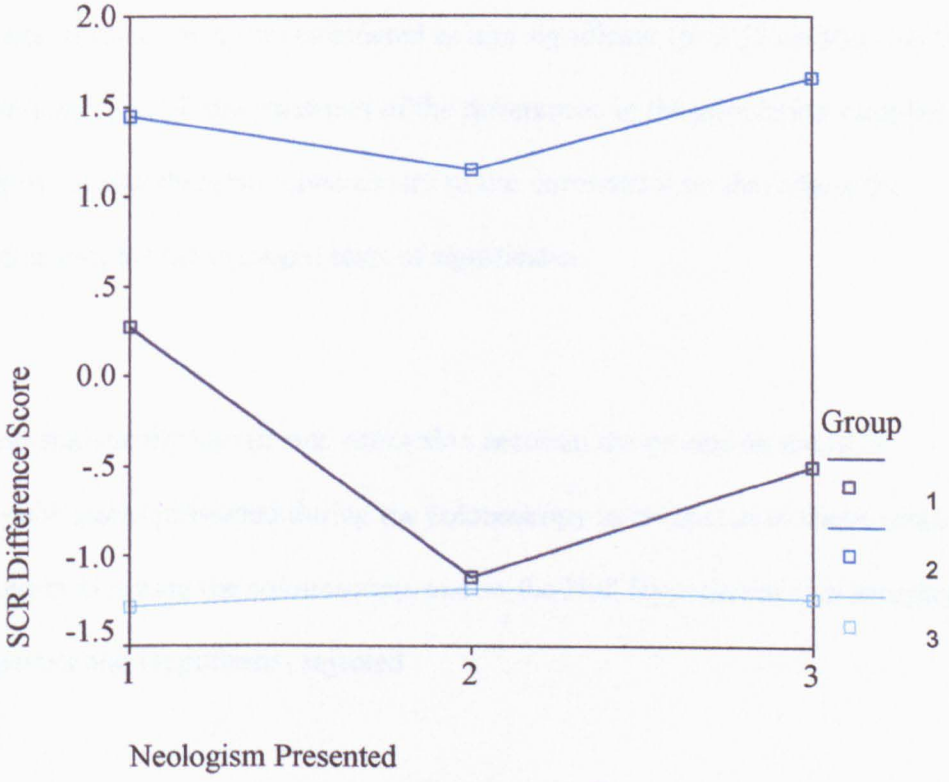


Figure 9 (on the previous page) shows that there may be some interaction effects between the changes in SCR from pre- to post-colonoscopy in relation to the all three neologisms according to the group participants were in (i.e. the word they were presented during the procedure) as the lines do not run parallel to each other.

Table 8 – Repeated Measures ANOVA (within-subjects effects)

Source	Degrees of Freedom	Mean Sum of Squares	F Value	P value
Neologism presented	2	2.06	0.42	0.66
Neologism presented x Group	4	1.53	0.31	0.87
Error (neologism)	50	4.90	~~~~~~~~~~	~~~~~~~~~~

Key: ~~~~~ denotes incalculable statistics.

Sphericity was assumed as it was calculated as non significant (p=0.58 on Mauchly's Test of Sphericity) i.e., all the variances of the differences in the population sampled are assumed equal. It was therefore unnecessary to use corrected tests that adjust the degrees of freedom for the averaged tests of significance.

There was no statistically significant interaction between the groups on the SCR reaction to neologisms presented during the colonoscopy as compared to those which were not presented during the colonoscopy, and so the Null Hypothesis$_1$ was accepted and the Experimental Hypothesis$_1$ rejected.

Null Hypothesis$_2$

- There will be no significant difference in skin conductance response change from pre- to post-colonoscopy between intra-operatively presented neologisms designed to provoke an emotional association and 'neutral' neologisms.

Experimental Hypothesis$_2$

- There will be a significant difference in skin conductance response change from pre- to post-colonoscopy between intra-operatively presented neologisms designed to provoke an emotional association and 'neutral' neologisms.

Table 9 – Repeated Measures ANOVA (within-subjects contrasts)

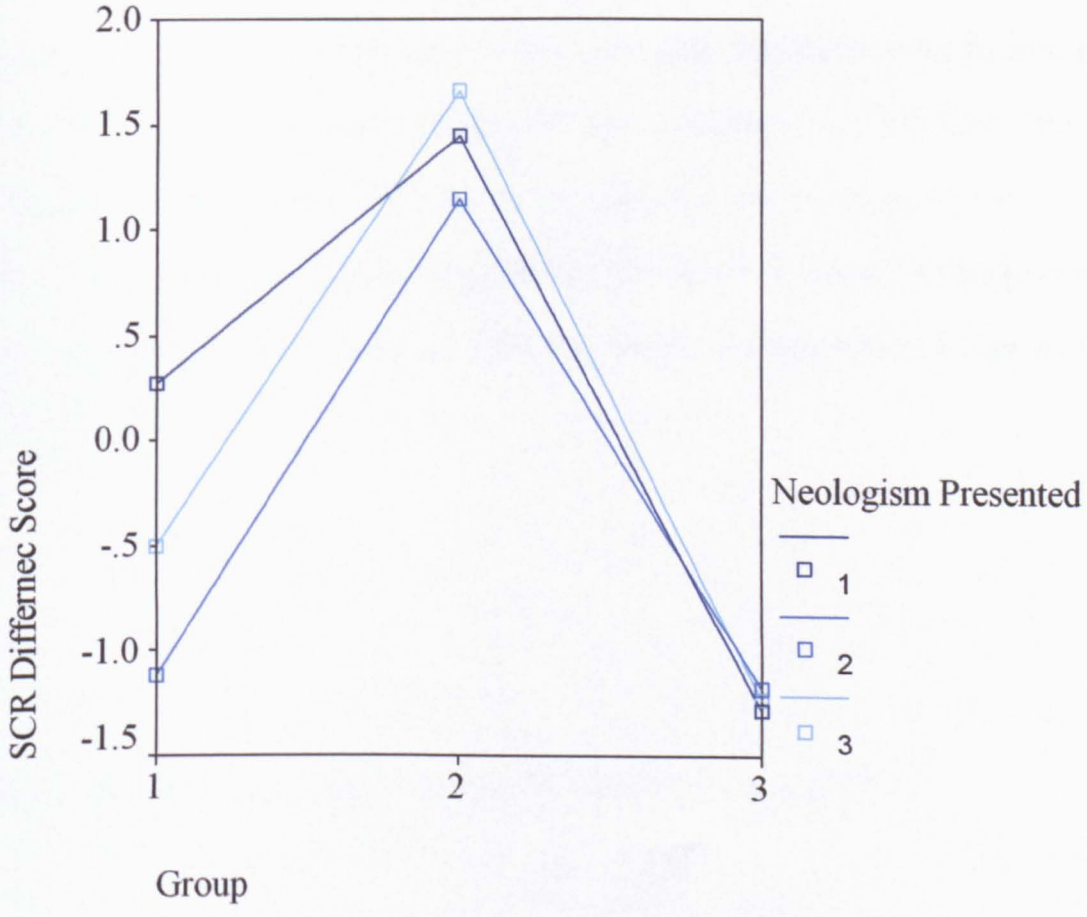
Source	Degrees of Freedom	Mean Sum of Squares	F Value	P value
Neologism presented	1	3.72	0.94	0.34
Neologism presented x Group	2	1.75	0.44	0.65
Error (neologism)	25	3.98	~~~~~	~~~~~

Key: ~~~~~ denotes incalculable statistics.

A quadratic contrast has been cited as this compares the mean of the averages of the SCR difference scores for pote and scrate (the emotive neologisms) with the mean of the SCR difference score for moof. A linear contrast in this programme would only compare the mean SCR difference scores between pote and scrate and is therefore not useful in answering hypothesis$_2$.

There is no statistically significant difference between the SCR responses from pre- to post-colonoscopy when comparing the 'emotive' (i.e. pote and scrate) and 'neutral' (i.e. moof) neologisms presented during the procedure. Therefore, the Null Hypothesis$_2$ was accepted and the Experimental Hypothesis$_2$ was rejected.

Figure 10 – Profile Plot B - Illustrating the Relationship Between the Neologism Presented and the Group Membership According to the SCR Difference Scores



As can be seen more clearly in *Figure 10* (on the previous page) (as opposed to *Figure 9*) there is a fairly noticeable difference between the groups when looking at variability of the SCR responses to each of the three neologisms and the mean SCR difference scores for all three neologisms combined.

Table 10 – Repeated Measures ANOVA (between-subjects effects)

Source	Degrees of Freedom	Mean Sum of Squares	F Value	P value
Intercept	1	0.66	0.07	0.79
Group	2	53.15	5.92	0.008**
Error	25	8.98	~~~~~	~~~~~

Key: ~~~~~ denotes incalculable statistics.
** denotes statistical significance at the 1% level

This difference between the groups is in fact statistically significant (as can be seen in *Table 10* above) and although this result does not prove interesting in the light of the hypotheses, it does warrant further inspection of the raw data (*see Appendix IX*). However, eyeballing the raw data suggests that this difference is purely coincidence or that there are other factors acting such that they may be unevenly dispersed between the three groups.

For a full Repeated Measures ANOVA SPSS output see *Appendix XI*.

Potential Covariates Analysis

- Descriptive Statistics

Table 11 – Descriptive Statistics for Group 1

	N	Mean	SD	Skewness
EPI - Extroversion	9	15.11	4.37	-0.26
EPI – Neuroticism	9	12.00	5.79	-0.63
EPI – Lie Scale	9	2.22	2.33	0.57
HADS – Anxiety	9	6.44	3.91	0.70
HADS – Depression	9	3.89	3.26	0.18
BDS	9	0.30	1.28	0.10
Anxiety rating before procedure	9	4.00	1.32	-0.83
Anxiety rating after procedure	9	1.89	1.62	2.51
Anxiety rating at 1-week follow-up	9	2.11	1.27	1.63
Pain rating after procedure	7	2.43	2.70	1.71
Pain rating at 1-week follow-up	5	2.00	2.74	0.61

Group 1 had the highest Behavioural Distress Scale score. The group averaged within the normal range on both the anxiety and depression subscales of the HADS. Extroversion and neuroticism average scores are fairly similar across all three groups.

Table 12 – Descriptive Statistics for Group 2

	N	Mean	SD	Skewness
EPI - Extroversion	10	14.30	3.59	-0.23
EPI – Neuroticism	10	12.40	4.22	0.53
EPI – Lie Scale	10	3.10	2.13	0.27
HADS – Anxiety	10	5.90	3.78	0.79
HADS – Depression	10	3.70	3.40	0.79
BDS	10	0.01	1.49	0.71
Anxiety rating before procedure	10	4.90	3.07	-0.40
Anxiety rating after procedure	10	1.50	0.92	2.27
Anxiety rating at 1-week follow-up	10	1.60	0.84	1.00
Pain rating after procedure	10	2.20	2.25	0.86
Pain rating at 1-week follow-up	8	2.13	2.30	0.65

Group 2 showed the lowest Behavioural Distress Scale score of the three groups. Again the group averaged within the normal range on both the anxiety and depression subscales of the HADS.

Table 13 – Descriptive Statistics for Group 3

	N	Mean	SD	Skewness
EPI – Extroversion	9	14.33	3.81	-0.26
EPI – Neuroticism	9	11.67	5.36	-0.07
EPI – Lie Scale	9	3.44	1.81	-0.21
HADS – Anxiety	9	8.56	4.88	0.44
HADS – Depression	9	4.78	3.63	1.72
BDS	9	0.12	1.13	0.21
Anxiety rating before procedure	9	3.67	2.18	-0.01
Anxiety rating after procedure	9	1.44	0.73	1.50
Anxiety rating at 1-week follow-up	9	1.22	0.44	1.62
Pain rating after procedure	9	2.78	2.59	0.98
Pain rating at 1-week follow-up	9	2.00	1.66	0.85

Group 3 were the only group who displayed an averaged anxiety score on the HADS above the normal range, falling instead into the 'mildly' anxious category.

For a full Descriptive Statistics (including total sample statistics) SPSS output see *Appendix X.*

- Inferential Statistical Analysis of the Hypotheses 3-5

Table 14 – Pearson Correlations of Potential Covariates with SCR Change from Pre to Post-Procedure

	N	Pearson Correlation (r)	Significance (p) - two-tailed
EPI – Extroversion	28	-0.010	0.958
EPI – Neuroticism	28	0.015	0.940
EPI – Lie Scale	28	-0.120	0.543
HADS – Anxiety	28	0.020	0.918
HADS – Depression	28	-0.150	0.447
BDS	28	0.047	0.811
Anxiety rating before procedure	28	-0.147	0.455
Anxiety rating after procedure	28	-0.037	0.851
Anxiety rating at 1-week follow-up	28	-0.005	0.978
Pain rating after procedure	26	-0.093	0.650
Pain rating at 1-week follow-up	22	0.059	0.795

The SCR change only for the neologisms presented during the colonoscopies, regardless of group, was correlated with all other variables collected to investigate the possibility of any relationships. However none were found to be significant. Also, when looking at the corresponding scatterplots there were no outliers detected.

NB: - Five separate ANCOVAs were conducted to answer hypotheses 3-5. The reason for this was due to the small number of participants. A single ANOVA interpreting all five pertinent variables, although calculable on SPSS, would be unreliable in respect to interpretation.

Null Hypothesis$_3$

- There will be no significant effect of mood on implicit memory formation for neologisms presented during colonoscopy, as detected by skin conductance response, following intravenous administration of midazolam.

Experimental Hypothesis$_3$

- There will be a significant effect of mood on implicit memory formation for neologisms presented during colonoscopy, as detected by skin conductance response, following intravenous administration of midazolam.

Table 15 – Repeated Measures ANCOVA with HADS Anxiety as a Covariate (within subjects effects)

Source	Degrees of Freedom	Mean Sum of Squares	F Value	P value
Neologism presented	2	0.60	0.12	0.89
Neologism presented x HADS anxiety	2	0.34	0.07	0.94
Neologism presented x Group	4	1.57	0.31	0.87
Error (neologism)	48	5.09	~~~~~	~~~~~

Key: ~~~~~ denotes incalculable statistics.

Anxiety, as measured by the HADS had no statistically significant effect on SCR change from pre- to post-colonoscopy in relation to the group (i.e. the word presented to participants intra-operatively) and the stimulus neologisms (i.e. all three words presented before and after the procedure).

Table 16 – Repeated Measures ANCOVA with HADS Depression as a Covariate (within subjects effects)

Source	Degrees of Freedom	Mean Sum of Squares	F Value	P value
Neologism presented	2	4.07	0.83	0.44
Neologism presented x HADS depression	2	4.87	0.94	0.38
Neologism presented x Group	4	1.51	0.31	0.87
Error (neologism)	48	4.90	~~~~~	~~~~~

Key: ~~~~~ denotes incalculable statistics.

Table 16 shows that depression, as measured by the HADS, had no statistically significant effect on SCR change from pre- to post-colonoscopy in relation to the group (i.e. the word presented to participants intra-operatively) and the stimulus neologisms (i.e. all three words presented before and after the procedure).

The ANCOVA pertaining to mood as measured by the HADS suggest that the Null Hypothesis$_3$ should be accepted and the Experimental Hypothesis$_3$ rejected.

Null Hypothesis$_4$

- There will be no significant effect of personality on implicit memory formation for neologisms presented during colonoscopy, as detected by skin conductance response, following intravenous administration of midazolam.

Experimental Hypothesis$_4$

- There will be a significant effect of personality on implicit memory formation for neologisms presented during colonoscopy, as detected by skin conductance response, following intravenous administration of midazolam.

Table 17 – Repeated Measures ANCOVA with EPI Extroversion as a Covariate (within subjects effects)

Source	Degrees of Freedom	Mean Sum of Squares	F Value	P value
Neologism presented	2	3.06	0.62	0.54
Neologism presented x EPI extroversion	2	2.97	0.60	0.55
Neologism presented x Group	4	1.44	0.29	0.88
Error (neologism)	48	4.98	~~~~~	~~~~~

Key: ~~~~~ denotes incalculable statistics.

Extroversion, as measured by the EPI had no statistically significant effect on SCR change from pre- to post-colonoscopy in relation to the group (i.e. the word presented to participants intra-operatively) and the stimulus neologisms (i.e. all three words presented before and after the procedure).

Table 18 – Repeated Measures ANCOVA with EPI Neuroticism as a Covariate (within subjects effects)

Source	Degrees of Freedom	Mean Sum of Squares	F Value	P value
Neologism presented	2	2.78	0.56	0.57
Neologism presented x EPI neuroticism	2	4.22	0.86	0.43
Neologism presented x Group	4	1.56	0.32	0.87
Error (neologism)	48	4.92	~~~~~	~~~~~

Key: ~~~~~ denotes incalculable statistics.

Table 18 shows that neuroticism, as measured by the EPI, had no statistically significant effect on SCR change from pre- to post-colonoscopy in relation to the group (i.e. the word presented to participants intra-operatively) and the stimulus neologisms (i.e. all three words presented before and after the procedure).

Table 19 – Repeated Measures ANCOVA with EPI Lie Scale as a Covariate (within subjects effects)

Source	Degrees of Freedom	Mean Sum of Squares	F Value	P value
Neologism presented	2	4.94	1.01	0.37
Neologism presented x EPI lie scale	2	4.99	1.02	0.37
Neologism presented x Group	4	1.66	0.34	0.85
Error (neologism)	48	4.89	~~~~~	~~~~~

Key: ~~~~~ denotes incalculable statistics.

Table 19 (on the previous page) illustrates that a tendency to 'fake good' or lie on a psychometric scale, as measured by the EPI, had no statistically significant effect on SCR change from pre- to post-colonoscopy in relation to the group (i.e. the word presented to participants intra-operatively) and the stimulus neologisms (i.e. all three words presented before and after the procedure).

The ANCOVA pertaining to personality as measured by the EPI suggest that the Null Hypothesis$_4$ should be accepted and the Experimental Hypothesis$_4$ rejected.

Null Hypothesis$_5$

- There will be no significant effect of objectively rated behavioural distress on implicit memory formation for neologisms presented during colonoscopy, as detected by skin conductance response, following intravenous administration of midazolam.

Experimental Hypothesis$_5$

- There will be a significant effect of objectively rated behavioural distress on implicit memory formation for neologisms presented during colonoscopy, as detected by skin conductance response, following intravenous administration of midazolam.

Table 20 – Repeated Measures ANCOVA with Behavioural Distress Scale as a Covariate (within subjects effects)

Source	Degrees of Freedom	Mean Sum of Squares	F Value	P value
Neologism presented	2	1.87	0.37	0.69
Neologism presented x BDS	2	2.35	0.47	0.63
Neologism presented x Group	4	1.58	0.32	0.87
Error (neologism)	48	5.00	~~~~~	~~~~~

Key: ~~~~ denotes incalculable statistics.

Table 20 shows that behavioural distress, as measured by the BDS, had no statistically significant effect on SCR change from pre- to post-colonoscopy in relation to the group (i.e. the word presented to participants intra-operatively) and the stimulus neologisms (i.e. all three words presented before and after the procedure).

The ANCOVA pertaining to objectively rated behavioural distress as measured by the BDS suggest that the Null Hypothesis$_5$ should be accepted and the Experimental Hypothesis$_5$ rejected.

For a full Repeated Measures ANCOVA SPSS output see *Appendix XII*

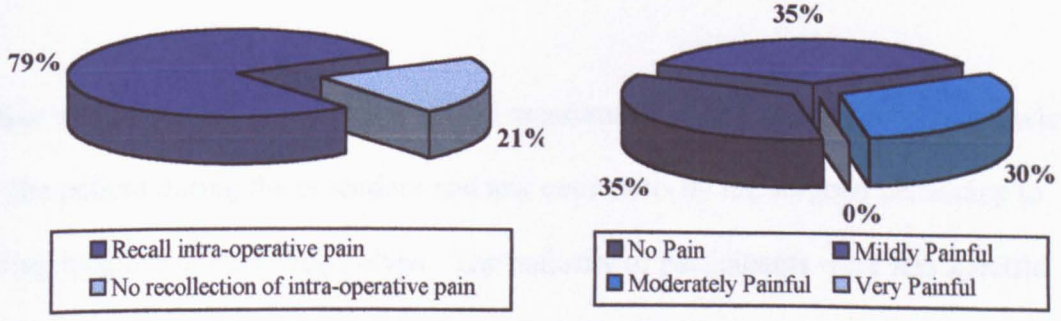
Qualitative Data - Explicit Memory of the Procedure

Six participants (21% of the total sample) recalled nothing at all, from the moment the midazolam was administered to waking up in recovery. The remaining 22 (79% of the total sample) had some explicit recall of intra-operative events, details of which are described below.

- Intra-Operative Explicit Memory of Pain

The main intra-operative explicit memory, and one which was directly measured by this study (on a ten point Likert scale – see Post-Colonoscopy Questionnaire – *Appendix V*), was the presence of pain, with over ¾ of the total sample recalling pain to some degree. Just over $^1/_3$ reported no pain, $^1/_3$ mild pain and $^1/_3$ moderate pain.

Figure 11 – Pain Ratings Following Colonoscopy



However, some participants who had had a colonoscopy before mentioned that they felt they had remembered more or less of their current procedure and they felt this may have

been because they were more aroused i.e. due to pain or anxiety, and therefore this penetrated the sedation.

- Recall of the Neologism Presented Intra-Operatively

Despite recalling pain, interestingly, none of the participants could remember the neologism they had been presented during the colonoscopy and some could not recall even listening to the tape at all, when asked about it in the Post Colonoscopy Questionnaire (*see Appendix V*). On several occasions when taking the headphones off the participants, having finished the tape but not the procedure, participants even commented that they did not think the personal stereo was working as they had not heard a thing. The personal stereo was checked before, during and after the procedure with every participant to ensure the tape was played correctly.

- Other Intra-Operative Explicit Memory

Other intra-operative memories included reassurance from the assessment nurse who sat by the patient during the procedure and any comments by the surgeon pertaining to taking biopsies or removing polyps. The majority of participants were less specific reporting the presence of people or the sounds of voices.

- First Continuous Memory Following Colonoscopy

Figure 12 – First Memory After Colonoscopy

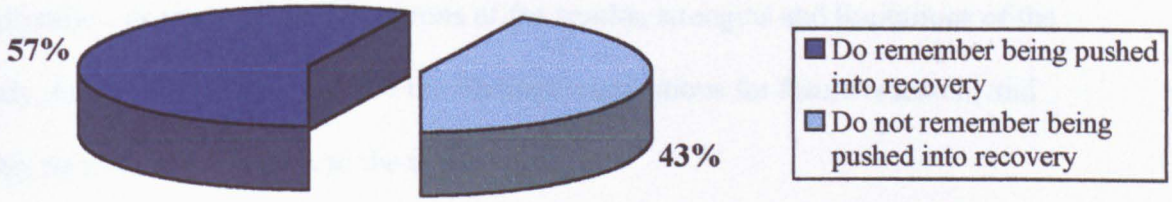


Figure 12 illustrates that over 50% of participants recall being wheeled into the recovery ward after their colonoscopy. The remaining participants' first continuous memory is of actually being in the recovery ward.

DISCUSSION

This study aimed to investigate whether implicit emotional memory could be demonstrated in patients undergoing a colonoscopy with benzodiazepine sedation. The discussion of the study's findings is divided into five sections: hypotheses testing and exploration of alternative explanations of the results; strengths and limitations of the study; the clinical implications of the findings; suggestions for future research; and lastly an overall conclusion to the thesis.

Hypothesis Testing

In respect to hypothesis testing the five accepted hypotheses will be taken in turn and discussed in relation to the literature delineated in the *Introduction* section and alternative explanations will be proffered where appropriate.

Accepted Null Hypothesis$_1$

- Participants will have no implicit memory for words presented during colonoscopy, as detected by skin conductance response, following intravenous administration of midazolam.

Only Group 1 responded in the way predicted by the corresponding experimental hypothesis to the accepted null hypothesis stated above, in that they showed a larger increase in skin conductance response (SCR) from pre- to post-procedure to the neologism they had been presented with during the colonoscopy compared to the other two neologisms. However, this difference was not statistically significant. This finding

may be taken to suggest that in the small sample it may be that all those most likely to form implicit emotional memories have all been allocated to one group simply by chance. However, as in each group there are those that both respond in the pattern one would predict by having the greatest change in SCR to the neologism presented during the colonoscopy compared to ones that were not, there are also participants in each group who show greatest change in SCR to one of the words they did not get presented during the colonoscopy and therefore cannot be ascribed to implicit memory formation, but purely chance.

This finding goes against Fang et al (1987) who found evidence for implicit memory as measured on priming tasks (i.e. word completion and category-generation) for words presented under a single oral administration of diazepam. Despite a difference in the benzodiazepine, dose and the route of administration which probably had a negligible effect (unless the to-be-remembered words were presented too early after the administration of the drug or if the dose was small enough not to cause the same level of impairments as those found in the current study) there were significant differences in the mean age of participants, the situations and conditions in which the study was conducted, and material to be remembered. The fact that this study used patients who were undergoing a painful and worrisome non-surgical procedure while presented the to-be-remembered stimulus may have had an adverse effect on their ability to form implicit memories due to distraction or lack of relevance to them. The stimuli were after all neologisms not true words and therefore may have been more difficult to encode implicitly and unlike those young and healthy participants in Fang et al's study had no real incentive to attend to the tape being played to them; not being paid for their participation and it not affecting the level of their medical treatment. Also as their explicit memories were characterised by what they heard the nurse or surgeons saying

to them they may not have processed any other auditory information, being too intent, understandably, on seeking reassurance on the progress of their procedure. Tests of implicit memory targeted at the information discussed during the colonoscopy may have procured a different result in agreement with the experimental hypothesis (see *Suggestions for Future Research*). Importantly, Fang et al's study measured implicit memory on a primary task using neutral target words unrelated to the stress of a medical procedure. The current study was designed on the basis of an aversive associative conditioning paradigm (Jacobs & Nadel, 1985). However, it may be that the neologisms themselves did not relate to the stress associated with colonoscopies, despite being designed to do so. Therefore, the results are in agreement with Ghoneim et al (1992) who despite using a conditioning paradigm failed to find conclusive evidence of implicit memory as indicated by change in skin conductance response.

Accepted Null Hypothesis$_2$

- There will be no significant difference in skin conductance response change from pre- to post-colonoscopy between intra-operatively presented neologisms designed to provoke an emotional association and 'neutral' neologisms.

As neologisms rather than true words were selected due to the ethical considerations of using real words, the research design assumed that participants would link the neologisms to their real word counterparts. However, this may have not occurred making all three neologisms 'neutral' to the participants listening to them and therefore little difference would be detected between those deemed emotive compared to those deemed neutral. Alternatively, as the neologisms were possibly not emotive they may

have been processed by the affected cognitive hippocampal system and therefore transfer from short-term to long-term memory did not occur (Brown, Lewis, Brown, Horn & Bowes, 1982; Ghoneim & Mewaldt, 1975). This may have also led to no conditioning and therefore no change in SCR from pre- to post-procedure.

Accepted Null Hypothesis$_3$

- There will be no significant effect of mood on implicit memory formation for words presented during colonoscopy, as detected by skin conductance response, following intravenous administration of midazolam.

Many of the people who did not want to participate in the research chose not to do so on the basis of feeling too anxious about the procedure to be involved in anything else. This may suggest that the sample collected was missing any participants who would be more disposed to conditioning during an aversive event (O'Malley, Wang, Kroenke, Roy & Wong, 1998). Also, it is possible that the anxiolytic effects of the midazolam may have reduced the moderately anxious participants' anxiety levels low enough to impair their performance with respect to attending to and remembering the neologism presented on the tape (Yerkes & Dodson, 1908).

With regard to depression, none of the groups averaged a group mean depression rating on the HADS any higher than that deemed normal in the general population. However, Group 3 scored a mean average of anxiety in the mildly anxious range, clinically speaking. The researcher noted that when talking to the participants at the end of the final stage of the experiment a large proportion of individuals reported feeling anxious about future results not depressed about results already given. It might be interesting to

see how their mood ratings changed over time and after diagnoses and treatment prescribed as one might predict that anxiety may reduce due to losing the "not knowing" feeling and depression may increase with any negative results.

Accepted Null Hypothesis$_4$

- There will be no significant effect of personality on implicit memory formation for words presented during colonoscopy, as detected by skin conductance response, following intravenous administration of midazolam.

Personality did not play a role in the change in SCR to the neologisms presented but that is not to say that it does not have bearing on implicit emotional memory formation (Wilson, Whiteoak, Dewey & Watson, 1989). Again, with the small sample recruited the distribution of representative personalities of the true population may not have been gathered. Like the distribution of mood ratings, it may be that those introverted and neurotic individuals are also those more likely to refuse to partake or to withdraw during the experiment. It would have been interesting to get empirical data to evaluate the profiles of those who chose not to take part compared to those who consented.

Accepted Null Hypothesis$_5$

- There will be no significant effect of objectively rated behavioural distress on implicit memory formation for words presented during colonoscopy, as detected by skin conductance response, following intravenous administration of midazolam.

The Behavioural Distress Scale is, as mentioned below, not a standardised test and it cannot therefore be assumed to be truly valid and reliable despite its face validity. Also, as noted by the researcher, the apparent discomfort endured during the colonoscopies varied considerably from patient to patient. This seemed to vary according to expectation of pain prior to the procedure and likelihood to express pain overtly. This was not measured explicitly by the current research design, and although midazolam does disinhibit behaviour to a degree, some patients seemed very aware of themselves and apologised for their verbalisations of pain or embarrassing aspects of the procedure such as unclean bowels or the passing of wind that had been injected into the colon via the endoscope to inflate the area under investigation.

Strengths and Limitations

The main strengths of this study were that it attempted to investigate a fairly specific and well defined aspect of implicit memory, under ethically sound conditions, in a clinically relevant field setting, using measures of memory that have been found to be both sensitive and specific to what they were designed to measure. The methodology maximised the relatively small number of participants utilising a repeated measured method with random allocation to the groups and minimised demand characteristics through the application of a double blind design.

However, despite using a repeated measures design, which allows each participant to act as their own control, no separate control group was adopted. Also the group sampled was relatively small at twenty-eight making statements of generalisation extremely limited. The difficulty in sampling was due in part to the lack of incentive to partake (e.g. it was of course optional and refusal to participate would not effect their treatment

at all, the research was being conducted by someone not involved in their aftercare or working in any other capacity than researcher in the department). Another contributor to the recruitment problem was attrition due to the lack of incentive to return for the one-week follow-up session (e.g. no other need to come to the hospital other than to do the twenty minute follow-up, travel expenses were not reimbursed due to financial limitations of the study etc.). Approximately one in every five patients approached to participate in the research declined to take part. Reasons given included an unwillingness to return for the one-week follow-up, the added anxiety of having to be involved in a research project when the procedure already felt overwhelming, not wanting to wear headphones during the colonoscopy, and not fitting the inclusion criteria. Fifteen participants who did complete the first three stages of the research did not return for the follow-up.

Another weakness of the current study was that the Behavioural Distress Scale has not been tested statistically for reliability and validity with respect to what it is measuring and it may have been useful to have at least gauged inter-rater reliability. Further to this point, it may have been useful to use some objective measure of the level of "consciousness" of the participants during the colonoscopy procedure e.g. Glasgow Coma Scale or some reliable and valid physiological measure. The researcher observed that apparent "consciousness" of the participant varied quite considerably despite them being given roughly equivalent doses of medication. As discussed in the *Introduction* individual differences may affect the level of potency and resultant impairment in performance of the drug. Also there has been some research, which suggests that fentanyl may have an impact on memory consolidation (Richardson, 1989) and the effects of this, although unavoidable in the participant sample used, may account for why no evidence of implicit memory was found on the measures used.

Another issue to question was the use of SCR, which may not have been an appropriate measure in the group sampled. Although SCR is the response paradigm most commonly sensitive to autonomic arousal as a function of emotional reaction (Edelberg, 1967), it is possible that a larger proportion of non-responders were sampled.

Lastly, although the one-week follow was chosen to ensure that all residual traces of midazolam would have been metabolised and eliminated from the body the time delay may have caused any implicit memory trace to decay. Therefore, such a decay may have resulted in no change in the SCR from pre- to post-procedure and caused the null hypotheses to be accepted unnecessarily.

Clinical Implication of the Findings

Studies that support their null hypotheses make it difficult to draw any conclusions regarding the wider clinical implication of the research. However, the notable finding that a large proportion of participants have explicit recall of pain and definitive comments from nursing staff and surgeons e.g. "Got it all out" (referring to a polypectomy) and "Everything is fine", has implications for both better pain control and being more careful about any comments with negative connotations being passed until the patient is fully awake and conscious.

Suggestions for Future Research

Although there were no significant findings with regard to this research, larger scale studies which addressed the methodological problems and difficulties of implementation encountered with this one would be required before any definite

conclusions could be drawn regarding the post-procedure memory and resultant psychological sequelae of colonoscopy involving conscious sedation and the factors that mediate these. However, this study does raise some interesting questions regarding future research.

Methodologically speaking, in addition to larger samples, the use of proper words or testing emotionally relevant information presented during the procedure by nursing staff and surgeons may illustrate implicit memory. This may be carried out by taping what is said during each procedure, so the voice and what is said is exactly as it was during the colonoscopy. Excerpts from this tape, combined with random statements made by the same surgeon (possibly from other procedures together with neutral statements not related to the colonoscopies), could then be played back to the participant, once the midazolam had metabolised out of their system, whilst skin conductance response is measured. This data could be compared to a matched control group.

It may also, as mentioned above, be useful to standardise the BDS and use additional measures of consciousness. To help with the recruitment problem, financial incentives may encourage more people to take part, or arranging with the surgeons to have those who wish to participate to have follow-up appointments shortly after the procedure not weeks and month down the line. Also the addition of other measures of implicit memory may help show which method is most sensitive and help comparisons to be made to other studies.

Theoretically, it would be interesting to see if time and lack of rehearsal had a similar impact on implicit memory as explicit memory. Varying the length of time post-procedure to carry out stage four of the study may answer this question.

Academically and clinically it would be interesting to investigate in more depth the potential impact of fentanyl (opioid analgesic) on memory formation and whether this interacts with the midazolam or the formation of implicit emotional memory as opposed to neutral emotional memory.

Lastly, it would be useful to look at the individual differences of those that recall pain and personally relevant comments and those that don't. This may highlight why some people and certain types of information can be explicitly recalled through what is otherwise a fairly dense drug-induced amnesia. Is it just the quality of the information or is the person i.e. those that recalled pain may have felt more pain and those that recalled significantly relevant statements may have just had them discussed by the staff during the procedure as opposed to not; instead of it being mediated by personality characteristics, mood, or individual sensitivity to amnestics.

Conclusions

Although all the experimental hypotheses were rejected, it is not possible to suggest that implicit memory, and more specifically implicit emotional memory, does not exist under midazolam amnesia. The gap in the literature on the effectiveness in suppression of memory for aversive events under midazolam induced conscious sedation remains 'unfilled' (Pain et al, 2000). However, the current study has certainly found evidence of some intra-operative explicit memory and somewhat disturbingly this has centred on pain awareness and some personally significant comments passed about the progress and prognosis of the participants' by the surgeons and nursing staff.

The variability in research design, methodology and resultant findings of the studies that have been published to date highlight the need to standardise definitions and best methods of measurement to create a more cohesive effort in answering some fundamental questions attempted in this study and others conducted prior to it. The rationale for this, despite the area being interesting from an academic and theoretical view point, is that it is vital for patient care to remain optimal and medical professionals to remain up to date in the latest knowledge on the effects of the drugs they prescribe and remain safe from the threat litigation over charges of malpractice (Ghoneim & Mewaldt, 1990).

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Appendix I – Hospital Anxiety and Depression Scale (HADS)

Mood Questionnaire

Emotions can play an important part in our physical health. This questionnaire asks about how you feel. Please read each item and tick the reply, which comes closest to how you have been feeling in the PAST WEEK. Don't take too long over your replies; your immediate reaction to each item will probably be more accurate than a long thought-out response.

1. I feel tense or 'wound up'...
a)...most of the time..... [ ]
b)...a lot of the time..... [ ]
c)...time to time, occasionally..... [ ]
d)...not at all..... [ ]

2. I feel as if I am slowed down...
a)...nearly all the time..... [ ]
b)...very often..... [ ]
c)...sometimes..... [ ]
d)...not at all..... [ ]

3. I still enjoy the things that I used to enjoy...
a)...definitely as much..... [ ]
b)...not quite so much..... [ ]
c)...only a little..... [ ]
d)...hardly at all..... [ ]

4. I get a sort of frightened feeling like 'butterflies' in the stomach...
a)...not at all..... [ ]
b)...occasionally..... [ ]
c)...quite often..... [ ]
d)...very often..... [ ]

5. I get a sort of frightened feeling as if something awful is about to happen...
a)...very definitely and quite badly.... [ ]
b)...yes, but not too badly..... [ ]
c)...a little, but it doesn't worry me... [ ]
d)...not at all..... [ ]

6. I have lost interest in my appearance...
a)..definitely..... [ ]
b)..I don't take so much care as I should [ ]
c)..I may not take quite so much care... [ ]
d)..I take just as much care as ever..... [ ]

7. I can laugh and see the funny side of things...
a)...as much as I always could..... [ ]
b)...not quite so much now..... [ ]
c)...definitely not so much now..... [ ]
d)...not at all..... [ ]

8. I feel restless as if I have to be on the move...
a)...very much indeed..... [ ]
b)...quite a lot..... [ ]
c)...not very much..... [ ]
d)...not at all..... [ ]

9. Worrying thoughts go through my mind...
a)...a great deal of the time..... [ ]
b)...a lot of the time..... [ ]
c)...from time to time but not too often..[ ]
d)...only occasionally..... [ ]

10. I look forward with enjoyment to things...
a)...as much as I ever did..... [ ]
b)...rather less than I used to..... [ ]
c)...definitely less than I used to..... [ ]
d)...hardly at all..... [ ]

11. I feel cheerful...
a)...not at all..... [ ]
b)...not often..... [ ]
c)...sometimes..... [ ]
d)...most of the time..... [ ]

12. I get sudden feelings of panic...
a)...very often indeed..... [ ]
b)...quite often..... [ ]
c)...not very often..... [ ]
d)...not at all..... [ ]

13. I can sit at ease and feel relaxed...
a)...definitely..... [ ]
b)...usually..... [ ]
c)...not often..... [ ]
d)...not at all..... [ ]

14. I can enjoy a good book or radio or TV programme...
a)...often..... [ ]
b)...sometimes..... [ ]
c)...not often..... [ ]
d)...very seldom..... [ ]

Tick Only One Box In Each Section

Appendix II – Eysenck Personality Inventory (EPI)

Personality Questionnaire

Here are some questions regarding the way you behave, feel and act. After each question is a space for answering "YES" or "NO".

Try to decide whether "YES" or "NO" represents your usual way of acting or feeling. Then put a cross in the circle under the column headed "YES" or "NO". Work quickly and don't spend too much time over any question; I want your first reaction, not a long-drawn out thought process. The whole questionnaire shouldn't take more than a few minutes. Be sure to answer all the questions. There are no right or wrong answers, and this isn't a test of intelligence or ability, but simply a measure of the way you behave.

		YES	NO
1.	Do you like plenty of excitement and bustle around you?		
2.	Have you often got a restless feeling that you want something but do not know what?		
3.	Do you nearly always have a "ready answer" when people talk to you?		
4.	Do you sometimes feel happy, sometimes sad, without any real reason?		
5.	Do you usually stay in the background at parties and "get-togethers"?		
6.	As a child, did you always do as you were told immediately and without grumbling?		
7.	Do you sometimes sulk?		
8.	When you are drawn into a quarrel, do you prefer to "have it out" to being silent, hoping things will blow over?		
9.	Are you moody?		
10.	Do you like mixing with people?		
11.	Have you often lost sleep over your worries?		
12.	Do you sometimes get cross?		
13.	Would you call yourself happy-go-lucky?		
14.	Do you often make up your mind too late?		
15.	Do you like working alone?		
16.	Have you often felt listless and tired for no good reason?		
17.	Are you rather lively?		
18.	Do you sometimes laugh at a dirty joke?		
19.	Do you often feel fed-up?		
20.	Do you feel uncomfortable in anything but everyday clothes?		
21.	Does your mind often wander when you are trying to attend closely to something?		
22.	Can you put thoughts into words quickly?		
23.	Are you often "lost in thought"/		
24.	Are you completely free from prejudices of any kind?		
25.	Do you like practical jokes?		
26.	Do you often think about your past?		
27.	Do you very much like good food?		
28.	When you get annoyed, do you need someone friendly to talk to about it?		
29.	Do you mind selling things or asking people for money for a good cause?		
30.	Do you sometimes boast a little?		
31.	Are you touchy about some things?		
32.	Would you rather be at home on your own than go to a boring party?		
33.	Do you sometimes get so restless that you cannot sit long in a chair?		
34.	Do you like planning things carefully, well ahead of time?		
35.	Do you have dizzy turns?		
36.	Do you *always* answer a personal letter as soon as you can after you have read it?		

37.	Can you usually do things better by figuring them out alone than by talking to others about it?		
38.	Do you ever get short of breath without having done heavy work?		
39.	Are you an easy-going person, not generally bothered about having everything "just-so"?		
40.	Do you suffer from "nerves"?		
41.	Would you rather plan things than do things?		
42.	Do you sometimes put off until tomorrow what you ought to do today?		
43.	Do you nervous in places like lifts, trains or tunnels?		
44.	When you make new friends, is it usually *you* who makes the first move, or does the inviting?		
45.	Do you get very bad headaches?		
46.	Do you generally feel that things will sort themselves out and come right in the end somehow?		
47.	Do you find it hard to fall asleep at bedtime?		
48.	Have you sometimes told lies in your life?		
49.	Do you sometimes say the first thing that comes into your head?		
50.	Do you worry too long after an embarrassing experience?		
51.	Do you usually keep "yourself to yourself" except with very close friends?		
52.	Do you often get into a jam because you do things without thinking?		
53.	Do you like cracking jokes and telling funny stories to your friends?		
54.	Would you rather win than lose a game?		
55.	Do you often feel self-conscious when you are with superiors?		
56.	When the odds are against you, do you still usually think it worth taking a chance?		
57.	Do you often get "butterflies in your tummy" before and important occasion?		

PLEASE CHECK TO SEE THAT YOU HAVE ANSWERED ALL THE QUESTIONS

Appendix III - Behavioural Distress Scale (BDS)

Measured for time tape is playing during the colonoscopy

Behaviour		**1 min**	**2 min**	**3 min**	**4 min**	**5 min**	**6 min**	**7 min**	**8 min**	**9 min**	**10 min**
face grimacing											
groaning	slight										
	moderate										
	frequent										
arm mvt	slight										
	moderate										
	frequent										
face	pale										
	flushed										
	sweating										
eyes	open										
	semi-open										
	closed										
awareness	alert/speak										
	semi-sleep										
	sleep										

HEART RATE : -

Time midazolam 1 given =

Dosage of midazolam 1 =

Dosage of fentanyl 1 =

Time midazolam 2 given =

Dosage of midazolam 2 =

Dosage of fentanyl =

Time tape started =

Appendix IV – Pre-Colonoscopy Questionnaire

1. Age
2. Gender
3. Weight
4. Do you have any current health problems?

5. Are you currently taking any prescribed medications?

6. Do you have a hearing impairment?

7. Have you had a colonoscopy before?

8. Why are you having a colonoscopy?

9. How would you rate your anxiety level now on a scale of 1-10 (1=relaxed, 10=panic)

10. Do you have any further questions about the research study?

ARRANGE FOLLOW-UP & GET PHONE NUMBER

Appendix V – Post - Colonoscopy Questionnaire

1. How would you rate your anxiety level now on a scale of 1-10 (1=relaxed, 10=panic)

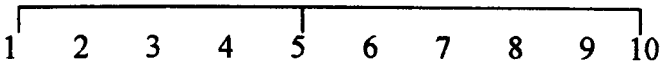
2. How did you feel before your examination?

3. Can you remember having your injection?

4. Can you remember what you heard through the headphones during the examination?

5. How painful was your colonoscopy?

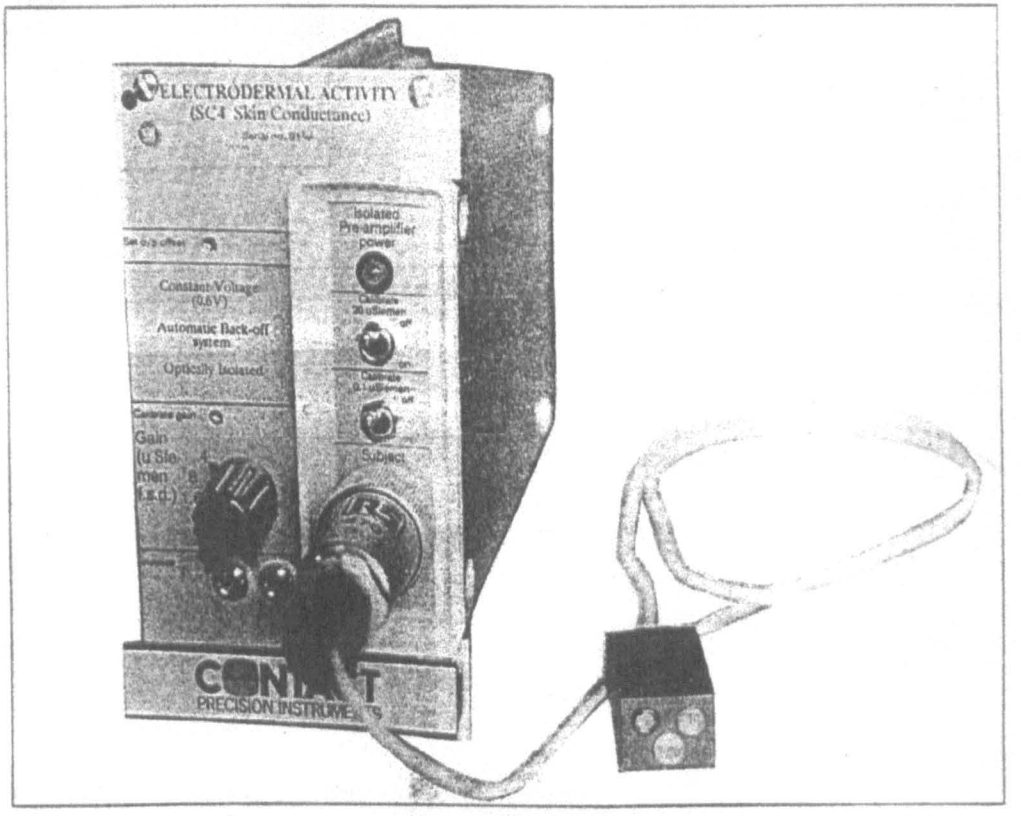
Can't remember No Pain Mildly painful (1) Moderately painful (5) Very painful (10)



6. What can you remember about the whole procedure from when you went into the surgical room to when you went into the recovery room? (what did you hear, feel, see?)

TURN OVER FOR MORE SPACE

PsyLab
SC4 Skin Conductance Amplifier



CONTACT
PRECISION INSTRUMENTS

SC4 measures directly in conductance, using direct coupling with constant voltage electrode excitation. Instantaneous adjustment of base-line suppression is achieved via the PsyLab digital link to permit use of very high sensitivity setting without risk of signal blocking.

SC4 is designed to solve the problem of large skin conductance responses (SCRs) which go off scale with conventional apparatus and was originally designed in 1979 to comply with specifications given by Lykken and Venables. Further useful information, including recommendation of electrode type, conductive paste etc. may be found in pages 4 - 62 of "Techniques in Psychophysiology"; Martin & Venables (published by Wiley, 1980).

Back-off level (base line) is automatically increased by the computer in 0.2 micro Siemen steps to reach a level near to the subject's basal level (SCL). This level is detected by monitoring the high sensitivity response signal which will be out-of-range until this balance is achieved. At this point, small responses (SCRs) may be greatly amplified and are recorded without the distortion introduced by AC coupling the signal, an inacurate method for base-line suppression. If a large SCR occurs, instantaneous back-off adjustment prevents loss of SCR data.

Output

Response signal output from the amplifier is set to suit an input of MC8, or a low resolution channel of MC24. This allows 1 part in 200 resolution for the active range of response signal, equivalent to 0.008 micro Siemen when used with the response sensitivity set to 1.6 micro Siemen full scale deflection (F.S.D.). A 3.5 mm jack lead is plugged into one output socket with the other end plugged into the interface.

Functional Details

The pre-amplifier is contained in an isolated plastic box, with electrical power conveyed to the circuit by a high frequency magnetic coupling through the wall of the box. This ensures complete safety and individual isolation of electrode connections to prevent interaction with other amplifiers.

A 10 Hz filter is applied to the response signal to prevent aliasing at low data rates. Position of the gain control setting is automatically communicated to the computer via the rear connecting system which also transmits back-off level to SC4. The same connecting system conveys power to the coupler. Gain control position is given in units of full scale deflection of the response signal. Software can therefore use half this value as the "step size" used when adjusting back-off, so that one "step" will cause the response signal to jump from the extremity of its range to range centre.

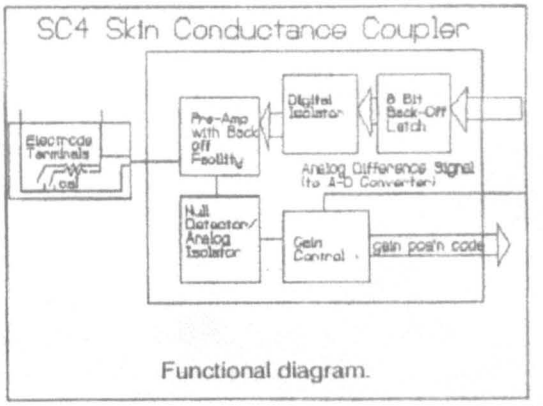
Two calibrators are supplied in the pre-amplifier which connect directly to the subject connection terminals. The large value can be used to check back-off accuracy and function, the small value is used to check accuracy of response signal gain calibration. For example, on gain setting 0.4 micro Siemen FSD, operating the 0.1 micro Siemen calibrator switch should cause a step in the response signal of a quarter of the scale range (providing that it does not go out of range, and then re-balance).

Specifications:

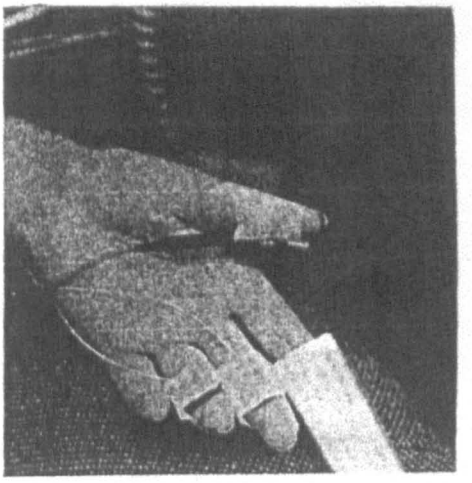
Measurement units	micro Siemen
Absolute accuracy	+/- 0.3 micro Siemen
SCR resolution	0.005 micro Siemen
Frequency response	DC - 10 Hz
Calibrator accuracy	(20) .05%, (0.1) 5%
Subject excitation	constant 0.6V DC
Voltage output	0 - 4V adjustable
Range	0 - 52 micro Siemen
Subject Isolation	> 2000V, 100 M Ohm

Contact Precision Instruments
4 Shillingford Street
London N1 2DP
England

Tel (071) + 354 3028
Tel (071) + 226 3049
Fax (071) + 226 0078
International (44 71) +



Functional diagram.



Electrodes positioned on the medial phalanges.

Gain Control Ranges (micro Siemen FSD)
0.4, 0.8, 1.6, 3.2

Contact Precision Instruments
(U.S.A. service)
8401 Colesville Road
Suite 504
Silver Spring, MD 20910
U.S.A.

tel (301) 650 7714

Appendix VII – Participant Information Sheet

THE UNIVERSITY OF HULL
ACADEMIC SURGICAL UNIT
CASTLE HILL HOSPITAL · CASTLE ROAD · COTTINGHAM · HULL HU16 5JQ
TELEPHONE 01482 623225/623247/623077 · FACSIMILE 01482 623274

Study Title: Memory effects following a colonoscopy

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not to take part

Thank you for reading this.

What is the purpose of this study?

I am a Trainee Clinical Psychologist studying for my Doctorate in Clinical Psychology at the University of Hull. As part of my course I work within the NHS with both adult and children with a variety of health related and psychological problems. Another major part of my course is a research project, which I am carrying out in the Endoscopy Department of Castle Hill Hospital.

This study is looking at memory associated with colonoscopy. Normally, due to the drugs given prior to the colonoscopy it is not possible to remember anything that happens during the procedure, except for possibly being aware of some discomfort. However, there is another kind of memory called 'implicit memory', which is when something is learnt but you are not aware of remembering how you learnt it. This type of memory can be detected in many different ways and it is this type of memory that we are investigating in this study to test how effective the drugs are at preventing it.

The study shall involve approximately 90 participants, which will be tested over a period of about 3 months.

Why have I been chosen?

You have been invited to for this study simply due to you being an outpatient at Castle Hill Hospital requiring a colonoscopy and are over 18 years of age.

Do I have to take part?

It is up to you to decide whether or not to take part. If you decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time or a decision not to take part will not affect the standard of care you receive.

What will happen to me if I take part?

Immediately before your colonoscopy, you will attend a very short interview in which you will you be asked some basic questions about your health and colonoscopy. You will also be asked to listen to a tape recording of some words whilst a machine measures the sweating on your hand. Some stick-on surface pads will be placed on your fingers. This is not harmful or painful in any way. During your colonoscopy you will also listen to another tape recording using a personal stereo and headphones. After your colonoscopy you will be given a very short questionnaire to complete in the recovery ward before you leave the hospital.

On the day of your Colonoscopy an appointment will be arranged for you to come back to the Endoscopy Department within 1-2 weeks after your Colonoscopy to see what you remember about the procedure and the words you were presented with in the headphones and to redo the test that measures sweating on your fingers whilst listening to word tapes. You will also be asked to complete a couple of short questionnaires about mood and personality. It should only take about 10 minutes but it is essential to the study, without this follow-up meeting the initial information taken on the day of your colonoscopy will not be able to be used for the research.

This type of study is called a double blind trial. This means that neither you, your doctor or the researcher will know which group you are in i.e. what words are going to be presented to you by the personal stereo during the colonoscopy. However, we will be able to find out if it is necessary.

What are the possible disadvantages and risks of taking part?

There are no risks or disadvantages of taking part in this study.

What are the possible benefits of taking part?

No, there are no individual benefits but the results may have wider implications and help other people who will be undergoing colonoscopies in the future.

Will my taking part in this study be kept confidential?

If you consent to take part in the research any of your medical records regarding the colonoscopy may be looked at by myself where it is relevant to your taking part in this research. However, all information that is collected about you during the course of the research will be kept strictly confidential. Any information about you will have your name and address removed and a participant number put in its place so that you cannot be recognized from it. The information you provide will not be passed onto another party.

What will happen to the results of the research study?

The results of this study will be written up as a doctoral thesis for the course and as a journal article to submit for possible publication. However, you will not be identified and your data will be labeled with an anonymous participant number, for which, only I will be aware of. If my journal article is published you can obtain a copy by writing or telephoning the Department of Clinical Psychology at the University of Hull.

Who has reviewed the study?

The Hull and East Riding Local Research Ethics Committee has approved this study.

Contact for Further Information.

You can contact me (Joanne Beckett, Trainee Clinical Psychologist) at:

Department of Clinical Psychology
School of Medicine
Robert Blackburn Building
The University of Hull
Cottingham Road
Hull
HU6 7RX
Tel: 01482 465933
Fax: 01482 466155

Thank you for taking part in my study.

You will be provided with a copy of this information sheet and your signed consent form to keep should you agree to participate in this study.

Appendix VIII – Consent Form

THE UNIVERSITY OF HULL
ACADEMIC SURGICAL UNIT
CASTLE HILL HOSPITAL · CASTLE ROAD · COTTINGHAM · HULL HU16 5JQ
TELEPHONE 01482 623225/623247/623077 · FACSIMILE 01482 623274

Consent Form

Title of Project: **Memory effects following a colonoscopy**

Name of Researcher: Joanne Beckett BSc (HONS)
Trainee Clinical Psychologist

1. I confirm that I have read and understood the information sheet for the above study and have had the opportunity to ask questions. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐
3. I understand that sections of my medical notes relating to my taking part in the study may be looked at by the researcher. I give permission for these individuals to have access to my records. ☐
4. I agree to take part in the above study. ☐

Name of Patient	Date	Signature
Name of Person taking consent	Date	Signature
Researcher	Date	Signature

Copies will be provided for the patient, the researcher and the hospital notes.

THE SCHOOL OF MEDICINE IS PART OF THE FACULTY OF HEALTH
PROFESSOR JOHN R T MONSON MD FRCS FRCSI FACS FRCPS(Glas)Hon) • HEAD OF DEPARTMENT • DIRECT LINE 01482 623225
PROFESSOR NICHOLAS D STAFFORD MB FRCS • PROFESSOR OF OTOLARYNGOLOGY & HEAD AND NECK SURGERY • DIRECT LINE 01482 674456
PROFESSOR P T McCOLLUM MCh FRCSI • PROFESSOR OF VASCULAR SURGERY • DIRECT LINE 01482 674784
PROFESSOR PETER W A LEE MD FRCS • PROFESSOR OF SURGERY • DIRECT LINE 01482 623077
MR GRAEME S DUTHIE MD HONS FRCS(Ed) • READER IN SURGERY • DIRECT LINE 01482 623247
MR STEPHEN R ELL BSc MB FRCS(ORL) • SENIOR LECTURER IN OTOLARYNGOLOGY • DIRECT LINE 01482 674456
MR PHILIP J DREW BSc MD(Hons) MS FRCS(Ed) ENG & GLAS) FRCS (GEN) • SENIOR LECTURER IN SURGICAL ONCOLOGY • DIRECT LINE 01482 623077

Appendix IX – Raw Data

Key: -

Variable	Label
Group	Group 1 heard POTE during colonoscopy Group 2 heard MOOF during colonoscopy Group 3 heard SCRATE during colonoscopy
EPIE	EPI – Extroversion
EPIN	EPI – Neuroticism
EPIL	EPI – Lie Scale
HADS anx	HADS – Anxiety
HADS dep	HADS – Depression
SUDS pre	Anxiety rating before colonoscopy
SUDS post1	Anxiety rating after colonoscopy, before discharge
SUDS post2	Anxiety rating 1-week follow-up
PAIN post1	Pain rating after colonoscopy, before discharge
PAIN post2	Pain rating 1-week follow-up
BDS	Behavioural Distress composite score
POTE	Difference score = skin conductance at 1-week follow-up minus skin conductance before colonoscopy
SCRATE	As above
MOOF	As above
CR	Cannot remember

N	Group	EPI – E	EPI – N	EPI – L	HADS anx	HADS dep	SUDS pre	SUDS post1	SUDS post2	Pain post1	Pain post2	BDS	Pote	Scrate	Moof
1	1	9	7	1	7	3	4	1	1	2	0	-0.9	0.000000	3.400000	1.900000

N	Group	EPI -E	EPI -N	EPI -L	HADS anx	HADS dep	SUDS pre	SUDS post1	SUDS post2	Pain post1	Pain post2	BDS	Pote	Scrate	Moof
2	1	9	2	5	2	0	5	2	2	CR	CR	0.18	0.068010	0.124005	-1.52796
3	1	17	12	0	6	6	5	2	3	0	CR	0.40	0.000000	1.599950	1.800000
4	1	20	6	6	3	3	5	1	1	3	CR	1.35	0.000000	-0.640005	-1.40296
5	1	13	18	1	2	0	3	1	2	2	CR	-1.05	2.799950	0.000000	0.000000
6	1	17	13	0	10	9	5	2	2	2	5	-0.37	-0.107000	-0.113005	-3.50196
7	1	21	18	0	14	7	2	1	2	8	5	2.31	-0.120995	-4.99000	-8.100000
8	1	17	17	3	7	1	2	6	1	CR	0	-1.65	-0.181995	-1.49995	-0.151000
9	1	13	15	4	7	6	5	1	5	0	0	1.58	-0.012995	-2.39701	0.900050
10	2	16	14	1	5	1	1	1	1	3	2	-0.54	0.000000	0.000000	0.000000
11	2	17	8	2	5	1	7	1	3	7	6	-0.95	-1.49995	0.199950	0.000000
12	2	15	13	7	8	9	6	2	2	0	1	-0.74	4.300000	1.599500	2.499950
13	2	10	19	4	11	9	8	4	2	3	4	-1.56	0.676000	0.290995	0.752000
14	2	9	8	3	4	0	8	1	1	3	4	1.83	3.775005	8.094005	1.882950
15	2	20	13	1	4	3	8	1	3	0	CR	-1.37	4.410000	1.322000	0.82000
16	2	10	19	4	2	3	3	1	1	3	CR	2.23	-0.096000	-0.052000	-1.08100
17	2	15	8	4	1	7	1	1	1	0	0	-1.09	0.320995	0.104000	1.680995
18	2	17	13	0	13	3	6	2	1	0	0	0.18	0.000000	5.200000	3.100000
19	2	14	9	5	6	1	1	1	1	3	0	2.11	-0.132955	-0.132955	2.499950
20	3	12	15	4	12	7	5	2	2	4	2	-0.55	-1.29996	-1.29996	-6.39995
21	3	10	3	3	3	3	1	1	1	1	1	1.72	-0.7999500	-0.799950	2.776950
22	3	17	10	4	5	3	5	1	1	3	1	0.98	-2.10005	-2.10005	-3.84600
23	3	16	10	1	8	3	1	1	1	0	1	0.56	1.540955	1.540955	-5.20000
24	3	14	14	2	9	2	2	1	1	2	3	-0.28	2.000000	2.000000	0.000000
25	3	13	20	5	15	3	2	1	1	5	4	-1.16	0.183000	0.183000	1.330050
26	3	17	10	5	3	2	5	1	1	2	1	-0.38	-7.49990	-7.49990	-3.26890
27	3	13	6	6	6	7	5	2	1	8	5	1.55	0.103995	0.13995	0.681000
28	3	10	17	1	16	13	7	3	2	0	0	-1.37	-3.19150	-3.19150	3.299950

Appendix X – Descriptive Statistics

* For key to variables *see Appendix IX*

Descriptive Statistics – Total Sample

Descriptive Statistics

	N	Range	Minimum	Maximum	Sum	Mean		Std.	Variance	Skewness		Kurtosis	
	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic	Statistic	Statistic	Std. Error	Statistic	Std. Error
EPIE	28	12	9	21	408	14.57	.72	3.795	14.402	-.168	.441	-1.094	.858
EPIN	28	18	2	20	337	12.04	.94	4.948	24.480	-.213	.441	-.763	.858
EPIL	28	7	0	7	82	2.93	.39	2.089	4.365	.102	.441	-1.148	.858
HADSANX	28	15	1	16	194	6.93	.80	4.207	17.698	.677	.441	-.435	.858
HADSDEP	28	13	0	13	115	4.11	.63	3.337	11.136	.865	.441	.202	.858
SUDSPRE	28	7	1	8	118	4.21	.44	2.315	5.360	.028	.441	-1.118	.858
SUDPOST1	28	5	1	6	45	1.61	.21	1.133	1.284	2.674	.441	8.178	.858
SUDPOST2	28	4	1	5	46	1.64	.18	.951	.905	1.921	.441	4.552	.858
PAINPRE	26	8	0	8	64	2.46	.47	2.404	5.778	1.034	.456	.644	.887
PAINPOST	22	6	0	6	45	2.05	.44	2.058	4.236	.582	.491	-1.198	.953
BDS	28	3.96	-1.65	2.31	3.83	.1368	.2405	1.27254	1.619	.352	.441	-1.236	.858
POTE	28	9.509900	5.099900	4.410000	5.332155	19043411	40881994	********	4.680	-.084	.441	.787	.858
SCRATE	28	5.593905	7.499900	8.094005	1.046077	03735989	54435778	********	8.297	.166	.441	2.769	.858
MOOF	28	1.399950	8.100000	3.299950	-9.293880	-.331924	55313788	********	8.567	-1.112	.441	.748	.858
Valid N (listwise)	21												

Descriptive Statistics – Group 1

Descriptive Statistics

	N	Range	Minimum	Maximum	Sum	Mean		Std.	Variance	Skewness		Kurtosis	
	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic	Statistic	Statistic	Std. Error	Statistic	Std. Error
EPIE	9	12	9	21	136	15.11	1.46	4.372	19.111	-.258	.717	-1.168	1.400
EPIN	9	16	2	18	108	12.00	1.93	5.788	33.500	-.627	.717	-.939	1.400
EPIL	9	6	0	6	20	2.22	.78	2.333	5.444	.568	.717	-1.398	1.400
HADSANX	9	12	2	14	58	6.44	1.30	3.909	15.278	.700	.717	.409	1.400
HADSDEP	9	9	0	9	35	3.89	1.09	3.257	10.611	.183	.717	-1.374	1.400
SUDSPRE	9	3	2	5	36	4.00	.44	1.323	1.750	-.833	.717	-1.248	1.400
SUDPOST1	9	5	1	6	17	1.89	.54	1.616	2.611	2.513	.717	6.774	1.400
SUDPOST2	9	4	1	5	19	2.11	.42	1.269	1.611	1.626	.717	3.152	1.400
PAINPRE	7	8	0	8	17	2.43	1.02	2.699	7.286	1.711	.794	3.684	1.587
PAINPOST	5	5	0	5	10	2.00	1.22	2.739	7.500	.609	.913	-3.333	2.000
BDS	9	3.96	-1.65	2.31	2.66	.2956	.4254	1.27628	1.629	.102	.717	-.710	1.400
POTE	9	2.981945	-.181995	2.799950	2.444975	27166389	31709431	********	.905	2.961	.717	8.830	1.400
SCRATE	9	8.390000	4.990000	3.400000	4.516013	-.501779	79221165	********	5.648	-.348	.717	1.064	1.400
MOOF	9	0.000000	8.100000	1.900000	-10.0638	-1.12043	1.044572	********	9.820	-1.518	.717	2.596	1.400
Valid N (listwise)	4												

Descriptive Statistics – Group 2

Descriptive Statistics

	N	Range	Minimum	Maximum	Sum	Mean		Std.	Variance	Skewness		Kurtosis	
	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic	Statistic	Statistic	Std. Error	Statistic	Std. Error
EPIE	10	11	9	20	143	14.30	1.14	3.592	12.900	-.233	.687	-.872	1.334
EPIN	10	11	8	19	124	12.40	1.33	4.222	17.822	.526	.687	-.862	1.334
EPIL	10	7	0	7	31	3.10	.67	2.132	4.544	.268	.687	-.333	1.334
HADSANX	10	12	1	13	59	5.90	1.20	3.784	14.322	.788	.687	-.006	1.334
HADSDEP	10	9	0	9	37	3.70	1.08	3.401	11.567	.787	.687	-1.004	1.334
SUDSPRE	10	7	1	8	49	4.90	.97	3.071	9.433	-.400	.687	-1.871	1.334
SUDPOST1	10	3	1	4	15	1.50	.31	.972	.944	2.270	.687	5.356	1.334
SUDPOST2	10	2	1	3	16	1.60	.27	.843	.711	1.001	.687	-.665	1.334
PAINPRE	10	7	0	7	22	2.20	.71	2.251	5.067	.859	.687	.988	1.334
PAINPOST	8	6	0	6	17	2.13	.81	2.295	5.268	.648	.752	-1.033	1.481
BDS	10	3.79	-1.56	2.23	.10	.0100	.4719	1.49241	2.227	.708	.687	-1.386	1.334
POTE	10	5.909950	1.499950	4.410000	4.410050	1.441005	37175942	********	4.513	.386	.687	-1.483	1.334
SCRATE	10	8.226960	-.132955	8.094005	6.625495	1.662550	87796575	********	7.708	1.852	.687	2.670	1.334
MOOF	10	4.181000	1.081000	3.100000	1.416845	1.141685	43699659	********	1.910	-.112	.687	-1.288	1.334
Valid N (listwise)	8												

Descriptive Statistics – Group 3

Descriptive Statistics

	N	Range	Minimum	Maximum	Sum	Mean		Std.	Variance	Skewness		Kurtosis	
	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic	Statistic	Statistic	Std. Error	Statistic	Std. Error
EPIE	9	11	9	20	129	14.33	1.27	3.808	14.500	-.260	.717	-1.189	1.400
EPIN	9	17	3	20	105	11.67	1.79	5.362	28.750	-.070	.717	-.527	1.400
EPIL	9	5	1	6	31	3.44	.60	1.810	3.278	-.210	.717	-1.322	1.400
HADSANX	9	13	3	16	77	8.56	1.63	4.876	23.778	.439	.717	-1.234	1.400
HADSDEP	9	11	2	13	43	4.78	1.21	3.632	13.194	1.718	.717	2.780	1.400
SUDSPRE	9	6	1	7	33	3.67	.73	2.179	4.750	-.010	.717	-1.572	1.400
SUDPOST1	9	2	1	3	13	1.44	.24	.726	.528	1.501	.717	1.467	1.400
SUDPOST2	9	1	1	2	11	1.22	.15	.441	.194	1.620	.717	.735	1.400
PAINPRE	9	8	0	8	25	2.78	.86	2.587	6.694	.982	.717	.809	1.400
PAINPOST	9	5	0	5	18	2.00	.55	1.658	2.750	.846	.717	-.392	1.400
BDS	9	3.09	-1.37	1.72	1.07	.1189	.3774	1.13223	1.282	.208	.717	-1.437	1.400
POTE	9	6.832895	5.099900	1.732995	-11.5229	-1.28032	77579207	********	5.417	-.225	.717	-.875	1.400
SCRATE	9	9.499900	7.499900	2.000000	-11.0634	-1.22927	95737742	********	8.249	-1.320	.717	2.263	1.400
MOOF	9	9.699900	6.399950	3.299950	-10.6269	-1.18077	1.188853	********	12.720	-.210	.717	-1.634	1.400
Valid N (listwise)	9												

Appendix XI - Repeated Measures ANOVA SPSS output

Within-Subjects Factors

Measure: MEASURE_1

WORD	Dependent Variable
1	POTE
2	MOOF
3	SCRATE

Between-Subjects Factors

		N
GROUP	1	9
	2	10
	3	9

Multivariate Tests

Effect		Value	F	Hypothesis df	Error df	Sig.
WORD	Pillai's Trace	.041	.510[a]	2.000	24.000	.607
	Wilks' Lambda	.959	.510[a]	2.000	24.000	.607
	Hotelling's Trace	.043	.510[a]	2.000	24.000	.607
	Roy's Largest Root	.043	.510[a]	2.000	24.000	.607
WORD * GROUP	Pillai's Trace	.055	.354	4.000	50.000	.840
	Wilks' Lambda	.945	.344[a]	4.000	48.000	.847
	Hotelling's Trace	.058	.333	4.000	46.000	.854
	Roy's Largest Root	.054	.670[b]	2.000	25.000	.521

a. Exact statistic

b. The statistic is an upper bound on F that yields a lower bound on the significance level.

c.
Design: Intercept+GROUP
Within Subjects Design: WORD

Mauchly's Test of Sphericity

Measure: MEASURE_1

Within Subjects Effect	Mauchly's W	Approx. Chi-Square	df	Sig.	Epsilon[a]		
					Greenhouse-Geisser	Huynh-Feldt	Lower-bound
WORD	.955	1.096	2	.578	.957	1.000	.500

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependent proportional to an identity matrix.

a. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tes Tests of Within-Subjects Effects table.

b.
Design: Intercept+GROUP
Within Subjects Design: WORD

Tests of Within-Subjects Effects

Measure: MEASURE_1

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
WORD	Sphericity Assumed	4.112	2	2.056	.420	.659
	Greenhouse-Geisser	4.112	1.914	2.148	.420	.651
	Huynh-Feldt	4.112	2.000	2.056	.420	.659
	Lower-bound	4.112	1.000	4.112	.420	.523
WORD * GROUP	Sphericity Assumed	6.130	4	1.532	.313	.868
	Greenhouse-Geisser	6.130	3.829	1.601	.313	.860
	Huynh-Feldt	6.130	4.000	1.532	.313	.868
	Lower-bound	6.130	2.000	3.065	.313	.734
Error(WORD)	Sphericity Assumed	244.808	50	4.896		
	Greenhouse-Geisser	244.808	47.860	5.115		
	Huynh-Feldt	244.808	50.000	4.896		
	Lower-bound	244.808	25.000	9.792		

Tests of Within-Subjects Contrasts

Measure: MEASURE_1

Source	WORD	Type III Sum of Squares	df	Mean Square	F	Sig.
WORD	Linear	.389	1	.389	.067	.798
	Quadratic	3.723	1	3.723	.936	.342
WORD * GROUP	Linear	2.621	2	1.311	.225	.800
	Quadratic	3.509	2	1.754	.441	.648
Error(WORD)	Linear	145.418	25	5.817		
	Quadratic	99.391	25	3.976		

Tests of Between-Subjects Effects

Measure: MEASURE_1

Transformed Variable: Average

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	.655	1	.655	.073	.789
GROUP	106.300	2	53.150	5.920	.008
Error	224.444	25	8.978		

Transformation Coefficients (M Matrix)

Average

Measure: MEASURE_1
Transformed Variable: AVERAGE

POTE	.577
MOOF	.577
SCRATE	.577

WORD[a]

Measure: MEASURE_1

	WORD	
Dependent Variable	Linear	Quadratic
POTE	-.707	.408
MOOF	.000	-.816
SCRATE	.707	.408

a. The contrasts for the within subjects factors are:
WORD: Polynomial contrast

Hospital Anxiety and Depression Scale - Anxiety

Within-Subjects Factors

Measure: MEASURE_1

WORD	Dependent Variable
1	POTE
2	MOOF
3	SCRATE

Between-Subjects Factors

		N
GROUP	1	9
	2	10
	3	9

Multivariate Tests

Effect		Value	F	Hypothesis df	Error df	Sig.
WORD	Pillai's Trace	.010	.116[a]	2.000	23.000	.889
	Wilks' Lambda	.990	.116[a]	2.000	23.000	.889
	Hotelling's Trace	.010	.116[a]	2.000	23.000	.889
	Roy's Largest Roo	.010	.116[a]	2.000	23.000	.889
WORD * HADSAN	Pillai's Trace	.005	.055[a]	2.000	23.000	.947
	Wilks' Lambda	.995	.055[a]	2.000	23.000	.947
	Hotelling's Trace	.005	.055[a]	2.000	23.000	.947
	Roy's Largest Roo	.005	.055[a]	2.000	23.000	.947
WORD * GROUP	Pillai's Trace	.056	.348	4.000	48.000	.844
	Wilks' Lambda	.944	.336[a]	4.000	46.000	.852
	Hotelling's Trace	.059	.324	4.000	44.000	.860
	Roy's Largest Roo	.053	.631[b]	2.000	24.000	.541

a. Exact statistic

b. The statistic is an upper bound on F that yields a lower bound on the significance level.

c.

Design: Intercept+HADSANX+GROUP
Within Subjects Design: WORD

Mauchly's Test of Sphericity

Measure: MEASURE_1

Within Subjects E	Mauchly's W	Approx. Chi-Square	df	Sig.	Epsilon[a] Greenhous e-Geisser	Huynh-Feldt	Lower-bound
WORD	.956	1.035	2	.596	.958	1.000	.500

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed depen proportional to an identity matrix.

a. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected Tests of Within-Subjects Effects table.

b.
Design: Intercept+HADSANX+GROUP
Within Subjects Design: WORD

Tests of Within-Subjects Effects

Measure: MEASURE_1

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
WORD	Sphericity Assumed	1.190	2	.595	.117	.890
	Greenhouse-Geiss	1.190	1.916	.621	.117	.882
	Huynh-Feldt	1.190	2.000	.595	.117	.890
	Lower-bound	1.190	1.000	1.190	.117	.735
WORD * HADSAN	Sphericity Assumed	.673	2	.336	.066	.936
	Greenhouse-Geiss	.673	1.916	.351	.066	.930
	Huynh-Feldt	.673	2.000	.336	.066	.936
	Lower-bound	.673	1.000	.673	.066	.799
WORD * GROUP	Sphericity Assumed	6.261	4	1.565	.308	.871
	Greenhouse-Geiss	6.261	3.831	1.634	.308	.864
	Huynh-Feldt	6.261	4.000	1.565	.308	.871
	Lower-bound	6.261	2.000	3.131	.308	.738
Error(WORD)	Sphericity Assumed	244.136	48	5.086		
	Greenhouse-Geiss	244.136	45.976	5.310		
	Huynh-Feldt	244.136	48.000	5.086		
	Lower-bound	244.136	24.000	10.172		

Tests of Within-Subjects Contrasts

Measure: MEASURE_1

Source	WORD	Type III Sum of Squares	df	Mean Square	F	Sig.
WORD	Linear	.844	1	.844	.140	.712
	Quadratic	.346	1	.346	.084	.775
WORD * HADSANX	Linear	.493	1	.493	.082	.778
	Quadratic	.180	1	.180	.043	.837
WORD * GROUP	Linear	2.575	2	1.287	.213	.810
	Quadratic	3.686	2	1.843	.446	.645
Error(WORD)	Linear	144.925	24	6.039		
	Quadratic	99.211	24	4.134		

Tests of Between-Subjects Effects

Measure: MEASURE_1
Transformed Variable: Average

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	7.239E-02	1	7.239E-02	.008	.931
HADSANX	2.310E-02	1	2.310E-02	.002	.961
GROUP	99.713	2	49.856	5.332	.012
Error	224.421	24	9.351		

Transformation Coefficients (M Matrix)

Average

Measure: MEASURE_1
Transformed Variable: AVERAGE

POTE	.577
MOOF	.577
SCRATE	.577

WORD[a]

Measure: MEASURE_1

	WORD	
Dependent Variable	Linear	Quadratic
POTE	-.707	.408
MOOF	.000	-.816
SCRATE	.707	.408

a. The contrasts for the within subjects factors are:
WORD: Polynomial contrast

Hospital Anxiety and Depression Scale - Depression

Within-Subjects Factors

Measure: MEASURE_1

WORD	Dependent Variable
1	POTE
2	MOOF
3	SCRATE

Between-Subjects Factors

		N
GROUP	1	9
	2	10
	3	9

Multivariate Tests

Effect		Value	F	Hypothesis df	Error df	Sig.
WORD	Pillai's Trace	.064	.786[a]	2.000	23.000	.467
	Wilks' Lambda	.936	.786[a]	2.000	23.000	.467
	Hotelling's Trace	.068	.786[a]	2.000	23.000	.467
	Roy's Largest Roo	.068	.786[a]	2.000	23.000	.467
WORD * HADSDEI	Pillai's Trace	.067	.821[a]	2.000	23.000	.453
	Wilks' Lambda	.933	.821[a]	2.000	23.000	.453
	Hotelling's Trace	.071	.821[a]	2.000	23.000	.453
	Roy's Largest Roo	.071	.821[a]	2.000	23.000	.453
WORD * GROUP	Pillai's Trace	.054	.332	4.000	48.000	.855
	Wilks' Lambda	.946	.322[a]	4.000	46.000	.862
	Hotelling's Trace	.057	.312	4.000	44.000	.869
	Roy's Largest Roo	.055	.665[b]	2.000	24.000	.524

a. Exact statistic

b. The statistic is an upper bound on F that yields a lower bound on the significance level.

c.
Design: Intercept+HADSDEP+GROUP
Within Subjects Design: WORD

Mauchly's Test of Sphericity

Measure: MEASURE_1

Within Subjects Ef	Mauchly's W	Approx. Chi-Square	df	Sig.	Epsilon[a] Greenhous e-Geisser	Huynh-Feldt	Lower-bound
WORD	.967	.771	2	.680	.968	1.000	.500

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed depende proportional to an identity matrix.

a. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected te Tests of Within-Subjects Effects table.

b.
Design: Intercept+HADSDEP+GROUP
Within Subjects Design: WORD

Tests of Within-Subjects Effects

Measure: MEASURE_1

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
WORD	Sphericity Assumed	8.147	2	4.073	.832	.441
	Greenhouse-Geisse	8.147	1.936	4.208	.832	.438
	Huynh-Feldt	8.147	2.000	4.073	.832	.441
	Lower-bound	8.147	1.000	8.147	.832	.371
WORD * HADSDE	Sphericity Assumed	9.733	2	4.866	.994	.378
	Greenhouse-Geisse	9.733	1.936	5.027	.994	.376
	Huynh-Feldt	9.733	2.000	4.866	.994	.378
	Lower-bound	9.733	1.000	9.733	.994	.329
WORD * GROUP	Sphericity Assumed	6.035	4	1.509	.308	.871
	Greenhouse-Geisse	6.035	3.872	1.559	.308	.866
	Huynh-Feldt	6.035	4.000	1.509	.308	.871
	Lower-bound	6.035	2.000	3.018	.308	.738
Error(WORD)	Sphericity Assumed	235.076	48	4.897		
	Greenhouse-Geisse	235.076	46.467	5.059		
	Huynh-Feldt	235.076	48.000	4.897		
	Lower-bound	235.076	24.000	9.795		

Tests of Within-Subjects Contrasts

Measure: MEASURE_1

Source	WORD	Type III Sum of Squares	df	Mean Square	F	Sig.
WORD	Linear	3.484	1	3.484	.609	.443
	Quadratic	4.663	1	4.663	1.143	.296
WORD * HADSDEP	Linear	8.223	1	8.223	1.438	.242
	Quadratic	1.510	1	1.510	.370	.549
WORD * GROUP	Linear	3.002	2	1.501	.263	.771
	Quadratic	3.034	2	1.517	.372	.693
Error(WORD)	Linear	137.195	24	5.716		
	Quadratic	97.881	24	4.078		

Tests of Between-Subjects Effects

Measure: MEASURE_1

Transformed Variable: Average

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	3.886E-02	1	3.886E-02	.004	.949
HADSDEP	.789	1	.789	.085	.774
GROUP	102.645	2	51.323	5.507	.011
Error	223.654	24	9.319		

Transformation Coefficients (M Matrix)

Average

Measure: MEASURE_1

Transformed Variable: AVERAGE

POTE	.577
MOOF	.577
SCRATE	.577

WORD[a]

Measure: MEASURE_1

	WORD	
Dependent Variable	Linear	Quadratic
POTE	-.707	.408
MOOF	.000	-.816
SCRATE	.707	.408

a. The contrasts for the within subjects factors are:
WORD: Polynomial contrast

Within-Subjects Factors

Measure: MEASURE_1

WORD	Dependent Variable
1	POTE
2	MOOF
3	SCRATE

Between-Subjects Factors

		N
GROUP	1	9
	2	10
	3	9

Multivariate Tests

Effect		Value	F	Hypothesis df	Error df	Sig.
WORD	Pillai's Trace	.044	.535[a]	2.000	23.000	.593
	Wilks' Lambda	.956	.535[a]	2.000	23.000	.593
	Hotelling's Trace	.046	.535[a]	2.000	23.000	.593
	Roy's Largest Root	.046	.535[a]	2.000	23.000	.593
WORD * EPIE	Pillai's Trace	.041	.491[a]	2.000	23.000	.618
	Wilks' Lambda	.959	.491[a]	2.000	23.000	.618
	Hotelling's Trace	.043	.491[a]	2.000	23.000	.618
	Roy's Largest Root	.043	.491[a]	2.000	23.000	.618
WORD * GROUP	Pillai's Trace	.053	.330	4.000	48.000	.857
	Wilks' Lambda	.947	.319[a]	4.000	46.000	.864
	Hotelling's Trace	.056	.309	4.000	44.000	.871
	Roy's Largest Root	.052	.630[b]	2.000	24.000	.541

a. Exact statistic

b. The statistic is an upper bound on F that yields a lower bound on the significance level.

c.

Design: Intercept+EPIE+GROUP
Within Subjects Design: WORD

Mauchly's Test of Sphericity[b]

Measure: MEASURE_1

Within Subjects Ef	Mauchly's W	Approx. Chi-Square	df	Sig.	Epsilon[a]		
					Greenhous e-Geisser	Huynh-Feldt	Lower-bound
WORD	.962	.882	2	.643	.964	1.000	.500

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependen proportional to an identity matrix.

a. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tes Tests of Within-Subjects Effects table.

b.

Design: Intercept+EPIE+GROUP
Within Subjects Design: WORD

Tests of Within-Subjects Effects

Measure: MEASURE_1

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
WORD	Sphericity Assumed	6.128	2	3.064	.616	.544
	Greenhouse-Geisse	6.128	1.927	3.179	.616	.539
	Huynh-Feldt	6.128	2.000	3.064	.616	.544
	Lower-bound	6.128	1.000	6.128	.616	.440
WORD * EPIE	Sphericity Assumed	5.949	2	2.974	.598	.554
	Greenhouse-Geisse	5.949	1.927	3.086	.598	.548
	Huynh-Feldt	5.949	2.000	2.974	.598	.554
	Lower-bound	5.949	1.000	5.949	.598	.447
WORD * GROUI	Sphericity Assumed	5.765	4	1.441	.290	.883
	Greenhouse-Geisse	5.765	3.855	1.496	.290	.877
	Huynh-Feldt	5.765	4.000	1.441	.290	.883
	Lower-bound	5.765	2.000	2.883	.290	.751
Error(WORD)	Sphericity Assumed	238.860	48	4.976		
	Greenhouse-Geisse	238.860	46.259	5.164		
	Huynh-Feldt	238.860	48.000	4.976		
	Lower-bound	238.860	24.000	9.952		

Tests of Within-Subjects Contrasts

Measure: MEASURE_1

Source	WORD	Type III Sum of Squares	df	Mean Square	F	Sig.
WORD	Linear	3.955	1	3.955	.675	.419
	Quadratic	2.173	1	2.173	.530	.474
WORD * EPIE	Linear	4.888	1	4.888	.835	.370
	Quadratic	1.060	1	1.060	.259	.616
WORD * GROUP	Linear	1.939	2	.970	.166	.848
	Quadratic	3.826	2	1.913	.467	.633
Error(WORD)	Linear	140.529	24	5.855		
	Quadratic	98.330	24	4.097		

Tests of Between-Subjects Effects

Measure: MEASURE_1

Transformed Variable: Average

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	5.055	1	5.055	.556	.463
EPIE	6.381	1	6.381	.702	.410
GROUP	104.777	2	52.389	5.766	.009
Error	218.062	24	9.086		

Transformation Coefficients (M Matrix)

Average

Measure: MEASURE_1

Transformed Variable: AVERAGE

POTE	.577
MOOF	.577
SCRATE	.577

WORD[a]

Measure: MEASURE_1

	WORD	
Dependent Variable	Linear	Quadratic
POTE	-.707	.408
MOOF	.000	-.816
SCRATE	.707	.408

a. The contrasts for the within subjects factors are:
WORD: Polynomial contrast

Eysenck Personality Inventory – Neuroticism

Within-Subjects Factors

Measure: MEASURE_1

WORD	Dependent Variable
1	POTE
2	MOOF
3	SCRATE

Between-Subjects Factors

		N
GROUP	1	9
	2	10
	3	9

Multivariate Tests

Effect		Value	F	Hypothesis df	Error df	Sig.
WORD	Pillai's Trace	.039	.472[a]	2.000	23.000	.630
	Wilks' Lambda	.961	.472[a]	2.000	23.000	.630
	Hotelling's Trace	.041	.472[a]	2.000	23.000	.630
	Roy's Largest Root	.041	.472[a]	2.000	23.000	.630
WORD * EPIN	Pillai's Trace	.064	.791[a]	2.000	23.000	.465
	Wilks' Lambda	.936	.791[a]	2.000	23.000	.465
	Hotelling's Trace	.069	.791[a]	2.000	23.000	.465
	Roy's Largest Root	.069	.791[a]	2.000	23.000	.465
WORD * GROUP	Pillai's Trace	.058	.358	4.000	48.000	.838
	Wilks' Lambda	.942	.346[a]	4.000	46.000	.845
	Hotelling's Trace	.061	.334	4.000	44.000	.853
	Roy's Largest Root	.055	.662[b]	2.000	24.000	.525

a. Exact statistic

b. The statistic is an upper bound on F that yields a lower bound on the significance level.

c.

Design: Intercept+EPIN+GROUP
Within Subjects Design: WORD

Mauchly's Test of Sphericity

Measure: MEASURE_1

Within Subjects Eff	Mauchly's W	Approx. Chi-Square	df	Sig.	Epsilon[a]		
					Greenhouse-Geisser	Huynh-Feldt	Lower-bound
WORD	.959	.968	2	.616	.960	1.000	.500

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependent proportional to an identity matrix.

a. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tests Tests of Within-Subjects Effects table.

b.

Design: Intercept+EPIN+GROUP
Within Subjects Design: WORD

Tests of Within-Subjects Effects

Measure: MEASURE_1

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
WORD	Sphericity Assumed	5.555	2	2.778	.564	.573
	Greenhouse-Geisser	5.555	1.921	2.892	.564	.566
	Huynh-Feldt	5.555	2.000	2.778	.564	.573
	Lower-bound	5.555	1.000	5.555	.564	.460
WORD * EPIN	Sphericity Assumed	8.442	2	4.221	.857	.431
	Greenhouse-Geisser	8.442	1.921	4.395	.857	.427
	Huynh-Feldt	8.442	2.000	4.221	.857	.431
	Lower-bound	8.442	1.000	8.442	.857	.364
WORD * GROUP	Sphericity Assumed	6.224	4	1.556	.316	.866
	Greenhouse-Geisser	6.224	3.842	1.620	.316	.859
	Huynh-Feldt	6.224	4.000	1.556	.316	.866
	Lower-bound	6.224	2.000	3.112	.316	.732
Error(WORD)	Sphericity Assumed	236.367	48	4.924		
	Greenhouse-Geisser	236.367	46.100	5.127		
	Huynh-Feldt	236.367	48.000	4.924		
	Lower-bound	236.367	24.000	9.849		

Tests of Within-Subjects Contrasts

Measure: MEASURE_1

Source	WORD	Type III Sum of Squares	df	Mean Square	F	Sig.
WORD	Linear	5.555	1	5.555	.969	.335
	Quadratic	2.890E-04	1	2.890E-04	.000	.993
WORD * EPIN	Linear	7.805	1	7.805	1.361	.255
	Quadratic	.636	1	.636	.155	.698
WORD * GROUP	Linear	2.787	2	1.393	.243	.786
	Quadratic	3.437	2	1.719	.418	.663
Error(WORD)	Linear	137.612	24	5.734		
	Quadratic	98.755	24	4.115		

Tests of Between-Subjects Effects

Measure: MEASURE_1

Transformed Variable: Average

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	5.481	1	5.481	.608	.443
EPIN	8.131	1	8.131	.902	.352
GROUP	109.531	2	54.766	6.076	.007
Error	216.312	24	9.013		

Transformation Coefficients (M Matrix)

Average

Measure: MEASURE_1

Transformed Variable: AVERAGE

POTE	.577
MOOF	.577
SCRATE	.577

WORD[a]

Measure: MEASURE_1

	WORD	
Dependent Variable	Linear	Quadratic
POTE	-.707	.408
MOOF	.000	-.816
SCRATE	.707	.408

a. The contrasts for the within subjects factors are:
WORD: Polynomial contrast

Within-Subjects Factors

Measure: MEASURE_1

WORD	Dependent Variable
1	POTE
2	MOOF
3	SCRATE

Between-Subjects Factors

		N
GROUP	1	9
	2	10
	3	9

Multivariate Tests

Effect		Value	F	Hypothesis df	Error df	Sig.
WORD	Pillai's Trace	.081	1.010[a]	2.000	23.000	.380
	Wilks' Lambda	.919	1.010[a]	2.000	23.000	.380
	Hotelling's Trace	.088	1.010[a]	2.000	23.000	.380
	Roy's Largest Root	.088	1.010[a]	2.000	23.000	.380
WORD * EPIL	Pillai's Trace	.072	.894[a]	2.000	23.000	.423
	Wilks' Lambda	.928	.894[a]	2.000	23.000	.423
	Hotelling's Trace	.078	.894[a]	2.000	23.000	.423
	Roy's Largest Root	.078	.894[a]	2.000	23.000	.423
WORD * GROUP	Pillai's Trace	.054	.333	4.000	48.000	.854
	Wilks' Lambda	.946	.323[a]	4.000	46.000	.861
	Hotelling's Trace	.057	.312	4.000	44.000	.868
	Roy's Largest Root	.053	.633[b]	2.000	24.000	.540

a. Exact statistic

b. The statistic is an upper bound on F that yields a lower bound on the significance level.

c.

Design: Intercept+EPIL+GROUP
Within Subjects Design: WORD

Mauchly's Test of Sphericity

Measure: MEASURE_1

Within Subjects Eff	Mauchly's W	Approx. Chi-Square	df	Sig.	Epsilon[a]		
					Greenhouse-Geisser	Huynh-Feldt	Lower-bound
WORD	.963	.858	2	.651	.965	1.000	.500

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependent proportional to an identity matrix.

a. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tests Tests of Within-Subjects Effects table.

b.

Design: Intercept+EPIL+GROUP
Within Subjects Design: WORD

Tests of Within-Subjects Effects

Measure: MEASURE_1

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
WORD	Sphericity Assumed	9.871	2	4.935	1.009	.372
	Greenhouse-Geisser	9.871	1.929	5.116	1.009	.370
	Huynh-Feldt	9.871	2.000	4.935	1.009	.372
	Lower-bound	9.871	1.000	9.871	1.009	.325
WORD * EPIL	Sphericity Assumed	9.984	2	4.992	1.020	.368
	Greenhouse-Geisser	9.984	1.929	5.175	1.020	.366
	Huynh-Feldt	9.984	2.000	4.992	1.020	.368
	Lower-bound	9.984	1.000	9.984	1.020	.323
WORD * GROUP	Sphericity Assumed	6.619	4	1.655	.338	.851
	Greenhouse-Geisser	6.619	3.859	1.715	.338	.845
	Huynh-Feldt	6.619	4.000	1.655	.338	.851
	Lower-bound	6.619	2.000	3.309	.338	.716
Error(WORD)	Sphericity Assumed	234.825	48	4.892		
	Greenhouse-Geisser	234.825	46.304	5.071		
	Huynh-Feldt	234.825	48.000	4.892		
	Lower-bound	234.825	24.000	9.784		

Tests of Within-Subjects Contrasts

Measure: MEASURE_1

Source	WORD	Type III Sum of Squares	df	Mean Square	F	Sig.
WORD	Linear	3.199	1	3.199	.554	.464
	Quadratic	6.671	1	6.671	1.666	.209
WORD * EPIL	Linear	6.704	1	6.704	1.160	.292
	Quadratic	3.279	1	3.279	.819	.375
WORD * GROUP	Linear	4.708	2	2.354	.407	.670
	Quadratic	1.910	2	.955	.239	.790
Error(WORD)	Linear	138.713	24	5.780		
	Quadratic	96.112	24	4.005		

Tests of Between-Subjects Effects

Measure: MEASURE_1

Transformed Variable: Average

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	3.526E-02	1	3.526E-02	.004	.952
EPIL	.105	1	.105	.011	.916
GROUP	106.260	2	53.130	5.684	.010
Error	224.339	24	9.347		

Transformation Coefficients (M Matrix)

Average

Measure: MEASURE_1

Transformed Variable: AVERAGE

POTE	.577
MOOF	.577
SCRATE	.577

WORD[a]

Measure: MEASURE_1

	WORD	
Dependent Variable	Linear	Quadratic
POTE	-.707	.408
MOOF	.000	-.816
SCRATE	.707	.408

a. The contrasts for the within subjects factors are:
WORD: Polynomial contrast

Behavioural Distress Scale

Within-Subjects Factors

Measure: MEASURE_1

WORD	Dependent Variable
1	POTE
2	MOOF
3	SCRATE

Between-Subjects Factors

		N
GROUP	1	9
	2	10
	3	9

Multivariate Tests

Effect		Value	F	Hypothesis df	Error df	Sig.
WORD	Pillai's Trace	.037	.442[a]	2.000	23.000	.648
	Wilks' Lambda	.963	.442[a]	2.000	23.000	.648
	Hotelling's Trace	.038	.442[a]	2.000	23.000	.648
	Roy's Largest Root	.038	.442[a]	2.000	23.000	.648
WORD * BDS	Pillai's Trace	.035	.419[a]	2.000	23.000	.663
	Wilks' Lambda	.965	.419[a]	2.000	23.000	.663
	Hotelling's Trace	.036	.419[a]	2.000	23.000	.663
	Roy's Largest Root	.036	.419[a]	2.000	23.000	.663
WORD * GROUP	Pillai's Trace	.056	.343	4.000	48.000	.848
	Wilks' Lambda	.945	.332[a]	4.000	46.000	.855
	Hotelling's Trace	.058	.320	4.000	44.000	.863
	Roy's Largest Root	.052	.627[b]	2.000	24.000	.543

a. Exact statistic

b. The statistic is an upper bound on F that yields a lower bound on the significance level.

c.

Design: Intercept+BDS+GROUP
Within Subjects Design: WORD

Mauchly's Test of Sphericity

Measure: MEASURE_1

Within Subjects Ef	Mauchly's W	Approx. Chi-Square	df	Sig.	Epsilon[a] Greenhouse-Geisser	Huynh-Feldt	Lower-bound
WORD	.958	.985	2	.611	.960	1.000	.500

Tests the null hypothesis that the error covariance matrix of the orthonormalized transformed dependen proportional to an identity matrix.

a. May be used to adjust the degrees of freedom for the averaged tests of significance. Corrected tes Tests of Within-Subjects Effects table.

b.

Design: Intercept+BDS+GROUP
Within Subjects Design: WORD

Tests of Within-Subjects Effects

Measure: MEASURE_1

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
WORD	Sphericity Assumed	3.740	2	1.870	.374	.690
	Greenhouse-Geisse	3.740	1.920	1.948	.374	.682
	Huynh-Feldt	3.740	2.000	1.870	.374	.690
	Lower-bound	3.740	1.000	3.740	.374	.547
WORD * BDS	Sphericity Assumed	4.691	2	2.346	.469	.629
	Greenhouse-Geisse	4.691	1.920	2.444	.469	.621
	Huynh-Feldt	4.691	2.000	2.346	.469	.629
	Lower-bound	4.691	1.000	4.691	.469	.500
WORD * GROUI	Sphericity Assumed	6.303	4	1.576	.315	.867
	Greenhouse-Geisse	6.303	3.839	1.642	.315	.860
	Huynh-Feldt	6.303	4.000	1.576	.315	.867
	Lower-bound	6.303	2.000	3.151	.315	.733
Error(WORD)	Sphericity Assumed	240.117	48	5.002		
	Greenhouse-Geisse	240.117	46.069	5.212		
	Huynh-Feldt	240.117	48.000	5.002		
	Lower-bound	240.117	24.000	10.005		

Tests of Within-Subjects Contrasts

Measure: MEASURE_1

Source	WORD	Type III Sum of Squares	df	Mean Square	F	Sig.
WORD	Linear	.649	1	.649	.109	.744
	Quadratic	3.091	1	3.091	.762	.391
WORD * BDS	Linear	2.705	1	2.705	.455	.506
	Quadratic	1.986	1	1.986	.489	.491
WORD * GROUP	Linear	3.111	2	1.556	.262	.772
	Quadratic	3.191	2	1.596	.393	.679
Error(WORD)	Linear	142.713	24	5.946		
	Quadratic	97.404	24	4.059		

Tests of Between-Subjects Effects

Measure: MEASURE_1
Transformed Variable: Average

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Intercept	.395	1	.395	.043	.838
BDS	2.418	1	2.418	.261	.614
GROUP	104.162	2	52.081	5.630	.010
Error	222.026	24	9.251		

Transformation Coefficients (M Matrix)

Average

Measure: MEASURE_1
Transformed Variable: AVERAGE

POTE	.577
MOOF	.577
SCRATE	.577

WORD[a]

Measure: MEASURE_1

	WORD	
Dependent Variable	Linear	Quadratic
POTE	-.707	.408
MOOF	.000	-.816
SCRATE	.707	.408

a. The contrasts for the within subjects factors are:
WORD: Polynomial contrast

Do I have to take part?

It is up to you to decide whether or not to take part. If you decide to take part you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time or a decision not to take part will not affect the standard of care you receive.

What will happen to me if I take part?

Immediately before your colonoscopy, you will attend a very short interview in which you will you be asked some basic questions about your health and colonoscopy. You will also be asked to listen to a tape recording of some words whilst a machine measures the sweating on your hand. Some stick-on surface pads will be placed on your fingers. This is not harmful or painful in any way. During your colonoscopy you will also listen to another tape recording using a personal stereo and headphones. After your colonoscopy you will be given a very short questionnaire to complete in the recovery ward before you leave the hospital.

On the day of your Colonoscopy an appointment will be arranged for you to come back to the Endoscopy Department within 1-2 weeks after your Colonoscopy to see what you remember about the procedure and the words you were presented with in the headphones and to redo the test that measures sweating on your fingers whilst listening to word tapes. You will also be asked to complete a couple of short questionnaires about mood and personality. It should only take about 10 minutes but it is essential to the study, without this follow-up meeting the initial information taken on the day of your colonoscopy will not be able to be used for the research.

This type of study is called a double blind trial. This means that neither you, your doctor or the researcher will know which group you are in i.e. what words are going to be presented to you by the personal stereo during the colonoscopy. However, we will be able to find out if it is necessary.

What are the possible disadvantages and risks of taking part?

There are no risks or disadvantages of taking part in this study.

What are the possible benefits of taking part?

No, there are no individual benefits but the results may have wider implications and help other people who will be undergoing colonoscopies in the future.

Will my taking part in this study be kept confidential?

If you consent to take part in the research any of your medical records regarding the colonoscopy may be looked at by myself where it is relevant to your taking part in this research. However, all information that is collected about you during the course of the research will be kept strictly confidential. Any information about you will have your name and address removed and a participant number put in its place so that you cannot be recognized from it. The information you provide will not be passed onto another party.

What will happen to the results of the research study?

The results of this study will be written up as a doctoral thesis for the course and as a journal article to submit for possible publication. However, you will not be identified and your data will be labeled with an anonymous participant number, for which, only I will be aware of. If my journal article is published you can obtain a copy by writing or telephoning the Department of Clinical Psychology at the University of Hull.

Who has reviewed the study?

The Hull and East Riding Local Research Ethics Committee has approved this study.

Contact for Further Information.

You can contact me (Joanne Beckett, Trainee Clinical Psychologist) at:

Department of Clinical Psychology
School of Medicine
Robert Blackburn Building
The University of Hull
Cottingham Road
Hull
HU6 7RX
Tel: 01482 465933
Fax: 01482 466155

Thank you for taking part in my study.

You will be provided with a copy of this information sheet and your signed consent form to keep should you agree to participate in this study.

Appendix VIII – Consent Form

THE UNIVERSITY OF HULL
ACADEMIC SURGICAL UNIT
CASTLE HILL HOSPITAL • CASTLE ROAD • COTTINGHAM • HULL HU16 5JQ
TELEPHONE 01482 623225/623247/623077 • FACSIMILE 01482 623274

Consent Form

Title of Project: **Memory effects following a colonoscopy**

Name of Researcher: Joanne Beckett BSc (HONS)
Trainee Clinical Psychologist

1. I confirm that I have read and understood the information sheet for the above study and have had the opportunity to ask questions. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐
3. I understand that sections of my medical notes relating to my taking part in the study may be looked at by the researcher. I give permission for these individuals to have access to my records. ☐
4. I agree to take part in the above study. ☐

Name of Patient	Date	Signature
Name of Person taking consent	Date	Signature
Researcher	Date	Signature

Copies will be provided for the patient, the researcher and the hospital notes.