

The relationship between traumatic life events, high cortisol and Alzheimer's disease: A case
study

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ABSTRACT

This case study serves as the first stage of a pilot study for a large research project that aims to determine whether there is an underlying link between stressful life events, the levels of cortisol (a stress hormone), and risk of developing Alzheimer's disease (AD). In this study, an individual previously and independently diagnosed with AD (patient HA) and a matched control group consisting of 4 healthy participants were administered a battery of cognitive and memory tests, a life events questionnaire, a resilience questionnaire, and a subjective stress measurement. Afterwards, they were asked to swab their saliva at 9am for three consecutive days so to obtain a measurement of their cortisol. It was hypothesized that the patient HA would have lower cognitive and memory scores, higher neuroticism, lower resilience and experienced more stressful life events than the control group. However, results indicate that patient HA had lower memory scores, but not higher neuroticism, lower resilience or experienced more stressful life events.

There is much interest in the adverse effects of stress on the human body. It is commonly known that too much stress is bad for one's health, and many precautions can be taken to relieve stress. Stress not only affects the physical body, but also results in impaired cognition as well. The body reacts to stress by releasing a hormone, cortisol, which assists in survival. However, excessive cortisol levels have been related to cognitive impairments, suggesting that the more stress one experiences, the worse one's cognitive performance. Patients with Alzheimer's disease (AD) experience memory impairment and some studies have illustrated that they have higher cortisol levels. If cortisol levels predict memory impairment, it would be interesting to see whether cortisol levels play a predictive role in the development of AD. This research is particularly relevant in the South African context, as South Africa was governed by a cruel apartheid regime, and now battles with a high crime rate, unemployment, and poverty – resulting in much distress for most South Africans. If excessive cortisol is a risk factor for the development of AD, then South Africans may be at a greater risk for developing AD than other population. No South African studies have outlined the relationship of cortisol levels of patients with Alzheimer's disease with the lifestyle and events that they have experienced.

LITERATURE REVIEW

Stress and Glucocorticoids

Kemeny (2003, p. 124) defines stressors as “circumstances that threaten a major goal, including the maintenance of one's physical integrity (physical stressors) or one's psychological well-being (psychological stressors).” She states that a possible response to these stressors is distress, “a negative psychological response to such threats [that] can include a variety of affective and cognitive states, such as anxiety, sadness, frustration, the sense of being overwhelmed, or helplessness” (p. 124). When the body responds to a stressor, the hypothalamic-pituitary-adrenal (HPA) axis is stimulated. A chain effect occurs, in which the hypothalamus secretes corticotrophin releasing factor (CRF), which stimulates the secretion of adrenocorticotropin hormone (ACTH) from the pituitary gland. ACTH triggers the release of glucocorticoids (GCs) from the adrenal cortex (Lupien et al., 2005). In humans, GCs occur are called cortisol. GCs follow a circadian rhythm, with humans having maximum GCs levels in the morning (circadian peak), which decline throughout the day (circadian trough) but peak again during sleep.

GCs bind to two different receptors, mineralocorticoid (MRs) and glucocorticoid receptors (GRs). During the circadian trough, GCs bind to 90% of MRs and 10% of GRs; during the circadian peak, MRs are saturated with GCs, whereas 67-74% of GRs are occupied. The MR and GR occupation during the circadian peak of GC secretion are replicated with exposure to stress. Essentially, GCs enhance the bodily processes which would lead to survival. That is to say, heart rate increases, blood pressure increases, and muscle tone increases; these are only some of the processes that enhance chances of survival during a critical period. The increase in glucose and oxygen in the blood, due to stress, also affects the brain, resulting in improved memory formation and retrieval. Both the hippocampus and the medial prefrontal cortex contain a large amount of glucocorticoid receptors (Cook & Wellman, 2004, Lyons, Lopez, Yang, & Scgatzburg, 2000). Specifically, MRs are situated in the limbic system, predominantly in the hippocampus, parahippocampal gyrus, entorhinal, and insular cortices, while GRs are found in subcortical structures (paraventricular nucleus and other hypothalamic nuclei, the hippocampus and parahippocampal gyrus) and cortical structures, predominately the prefrontal cortex (Lupien et al. 2005). Cognitive function improves when most of the MRs, and few GRs are stimulated. Conversely, significantly high or low amounts of GCs within the body result in cognitive impairments (de Kloet, Oitzl, & Joëls, 1999).

Brain structures and functions

The hippocampally based memory system is one of multiple memory systems in the brain. It is believed that the hippocampus and its neighbouring regions are responsible for new learning and declarative memory, especially episodic memory processes (Bäckham, Jones, Berger, Laukka, & Small, 2005). It has been suggested that the right hippocampus plays a primary role in allocentric visual-spatial mapping, while the left hippocampus is responsible for episodic/autobiographical memory (Burgess, Maguire, & O'Keefe, 2002).

GCs and impaired memory

It is believed that excessive exposure to GCs results in neuronal damage in regions which contain GC receptors, specifically the hippocampus and medial prefrontal cortex (Lupien et al., 1998). These excessive levels of glucocorticoids are associated with hippocampal atrophy in

both rats and humans (Seckl & Olsson, 1995; Lupien et al., 1998 as cited in MacLulich et al., 2005), and may have an adverse effect on the temporal lobes in general (van der Beek et al., 2004).

This relationship between GCs and memory has been demonstrated in research on individuals using corticosteroid treatment and people diagnosed with Cushing's disease (which involves the oversecretion of GCs) (Starkman, Gebarski, Berent, Schteingart, 1992; Ling, Perry, & Tsuang, 1981, cited in Lupien et al., 2005). Both sets of patients reported memory impairments and displayed hippocampal atrophy. Other studies have illustrates the relationship between high glucocorticoids and deficits in attention (Wolkowitz, 1994), working memory (Lupien, Gillin, & Hauger, 1999) and declarative memory (Newcomer et al., 1999, as cited in MacLulich et al., 2005).

In a study on the relationship between plasma cortisol levels, brain volumes, and cognition in 97 healthy older men (mean age 65-70 years), correlations were found that supported the suggested effect of GCs on memory. Each man's performance on nine cognitive scales (each describing a different domain) was recorded, and blood was drawn on the same day at 09h00 and 14h30. A significant, negatively correlated relationship was found between cortisol levels at 09h00 and scores on measures of attention and processing speed and of delayed paragraph recall. The researchers suggest that the 09h00 cortisol level was correlated with delayed paragraph recall because delayed memory is influenced by the functioning of the hippocampus. Furthermore, left temporal lobe volume was significantly negatively correlated with 14h30 cortisol levels, a finding that corresponds with other studies that have found the left cerebral hemisphere to be particularly influenced by abnormalities in cortisol levels (Campbell, Marriott, Nahmias, MacQueen, 2004; van der Beek et al., 2004).

Similar results were found in a study examining the relationship between declarative memory and cortisol in 139 healthy elderly people (Wright, Kunz-Ebrecht, Iliffe, Foese, & Steptoe, 2005). Three cognitive tests were administered: verbal paired associates (VPA-I); matrix reasoning (MR); and Verbal Paired Associates recall & recognition (VPA-II). Results showed only a significant negative correlation between VPA-II scores and cortisol levels, independent of

age, sex, time of day, medication, chronic illness, education and task appraisals (individual's assessment of task difficulty and subject stress). The authors further stated that because of the lack of association between MR and cortisol levels, cortisol levels may only be related to memory (as opposed to general cognition). These results, therefore, support the notion that this relationship is controlled by the hippocampus.

The two studies reviewed above were cross-sectional, and therefore causality could not be supposed. To partially remedy this limitation, Karlamangla, Singer, Chodos, McEwen, and Seeman's (2005) longitudinal study examined cortisol urinary excretion in 538 people, and assessed their cognitive functioning. They found that the initial urinary cortisol level was positively correlated with the risk of cognitive impairment. Similarly, Li et al. (2006) conducted a 3-year longitudinal study on 46 healthy elderly people to determine if memory function (which was assessed by numerous cognitive tests) was related to salivary cortisol levels. Groups were divided according to the initial cortisol level; the high cortisol group showed a steep decline in paragraph recall skills. People who had increasing cortisol levels across the 3 levels had the worst verbal recall skills.

Stress and Alzheimer's Disease

Dementia of the Alzheimer's type is characterized by memory impairment, which is often tested by asking the individual to learn new information, and by progressive deterioration of intellectual and emotional functioning. Dysfunction in another domain, such as language, executive function, motor and so forth, may be present as well (American Psychiatric Association, 2000; Sue et al., 2003).

The histology of brain tissue, removed during an autopsy, indicates extreme formations of amyloid plaques and neurofibrillary tangles. These two neuropathological features are hallmarks of AD. Neuroimaging and autopsy will demonstrate that atrophy of the frontal, parietal and temporal lobes occur.

Although age is the most prominent risk factor for AD, stress may also increase the risk of developing the disease (Green, Billings, Roozendaal, McGaugh, & LaFerla, 2006). In a study

consisting 806 elderly people, it was suggested that the tendency to experience psychological distress (i.e., stress) predicted cognitive decline and the likelihood of Alzheimer's disease (Wilson et al., 2003). In this particular study, distress proneness was associated with impairments in general cognition, episodic memory, working memory and perceptual speed.

Weiner, Vobach, Olsson, Svetlik, and Risser (1999) conducted a study on the relationship between cortisol secretion and AD, with a sample of 19 AD patients, of whom 9 were assessed longitudinally. They found that higher cortisol levels at 12h00 were associated with a rapid decline in cognitive skills. Umegaki et al. (2000) examined the plasma cortisol levels of 115 patients (66 were diagnosed with AD; 28 were diagnosed with vascular dementia (VD); 21 served as non-demented controls), in a cross-sectional and longitudinal study. Both AD and VD patients had significantly higher cortisol levels than the control group. The cortisol levels of the AD patients were reexamined after 40 months, and although these levels did not decline significantly, their MMSE scores had. AD patients who had higher cortisol levels in the initial testing also presented with a more rapid progression of AD.

There are concerns that the high cortisol levels in AD patients may be a result of the disease, and may not have preceded the disease. Green et al. (2006) dispute this notion, arguing that stress can be a causal factor, alongside other environmental and genetic factors. They administered glucocorticoid amounts, equivalent to the amount produced during stress, to *in vitro* and *in vivo* systems of rats. In the *in vitro* system, exposure to increased levels of GCs increased the formation of amyloid β -peptide ($A\beta$) plaques, which is a hallmark of AD.

Numerous studies have demonstrated that GCs have an effect on memory function, as the hippocampus is very sensitive to GCs. High levels of GCs result in a decline in memory function, in particular declarative memory. High levels of GCs also predict rapid future memory decline. Therefore, since that high cortisol levels may precede the development and be a potential risk factor of AD, it would be of significant interest to investigate the relationship between the cortisol levels of AD patients, their memory scores and their subjective life experiences.

SPECIFIC AIMS AND HYPOTHESES

This pilot study forms the foundation for a much larger project that will continue next year. One AD participant was recruited to see whether we could accurately test our hypotheses, and test materials. The specific aims of this pilot study are to determine whether patient HA, who has been diagnosed with Alzheimer's disease, has worse memory scores, higher neuroticism and experienced more stressful life events than the control group. The larger study, which this study forms part, aims to determine whether older adults diagnosed with Alzheimer's disease have higher cortisol levels than the control group, and have experienced many stressful events during their lifetimes, which could contribute to an overall higher level of cortisol. If these individuals have experienced a high number (and/or a more severe degree) of stressful events, then we can assume that lifetime psychosocial stress, and consequent high cortisol levels, may be a risk factor for the development of AD. This result will have many implications for AD patients; for instance, if cortisol levels can be regulated or decreased, the onset and/or progression of AD may be delayed.

My specific hypotheses are that (a) patient HA will have worse memory scores than the control group, (b) patient HA will have higher neuroticism than the control group, and (c) patient HA experienced more traumatic life events than the control group.

DESIGN AND METHODOLOGY

Design

This is a case study design where the memory test and questionnaire scores of 1 adult diagnosed with AD, patient HA, are contrasted with those of 4 healthy matched (age, SES) controls.

Participants

Five participants were recruited in this study – one case-study patient and four controls matched for age and SES. The patient, HA, is a 76-year-old woman independently diagnosed (By Dr

Marc Combrinck, a neurologist who works at Groote Schuur Hospital) with possible AD, and deemed eligible after the telephonic screening. The four control participants were healthy community-dwelling adults. In recruiting this AD patient, the following exclusion criteria were used: psychiatric disorders (e.g., current depression, or anxiety disorders), neurological disorders (e.g., Parkinson's disease, Huntington's disease, epilepsy not due to AD etc), stroke, loss of consciousness, HIV/AIDS, uncontrolled hypertension, uncontrolled diabetes, alcoholism, drug abuse, smoking \geq 12 cigarettes a day (resulting in cortisol being 40% higher than that of non-smoking population; Steptoe & Ussher, 2006), steroid treatment and not having English as their first language. The severity of patient HA's AD was assessed by Dr Combrinck and she was deemed eligible for the study.

The four control participants were healthy community-dwelling adults aged over 65 years. The exclusion criteria for the control group was similar to those of patient HA, and included a MMSE score <24 .

Ethical approval for the study procedures was granted by both the UCT Department of Psychology and the UCT Faculty of Health Sciences Ethics Committee. All participants in the control group gave their full informed consent for participation. Patient HA's husband, who is her legal guardian, consented for her to participate in the study.

Materials/ Apparatus

Demographic questionnaire: The participants of both groups (control and patient) were administered a demographic questionnaire developed for this study (see Appendix A).

Life events questionnaire: The Life events questionnaire used consisted of 11 statements, and the participant had to indicate whether or not they had experienced any of these events, and in which time slot (in the past 6 months, or longer than 6 months ago).

CD-RISC: The Connor-Davidson resilience scale (CD-RISC; Connor & Davidson, 2003) measures resilience, the ability to adapt to challenging situations. It consists of 25 statements

(such as “I like challenges”, “Not easily discouraged by failure”, and “See the humorous side of things”), each rated on a 5 point scale (0 indicates “not true at all” and 5 indicates “true all the time”) relating to the individual. These responses are tallied to determine a total score between 0 and 100. A high total score illustrates high resilience in an individual. The CD-RISC has demonstrated high test-retest reliability, and validity, and is successful in measuring resilience in both clinical and normal populations (Connor & Davidson, 2003). Although it has been translated into Afrikaans, no published South African studies have been found that used this scale.

CAMCOG-R. The *Cambridge Mental Disorders of the Elderly Examination-Revised* (CAMDEX-R) was developed to detect and track dementia in the elderly (Lezak et al., 2004). The CAMDEX-R consists of three sections, of which two are structured interviews (one with the patient, and the other with an individual who is knowledgeable about the patient’s condition, medical history, and family history) and the other is the CAMCOG-R (The *Cambridge Cognitive Examination-Revised*). The CAMCOG-R consists of 67 items, divided into 8 different domains: Orientation; Language; Memory; Attention; Praxis; Calculation; Abstract Thinking and Perception. Testing time is 25 minutes, and the maximum attainable score is 107. The 19 questions which make up the MMSE are present in the CAMCOG-R; therefore one can derive an MMSE score from the CAMCOG-R questions. The CAMCOG-R was altered so that it was more suitable for a South African population (see Appendix C for the changes). In accordance with these changes, the accompanying booklet (which contains pictures that relate to some of the test's questions) had to be reprinted with less culturally biased images.

BADLS. The *Bristol Activities of Daily Living Scale (BADLS)* is designed to measure the functional ability (finances, dressing, eating and so forth) of patients suffering from memory problems, and is completed by the caretaker (Brucks, Ashworth, Wilcock, & Siegfried, 1996). However, when this questionnaire was administered to the control group, they answered it about themselves. It consists of 20 questions, has high test-retest reliability and validity, and is strongly correlated to the MMSE (Lezak et al., 2004). The maximum score is 60, which indicates total dependence upon others.

CLOX. This cognitive test assesses visual spatial ability and executive functioning, and differentiates executive functioning from non-executive components (Royall, Cordes, & Polk, 1998). It consists of two drawing exercises, CLOX1 and CLOX2. In CLOX1, the patient is required to draw a clock without guidance from the test administrator. The patient has to interpret the instructions correctly (“Draw me a clock that says 1:45. Set the hands and numbers on the face so that a child could read them.”), decide how to draw the clock (shape, size), and has to plan ahead (e.g., by placing of 3, 6, 9 and 12 for orientation). CLOX2 involves the patient copying a clock drawn by the test administrator. Executive functioning problems are illustrated by a low score on CLOX1, but a high score on CLOX2, whereas visuospatial problems are evident with low scores on both CLOX1 and CLOX2. CLOX1's score is subtracted from CLOX2's score, and this new score illustrates how well the participant learnt to draw the clock. Both CLOX are marked using the same criteria.

Trail Making Test (TMT). This test is divided into two sections: Trail Making A (TMA) requires the participant to connect consecutively circled numbers with straight lines, and Trail Making B (TMB) requires the participant to connect consecutive circled letters and numbers by switching between the data sets (Lezak et al., 2004). When the participant makes a mistake on either section, the researcher must point out the mistake, mark it, and demonstrate the correct answer. This test is sensitive to cognitive decline consistent with dementia; for instance, errors on TMT B may suggest that there is difficulty in switching between sets, and that these participants may struggle with complex daily activities (e.g., driving; Stutts, Stewart & Martell, 1998). The types of mistakes that are made shed light upon the particular problems that each patient is experiencing (perseveration occurs when the participant struggles to switch between letters and numbers). Both tests are timed, and the time taken to complete each test serves as the score for that test. For this study, if the participant was unable to complete the test they were asked to stop, and were given a score of 300 seconds.

The Placing Test (TPT). The placing test is one of visual memory. Two versions of this test were administered – one using shoes, and the other using faces. A piece of paper is divided into quadrants, of which two contain a face/shoe. The participant is asked to make an assessment of each picture (Face: Is the person young, middle-aged or elderly?; Shoe: Does it belong to a man

or a woman?),but their answers are not scored. After 5 minutes, the participant is presented with a page divided into four quadrants and a large image of each face/shoe. They are asked to identify in which quadrant, the presented shoe/face had originally appeared. This test measures learning, and tests to see whether the participant is making associations between two items of the same event (i.e. the face and its relevant position on the page)(Andersen, de Jager, & Iversen, 2006). Afterwards, by providing a cue (face/shoe), it can be determined whether the participant correctly consolidated a memory. Administration time is 5 minutes, and the score is the number of correctly identified quadrants, with a maximum of 10. It is very adept at identifying AD, and was designed to identify AD in a group where it was suspected. This tests correlates with other tests of memory, but has a weak correlation with other tests of general cognition, thus displaying its strength as a test of memory.

Sorbettes. Saliva will be collected using sorbettes. These resemble cotton buds, with a spear-shaped cotton pad on the end, which is attached to a red plastic stick. Sorbettes are a preferred option when wanting to measure cortisol, as they can be stored in the freezer without damage occurring to the saliva, are less invasive than blood samples, and cause less distress (Ice, Katz-Stein, Himes, & Kane, 2004; Li et al, 2006). Each participant was given three sorbettes, three plastic containers and an instruction sheet that documented how to swab saliva (see Appendix D). Saliva was to be swabbed at 09:00. Participants were not allowed to eat 30 minutes before swabbing, or to brush their teeth 15 minutes before swabbing. Each participant had to place the cotton swab into the mouth, so that it touched the inside wall of the cheek, and leave it there for 1 minute so it could absorb enough saliva. Afterwards, the sorbette was placed in its plastic container, and then put in the freezer. Sorbettes can be stored in the freezer, without damage occurring to the saliva, and are a preferred option when wanting to measure cortisol (Ice, Katz-Stein, Himes, & Kane, 2004; Li et al, 2006), as it is less invasive than blood samples, and causes less distress. It also allows the participant to swab their own saliva at their house, as opposed to traveling to a hospital to have a 09:00 blood sample drawn.

Procedure

Patient HA was screened and referred by her private practitioner, and then referred to the researcher. The researcher screened the participant telephonically, and after determining her eligibility and gaining a verbal consent, a meeting was arranged at Groote Schuur Hospital (GSH) at 11h00 on a mutually convenient day.

One of the controls was the patient's husband, and after telephonically screening him, a meeting was arranged at GSH at 11:00 on a mutually convenient day. Both of these two participants were reimbursed with R150 for traveling expenses.

The other three participants in the control group were tested at a nursing home in a nearby suburb.

At the scheduled meeting, participants read and signed a consent form (see Appendix D). Each participant was then asked to complete the questionnaires outlined above. If someone accompanied the participant, they were allowed to stay in the testing room when the questionnaires were administered, but were asked to leave during the cognitive testing.

After the testing, each participant was given three sorbettes sets, which consisted of the cotton swab used to obtain their saliva, the plastic storage container, and an instruction sheet. They took these swab sets home with them, and every morning for the next 3 days, they had to swab their saliva at 09h00. After swabbing their saliva, they placed the sorbette in the plastic container, which was then stored in the freezer. After 3 days had passed, the sorbettes were fetched by the researcher from the participant's house, and transferred into a cooler box. Once she had arrived home, the salivettes were transferred into her freezer before going to the laboratory for analysis.

RESULTS

Demographic information

The control group ranged from 71-86 years of age, and their education ranged from 12-13 years (see Table 1). Three of the five participants indicated that they were white, whereas the remaining two (consisting of patient HA and her husband) declined answering. All five

participants grew up in an urban settings, however one of the control participants grew up in Northern Rhodesia (Zambia).

Patient HA is a married woman, 76 years old, who was diagnosed with Alzheimer's disease in September 1998. She presented with memory impairment for about 18 months prior to her diagnosis. She has high blood pressure, but it is controlled through the use of prescription medicine.

CAMCOG-R and subdomain scores

Patient HA performed worse than the control group on the CAMCOG-R, and most of its subdomains (see Table 2). She had a slightly higher score on Language-Comprehension than the control group (9 vs 8.75). Most of her scores on the CAMCOG-R and its subdomains are worse than those of the control group by more than 2 standard deviations (see Figure 1). Her CAMCOG-R score is more than 3 standard deviations less than that the score for a population matched on education (Huppert et al., 1996). When compared to a population of mild dementia (mean = 65.46; SD= 1.69), her CAMCOG-R score is worse by more than 2 standard deviations (Huppert et al., 1996), suggesting that the severity of her dementia not be considered as mild. All her subdomain scores (except for Memory Total, Remote Memory, and Memory Learning) fall within the range of the Mild dementia group. Her Memory Total score is more than 2 standard deviations less than that of the mild dementia group (M=14.74; SD = 4.55). Her Remote Memory score is 2 standard deviations less than that of the mild dementia group (M=2.94; SD=1.47). Lastly, her Memory Learning score is slightly more than 2 standard deviations less than the mean of the mild dementia group (M= 9.30; SD=3.55).

Neuropsychological tests

The control group had higher means on all the cognitive tests, and had lower times on both TMT A and TMT B (indicating that they completed the test in a shorter time) (see Table 3). Patient HA received a default time of 300 seconds on TMT B, as she began to struggle and repeatedly made mistakes. Thus, testing was ended before she completed the trail, resulting in her receiving a time of 300 seconds. Patient HA's TMT A and TMT B are both less than the 10th percentile for

her age (Strauss, Sherman, & Spreen, 2006). Her MMSE score is less than the 10th percentile, and 4 standard deviations less than the mean for a population matched on age and education (Crum & Anthony et al., 1993). Her CLOX1 score and CLOX2 score place her within the cut-off bracket for probable Alzheimer's disease (Royall, Cordes & Polk, 1998).

Questionnaires

Patient HA did not score much lower than the control group on any of the questionnaires (see Table 4). None of her scores are more than 2 standard deviations from the mean of the control group.

DISCUSSION

Only one of the hypotheses has shown to be true – that patient HA would have worse memory scores than the control group. Patient HA's low memory scores are typical of AD, and her MMSE is indicative of progression of her illness. Her BADLS scores is a result of her losing the ability to complete everyday tasks as proficiently as had before she was diagnosed. She has a higher score than the control group on the CAMCOG-R sub domain, Language expression, but this is a result of one of the control participants having one wrong answer, while the others had full marks. The cognitive scores are as expected, and do comply with the results from the literature. However, once the cortisol sorbettes have been analysed it will be possible to examine the relationship between them and the cognitive, and questionnaire scores. The cortisol samples have been taken, and are currently stored in the researcher's freezer. Once the credit forms have been processed by the Groote Schuur Laboratory, these samples will be analysed, and then examined alongside the other test scores.

The lack of participants with AD has resulted in no variance between scores in this group – hence the absent standard deviance. Additionally, t-tests could not be used to determine how significantly different the test scores were between groups. The small sample size does skew the results, and does not allow for further statistical tests to be run.

It should be noted that due to the patient's AD, she could not complete the questionnaires (NEO-FFI, CD-RISC, LEQ, Demographic), and these were filled out by her husband. The NEO-FFI and CD-RISC measure neuroticism and resiliency, subjectively experienced qualities, and there

is a risk that her data may accurately portray these personality traits. Additionally, her husband may not have been able to completely her LEQ accurately, which further sheds doubt upon these results.

The patient's husband was an eligible participant, and is one of the four participants in the control group. Since he his wife has AD, there is likelihood that this may be perceived an external stressor to him, thereby increasing his cortisol levels. However, without an actually measure of his cortisol at this time we can only speculate what effect this may have.

The largest obstacle that was experienced was that of the ethical documents. This project had to be ethically approved by the Research Ethical Committee of the Faculty of Health Sciences. Final official ethical approval was granted on 3 October 2007, which has contributed to the lack of time and small sample size. Arrangements with the doctors and laboratory could not be completed until ethical approval was granted. Additionally, the sorbettes arrived from USA in the last two weeks of September. Lastly, funding had to be arranged, because of the cortisol analyses, purchasing of the sorbettes, and reimbursing the participants' travel expenses.

Despite these limitations, this pilot study is a firm foundation for a much larger scale project. Our single patient who has been diagnosed with Alzheimer's disease has shown a great difference in the cognitive test scores, and when data collection continues in November, it is expected that the other patients diagnosed with AD will demonstrate these same differences. Once sufficient data has become available, significant difference between group test means can be determined and multiple regression will be used to determine whether neuroticism, traumatic life events and resiliency may be predictive of high cortisol, and subsequently, the cognitive decline associated with AD.

Lastly, possible future research should expand the basic premises of this project by using a longitudinal design that should make use of the same tests in this study. A large, healthy, elderly sample group should be administered these tests, and have their saliva swabbed at regularly intervals through the study (every 3 months, or every 6 months). As the study progresses, some of the participants may develop AD and it would be of interest to compare the cortisol levels, and

test scores before this disease developed. Thus, there may be a significant difference between groups, which may suggest that cortisol levels, and test scores predict the development of AD.

CONCLUSION

Despite the small sample size, patient HA has demonstrated severe cognitive impairment in different cognitive domains, as typical with AD. It has been shown that the tests used can illustrate the difference in cognitive scores between healthy controls and ill patients. However, this same result was not shown with the questionnaires employed. Due to the small sample size, no definitive conclusions can be drawn, but once more participants are recruited, it is anticipated that the difference between healthy and ill participants, regarding life events experienced, neuroticism, resilience, cortisol levels and cognitive scores, will become more evident. This pilot study is a stepping stone to a larger project that will hopefully shed more light on the relationship between cortisol, traumatic life events and Alzheimer's disease.

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Appendix A
Demographic Questionnaire

PARTICIPANT KEY: _____

Section A: BASIC DEMOGRAPHICS

1. Age: _____
2. Sex: MALE FEMALE
3. Home Language: _____
4. What is your race or ethnic background?
 WHITE
 AFRICAN
 COLOURED
 ASIAN
 INDIAN
 OTHER: (specify) _____
5. What term best describes the kind of neighbourhood in which you grew up?
 SUBURBAN
 URBAN
 TOWNSHIP
 INTERMEDIATE
6. What is the name of the neighbourhood in which you grew up?

Section B. EDUCATION

7. Education (highest degree or grade completed): _____
8. Was most of your school education completed in a rural or urban setting (circle one)?
 RURAL URBAN
9. In which language was most of your school education completed?

10. Did you have to repeat any grades? YES NO

a. If yes, please specify which grade(s): _____

ONLY COMPLETE QUESTIONS 11-12 IF YOU HAVE COMPLETED MATRIC.

11. Did you matriculate from a public high school or a private high school (circle one)?

PUBLIC

PRIVATE

12. What is the name of the school from which you matriculated?

***ONLY COMPLETE QUESTIONS 13- 15 IF YOU WERE ENROLLED IN
TERTIARY EDUCATION***

13. At what university/technikon/college (s) did you enroll after school?

14. For what did degree/s did you register?

15. Did you complete it? YES NO

16. How did you earn an income for most of your life?

Section C: HEALTH

17. Have you ever been involved in a motor vehicle accident? YES NO

If yes, how old were you at the time? _____

18. Have you ever had surgery?

YES

NO

If yes:

What type of surgery? _____

How old were you at the time of surgery? _____

19. Have you ever experienced a personal trauma (e.g., been the victim of a violent crime, witnessed a violent crime, etc.)?

YES

NO

If yes, can you say that it still affects you emotionally (e.g., you have nightmares or daydreams about it, you worry a lot about it happening again, etc.)?

YES

NO

Appendix B

Changed Questions in the CAMCOG

Table B1

CAMCOG Revisions

Question Number	Original Question	Revision
144	Can you tell me where we are now? For instance, what county (state) are we in?	Can you tell me where we are not? For instance, what province are we in?
146	What are two main streets nearby (or near your home)?	What country are we in?
155	Was there wireless/radio in this country before television was invented?	Was there radio in this country before television was invented?
157	I am going to show you some objects. Please tell me the name of each one. Show 'Pictures for naming' in booklet. [Pictures: (1) shoe,sandal; (2) typewriter; (3) scales; (4) suitcase, portmanteau; (5) barometer; (6) table lamp; lamp]	I am going to show you some objects. Please tell me the name of each one. Show 'Pictures for naming' in booklet. [Pictures: (1) shoe,sandal; (2) screwdriver; (3) clothes iron; (4) suitcase, portmanteau; (5) clock; (6) table lamp; lamp]
164	Can you tell me what were the objects in the coloured pictures I showed you a little while ago? [Answer: (1) shoe,sandal; (2) typewriter; (3) scales; (4) suitcase, portmanteau; (5) barometer; (6) table lamp; lamp]	Can you tell me what were the objects in the coloured pictures I showed you a little while ago? [Answer: (1) shoe,sandal; (2) screwdriver; (3) clothes iron; (4) suitcase, portmanteau; (5) clock; (6) table lamp; lamp]
165	Which of these objects did I show you below? [Pictures: (1) shoe,sandal; (2) screwdriver; (3) clothes iron; (4) suitcase, portmanteau; (5) clock; (6) table lamp; lamp]	Which of these objects did I show you below? [Answer: (1) shoe,sandal; (2) screwdriver; (3) clothes iron; (4) suitcase, portmanteau; (5) clock; (6) table lamp; lamp]
169	Who was the leader of the Russians in the Second World War? [Correct answer: Stalin]	Who was the Prime Minister of South Africa during the Second World War? [Correct answer: Jan Smuts]

170	What was Mae West famous for? [Correct answer: Entertainer, Film star, life jacket]	What was Louis Armstrong famous for? [Correct Answer: Singer, saxophonist, jazz singer]
171	Who was the famous flyer whose son was kidnapped? [Correct answer: Lindbergh]	Which famous film, starring Vivien Leigh and Clark Gable was released in the 1930s? [Correct answer: Gone with the Wind]
166a	Who was the US President who was shot in Texas? [Correct answer: John F. Kennedy]	What is the name of the South African prime minister that was stabbed in parliament? [Correct answer: Hendrik Verwoed]
167a	What is Yoko Ono famous for? [Correct Answer: Wife of beatle, John Lennon]	What is Steve Biko famous for? [Correct answer: Black activist, died in police custody]
169a	What was Edmund Hilary famous for? [Correct answer: First to reach summit of Mt Everest]	Who was the first South African to win a Nobel Peace Prize? [Correct answer: Albert Luthuli]
170a	Who was the first woman Prime Minister of India? [Correct answer: Indira Ghandi]	Who was the first surgeon to perform a heart transplant? [Correct answer: Christiaan (Chris) Bernard]
171a	Who was the famous cinema actress who married Prince Rainier of Monaco? [Correct Answer: Grace Kelly)	Which island off the coast of South Africa was used as a leper colony, military base and prison? (Correct answer: Robben Island)
172	What is the name of the present King or Queen?	What is the name of the present President of South Africa?
173	Who is likely to be the next King or Queen?	What was the full date when two planes flew into the Twin Towers in New York? (Correct answer: 11 September 2001)
174	What is the name of the current Prime Minister?	Who is the president of USA?
176	Name the following three objects taking one second to	Name the following three objects taking one second to

	say each: apple, table, penny.	say each: apple, table, pen.
190	Write this name and address on the envelope: Mr. John Brown 42 West Street, Bedford	Write this name and address on the envelope: Mr. John Brown 42 West Street, Bellville
195	If someone went shopping and was given 15 pence as change from £1, how much did they spend?	If some went shopping and was given 15 cents as change from R1, how much did they spend?
201	Who is this? (Show picture of [1] Queen; [2] Pope, Archbishop, Bishop)	Who is this? (Show picture: [1] Archbishop Desmond Tutu; [2] Nelson Mandela)
203	Can you tell me who this is, or what he/she does? (Indicate any two people available)	Can you tell me who this is, or what he/she does? (Show any two of following pictures: policeman, doctor, nurse, fireman, priest)

Appendix C
Telephone Screening Procedure

This telephone screener includes (a) telephone consent, (b) exclusionary criteria, and (c) basic demographic questions.

Participant Code: _____

Date of Screening: _____

Name of Researcher Conducting the Screening: _____

First, I would like to confirm some information about you.

Can you please give me your full name, address, and phone number?

Name: _____

Address: _____

Phone: _____

E-mail (if applicable):

ASK GENDER (QUESTION 2) ONLY IF NOT KNOWN OR UNABLE TO DETERMINE.
OTHERWISE, CODE QUESTION 2 AND THEN ASK PREFERRED TITLE QUESTION.

1. Are you male or female?

MALE.....1 [Is that Mr., Dr., Rev., or other?]
RECORD PREFERRED TITLE ON CONTACT RECORD.

FEMALE.....2 [Is that Mrs., Miss, Ms., Dr., Rev., or other?]
RECORD PREFERRED TITLE ON CONTACT RECORD.

2. What is your date of birth? ____/____/____
 MM DD YYYY

IS PARTICIPANT WITHIN 6 WEEKS OF 65TH BIRTHDAY OR OLDER TODAY?

YES.....1

NO.....2 **INELIGIBLE: READ SCRIPT BELOW
AND END INTERVIEW**

AGE INELIGIBILITY CLOSE-OUT SCRIPT:

These are the only questions I need to ask. This research study is designed for people who are age 65 or older. I would like to thank you for the time you have taken to speak with me. We will not need to contact you again. Thank you.

3. Is English your first language? YES.....1
NO.....2

4. What is your marital status?
[READ RESPONSE CATEGORIES IF PARTICIPANT IS UNABLE TO ANSWER]

MARRIED.....1
LIVING AS MARRIED.....2
SEPARATED.....3
DIVORCED.....4
WIDOWED.....5
SINGLE OR NEVER MARRIED.....6

IF 1 OR 2 ARE SCORED

**MENTION THAT THEIR SPOUSE
MAY BE ASKED TO PARTICIPATE
AS WELL AS A CONTROL SUBJECT.**

5. Does anyone live in the home with you?

YES.....1
NO.....2

6. What is highest grade of school or level of education that you completed?
[CODE ONLY ONE RESPONSE]

DID NOT GO TO SCHOOL	00
FIRST GRADE	01
SECOND GRADE	02
THIRD GRADE	03
FOURTH GRADE	04
FIFTH GRADE	05
SIXTH GRADE	06
SEVENTH GRADE	07
EIGHTH GRADE	08

NINTH GRADE	09
TENTH GRADE	10
ELEVENTH GRADE	11
TWELTH GRADE	12
GED	Enquire as to how many school years the participant completed prior to obtaining the GED; code that number.
VOCATIONAL TRAINING/ SOME COLLEGE AFTER HS GRAD	13
ASSOCIATE'S DEGREE	14
SOME COLLEGE	13-15
UNDERGRADUATE DEGREE (BA-BS)	16
SOME PROFESSIONAL SCHOOL AFTER AFTER COLLEGE GRADUATION	17
MASTER'S DEGREE	18
DOCTORAL DEGREE (e.g., Ph.D., MD, DVM, DDS, JD, etc.)	20

7. The next questions are about your vision. Do you wear glasses or contact lenses to read?

YES.....1
NO.....2

BEGINNING WITH ITEM 10, AND FOR ALL OTHERS, DO NOT TERMINATE INTERVIEW IF INELIGIBLE. COLLECT ALL DATA, THEN READ INELIGIBILITY SCRIPT BEFORE #29 AT END.

8. How much difficulty do you have reading ordinary print in the newspaper [wearing glasses or contact lenses?]? Would you say ...

No difficulty.....1
A little or some difficulty.....2
Extreme difficulty.....3 = **INELIGIBLE**
You stopped reading because of your eyesight.....4 = **INELIGIBLE**
You stopped reading for other reasons, or you are not interested in reading.....5

The next few questions are about medical conditions you might have.

9. Has a doctor or nurse ever told you that have:

	14.YES	NO	14.DK	N/A
Alzheimer's Disease or other severe dementing illness?	1	2	8	
neurological disease, including Parkinson's disease, Huntington's disease, or epilepsy?	1 = INELIGIBLE	2	8	
Asthma?	1 = INELIGIBLE			
Do you have high blood pressure?	1 = ASK NEXT QUESTION			
Are you on medication to control it?	1 = ASK NEXT QUESTION 1 = ELIGIBLE			
What medication are you on?				
Do you have diabetes?	1 = ASK NEXT QUESTION			
Are you on medication to control it?	1 = ASK NEXT QUESTION 1 = ELIGIBLE			
What medication are you on?				
heart attack or myocardial infarction?	1 = ASK NEXT QUESTION	2	8	
[Was it in the past year?]	1 = INELIGIBLE	2	8	-7
A stroke or a TIA?	1 = ASK NEXT QUESTION	2	8	
[Was it in the past year?]	1 = INELIGIBLE	2	8	-7
A head injury resulting in loss of consciousness?	1 = ASK NEXT QUESTION	2	8	
[Was it in the past year?]	1 = INELIGIBLE	2	8	-7

Drug or alcohol abuse?	1 = INELIGIBLE	2	8	
Do you smoke cigarettes?	1 = ASK NEXT QUESTION	2	8	
[How many do you smoke per day?]	TWELVE OR MORE = INELIGIBLE			
Cancer, other than skin cancer, within the past 5 years?	1 = ASK NEXT QUESTION	2	8	
[What kind of cancer (site of the cancer) is it?] CODE ALL PARTICIPANT MENTIONS.	LUNG.....1 = INELIGIBLE STOMACH.....2 = INELIGIBLE LIVER.....3 = INELIGIBLE PANCREAS.....4 = INELIGIBLE ESOPHAGUS.....5 = INELIGIBLE OTHER.....6 SPECIFY: _____ N/A.....-7			
[Are you currently receiving chemotherapy or radiation treatment for this (these) cancer(s)?]	YES.....1 = INELIGIBLE NO.....2 N/A.....-7			
Have you ever been hospitalized for psychiatric treatment?	1 = INELIGIBLE (=12)	2 (=14)	8 (=14)	

12. Do you have access to a freezer?

YES.....**ELIGIBLE**
NO.....**INELIGIBLE**

This study consists of a single testing session at a convenient location, where you will be administered a few tests of memory and other cognitive abilities. The blood sample needs to be drawn at 9am, and the testing will start at 11am. This test session will last approximately 2 hours. Your spouse, or caretaker should accompany you. You will be compensated R150 for your traveling expenses, if the testing session takes place at Groote Schuur Hospital.

10. Are you willing to participate in this testing session?

YES.....1

NO.....2 = **INELIGIBLE**

Are you willing to have your spouse or caretaker contacted by our staff to answer some questions about you?

YES.....1 (RECORD CONTACT BELOW)

NO.....2 = **POSSIBLY INELIGIBLE**

N/A.....-7

Informant Name: _____

Informant Address: _____

Informant Phone: _____

Informant E-mail (if applicable): _____

TAKE A PAUSE WHILE YOU BRIEFLY ASSESS THE FOLLOWING TWO ITEMS.

14. INTERVIEWER ASSESSMENT OF PARTICIPANT COMMUNICATION

USING THE SCORING CRITERIA ON THE NEXT PAGE, CODE YOUR ASSESSMENT OF PARTICIPANT'S ABILITY TO MAKE SELF UNDERSTOOD AND TO UNDERSTAND OTHERS. THESE JUDGMENTS CAN BE MADE BOTH ON THE BASIS OF COGNITIVE UNDERSTANDING, AND ALSO OF ENGLISH-AS-SECOND-LANGUAGE ISSUES.

12. MAKING SELF UNDERSTOOD

UNDERSTOOD.....0

USUALLY UNDERSTOOD.....1
(DIFFICULTY FINDING WORDS OR FINISHING
THOUGHTS.)

SOMETIMES UNDERSTOOD.....2 = **INELIGIBLE**
(ABILITY IS LIMITED TO MAKING CONCRETE
REQUESTS.)

RARELY/NEVER UNDERSTOOD.....3 = **INELIGIBLE**

13. ABILITY TO UNDERSTAND OTHERS

UNDERSTANDS.....0

USUALLY UNDERSTANDS.....1
(MAY MISS SOME PART/INTENT OF MESSAGE.)

SOMETIMES UNDERSTANDS.....2 = **INELIGIBLE**
(RESPONDS ADEQUATELY ONLY TO SIMPLE DIRECT
COMMUNICATION.)

RARELY/NEVER UNDERSTANDS.....3 = **INELIGIBLE**

14. MAKING SELF UNDERSTOOD SCORING

0	= Understood:	The participant expresses ideas clearly.
---	---------------	--

1	= Usually Understood:	The participant has difficulty finding the right words or finishing thoughts, resulting in delayed responses; or requires some prompting to make self understood.
2	= Sometimes Understood:	The participant has limited ability, but is able to express concrete requests regarding at least basic needs (e.g., food, drink, sleep, toilet).
3	= Rarely/Never Understood:	At best, understanding is limited to interpretation of highly individual, person-specific sounds (e.g., indicated presence of pain or need to toilet).

14. UNDERSTANDING OTHERS SCORING

0	= Understands:	The participant clearly comprehends the interviewer's message(s) and demonstrates comprehension by words or questions.
1	= Usually Understands:	May miss some part of intent of the message but comprehends most of it. The participant may have periodic difficulties integrating information but generally demonstrates comprehension by responding to words or questions.
2	= Sometimes Understands:	Demonstrates frequent difficulties integrating information, and responds adequately only to simple and direct questions or directions. When the message is rephrased or simplified, the participant's comprehension is enhanced.
3	= Rarely/Never Understands:	Demonstrates very limited ability to understand communication. Or, interviewer has difficulty determining whether the participant comprehends messages, based on verbal responses. Or, the participant can hear sounds by does not understand messages.

DETERMINE PARTICIPANT ELIGIBILITY AND GO TO APPROPRIATE SCRIPT ON NEXT PAGE.

FOR ELIGIBLE PARTICIPANTS

Thank you for answering the questions. As I have already mentioned, we would like to continue with you in the program. The single meeting at a convenient location starts at 11am. I shall ask you to fill out some questionnaires and complete some activities involving memory. The testing session should take approximately 2 hours. There will be many breaks, and I shall provide tea, coffee, juice and biscuits. We shall compensate you R150 for your traveling expenses if the testing location is not at your home, or nearby location. Would it alright with you, if I confirmed this meeting a day or two before the testing session?

Do you have any questions for me at this time?

You have already indicated that you would be willing to schedule this session.

To help me with scheduling an appointment, could you tell me what other commitments you typically have during the week, such as work, volunteering, caring for others, or social activities?

Could I schedule you for (date/time)?

14. Date: _____ / _____ / _____

15. Time: _____:_____ AM/

16. Test Site: _____

17. Person: _____ (Tester ID/Initials)

Do you know where (SITE) is located?

Thank you. If you wear glasses for distance or reading or wear a hearing aid, please bring them with you. We look forward to seeing you on (day/date).

Thank you very much for your time.

INELIGIBLE SCRIPT

This concludes your participation in this study. Thank you for answering these questions. This has been very helpful. Based on our interview today, you are not eligible to participate in the study at this time. This is typically because individuals have health conditions that have been identified as exclusion characteristics for this study, or because of difficulties in arranging for travel schedules, and so forth. We appreciate the time you have spent answering these questions. Although you are not participating in this study, we may want to call you in the future about your interest in other studies.

- 18.** May we have your permission to share your interest in research with other University of Cape Town researchers in our department, so that they may call you in the future?

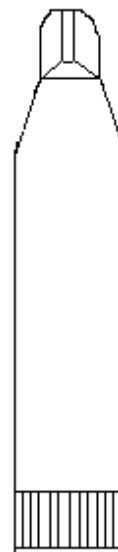
YES1
NO2

Appendix C

How to swab and store saliva samples.

EQUIPMENT:

A cotton swab



Plastic storage tube

1. Cotton swabs (long, red stick with a cotton tip shaped like a spear).
2. Plastic storage tube: a plastic tube that has a pointed end on the one side, and a detachable round cap. Each plastic tube will have a white sticker on it.

You will receive three cotton swabs, and three plastic tubes.

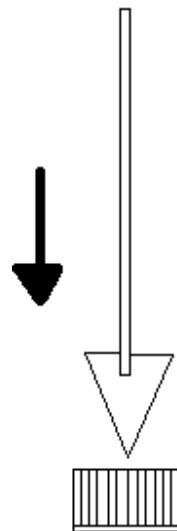
SWABBING SALIVA:

1. No eating/drinking/gum chewing up to **30min before** collection
2. No flossing or brushing teeth up to **15 min before** collection
3. If you have a sore in your mouth, or bleeding gums, please do not swab your saliva until it is healed. It is important not to have blood in your saliva when swabbing.
4. Before you start, open the plastic storage tube and place the lid on a flat surface.

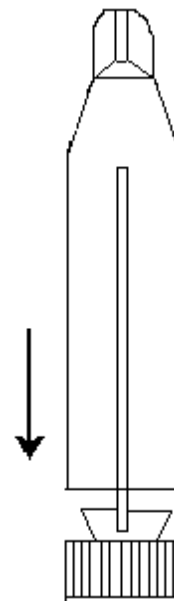
5. To swab your saliva, take the cotton swab and put it in your mouth, so that it touches your cheek. Let it touch your cheek for one minute, so that it absorbs enough saliva. Please, do not spit on the swab instead of putting it in your mouth.

STORAGE:

6. After one minute has passed, take the cotton swab out of your mouth. Put the spear-tipped side (the pointy side) of the cotton swab into the round plastic lid.



7. Hold the red stick of the cotton swab so that it is upright, and place the plastic tube over this red stick.



8. Clip the tube into the lid.



9. Place the plastic tube upright in the freezer, and make sure that the pointed end of the plastic tube is facing downwards.



10. Put one cotton swab into one plastic tube. Please, do not put all three cotton swabs into one plastic tube. It is important that each cotton swab is stored in its own tube.

11. Please, do not take the plastic tube out of the freezer until the researcher (Ms Nortje) fetches it from you.

If you have any questions, please phone Ms Alicia Nortje at (021) 975 9221, or 083 688 28 28. She will be happy to answer any questions that you may have.

Appendix D

Informed Consent Form

***Informed Consent to participate in research and authorization for the collection
and use of the results of cognitive tests and other personal information.***

UCT Faculty of Health Sciences Ethics Research Committee Approval Reference: 270/2007

You are being asked to take part in a research study. This form provides you with information about the study and seeks your authorization for the collection and use of your cognitive test results, your salivary cortisol levels, as well as other personal information necessary for the study. The Principal Investigator (Dr. Kevin Thomas, Ms. Alicia Nortje, or Dr. Marc Combrinck) will also describe this study to you and answer any questions you may have. Your participation is entirely voluntary. Before you decide whether or not to take part, read the information below and ask questions about anything you do not understand. By participating in this study you will not jeopardize any future treatment of your condition.

1. Name of Participant ("Study Subject")

2. Title of Research Study

The relationship between traumatic life events, high cortisol and Alzheimer's disease.

3. Principal Investigator(s) and Telephone Number(s)

Kevin G. F. Thomas, Ph.D.

Alicia Nortje

Senior Lecturer

Postgraduate student

Department of Psychology

Department of Psychology

University of Cape Town

Department of Psychology

021-650-4608

021 975 9221

Co-Investigator:

Marc Combrinck, M. D.
Neurology Division
Department of Medicine
Groote Schuur Hospital
021-404-3198

4. Source of Funding or Other Material Support

National Research Foundation

5. What will be done if you take part in this research study?

First, you will be screened by your doctor and by a study representative. The screening procedure takes place because it is important to know your medical history and other personal information. If your doctor thinks you may be eligible, he/she will send your contact details to the study representative. This person will then ask you some questions over the phone. If you are eligible, a meeting will be arranged between you and the researcher. You and an informant (your spouse/partner/close relative) will be asked to come to an accessible/familiar venue at 10:30am on a day that is mutually convenient.

At this meeting, a researcher will meet you at a prearranged location, and show you to the testing room. The researcher will then ask you and your informant to complete some paper-and-pencil questionnaires that ask about your background, levels of stress, ways in which you cope with stress, and your everyday activities.

After completing the questionnaires, the researcher will test your memory and other mental functions using paper-and-pencil instruments. The entire session should not take longer than two (2) hours. If you require breaks in between questionnaires or test instruments, please let the researcher know.

After completing the tests, the researcher will give you three sets of cotton bud swabs. They will look very similar to cotton buds, except that the tip will have a triangular piece of cotton on it.

You should take these cotton bud swabs home with you. The day after you have met the researcher, you must swab your saliva at 9 am. You should do this for three consecutive days, at 9am every day. You will be given detailed instructions about how to swab your saliva. If you think that you might forget to swab your saliva at 9am, the researcher will ask for your permission to phone you at 8:55 am on each of the collection days to remind you.

After three days, the researcher will phone you and arrange to pick up the swabs from you. Please do not take the swabs out of the freezer until the researcher comes to your house. It is important that the swabs do not defrost.

Remember, you are free to withdraw at any stage without having to give a reason. Your future treatment will not in any way be adversely affected if you decide to do so. Please contact the Principal Investigators listed above to let one of us know if you do not wish to take part in this study any longer.

The researcher will not be able to give your individual scores or cortisol levels. However, if you wish to know the overall results of the entire study, you can contact one of the Principal Investigators.

6. If you choose to participate in this study, how long will you be expected to participate in the research?

The testing session will take 2 hours, and you will be asked to swab your saliva for three days. The total duration is therefore four days.

7. How many people are expected to participate in the research?

20

8. What are the possible discomforts and risks?

There are no risks involved in this study. You might get tired from the tests. If you do feel tired and need to take a break, please feel free to tell us.

9. What are the possible benefits to you?

There is no immediate benefit in participating. However, the researcher will, with your permission, make available the results of the memory and cognitive test scores to your doctor.

10. What are the possible benefits to others?

We are interested in the relationship between stress levels, cortisol, cognitive/memory functions, and aging. This knowledge may allow for new risk factors for dementias such as Alzheimer's disease to be identified, and may lead to better management of these conditions in the long term. Additionally, it may result in better treatment options.

11. If you choose to take part in this research study, will it cost you anything?

No.

12. Will you receive compensation for taking part in this research study?

You will not be paid for participating in this study. However, if the meeting between you and the researcher is arranged at Groote Schuur Hospital, we will reimburse your R150.00 for your traveling expenses.

13. Can you withdraw from this research study?

You may withdraw from this study at any stage, and do not have to give a reason for doing so. Your future treatment will not be adversely affected by your decision.

If you have any questions regarding your rights as a research subject, you may phone the Psychology Department offices at 021-650-3430.

14. If you withdraw, can information about you still be used?

Yes, with your permission, your information may still be used.

15. Once information is collected, how will it be kept secret (confidential) in order to protect your privacy?

Information collected will be stored in locked filing cabinets or in computers with security passwords. All information will be stored by code number, rather than by name. Only the researchers involved in this study will have access to this information. The University of Cape Town has the right to verify the authenticity of the information collected.

16. What information about you may be collected, used and shared with others?

This information gathered from you will include a medical history, some personal information, your cognitive tests results and cortisol levels. The information will be kept and stored by research code. We are planning to expand this project in 2008 in a collaborative international study between University of Cape Town and the University of Oxford, and your information may be included in this study.

17. How will the researcher(s) benefit from your being in the study?

This research forms part of Ms. Nortje's Honours degree in Psychology. It is also part of a larger study that will commence in 2008.

19. Signatures

As a representative of this study, I have explained to the participant the purpose, the procedures, the possible benefits, and the risks of this research study; the alternatives to being in the study; and how the participant's protected health information will be collected, used, and shared with others:

Signature of Person Obtaining Consent & Authorization

Date

Consenting Adults. You have been informed about this study's purpose, procedures, possible benefits, and risks; the alternatives to being in the study; and how your protected health information will be collected, used and shared with others. You have received a copy of this Form. You have been given the opportunity to ask questions before you sign, and you have been told that you can ask other questions at any time.

Adult Consenting for Self. By signing this form, you voluntarily agree to participate in this study. You hereby authorize the collection, use and sharing of your protected health information as described in the sections above. By signing this form, you are not waiving any of your legal rights.

Signature of Adult Consenting & Authorizing for Self

Date

Parent/Adult Legally Representing the Subject. By signing this form, you voluntarily give your permission for the person named below to participate in this study. You hereby authorize the collection, use and sharing of protected health information for the person named below as described in the sections above. You are not waiving any legal rights for yourself or the person you are legally representing. After your signature, please print your name and your relationship to the subject.

Consent & Authorization Signature
of Parent/Legal Representative

Date

Print: Name of Legal Representative of and Relationship to Participant:

Please indicate below if you would like to be notified of future research projects conducted by our research group:

_____ (initial) Yes, I would like to be added to your research participation pool and be notified of research projects in which I might participate in the future.

Method of contact:

Phone number: _____

E-mail address: _____

Mailing address: _____

Author Note

I would like to acknowledge the assistance of Dr Kevin Thomas, Dr Marc Combrinck and Helen Matuszek. Each of these people guided me when I lost, and have contributed significantly to this project. Lastly, I have to thank my family and friends who supported and always believed in me – I really needed it!

Table 1

Demographic Characteristics of Participants in the Current Study

Demographic variable	Patient HA	Control Group (n=4)
Age	76	78.5 (7.14)
Gender	F	1 M; 3 F
Years of education	8	12.5 (0.58)
Area brought up in	Urban	All urban

Note. For age and years of education, means are presented with standard deviations in parentheses.

Table 2

CAMCOG-R and subdomain scores

CAMCOG-R & Domains	Patient HA	Control Group (n=4)
CAMCOG-R	47 (none)	95.0(6.48)
Orientation	5 (none)	9.25(0.5)
Language Total	21(none)	29.5(0.577)
Language-Comprehension	9(none)	8.75(0.5)
Language-Expression	12.0(none)	20.75(0.5)
Memory Total	4(none)	24.0(1.83)
Memory-Remote	0(none)	5.75(0.5)
Memory Recent	2(none)	3.50(0.577)
Memory Learning	2(none)	14.75(0.957)
Attention/Calculation	4(none)	7.75 (1.5)
Praxis	8(none)	11.25 (0.957)
Abstract	0(none)	7.75 (0.5)
Perception	5(none)	7.5 (1.0)

Note. For each test and subdomain, means are presented with standard deviations in parentheses.

Table 3

Neuropsychological test scores of the patient group, and control group.

Test/Questionnaire	Patient HA	Control Group (n=4)
MMSE	16 (none)	27.75 (0.957)
CLOX 1	5 (none)	12.50 (1.290)
CLOX 2	8 (none)	13.50 (0.58)
TPT shoe	1 (none)	8.75 (0.5)
TPT face	4 (none)	8.5 (1.29)
TMT A	90 (none)	57.25 (19.41)
TMT B	300(none)	108.5 (51.05)

Note. For each test, means are presented with standard deviations in parentheses

Table 4

Questionnaire scores for patient HA, and control group.

Questionnaire	Patient HA	Control group (n=1)
BADLS	19 (none)	0 (none)
Life event occurrence	24 (none)	26.75 (3.096)
Life event impact	1 (none)	6.5 (5.97)
CD-RISC	76 (none)	82.25 (9.07)
NEO-FFI	8.0(none)	8.25 (3.30)

Note. For each questionnaire, means are presented with standard deviations in parentheses

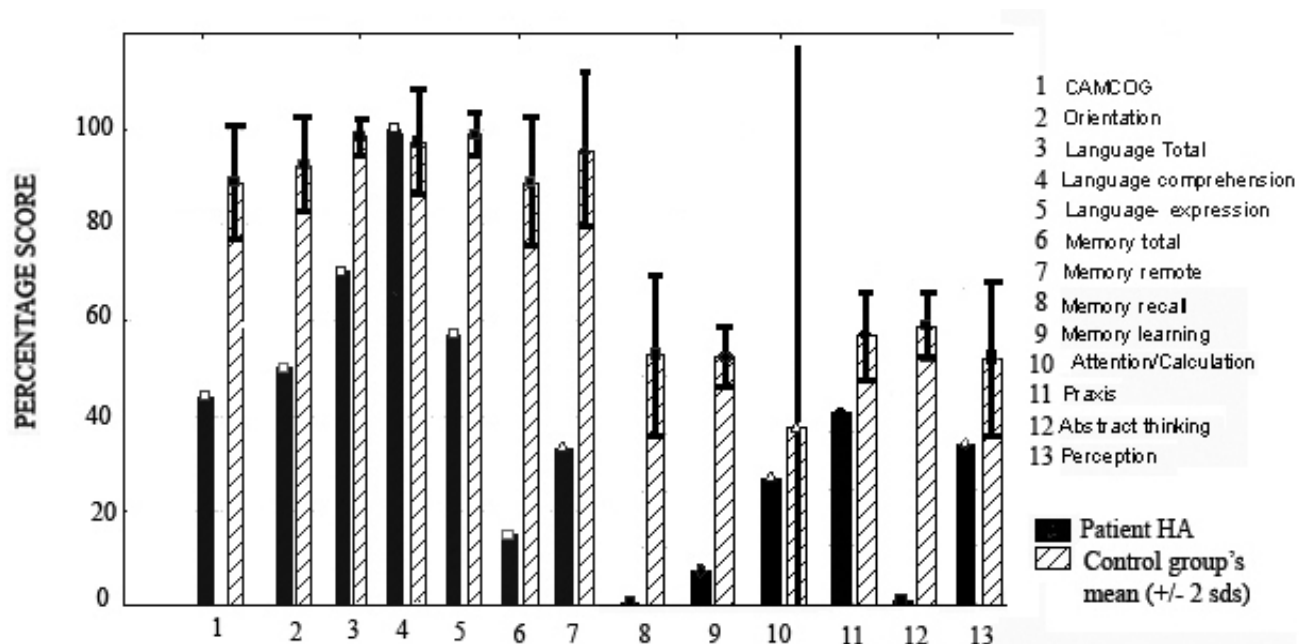


Figure 1

Patient HA's performance on CAMCOG and domains, compared to Control group performance.