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NAME: Musaddiqah Brown and Tayla Page

STUDENT NUMBER: BRWMUS001 and PGXTAY001

SIGNATURE: M. Brown and T. Page

Associations between Sleep Disruption, Poor Quality of Life, Affective
Dysregulation, and Cognitive Dysfunction in Patients with Pituitary Diseases

Musaddiqah Brown and Tayla Page

ACSENT Laboratory
Department of Psychology
University of Cape Town

Supervisor: Kevin G. F. Thomas

Co-supervisors: Michelle Henry, Ian Ross, Thuran Naiker, and Patrick Semple

Word count: [7740]

Abstract

Sleep is a crucial biological process that plays an important role in promoting physical and mental health. Separate lines of research indicate that patients with pituitary disease experience (a) poor quality of life, (b) disrupted sleep patterns, (c) cognitive impairment, and (d) affective disorders. Of primary interest for us, however, are preliminary suggestions that the poor quality of life experienced by patients with pituitary disease (including, in some cases, cognitive and affective deficits) is associated with sleep disruption. In an attempt to explore such associations, we recruited 12 patients with pituitary disease (age $M = 45.25 \pm 14.61$ years) from the Radiotherapy Clinic at Groote Schuur Hospital and 12 age-, sex- and education-matched healthy controls from the University of Cape Town community. We administered a short test battery (Quality of Life Scale; Global Sleep Assessment Questionnaire; Brief Test of Adult Cognition by Telephone; Beck Depression Inventory-Short Form) either telephonically or in person. Analyses detected significant between-group differences on the executive function aspect of cognition, $p = .03$, and a trend towards significance on measures of sleep, $p = .05$. Within the patient group, analyses detected a trend towards a significant association between sleep quality and overall quality of life, $r = .57$, $p = .05$. Future research should investigate this association, as well as those between sleep disruption, cognitive dysfunction, and affective disorders, in a larger sample of patients to gain a better understanding of ways in which sleep problems might affect overall quality of life.

Sleep is a naturally occurring biological process that plays a crucial role in the promotion of health, metabolic functioning, and overall well-being (Walker, 2017). Of particular concern to psychologists is the fact that healthy sleep supports appropriate affective regulation and intact cognitive functioning (Anderson & Horne, 2006; Djonlagic, Rosenfeld, Shohamy, Myers, Gluck, & Stickgold, 2009; Stickgold, 2005; Stickgold & Walker, 2005; Mukherjee et al., 2015). Sleep disturbances or disruptions can therefore accelerate the progression of medical diseases, increase the risk of depression, and impair memory consolidation (Ellenbogen, 2005; Irwin, 2015).

The hypothalamic-pituitary-adrenal (HPA) axis is one of the primary physiological mechanisms involved in the regulation of sleep-wake cycles and sleep stages (Balbo, Leproult, & Van Cauter, 2010). In fact, there is a bidirectional relationship between sleep regulation and HPA-axis activity. On the one hand, cycling between various sleep stages, and between sleep and waking, is associated with HPA axis-controlled hormonal inhibition and secretion; on the other, changes in sleep patterns affect the secretion of those hormones, which include growth hormone-releasing hormone (GHRH) and corticotrophin-releasing hormone (CRH; Leproult & Van Cauter, 2010; Nielsen, Lindholm, & Laurberg, 2007; Steiger, Dresler, Kluge, & Schüssler, 2013; Van Dalfsen & Markus, 2018).

It is for this reason that the pituitary gland, a pea-sized structure situated at the base of the skull with primary functions of hormone production and secretion (Emerald, 2016), is of interest to sleep neuroscientists. Diseases of the pituitary gland (e.g., Cushing's disease, acromegaly, and apoplexy) are accompanied by changes in hormone secretion (e.g., excessive GH; Melmed, 2006), and, therefore, are often the cause of sleep disturbance and consequent declines in overall quality of life (QoL).

The purpose of this study was to explore the possible associations between poor QoL, sleep disruption, cognitive dysfunction, and affective disorders in patients with pituitary disease. In the literature review below, we first give a brief description of pituitary diseases and hormones implicated in them. Thereafter, we discuss sleep disruptions and compromised QoL that occur within pituitary disease, with additional focus on how sleep disruption may be a mediating factor between disease presence and poor QoL in these patients. Finally, because cognitive impairment and affective dysregulation are often (a) caused by sleep disruption, and (b) associated with poor QoL, we review studies investigating cognitive and affective function in patients with pituitary disease.

Pituitary Diseases

Pituitary diseases are commonly caused by either secretory or non-secretory tumours on the pituitary gland. *Secretory tumours* cause an imbalance in hormone secretion, leading to neuroendocrine disorders such as Cushing's disease and acromegaly (Nielsen et al., 2007). Cushing's disease is characterized by over-secretion from the pituitary gland of adrenocorticotrophic hormone (ACTH), the hormone that stimulates the production of cortisol (Bertagna, Guignat, Groussin, & Bertherat, 2009). Of particular concern here is that cortisol, a steroid hormone, plays a crucial role in regulating the memory processing that occurs during sleep. Specifically, cortisol concentrations that are elevated above normal physiological levels disrupt sleep-dependent memory consolidation (Harand et al., 2012; Harbeck, Kropp, & Mönig, 2009). This is likely a primary reason why patients with Cushing's disease perform poorly on memory tasks (Wamsley & Stickgold, 2011).

Non-secretory tumours are microadenomas (< 1cm in size) and macroadenomas (> 1cm in size; Jaffe, 2006). Macroadenomas put immense pressure on the pituitary gland, causing visual defects in 70% of patients who experience them. Treatment for secretory and non-secretory adenomas includes surgical removal, radiotherapy, and medication (Melmed et al., 2002).

Sleep Disruption in Pituitary Disease

Recent estimates suggest that 40-80% of patients diagnosed with acromegaly experience Sleep Apnea Syndrome (Galerneau et al., 2016). Sleep apnea (defined as airway obstructions or breathing problems occurring during sleep; Barkan, 1997) occurs because of the overgrowth of soft tissue in the upper airway. This overgrowth tends to obstruct the airway when the patient is lying down, leading to fragmented sleep and impaired daytime functioning due to fatigue (Grunstein, Ho, & Sullivan, 1991; Romijn, 2016).

Patients with other pituitary diseases also experience various kinds of sleep disruption. For instance, in one study patients treated for non-functioning pituitary macroadenoma (NFMA) reported subjective deficits (viz., decreased sleep quality and daytime fatigue) and were observed, using polysomnography and actigraphy, to experience disturbed distribution of sleep stages (Biermasz et al., 2011).

Quality of Life in Pituitary Disease

Numerous studies suggest that people with pituitary disease experience poor QoL (Andela, Lobatto, Pereira, van Furth, & Biermasz, 2018; Chanson & Salenave, 2008; Page, Hammersley, Burke, & Wass, 1997; Rowels, Prieto, Badia, Shalet, Webb, & Trainer, 2005). In one widely-cited example from this literature, Johnson and colleagues (2003) used the

standard Short Form 36 (SF-36) health survey (Ware & Sherbourne, 1992) to investigate patients' perceptions of the impact of a pituitary adenoma on mental and physical wellbeing prior to their receiving any treatment. Results suggested that those with pituitary adenomas had impaired QoL compared to norms from the general US population, and that there were differences in QoL among patients with different pituitary diseases (e.g., Cushing's disease patients reported the highest level of impairment in both physical and mental QoL; patients with acromegaly reported greater impairment in physical than mental QoL; and patients with prolactinomas and NFMA reported greater impairment in mental than physical QoL).

Van Aken and colleagues (2005) also used the SF-36, as well as the Multidimensional Fatigue Index (MFI-20; Smets, Garssen, Bonke, & De Haes, 1995), the Nottingham Health Profile (NHP; Wiklund, 1990), and the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) to explore QoL in patients after long-term cure of Cushing's disease. They found that even after being cured patients still reported a diminished QoL, particularly on items relating to fatigue or physical ability. Dekkers et al. (2006) used the same set of questionnaires and replicated this set of results in post-treatment patients with NFMA.

Association between Sleep Disruption and Quality of Life in Pituitary Disease

A small body of literature describes potential associations between sleep disruption and compromised QoL in pituitary disease patients. In the sample of treated NFMA patients studied by Biermasz et al. (2011), subjective and objective sleep disruptions were accompanied by self-reports of impaired physical and mental function, depressed mood, and restrictions in everyday activities, all of which contributed to poor QoL.

Van der Klaauw and colleagues (2007) partially replicated these findings, reporting that despite their NFMA patients having regular sleeping patterns they also experienced increased daytime sleepiness and fatigue, both of which contributed to diminished QoL. Similarly, Leistner et al. (2015) reported that poor QoL was associated with poor sleep quality in patients with acromegaly, Cushing's disease, prolactinomas, and non-functioning pituitary adenomas (NFPA).

Cognitive Impairment in Pituitary Disease

Cognition has been assessed both subjectively and objectively in patients with pituitary diseases (see, e.g., Bulow et al., 2002; Noad et al., 2004; Pivonello et al., 2015). In terms of subjective reports, Yedinak and Fleseriu (2014) investigated self-perception of cognitive function among patients with active acromegaly, controlled acromegaly, and NFPA using the Functional Assessment of Cancer Therapy Cognitive Scale (FACT-Cog; Wagner et

al., 2013). They found that perception of cognitive dysfunction was highest among patients with NFPA, specifically in the areas of mental agility (speed of thought processing, problem solving, and reasoning) and verbal memory recall. Patients with active acromegaly reported the highest perception of dysfunction with respect to concentration and the ability to learn new information and skills.

In terms of objective reports, Tiemensma et al. (2010) used a neuropsychological test battery to evaluate cognitive function after long-term cure of Cushing's disease. They found that cured patients had significantly lower scores on the Mini Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975) and the Wechsler Memory Scale (WMS; Wechsler, 1945) than matched healthy controls and patients who were being treated for NFMA. Moreover, the cured Cushing's disease patients performed more poorly on tasks assessing planning, perception, and reasoning. These findings suggest that impairment in cognitive functioning is not necessarily due to the presence of a pituitary disease itself, but instead in cases like this may be attributed to the irreversible effects hypercortisolism has on the brain.

Affective Disorders in Pituitary Disease

Affective disorders represent a major complication of pituitary disease (see, e.g., Bulow et al., 2002; Kars et al., 2007; Sonino, Fallo, & Fava, 2010). Sonino and colleagues (2007) compared pituitary disease patients who were in remission to healthy controls and to patients being treated for a non-pituitary endocrine disease. They found that psychological distress (e.g., that associated with DSM diagnoses of major depressive disorder and generalized anxiety disorder) was significantly more prevalent in pituitary disease patients than in healthy controls. Similarly, Pivonello et al. (2015) found that, even after treatment, patients with Cushing's disease experience persistent depression, generalized anxiety, and panic attacks.

The Current Study: Rationale, aims and hypothesis

Sleep disruption is detrimental to physical and psychological well-being. Separate lines of research indicate that patients with pituitary disease experience (a) poor quality of life, (b) disrupted sleep patterns, (c) cognitive impairment, and (d) affective disorders. Of more interest here, however, are preliminary suggestions that the poor quality of life experienced by patients with pituitary disease (including, in some cases, cognitive deficits and affective disorders) is associated with sleep disruption.

In an attempt to explore the possibility of such associations, we recruited a group of patients with pituitary disease and a group of demographically-matched healthy controls.

Using standardized measures of QoL, sleep quality, cognition, and mood we tested these specific hypotheses: (1) disease status will negatively impact QoL, sleep quality, cognition, and mood (i.e., patients will score more poorly on measures of those constructs than controls), and (2) disrupted sleep will be associated with cognitive impairment, affective disorder, and compromised QoL.

Methods

Design and Setting

We used a correlational case-control design, collecting data via telephonic or face-to-face administration of standardized clinical questionnaires and cognitive tests. Face-to-face test sessions were conducted in a private room at Groote Schuur Hospital's Radiotherapy Clinic. Telephone sessions were conducted from a private office in the Numeracy Centre at the University of Cape Town.

Participants

Recruitment. We recruited adult patients diagnosed with a pituitary disease ($n = 12$; 6 women and 6 men) from the Radiotherapy Clinic at Groote Schuur Hospital (GSH). Recruitment was either via telephone or in person. Regarding telephone recruitment, doctors at the Radiotherapy Clinic asked patients who met the study's eligibility criteria for permission to provide us with their contact details. They were assured that providing their contact details would not equate to consenting to participate; it would only mean agreeing to receive a call from a researcher who would further inform them about the nature of the study. Individuals who received a phone call were asked for their verbal consent to participate. After consent was given, the researcher scheduled an appointment for the telephonic test session.

Regarding in-person patient recruitment, we approached individuals waiting for an appointment at the Radiotherapy Clinic. We informed them about the study and asked if they were interested in participating. If they agreed, we invited them to a private room at the clinic where we administered the tests.

We recruited healthy controls ($n = 12$; 6 women and 6 men) from the University of Cape Town community. We recruited these individuals by informing peers, friends, or family members about the nature of the study and asking them whether they knew individuals who met the eligibility criteria. After receiving their contact details, we then called these individuals and asked them if they would be willing to participate. If they replied in the affirmative, we arranged for a time and place that best suited them. Tests were administered via face-to-face interviews for all of these individuals.

Eligibility criteria. All participants were aged between 18 and 65 years. We enforced this criterion strictly because both cognitive function and sleep architecture are much more variable in children, adolescents, and older adults than in young or middle-aged adults (Crowley, 2011; Naveh-Benjamin, Hussain, Guez, & Bar-On, 2003). All participants were required to be fluent English speakers because all study instruments are only validated for use in that language.

All patients were required to have a pituitary disease. To ensure that this criterion be met, doctors from the Radiotherapy Clinic provided us with the clinical background of patients who consented to participate in the study. Furthermore, we obtained the relevant medical information from the patients via the sociodemographic questionnaire (see Appendix A).

Individuals prescribed any medication known to affect sleep and mood were excluded from participation. Additionally, in order to avoid any potential impact of medication changes affecting outcome variables, patients were required to have been on stable treatment for at least 3 months prior to study enrolment.

Healthy controls were required to be free of chronic disease. Any individual with a history of neurological disorder that could negatively affect cognition (e.g., dementia, epilepsy, moderate-to-severe head injury, and stroke) was excluded from participation. Those with a history of psychiatric illness (e.g., affective and psychotic disorders) were also excluded because altered mood states and disrupted sleep are characteristic of such illnesses (Regier, Rae, Narrow, Kaelber, & Schatzberg, 1998).

Finally, pregnant women were not permitted to participate due to the changed sleeping patterns they experience during the gestational period (Hall, Hauck, Carty, Hutton, Fenwick, & Stoll, 2009).

Group matching. We first recruited patients and thereafter sought to recruit demographically-matched healthy controls. Groups were matched on age, level of education, and sex. A large literature describes age-related declines in cognition, even in otherwise healthy individuals (Deary et al., 2009; Murman, 2015). A similarly large literature describes strong associations between level of education and cognitive performance (Guerra-Carrillo, Katovich, & Bunge, 2017; Kiernan & Huerta, 2008; Wilson, Herb, Scherr & Barnes, 2009). The sleep patterns of men and women are frequently found to be different (Guidozzi, 2015). For instance, women have longer sleep latency, experience more daytime sleepiness, have less NREM sleep (specifically with regard to stages 1 and 2), complain about a poorer quality

of sleep, and have a 40% greater risk of developing insomnia (Guidozzi, 2015; Mallampalli, & Carter, 2014).

Measures

To ensure that participant burden was not unduly high and to thereby increase the likelihood of enrolment and reduce the possibility of attrition, we chose the briefest possible psychometrically sound instruments that assessed the constructs of interest.

Sociodemographic and medical questionnaire. We used a self-designed study-specific questionnaire to obtain the necessary demographic information (e.g., age, sex, education) from all participants, and the relevant medical information (e.g., type of illness, type of treatment, and how long they have been on that regimen) from patients. Information obtained from this questionnaire was used to ensure that participants met the study's eligibility criteria and that the groups were well matched.

The Quality of Life Scale (QOLS). This interview-based instrument is adapted from Flanagan's (1982) instrument, and is designed to measure QoL in adult patients with chronic diseases (Burckhardt, Woods, Schultz, & Ziebarth, 1989; see Appendix B). The scale comprises 16 items that measure QoL across five dimensions: material and physical well-being, relationships with others, social activities, personal development, and leisure. Each item is rated on a seven-point Likert-type scale, with higher scores equating to better QoL. Administration time is approximately 5 mins.

The QOLS is internally consistent ($\alpha = .82$ to $.92$) and has high 3-week test-retest reliability ($r = .78$ to $.84$; Burckhardt & Anderson, 2003). The QOLS has successfully been used in patient groups with various clinical backgrounds. It has also been translated into 16 different languages, including Arabic, French, German, Greek, Hebrew, Mandarin, Portuguese, Spanish, and Swedish. This suggests the QOLS has reasonable cross-cultural validity (Burckhardt & Anderson, 2003).

Global Sleep Assessment Questionnaire (GSAQ). This self-report screening tool was developed to help clinicians diagnose sleeping disorders in adults (Roth et al., 2002; see Appendix C). It comprises 11 items that measure sleep quality and its effects on mood, everyday life activities, and physical health problems. Each item is scored on a 4-point Likert-type scale, with higher scores indicating better quality of sleep. Administration time is approximately 5 minutes.

The GSAQ accurately distinguishes between different sleep-related diagnoses (including the absence of a sleep disorder) and has test-retest reliability ranging from $.51$ to $.92$ over spans ranging from 1 to 2 weeks (Roth et al., 2002). Regarding cross-cultural

validity, the developers administered the GSAQ to a mixed clinical and community sample ($N = 212$) from two different primary care centres and five different sleep centres in the US Population. The sample comprised of people of different ethnicities, levels of education, genders, and ages. Results indicated that it was able to detect the presence of a possible sleeping disorder across the different groups (Roth et al., 2002). In addition, the GSAQ was used in a cross-sectional study exploring the prevalence of sleep disorders in pregnant women with preeclampsia ($n = 102$), healthy pregnant women ($n = 106$) and non-pregnant women ($n = 103$). It was found that the GSAQ was able to detect different sleeping problems across all three groups (Khazaie et al., 2013), which shows that the GSAQ can be administered to patient and healthy groups.

Brief Test of Adult Cognition by Telephone (BTACT). This instrument is suited for administration to adults of all ages and from different educational backgrounds, and it can be administered to both cognitively competent and cognitively impaired individuals as well as those with visual impairment (Castanho, Amorim, Zihl, Palha, Sousa, & Santos, 2014; Gurnani, John, & Gavett, 2015; Tun & Lachman, 2006; see Appendix D). It comprises the six subtests listed below. Administration time is approximately 10-15 minutes.

The *Rey Auditory Verbal Learning Test (RAVLT)* is a test of verbal episodic memory consists of a 15-word list that measures both immediate and delayed recall. The researcher reads a list of words to the participant. After all the words have been read the participant is asked to repeat as many words as they can remember. After a 15-min filled delay, the participants are again asked to repeat as many words on the list as they can remember. The outcome measure here is the number of words retained over the delay (i.e., number of words remembered on the delayed recall trial minus the number of words remembered on the immediate recall trial; a larger sum indicates better performance).

The *Digits Backward* subtest assesses working memory. The examiner reads a sequence of numbers to the test-taker, who then has to repeat the sequence in reverse order. Administration begins with a 2-digit sequence and proceeds incrementally up to maximum of an 8-digit sequence. The test is discontinued if the participant succeeds at the 8-digit sequence or fails any sequence length twice. The outcome measure here is the amount of digit- sequences that they got correct.

The *Category Fluency* task assesses the verbal generativity domain of executive functioning. The test-taker is required to name as many animals as s/he can within 90 seconds. The outcome measure here is the number of correct words generated.

The *Stop and Go Task* assesses the inhibition domain of executive functioning. On the first (acquisition) trial, the test-taker must respond with ‘go’ when the examiner says the word ‘green’ and must respond with ‘stop’ when the examiner says ‘red.’ On the subsequent reverse trial, the test-taker must respond with ‘go’ when the examiner says the ‘red’ and must respond with ‘stop’ when the examiner says ‘green.’ The third trial is a mixture of acquisition and reverse phases alternating unexpectedly. This measures the ability to control automatic responses. The outcome measure here is the number of correct responses.

The *Number Series* task measures inductive reasoning. The examiner reads a sequence of five digits and the test-taker is required to provide a sixth digit that completes or continues the sequence. The task consists of five trials of graded difficulty. The outcome measure here is the number of trials on which the participant provides a correct response.

The *Backward Counting* task measures processing speed. The examiner instructs the test-taker to count backwards from 100 for 45 seconds. The outcome measure here is the number that is reached (i.e., lower scores are better).

Telephonic administration of the BTACT yields similar results to in-person administration, with correlations for different subtests ranging from .55 to .95 (Lachman, Agrigoroaei, Tun, & Weaver, 2014; Tun & Lachman, 2006). Moreover, Lachman et al. (2014) showed that it can be administered to both healthy and patient populations. The instrument was used successfully in a South African study investigating memory impairment in patients with Addison’s disease (Henry, Thomas, & Ross, 2014).

Beck Depression Inventory-Short Form (BDI-SF). This 13-item self-report instrument measures intensity and depth of depression in clinical and non-clinical populations (Beck & Beck, 1972; see Appendix E). Each item consists of a statement and four response options. Each option is associated with a score ranging from 0–3. Higher scores are associated with more severe depression. Administration time is approximately 5 minutes.

Knight (1984) reported the instrument's internal consistency reliability to be .81 in a health survey of a large sample of men and women ($N = 1091$). Moreover, the BDI-SF is a valid substitute for the full BDI, with total-score correlations ranging from .89 to .97 (Beck, Rial, & Rickels, 1974). The BDI-SF has excellent psychometric properties in identifying moderate and severe depression (Furlanetto, Mendlowicz, & Bueno, 2005). The full version of the BDI has been used successfully in South African studies investigating clinical and non-clinical populations (de Klerk, du Plessis, Steyn, & Botha, 2004; Kagee, Nel, & Saal, 2014; Makhubela & Mashegoane, 2016; Stein et al., 2015).

Procedure

Study procedures lasted about 20 minutes in total, regardless of whether we administered the measures over the telephone ($n = 7$; 7 patients) or in person ($n = 17$; 5 patients).

Telephone administration. We called individuals who had earlier indicated their willingness to participate and asked them to give verbal consent (Appendix F). After receiving consent and completing the sociodemographic and medical questionnaire, we administered the study instruments, following standardized instructions in the relevant test manuals, in this order: QOLS, GSAQ, BDI-SF, and BTACT. When administration was complete, we thanked them for participating and encouraged them to ask questions. Thereafter we debriefed them and ended the phone call.

Face-to-face administration. We conducted the interview in a private room at the GSH Radiotherapy Clinic. We administered the measures in the same order as described above for the telephone administration. When administration was complete, we thanked them and encouraged them to ask questions. Thereafter, we debriefed and dismissed them.

Ethical Considerations

Ethical approval for the study procedures was granted by the Research Ethics Committees of the University of Cape Town's Department of Psychology (PSY2019-033) and Faculty of Health Sciences (462/2019).

Consent and confidentiality. All consent procedures were completed prior to administration of the study measures. Before asking individuals to verbally consent to participation we informed them about the nature of the study and told them that participation included facilitating data collection, allowing use of the data, and permitting publication of the results. We also informed them that their participation was voluntary, that they could refuse to answer any question they found uncomfortable, and that they could withdraw at any

time without penalty and without having to give an explanation. We emphasized to patients that discontinuing participation would have no bearing on their treatment.

The collected data are held strictly confidential. We anonymized the data by assigning each participant a unique study identification number. The data are kept on a password-protected external hard drive accessible only to the researchers and their supervisors. A copy of the complete dataset is held on another external hard drive for back-up purposes.

Risks and benefits. Participation did not pose any foreseeable social, psychological, or physical risks. Participants received no direct compensation for their involvement.

Debriefing. We debriefed each participant individually when administration of all study measures had been completed. We also sent them a debriefing letter (see Appendix G), either via post or email. When write-up was complete, they received a summary of the study results, again either via post or email.

Data Management and Statistical Analysis

We used SPSS (v. 25.0) to complete all analyses, with the threshold for statistical significance (α) set at .05 unless noted otherwise.

Deriving outcome variables. The set of major outcome variables was comprised of the total scores on the QOLS, GSAQ, and BDI-SF, as well as individual scores for each BTACT subtest. We scored each instrument following standard methods described in the relevant test manual.

Descriptive and inferential analyses. As an initial step, we generated descriptive statistics (measures of central tendency and variation) for all of the data to describe the sample and to identify outliers. We defined outliers as any score $\pm 3 SD$ from the group mean. Thereafter, inferential analyses proceeded across three steps. First, a series of independent-sample *t*-tests confirmed the groups were well matched on key sociodemographic characteristics (age, highest level of education). Second, a series of one-tailed independent-sample *t*-tests assessed the magnitude of between-group differences on the QOLS, GSAQ, BTACT, and BDI-SF (i.e., they tested Hypothesis 1). Third, a series of bivariate correlational analyses (estimated using Pearson's coefficient) assessed, for the entire sample and within each group separately, the magnitude of association between scores on the GSAQ, QOLS, BTACT, and BDI-SF (i.e., they tested Hypothesis 2).

Results

Sample Characteristics

Table 1 summarises the sample sociodemographic characteristics. The sample's age range was 26–65 years ($M = 45.25 \pm 14.61$). Level of education was similarly variable, ranging from a participant who had not completed primary school to one who had obtained a university degree (5–16 years, $M = 11.46 \pm 3.40$). As expected given our study design and recruitment plan, analyses detected no significant between-group differences with regard to age and highest level of education.

Patient clinical characteristics. Patients had been diagnosed with Cushing's disease ($n = 1$), acromegaly ($n = 1$), hypopituitarism ($n = 5$), partial hypopituitarism ($n = 2$), or apoplexy ($n = 3$). All had been on stable treatment for at least 3 months prior to study enrolment. Most ($n = 10$; 83% of the sample) reported being prescribed hydrocortisone medication. No patient was receiving radiotherapy at the time of study participation, although two (17%) reported having received radiotherapy and eight (67%) reported having undergone surgery 8 in the past to treat their pituitary disease.

Table 1
Sample Sociodemographic Characteristics (N = 24)

Variable	Group		<i>t</i>	<i>P</i>	ESE
	Patients (<i>n</i> = 12)	Controls (<i>n</i> = 12)			
Age (years)					
<i>M</i> (<i>SD</i>)	47.42 (12.88)	46.99 (7.66)	-0.72	.24	-0.31
Range	26–65	30–60			
HLOE					
<i>M</i> (<i>SD</i>)	11.33 (3.08)	11.58 (3.82)	0.12	.45	0.05
Range	7–15	5–16			
Sex					
Female	6 (50%)	6 (50%)			
Male	6 (50%)	6 (50%)			

Note. For the variables *Age* and *HLOE*, means are presented with standard deviations in parentheses. ESE = effect size estimate (in this case, Cohen's *d*); HLOE = highest level of education (in years).

Between-group Comparisons: Quality of life, sleep quality, cognition, affect,

Although analyses detected no significant between-group differences (at either the conventional or the Bonferroni-corrected *p* threshold) on the QOLS and BDI-SF, they did detect a strong trend toward such differences for the GSAQ. Of note is that the magnitude of this trending difference was associated with a large effect size (see Table 2).

Regarding BTACT performance, descriptive statistics indicated that patients scored more poorly than controls on all subtests. However, the only statistically significant between-group difference (albeit only at the conventional *p* threshold) was on the Stop and Go task. Again, the magnitude of difference there was associated with a large effect size (see Table 2).

Table 2

Descriptive Statistics and Between-group Comparisons: Measures of quality of life, sleep quality, cognition, and depression (N = 24)

Variable	Group		<i>t</i>	<i>P</i>	ESE	95% CI	
	Patients (<i>n</i> = 12)	Controls (<i>n</i> = 12)				LL	UL
QOLS	87.33 (14.99)	84.00 (17.42)	-0.50	.30	0.21	-17.09	10.42
GSAQ	35.33 (6.00)	38.58 (2.39)	1.74	.05	0.91	-0.62	7.12
BTACT							
RAVLT	-2.08 (1.88)	-2.16 (1.89)	-0.11	.45	0.04	-1.68	1.51
Digits Backward	3.50 (1.88)	4.08 (2.15)	0.71	.24	0.30	-1.12	2.29
Category Fluency	10.92 (5.80)	13.18 (4.81) ^a	1.01	.16	0.44	-2.38	6.91
Stop and Go	30.00 (3.33)	32 (.00)	2.08	.03*	0.86	-0.09	4.09
Number Series	1.00 (1.34)	1.67 (1.67)	1.08	.15	0.45	-0.62	1.95
Counting Backwards	28.18 (11.72) ^b	31.33 (10.20) ^c	0.69	.25	0.30	-6.36	12.66
BDI-SF	2.42 (3.77)	2.58 (2.19)	-0.13	.44	0.05	-2.44	2.78

Note. In the second and third columns, means are presented with standard deviations in parentheses. ESE = effect size estimate (in this case, Cohen's *d*); CI = confidence interval; LL = lower limit; UL = upper limit; QOLS = Quality of Life Scale; GSAQ = Global Sleep Assessment Questionnaire; BTACT = Brief Test of Adult Cognition by Telephone; RAVLT = Rey Auditory Verbal Learning Test; BDI-SF = Beck Depression Inventory-Short Form.

^a*n* = 11; data from one participant in this group were not part of the analysis because they contained outlying values.

^b*n* = 11; data from one participant in this group were not part of the analysis because they contained outlying values.

^c*n* = 11; one participant in this group did not provide an answer to the relevant question.

**p* < .05. Bonferroni-corrected *p*-value = .05 / 9 = .006. All listed *p*-values are one-tailed.

Bivariate Correlations: Sleep quality, cognition, depression, and quality of life

For the entire sample, analyses detected a significant negative association between QOLS and BDI-SF scores ($p = .042$; those who reported better quality of life also reported lower levels of depression; see Table 3). Analyses also detected strong trends toward (a) a significant positive association between GSAQ and QOLS scores ($p = .054$; those who reported better quality of life also reported better sleep quality), and (b) a significant positive association between BTACT Backward Counting and BDI-SF scores ($p = .053$; those who performed better on the cognitive test also reported lower levels of depression). Finally, analyses detected moderate trends toward (a) a significant negative association between GSAQ and BDI-SF scores ($p = .075$; those who reported better sleep quality also reported lower levels of depression), (b) a significant positive association between GSAQ and BTACT Digits Backward scores ($p = .099$; those who reported better sleep quality performed better on the cognitive test), and (c) a significant negative association between BTACT Stop and Go and BDI-SF scores ($p = .077$; those who performed better on the cognitive test also reported lower levels of depression).

For the patient group, the analyses presented in Table 4 detected a significant positive association between GSAQ and QOLS scores ($p = .026$; those who reported better quality of life also reported better sleep quality). Analyses also detected a strong trend towards a significant positive association between the BDI and BTACT counting backward scores ($p = .058$; those who performed better on the cognitive test also reported lower levels of depression). Finally, analyses detected moderate trends toward (a) a significant negative association between QOLS and BDI-SF scores ($p = .085$; those who reported better quality of life also reported lower levels of depression), and (b) a significant positive association between QOLS and BTACT Stop and Go scores ($p = .068$; those who reported better quality of life performed better on the cognitive test).

For the control group, the analyses presented in Table 4 detected (a) a significant positive association between QOLS and BTACT Number Series scores ($p = .047$; those who reported better quality of life also performed better on the cognitive task), and (b) a significant negative association between QOLS and BTACT RAVLT scores ($p = .015$; those who reported better quality of life performed better on the cognitive test). Analyses also detected a moderate trend towards a significant negative association between GSAQ and RAVLT scores ($p = .078$; those who reported better quality of sleep performed poorly on the cognitive test).

Table 3

Bivariate Correlations for the Entire Sample: Associations between sleep quality, cognition, mood, and quality of life (N = 24)

	1	2	3	4	5	6	7	8	9
1. GSAQ	1.00								
2. BTACT RAVLT	-.445	1.00							
3. BTACT Digits Backwards	.273	.334	1.00						
4. BTACT Category Fluency ^a	.055	-.009	.137	1.00					
5. BTACT Stop and Go ^b	.249	-.183	-.155	.541*	1.00				
6. BTACT Number Series	.092	-.185	.138	.555*	.282	1.00			
7. BTACT Backward Counting ^c	-.023	.177	.472	.490*	-.064	.441*	1.00		
8. BDI-SF	-.303	.167	.234	.273	-.307	-.009	.346	1.00	
9. QOLS	.336	-.218	-.185	-.149	.219	.232	-.270	-.361*	1.00

Note. Data presented are Pearson's r correlation coefficients. Statistically significant associations (one-tailed) are highlighted in boldface font.

GSAQ = Global Sleep Assessment Questionnaire; BTACT = Brief Test of Adult Cognition by Telephone; RAVLT = Rey Auditory Verbal Learning Test; BDI-SF = Beck Depression Inventory-Short Form; QOLS = Quality of Life Scale.

^a $N = 23$; data from one participant in this group were not part of the analysis because they contained outlying values.

^b $N = 23$; data from one participant in this group were not part of the analysis because they contained outlying values.

^c $N = 23$; one participant in this group did not provide an answer to the relevant question.

* $p < .05$.

Table 4

Bivariate Correlations for the patient and control groups: Associations between sleep quality, cognition, mood, and quality of life (N = 24)

	1	2	3	4	5	6	7	8	9
1. GSAQ	1.00	.115	.281	.069	.145	-.112	-.249	-.327	.573*
2. BTACT RAVLT	-.437	1.00	.218	-.009	-.290	-.036	.460	.108	.245
3. BTACT Digits Backwards	.237	.449	1.00	-.406	-.391	.000	.382	.415	-.039
4. BTACT Category Fluency ^a	-.303	.563*	.284	1.00	.527*	.650*	.381	.230	.129
5. BTACT Stop and Go ^b	.d	.d	.d	.d	1.00	.304	-.240	-.405	.455
6. BTACT Number Series	.281	-.306	.186	.440	.d	1.00	.507	-.125	-.805
7. BTACT Backward Counting ^c	.319	-.086	.545*	.652*	.d	.364	1.00	.503	-.249
8. BDI-SF	-.383	.287	-.011	.363	.d	.132	.084	1.00	-.423
9. QOLS	.188	-.624*	-.272	-.407	.d	.506*	-.273	-.319	1.00

Note. Data presented are Pearson's r correlation coefficients. Statistically significant associations (one-tailed) are highlighted in boldface font. Data in the top right corner shaded light grey = patient group; data in the bottom left corner not shaded = control group. GSAQ = Global Sleep Assessment Questionnaire; BTACT = Brief Test of Adult Cognition by Telephone; RAVLT = Rey Auditory Verbal Learning Test; BDI-SF = Beck Depression Inventory-Short Form; QOLS = Quality of Life Scale.

^a $N = 23$; data from one participant in this group were not part of the analysis because they contained outlying values.

^b $N = 23$; data from one participant in this group were not part of the analysis because they contained outlying values.

^c $N = 23$; one participant in this group did not provide an answer to the relevant question.

^dCannot be computed because the variable is constant: All of the controls had the same score for this variable.

* $p < .05$.

Discussion

This study investigated sleep quality, quality of life (QoL), cognitive performance, and affective regulation (and associations among them) in patients with pituitary disease. Below, we discuss the status of our hypotheses and how the current findings relate to the existing literature. We conclude by noting some limitations of the study and by making recommendations for future research on this topic.

Hypothesis 1: Between-group comparisons

Hypothesis 1 stated that the presence of pituitary disease would negatively affect QoL, sleep quality, cognitive performance, and affect. This hypothesis was only partially confirmed: we observed a trend towards a significant between-group difference at the conventional level with regard to sleep quality, with patients experiencing poorer quality of sleep than controls. Patients with pituitary disease also scored significantly more poorly than controls on one of the measures of cognitive performance (the BTACT Stop and Go task, which assesses the inhibition and self-regulation component of executive functioning), but analyses detected no significant between-group differences in self-reported QoL or depression, and on objective cognitive measures of episodic verbal memory, working memory, the verbal generativity domain of executive functioning, reasoning, and processing speed.

Regarding the sleep quality finding, the current data are consistent with previous studies reporting that sleep complaints are frequently observed in patients with pituitary disease (Biermasz et al., 2011; Leistner et al., 2015; Romijn, 2016; Van der Klaauw et al., 2007). These studies reported that patients with pituitary disease experience decreased sleep quality due to breathing problems, fragmented sleep, delayed onset of sleep, fatigue and daytime sleepiness. Similar problems were described by our sample of patients, although none mentioned experiencing sleep-disordered breathing. Overall, then, the current findings taken alongside those from previous studies support the inference that patients with pituitary disease experience poor quality of sleep.

Regarding the cognitive findings, the current data are consistent with previous studies reporting that patients with pituitary disease perform more poorly on tasks assessing executive functioning. For instance, Tooze, Gittoes, Jones, and Toogood (2009) reported that patients with pituitary diseases experience impairments in the following domains of executive functioning: attention, control and direction of lower level automatic function.

In contrast to previous studies (e.g., Guinan, Lowy, Stanhope, Lewis & Kopelman, 1998; Tiemensma et al., 2010), the current analyses detected no significant impairment

among pituitary disease patients on tasks assessing verbal episodic memory, working memory, inductive reasoning, and processing speed.

Overall, then, the current findings taken alongside those from previous studies suggest that pituitary disease negatively affects cognitive function within particular domains, but does not affect cognitive performance generally.

Regarding the QoL finding, the current data stand in contrast to a large body of research suggesting that patients with pituitary disease experience relatively poor quality of life (see, e.g., Andela et al., 2018; Chanson & Salenave, 2008; Johnson et al., 2003; Rowels et al., 2005). For instance, Pivonello et al. (2015) found that patients with Cushing's disease experience an impaired quality of life in the family, social, and work domains. One possible reason for the disparity between our QoL results and those of previous studies is that one of our eligibility criteria was that patients were on stable treatment for at least 3 months prior to enrolment. There is some evidence that treatment might improve QoL. For example, Pereira, Tiemensma, Romijn, and Biermasz (2012) found that while the QoL of pituitary adenoma patients may remain impaired after successful treatment, there are some instances in which it improves after treatment.

Another explanation for this finding might be that the brief self-report measure that we used to assess QoL, the Quality of Life Scale, was not sensitive to more subtle deficits that might be detected by other, more comprehensive measures. Other studies (Dekkers et al., 2006; Johnson et al., 2003; Van Aken et al., 2005) evaluating the QoL experienced by patients with pituitary disease made use of the SF-36, which comprises 36 statements assessing 8 health concepts (in contrast, the QOLS comprises 16 items assessing 5 domains).

Regarding the depression findings, again our current data stand in contrast to previous findings from this literature. Numerous studies indicate that patients with pituitary disease frequently experience depressive symptoms (see, e.g., Bulow et al., 2002; Kars et al., 2007; Sonino et al., 2010). For instance, Pivonello and colleagues (2015) found that in some cases of Cushing's disease, patients experience symptoms of depression, anxiety, or panic disorders even after successful treatment.

There are at least two possible explanations for the discrepancy between the current depression findings and those from previous studies. The first relates to the timeframe across which depressive symptoms were reported. The BDI-SF, which was used here, asks about symptoms experienced over the week prior to reporting. Previous studies that investigated depression in this patient population (e.g., Dekkers et al., 2006; Van Aken et al., 2005) used the Hospital and Anxiety Scale (HADS; Zigmond & Snaith, 1983). Although the HADS also

enquires about symptoms experienced 1 week prior to reporting, it is important to note that these studies used complementary mood information from the SF-36, which has a mental well-being component and enquires about symptoms experienced as much as 4 weeks prior to reporting (Ware & Sherbourne, 1992). Only examining 1 week of symptoms might reduce the sensitivity of enquiry.

A second possible explanation for these between-study discrepancies is that the depressive symptoms reported by patients in previous studies were not actually indicative of major depressive disorder, but rather by the fatigue- and apathy-dominated clinical syndrome that Weitzner and colleagues (2005) postulated is experienced by pituitary disease patients.

Hypothesis 2: Bivariate correlations

Hypothesis 2 stated that disrupted sleep is associated with cognitive impairment, affective disorder, and compromised QoL. This hypothesis was also partially confirmed: Analyses detected a significant positive association between sleep quality and QoL (i.e., patients who reported poorer sleep quality also reported poorer QoL). This association is consistent with previous findings in this literature (see, e.g., Biermasz et al., 2011; Leistner et al., 2015; Romjin, 2016). For instance, Van der Klaauw et al. (2007) reported that their NFMA patients experienced daytime sleepiness and fatigue, both of which contributed to diminished QoL. Hence, the current findings taken alongside those from previous studies support the inference that the poor QoL experienced by patients with pituitary disease might bear important relation to their disrupted sleep patterns.

Although the analyses detected no significant associations between sleep quality and cognitive performance, or between sleep quality and affective disorders, we observed in the patient group a strong trend towards a positive association between affective disorder and the processing speed aspect of cognition (those who performed better on the cognitive test also reported lower levels of depression). This finding is consistent with previously published findings indicating an increased prevalence of cognitive dysfunction and a high incidence of mental disorders among hypopituitary women (Bulow et al., 2002).

Analyses also detected a moderate trend toward a significant negative association between QoL and depression—those who reported better quality of life also reported lower levels of depression. This finding is also consistent with those reported in previously published studies (Johnson et al., 2003; Sonino et al., 2007). For instance, Kars and colleagues (2007) found that impaired QoL experienced by female patients treated for microprolactinoma is marked by increased anxiety and depression. .

Finally, analyses detected a significant positive association between QoL and the inhibition and self-regulation component of executive functioning (i.e. cognition) —those who reported better quality of life performed better on the cognitive test. Again, this finding is consistent with those reported in previously published studies (Noad et al., 2004; Pereira et al., 2012). For instance, Solomon et al. (2019) reported that patients with acromegaly experienced worse QoL and displayed poorer executive functioning than healthy controls.

Thus, the current findings taken alongside those from previous studies support the inference that depression experienced by patients with pituitary disease might bear important relation to their QoL and to their cognitive function. Further to this, cognitive dysfunction, particular in the area of executive function, might bear an important relation to overall QoL in these patients.

Limitations and Directions for Future Research

We acknowledge that the following limitations must temper the inferences one might draw from the current findings.

First, the current N of 24 means the study was statistically under-powered to achieve its aims. We calculated an ideal sample size for this study using G*Power software (Faul, Erdfelder, Lang, & Buchner, 2007). With type of analysis set at one-tailed independent-samples t -test and statistical parameters set at power $(1 - \beta) = .80$, $\alpha = .05$, and effect size (Cohen's d) = .20 (small in magnitude; an effect size of 0.2 would denote a 50–58% difference between groups; Cohen, 1962), the software determined that a minimum of 156 participants would be required. Hence, future research investigating these aims should recruit at least 78 patients and 78 controls. This might be difficult, however. As we discovered, it was a strenuous task to access patients because of the rarity of pituitary disease. Little is known about the base rate of pituitary diseases in the South African population, but global estimates suggest prevalence data ranges from <1% to 30% (Ezzat, Asa, Couldwell, Barr, Dodge, Vance & McCutcheon, 2004).

Second, our patient group included individuals with different forms of pituitary disease, as the patient database provided to us by the GSH Radiotherapy Clinic consisted of patients with various pituitary diseases. These different forms of diseases might introduce variability into at least some of the outcomes under consideration. For instance, Pereira and colleagues (2012) reported that cognitive dysfunction was present in patients treated for Cushing's disease, regardless of whether or for how long they had been in remission, but that no such deficits were detected in patients with a long-term cure of acromegaly. Future

research in the field should therefore aim to recruit patients with the same type of pituitary disease.

Third, the mode of administration of study instruments was inconsistent across participants (within both the patient and control groups). Because the clinic we sampled from ran only twice a month, we used telephonic recruitment and administration to supplement in-person recruitment and administration. Nonetheless, one must acknowledge that different modes of test administration place different demands on cognitive function: Whereas both in-person and telephonic testing require the test-taker to have basic verbal and language skills, the latter form of administration has a greater auditory demand which could be burdensome and affect the way the participant responds (Bowling, 2005). Future research in the field should therefore be careful to maintain a consistent mode of test and interview administration.

Summary and Conclusion

This study contributes to the existing pool of psychological research on patients with pituitary diseases. Our main aim was to investigate the possible associations between sleep disruption, poor QoL, cognitive dysfunction, and affective disorders in such patients. Results showed that, compared to matched healthy controls, patients with pituitary disease experience poorer sleep quality and specific cognitive impairment in the domain of executive functioning. These findings are consistent with previous research in the field. Similarly consistent were our findings of a significant positive correlation between sleep quality and overall quality of life in patients with pituitary disease.

Despite the fact that our hypotheses were not fully confirmed (in particular, there was a lack of statistical significance in analyses involving the measure of affect), the results do encourage further exploration of this topic. Descriptive statistics showed that, even for those inferential analyses that did not deliver statistically significant results, the order of means and direction of associations were, for the most part, in the predicted direction. Future studies using larger samples, homogeneous patient groups, and consistent modes of test administration are therefore encouraged and might shed further light on associations between sleep quality, cognition, affect, and overall QoL in patients with pituitary disease.

Acknowledgments

We would like to express our gratitude and appreciation to the following people:

To our supervisor: Dr Kevin Thomas and Co-supervisor: Dr Michelle Henry, for their consistent support and guidance throughout the research process.

To the doctors at the Radiotherapy Clinic at Groote Schuur Hospital, for accommodating us with data collection.

To all of our participants, for their time and contribution to this research.

Lastly, to our beloved parents, patient siblings and supportive partners, for their unconditional love and encouragement.

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Appendix A:
Sociodemographic Questionnaire

Section A. (for all participants)

Name.....

Participant Number.....

Age.....

Sex.....

Email address.....

Highest level of education obtained.....

What is the total monthly income of the household in which you live? If you are a student please take care to put your immediate caregiver’s monthly income not your own. (please circle only one option):

R0 – R499

R500 – R999

R1000 – R2499

R2500 – R5499

R5500 – R9999

R10000 – R20000

R20000 – R30000

R30000 +

Section B. (for patients only)

What forms of treatment are you currently on?

Provide more information about treatment

.....
.....

How long have you been on this treatment?

Section C. (for controls only)

Do you suffer from any chronic diseases?

If yes, please specify

.....
.....
.....

Are you on any type of medical treatment?

If yes, please provide more information

.....

Are you on any medication?

If yes, please specify which medication

.....

.....

.....

Appendix B:

QOLS

A seven point Likert-type scale is used to rate each item (shown below). The options are; (1) 'terrible' (2) 'unhappy' (3) 'mostly dissatisfied' (4) 'mixed' (5) 'mostly satisfied' (6) 'pleased' (7) 'delighted.'

The score is calculated by adding up the responses to each item to reach a total score. A high score is equated with a better QoL.

1. Material comforts home, food, conveniences, financial security
2. Health - being physically fit and vigorous
3. Relationships with parents, siblings & other relatives- communicating, visiting, helping
4. Having and rearing children
5. Close relationships with spouse or significant other
6. Close friends
7. Helping and encouraging others, volunteering, giving advice
8. Participating in organizations and public affairs
9. Learning- attending school, improving understanding, getting additional knowledge
10. Understanding yourself - knowing your assets and limitations - knowing what life is about
11. Work - job or in home
12. Expressing yourself creatively
13. Socializing - meeting other people, doing things, parties, etc
14. Reading, listening to music, or observing entertainment
15. Participating in active recreation
16. Independence, doing for yourself

Appendix C:

GSAQ

Each of the items below is presented next to a row of checkbox response options regarding symptom frequency over the last four weeks. The response options are (4) 'never' (3) 'sometimes' (2) 'usually' and (1) 'always' (Roth et al., 2002).

1. Did you have difficulty falling asleep, staying asleep, or did you feel poorly rested in the morning?
2. Did you fall asleep unintentionally or did you have to fight to stay awake during the day?
3. Did sleep difficulties or daytime sleepiness interfere with your daily activities?
4. Did work or other activities prevent you from getting enough sleep?
5. Did you snore loudly?
6. Did you hold your breath, have breathing pauses, or stop breathing in your sleep?
7. Did you have restless or "crawling" feelings in your legs at night that went away if you moved your legs?
8. Did you have repeated rhythmic leg jerks or leg twitches during your sleep?
9. Did you have nightmares, or did you scream, walk, punch, or kick in your sleep?
10. Did the following things disturb you in your sleep: pain, other physical symptoms, worries, medications, or other (specify)?
11. Did you feel sad or anxious?

Appendix D:

BTACT

Drum	
Curtain	
Bell	
Coffee	
School	
Parent	
Moon	
Garden	
Hat	
Farmer	
Nose	
Turkey	
Colour	
House	
river	

DIGITS BACKWARDS:

2-4	4-2	
5-7	7-5	
6-2-9	9-2-6	
4-1-5	5-1-4	
3 - 2 - 7 - 9	(9 - 7 - 2 - 3)	
4 - 9 - 6 - 8	(8 - 6 - 9 - 4)	
1 - 5 - 2 - 8 - 6	(6 - 8 - 2 - 5 - 1)	
6 - 1 - 8 - 4 - 3	3 - 4 - 8 - 1 - 6)	
5 - 3 - 9 - 4 - 1 - 8	(8 - 1 - 4 - 9 - 3 - 5)	
7 - 2 - 4 - 8 - 5 - 6	(6 - 5 - 8 - 4 - 2 - 7)	
8 - 1 - 2 - 9 - 3 - 6 - 5	5 - 6 - 3 - 9 - 2 - 1 - 8	
4 - 7 - 3 - 9 - 1 - 2 - 8	(8 - 2 - 1 - 9 - 3 - 7 - 4)	
9 - 4 - 3 - 7 - 6 - 2 - 5 - 8	8 - 5 - 2 - 6 - 7 - 3 - 4 - 9	
7 - 2 - 8 - 1 - 9 - 6 - 5 - 3	(3 - 5 - 6 - 9 - 1 - 8 - 2 - 7)	

NORMAL	G	GO
	R	STOP
	G	GO
REVERSE	R	GO
	R	GO
	G	STOP
	R	GO
	R	GO
NORMAL	R	STOP
	G	GO
	R	STOP
	G	GO
	G	GO
	R	STOP
REVERSE	G	STOP
	G	STOP
	R	GO
	G	STOP
NORMAL	G	GO
	R	STOP
	G	GO
	G	GO
	R	STOP
REVERSE	G	STOP
	G	STOP
	R	GO
	G	STOP
	R	GO
NORMAL	R	STOP
	G	GO
	R	STOP
	G	GO

NUMBER SERIES:

18, 20, 24, 30, 38.....(48)	
81, 78, 75, 72, 69.....(66)	
7, 12, 16, 19, 21.....(22)	
28, 25, 21, 16, 10.....(3)	
20, 37, 18, 38, 16.....(39)	

COUNTING:

Number reached –

Number errors –

DELAYED RECALL:

Drum	
Curtain	
Bell	
Coffee	
School	
Parent	
Moon	
Garden	
Hat	
Farmer	
Nose	
Turkey	
Colour	
House	
river	

Appendix E:
BDI-SF

Circle the statement that describes best how you've been feeling in the past week, including today.

1. 0 I do not feel sad.
1 I feel sad.
2 I am sad all the time and I cannot snap out of it.
3 I am so sad or unhappy that I cannot snap out of it.

2. 0 I am not particularly discouraged about the future.
1 I feel discouraged about the future
2 I feel I have nothing to look forward to
3 I feel the future is hopeless and that things cannot improve.

3. 0 I do not feel like a failure.
1 I feel I have failed more than the average person
2 As I look back on my life, all I can see is a lot of failure
3 I feel I am a complete failure as a person

4. 0 I get as much satisfaction out of things that I used to.
1 I don't enjoy things the way I used to.
2 I don't get real satisfaction out of anything anymore
3 I am dissatisfied or bored with everything.

5. 0 I don't feel particularly guilty.
1 I feel guilty a good part of the time.
2 I feel quite guilty most of the time.
3 I feel guilty all the time.

6. 0 I don't feel disappointed in myself.
1 I am disappointed in myself.
2 I am disgusted with myself.
3 I hate myself.

7. 0 I don't have any thoughts of killing myself
1 I do have thoughts of killing myself, but I would not carry it out.
2 I would like to kill myself.
3 I would kill myself if I had the chance

8. 0 I have not lost interest in other people.
1 I am less interested in other people than I used to be.
2 I have lost most of my interest in other people.
3 I have lost all of my interest in other people.

9. 0 I make decisions about as well as I ever could
1 I put off making decisions more than I used to.
2 I have greater difficulty in making decisions than before.
3 I cannot make decisions at all anymore
10. 0 I don't feel I look any worse than I used to
1 I am worried that I am looking old or unattractive
2 I believe that there are permanent changes in my appearance that make me look unattractive.
3 I believe that I look ugly.
11. 0 I can work about as well as before
1 it takes an extra effort to get started with doing something.
2 I have to push myself very hard to do anything.
3 I cannot do any work like before.
12. 0 I don't get more tired than I used to.
1 I get tired more easily than I used to.
2 I get tired doing almost anything
3 I am too tired to do anything.
13. 0 My appetite is no worse than usual.
1 My appetite is not as good as it used to be
2 My appetite is much worse than it used to be.
3 I have no appetite at all anymore.

Appendix F:
Consent Form
DEPARTMENT OF PSYCHOLOGY



1) Study title

Poor Quality of life, Cognitive Impairment and Affective Dysregulation may be mediated by Sleep Disruption in Patients with Pituitary Disease.

2) Investigator's

We are Psychology Honours students at the University of Cape Town and the information obtained from this study will be used for our thesis project.

3) Purpose

You are invited to participate in our study that aims to explore whether poor quality of life, memory and mood is affected by poor sleep in patients with pituitary disease. Before we start with the study questions there are a series of questions that we need to ask you to check whether you fit the study criteria.

4) Exclusion criteria

- Are you between the age of between 18- 65?
- Have you been on stable treatment for at least 3 months?
- Are you pregnant?
- Do you have a history of neurological disorders that could negatively affect memory, attention, learning, judgement, and reasoning?
- Do you have a history of psychiatric illness (e.g., affective and psychotic disorders)?
- Do you have any chronic diseases?
- What medication are you on?

5) Procedures

The telephonic survey will take approximately 60 minutes of your time. We will ask you a series of questions relating to your quality of sleep, memory and how you feel about life. Participation is completely voluntary and you may withdraw from the study at any time without penalty.

6) Privacy and Confidentiality

All the data obtained in this study will form part of a Psychology Honours research thesis. Your right to anonymity will be respected, which means that no names will be mentioned in the final write up of the study. Each participant will be assigned a number to therefore ensure their confidentiality.

7) Risks and Benefits

Participation does not pose any foreseeable psychological or physical risks. However, some questions might be considered personal and therefore if at any point in time you feel uncomfortable, you may terminate the interview or choose not to answer a specific question.

8) Questions and answers

You are encouraged to ask questions if you are unsure about certain details.

9) Signatures

The participant is well aware of the nature and purpose of the study. They have been informed about the procedures, confidentiality agreement, risks and benefits and, they are encouraged to ask further questions should they have any.

Researcher's Signature

Date.....

Do you agree to participate and consent to have your results used for the purpose of the research thesis and publication in an accredited journal? Are you aware that you are free to withdraw from this study at any given time should you feel the need to do so, and in doing so you will not encounter any penalties?

Participants verbal consent

Date.....

Appendix G:

Study Debriefing

This study is concerned with the detrimental effects of sleep disruption on cognition, quality of life and mood. Previous studies have found that in patients with pituitary disease, poor quality of life might be related to disrupted sleep patterns, no published study has examined the possible effects of sleep disruption on poor quality of life, cognitive dysfunction and emotion regulation difficulties in pituitary disease. The aim of this project is to investigate, in a sample of patients diagnosed with a non-functioning pituitary macroadenoma, the possibility of these effects.

How was this tested?

In this study, you were asked a series of questions, which tested cognition, depression, quality of life, quality of sleep and emotional regulation. All participants were asked the same questions in the same order during a phone call which lasted 1 hour.

Hypotheses and main questions:

We expect to find that not only does having pituitary disease negatively impact quality of life, sleep, emotion and cognition, but that impaired quality of life in these patients also arises due to sleep disruption, cognitive impairment and emotion regulation difficulties. Furthermore, cognitive impairment and emotion regulation difficulties are likely to occur, at least in part due to disrupted sleep.

Why is this important to study?

This study will not only contribute to the existing pool of psychological research on patients with pituitary disease, but will also lay a novel foundation for further research on the possible effects of sleep on cognitive impairment and emotion dysregulation in these patients. Moreover, should the results indicate that sleep plays an important role in quality of life, cognition and emotion, the study will promote the development of treatment targeted at improving sleep patterns (and thereby indirectly improving cognition, mood, and overall quality of life) in patients with pituitary disease.

What if I want to know more?

You will receive a summary of the findings when the research is completed, however if you have any concerns or questions regarding this research, please contact Musaddiqah Brown at 0798613947/ Brwmus001@myuct.ac.za or Tayla Page at 071 560 9312/ PGXTAY001@myuct.ac.za