An Investigation Into Sleep Quality After Stroke

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Abstract

Background:

It has been well established that sleep plays an important role in the consolidation of memory, which is useful for skill learning. Following stroke, many survivors are tasked with re-learning skills that have been affected by stroke. Many stroke survivors report difficulty sleeping, including difficulty initiating sleep, disrupted sleep and excessive daytime tiredness. If sleep quality is negatively affected by stroke, rehabilitation may be suboptimal as memory consolidation could be diminished and risk of long-term additional health problems could be increased.

Aims:

1. To establish whether there is a difference in the sleep quality between stroke survivors and healthy controls.
2. To understand whether there any neural correlates to poorer sleep after stroke.
3. To investigate whether a current digital Cognitive Behaviour Therapy treatment for sleep would be usable by a stroke cohort.

Methods and Results:

Study 1 – Sleep quality was measured for a group of 50 stroke survivors and 50 healthy controls with actigraphy monitors. It was found that the stroke group had significantly poorer sleep than the controls, even when accounting for age. Specifically, stroke survivors experienced reduced total sleep time and showed larger numbers of wakenings and total time spent awake during their sleep periods. No individual characteristics such as depression, daily activity or medications accounted for differences in objective sleep quality within the stroke group.

Study 2 - A subset of 15 stroke survivors from study 1 received structural MRI scans to test for relationships between lesion volume, grey matter volume and sleep quality. No significant relationships were found between any of the measures examined.

Study 3 - The feasibility of the dCBT programme 'Sleepio' was assessed amongst 11 stroke survivors. A significant relationship between age and time taken to complete the programme was found, suggesting that older users may find the programme more difficult to use. Of the 11 participants, 6 have completed the programme to date and were invited for an interview to discuss the feasibility of usage. It was found that the programme, while technically feasible to be used within this cohort, suggested implementing a number of changes that were not practical for stroke survivors with different disabilities, and aspects of the initial usage of the programme were difficult to follow.

Conclusions:

Given the multifaceted process of sleep it is very difficult to point to the driving component behind stroke that leads to poorer sleep. Aspects of stroke and its common outcomes, such as reduced mobility, pain, depression and location of lesion may collectively contribute to a reduction in sleep quality, although no single element has been identified as the main contributor to the change. Current therapies for sleep improvement appear to be appropriate to be used within this cohort, although some alterations may need to be made to make them more inclusive of stroke related disabilities. Given the overall feasibility of existing dCBT treatments for stroke survivors, efficacy research should be carried out on this cohort, as it has previously been shown to be effective within insomnia groups.

Chapter 1: An Introduction to Sleep after Stroke:

The process of sleep is one fundamental to human survival and functioning. A lack of adequate sleep quantity and quality is associated to the diagnosis of numerous diseases including Alzheimer's disease and cancer (Lucey & Bateman, 2014); Blask, 2009). Beyond the association of sleep loss and ill-health, a lack of sleep has been shown to be detrimental to functions of daily living, notably, sleep plays an integral role in consolidation of memory. This has been shown in studies looking at the effect of sleep on skill performance. In one study by Morita, Ogawa, & Uchida (2016) two groups of people were taught how to juggle. Both groups were given the same amount of teaching and time to practise but one group were allowed 70 minutes of sleep following the training while the other group stayed awake. The group that were allowed to sleep showed significant improvement at re-test in comparison to the group that had remained awake. This suggests that sleep may aid the consolidation of memory of motor skills. Memory consolidation refers to the process by which memory traces "may be reactivated, analysed and gradually incorporated into the brain's long-term event-memory" (Sutherland & McNaughton, 2000).

The process of sleep, within humans, can be broken up into two types of sleep Rapid Eye Movement (REM) sleep and non-REM sleep. Non-REM sleep is further divided into stages 1- 4 going from the lighter stages of 1 and 2 into the slow-wave sleep associated to stages 3 and 4. The different stages of sleep are cycled through in roughly 90 minutes throughout the night with the proportion of REM sleep increasing over the course of sleep. (Jürgen, 1980).

The different stages of sleep have been linked to different mechanisms of restoration and learning. For example, memory consolidation of a motor task has been linked to higher amounts of stage 2 light sleep (Walker et al., 2002). Whereas, memory consolidation on visual discrimination tasks have correlated with larger amounts of SWS and REM sleep (Stickgold et al., 2000), suggesting that the individual stages of sleep play different roles in consolidation of memory and learning enhancement.

The process of learning or re-learning skills is a key component of motor rehabilitation and has been shown to be aided by sleep within stroke patients. Siengsukon & Boyd (2009) showed that when groups of stroke survivors and controls are split into two groups: one being allowed to sleep after learning a movement task, the other being kept awake, the stroke survivors allowed to sleep showed off-line improvements in the task. Whereas, both the stroke survivors kept awake and both groups of controls showed no improvement. The authors later replicated these results in a paper assessing the specific sleep architecture between stoke survivors and controls (Siengsukon, Al-Dughmi, Al-Sharman & Stevens, 2015). It is surprising that no improvement was seen with the control sleep group in this study given previous literature supporting sleep for skill improvement in controls (Morita, Ogawa, & Uchida, 2016). However, the researchers suggest that the control group's older age could mean that sleep-dependent memory consolidation components such as Rapid Eye Movement (REM) sleep, Slow Wave Sleep (SWS) and sleep spindles could have been reduced thereby reducing the likelihood of sleep based improvements (Danker-Hopfe et al., 2005).

Stroke is a neurological condition that occurs following loss of oxygen-carrying blood to the brain. This happens through either a clot (ischemic stroke) blocking the flow of blood

to the brain or a bleed (haemorrhagic stroke) reducing the blood flow to the required areas. As the brain is deprived of oxygen the cells start to decay and die causing functional deficits in the stroke survivor. Depending on the location of the stroke different functions will be affected. The most common deficit associated to stroke is one-sided motor weakness to the contralateral upper limb, affecting 80% of survivors acutely and 40% chronically (Cramer et al., 1997).

Many stroke survivors complain of difficultly sleeping following stroke (Duss et al., 2017). A large body of research has been done into the most commonly diagnosed sleep disorders following stroke, which have been found to be Primary Insomnia, Restless Leg Syndrome (RLS) and Sleep Disordered Breathing (SDB) (Duss et al., 2017). However, despite the established prevalence of diagnosable sleep disorders amongst stroke survivors, there is little research into the effects that stroke has on general sleep quality. If sleep is impaired following stroke, consolidation of skills gained through rehabilitation therapies may be suboptimal. Stroke is the leading cause of adult disability in the UK (Adamson, Beswick, & Ebrahim, 2004) and it is estimated that rehabilitation after stroke costs the UK £26 billion per year (Patel et al., 2017). It is important, therefore, to investigate the effects stroke might be having on sleep as sleep interventions could offer a novel route for boosting all rehabilitation outcomes.

A longitudinal study tracking the sleep and health of 397 adults over 3 years found that sleep disturbance was linked to a poorer quality of life within a cohort of middle aged and older adults (Lee et al., 2009). This shows that sleep is an important function to be considered in the long-term for stroke survivors, going beyond the implications of diminished rehabilitation in early care. A number of health problems have been shown to

be associated to poorer sleep, including: increased risk of hypertension (Gangwisch et al., 2006), depression (Neckelmann, Mykletun & Dahl, 2007) and cognitive decline (Spira, Chen-Edinboro, Wu & Yaffe, 2014). Given that these health risks are commonly associated to stroke, with hypertension being the leading cause of stroke (O'donnell et al., 2010), targeting sleep could benefit long-term health as well as initial recovery.

This thesis aims to add more insight to three key questions in regards to the relationship between sleep and stroke:

1. Is sleep quality impaired at the chronic stage after stroke?
2. Does variation in sleep quality in stroke survivors relate to variation in brain structure?
3. Could a current digital Cognitive Behaviour Therapy (dCBT) programme for sleep be feasibly used by stroke survivors?

The first question will be addressed through a study comparing objective and subjective measures of sleep quality between stroke survivors and healthy controls. The second question will be addressed through a study investigating the neural correlates of objective sleep quality measures in a cohort of stroke survivors. To do this, variation in structural MRI data will be compared with variation in sleep actigraphy data. Finally, a mixed methods (quantitative/ qualitative interview) study will be run to investigate the third question. A group of stroke survivors are invited to complete a six-week dCBT programme focused on sleep improvement, then complete a semi-structured interview to assess the feasibility of the programme for individuals following stroke.

Investigating the relationship between sleep quality and stroke could open up new avenues for creating specified sleep therapies for stroke survivors thereby optimising the rehabilitation already being delivered and improving outcomes for stroke survivors.

Chapter 2: An Investigation into the Differences in Sleep Quality Between Stroke Survivors and Controls

Introduction

Sleep Disorders and Stroke

Literature on the effects of stroke on sleep have typically focused on the commonly diagnosed sleep disorders that many stroke survivors experience. A systematic review of sleep disorders after stroke identified the three most common sleep disorders following stroke as: Sleep Disordered Breathing (SDB), Restless Leg Syndrome (RLS) and Primary Insomnia (Duss et al., 2017). Sleep disorders have been well identified as risk factors for stroke (Gianfagna et al., 2016) but less research has investigated sleep disorders and problems following stroke.

Sleep Disordered Breathing

SDB describes the abnormal pattern of breathing that occurs during sleep due to reduced muscle tension in the airways leading to the lungs. Breathing can become reduced and pause frequently during the night, the lack of oxygen then causing individuals to wake up repeatedly during a period of sleep which interrupts the natural sleep cycle and reduces the quality of sleep.

A meta-analysis investigating the prevalence of SDB in stroke found that of the 2,343 patients included, 72% were classified by the Apnoea–Hypopnoea Index (AHI) as having at least mild SDB (>5 incidences per hour) with 38% being in the moderate range (>20

incidences per hour) (Johnson and Johnson, 2010). Studies of SDB in the general population have found the prevalence of mild SDB (5≤AHI<15) in men and women to be between 40.7% - 45.7% and 19.3% - 26.6% respectively; with moderate SDB (15≤AHI<30) being found in 11.8% - 15.7% of men and 4.2% - 4.4% of women (Bauters, Debuyzere, Chirinos, Hertegonne & Rietzschel, 2018; Heinzer et al., 2011). One study also found that at the 3 months stage of recovery, patients with SDB also showed worse independence in activities of daily living, using the Barthel Index (BI) in comparison to stroke survivors without SDB (Yin-fang and Yu-ping, 2009).

Restless Leg Syndrome

RLS is a condition of the nervous system that causes frequent urges to move the legs. This usually causes jerking movements of the legs and arms during sleep, known as Periodic Limb Movements in Sleep (PLMS). The presence of PLMS can be painful and disrupt the normal patterns of sleep leading to increased wakefulness during the night.

Lee et al. (2009a) found that in a cohort of 137 stroke survivors recruited whilst in hospital, 12.4% were reported as having stroke-related RLS, classified as a first-time diagnosis of RLS at one-month post stroke. Similarly, RLS was found in 12.5% of a longitudinal stroke cohort of 96 patients (Medeiros et al., 2010). None of these patients had previously received a medical diagnosis of RLS prior to the stroke and all RLS patients had worse sleep quality and lower improvement on the BI at 3 and 12 months post-stroke suggesting a potential relationship between poor sleep and functional recovery. A 2015 study also found a similar prevalence of RLS with 15% of their 149 patients having the syndrome after stroke/ TIA in comparison to 3% of controls (Schlesinger, Erikh, Nassar & Sprecher, 2015).

Insomnia

Primary Insomnia is another common sleep disorder affecting stroke survivors. This disorder is characterised by the increase in the time taken to fall asleep, the reduced number of total hours sleep and difficulty getting back to sleep after a nightly wakening.

A study investigating insomnia amongst ischemic stroke patients found that of 277 patients, 157 (56.7%) reported insomnia complaints or met diagnostic criteria for the disorder. Of these cases, 50 were determined as new insomnia cases based on the self-report of participants claiming they had not experienced sleep difficulties prior to the stroke (Leppävuori et al., 2002). This suggests a direct link between stroke and onset of insomnia complaint in 18.1% of the total patient sample of this study. This is, again, a higher rate than seen in the general population where reported insomnia prevalence was 9.3% in a study of 1246 individuals (Singareddy et al., 2012).

Given the large prevalence of these three disorders in stroke survivors in comparison to the general population, it appears that there is a link between stroke and poor sleep. More specifically, the number of studies reporting first time incidence of sleep disorders after stroke seems to suggest a causal link between stroke and the development of some sleep disorders. Further to this, the combination of research showing poor sleep as a risk factor for stroke and the findings of the first-time prevalence studies discussed could imply a bi-directional relationship between sleep problems and stroke, meaning that sleep problems could be both a cause and consequence of stroke. This idea is supported by a recent systematic review of 67 papers focussed on the relationship between sleep and stroke (Gottlieb et al., 2019). They found that chronic sleep dysfunction significantly increased risk

of ischemic stroke, while ischemic stroke was strongly related to a disruption of normal sleep architecture when compared to controls.

Sleep Quality and Stroke

The primary focus of sleep and stroke studies, typically, has been diagnosable sleep disorders and their effects on functional recovery. However, beyond the scope of these disorders, a wide number of stroke survivors have complained of difficulty sleeping outside of the categories of defined sleep disorders. Kim et al. (2015) reported that from 3 sleep quality questionnaires, not focused on specific disorders, between 48.8% and 71.5% of patients were classified as having a sleep problem. This indicates a larger group of stroke survivors experiencing sleep difficulty outside of the criteria for commonly diagnosed sleep disorders.

Three particular methods of assessing sleep quality are widely used in sleep literature:

1) Polysomnography (PSG) – biological measures of electrical activity in the brain, breathing and heart rate are monitored overnight to assess changes to the normal functioning of the brain and body during sleep.

2) Actigraphy – measures of activity obtained using accelerometers (typically from wrist-worn monitors) used to infer objective sleep duration and disruption.

3) Questionnaires – subjective ratings of sleep duration and quality given by participants.

Polysomnography

PSG studies allow for very detailed observations of the state of the brain and bodily function during periods of sleep. By using Electroencephalography (EEG) to monitor the brain, it is possible to measure not only the duration of sleep, but also the variations in sleep stages.

An average sleep cycle consists of 4 stages of Non-Rapid Eye Movement (NREM) sleep and 1 stage of Rapid Eye Movement (REM) sleep. The sleep cycle moves through stages of high frequency wave activity in periods of light sleep (stages 1&2) and moves to periods of low frequency wave activity during deep sleep (stages 3&4, also known as Slow Wave Sleep (SWS)). Following these stages of sleep, REM sleep occurs in which brain activity increases. The average sleep cycle lasts 90 minutes as shown by Březinová (1974) and is repeated throughout the night in healthy sleepers.

A systematic review and meta-analysis of PSG papers investigating sleep after stroke found that sleep quality is worse for stroke survivors in a number of measures (Baglioni et al., 2016). Total Sleep Time (TST), Sleep Efficiency (SE) (the proportion of time in bed, spent asleep) and Wake After Sleep Onset (WASO) were all found to be reduced in stroke groups in comparison to controls. When looking specifically at sleep stages the meta analyses found the duration of stage 2 sleep, SWS and REM sleep to be significantly reduced in stroke patients when compared to controls (Stage 2 = 36% vs 45%, SWS = 10% vs 12%). Although the differences in TST, SE and WASO between groups was found regardless of the participants' sleeping environment, the difference in SWS and REM duration was only found when comparing hospitalised stroke patients with hospitalised controls. As the controls assessed in those studies were assessed in sleep labs, it would suggest that the reduction in deep sleep and REM could be due to hospitals being a specifically detrimental environment to normal sleeping as opposed to just being purely novel environments.

Interestingly, when comparing the duration of Stage 1 sleep, stroke patients show a significantly larger percentage in relation to their whole night's sleep than controls (13% vs 10%) (Baglioni et al., 2016). This suggests that stroke could affect specific parts of sleep

architecture, reducing the amount of deep and REM sleep in exchange for larger periods of light sleep. This could be particularly detrimental to stroke patients' rehabilitation and recovery given that stage 2 sleep, SWS and REM have all been shown to be connected to memory consolidation leading to improved skill performance (Stickgold, 2005). Specifically, levels of stage 2 sleep correlate with improved performance on a motor task and levels of SWS and REM sleep correlate with improved performance on a visual discrimination task.

One study is of particular interest in understanding the cause for the difference in sleep outcomes after stroke. Terzoudi et al. (2009) looked specifically at sleep architecture after stroke compared to hospitalised controls. A group of 62 stroke survivors and 16 age matched controls had a single night's PSG sleep recording. Even when looking at just the stroke patients who did not have SDB they showed reductions in TST and SE. This study is particularly significant as the use of hospitalised controls removes the change in sleep environment as the only driving factor for the difficulties with sleep, suggesting that there is something uniquely connected to stroke that influences sleep mechanisms. However, the use of only one night's sleep recording may reduce the reliability of the results, given the variability between individual night's sleep within insomnia patients (Van Someren, 2007).

Van Someren (2007) investigated the reliability of actigraphy recording in insomnia over multiple nights. They concluded that multiple nights recordings are needed when investigating insomnia due to the high variability in sleep and sleep-wake rhythms within this cohort. Therefore, PSG studies recording for only one night such as Terzoudi et al. (2009), although richer in detail than actigraphy, may not be collecting representative data on the sleeping patterns of stroke survivors with sleep problems. Meaning that further

research with longer periods of sleep recordings is needed to reliably measure sleep problems.

Taken together, the evidence from PSG studies would seem to suggest that there is an established difference between the sleep architecture of stroke survivors when compared to controls, both when hospitalised and at home. Further evidence, however, is needed to compare groups of stroke survivors and controls outside of hospital environments and after the acute phase in order to determine whether there is something inherently connected to stroke that has a lasting impact on sleep.

Actigraphy

Sleep can also be measured by using motion as a measure of sleep vs wake periods. During sleep, the body is less physically active than during wake, with the body being physically paralysed during periods of REM sleep (Brooks & Peever, 2011). Motion detectors such as actigraph monitors can be used to predict when the body is in periods of sleep in comparison to wake under the assumption of the body being motionless during deep sleep. Therefore, sleep parameters such as onset, duration and disruption can reliably be measured by using actigraph data (Sadeh, 2011).

Actigraphy studies investigating sleep after stroke have found a link between stroke and poorer sleep. It has been reported that during the acute phase of stroke nightly wakenings are increased for hospitalised patients in comparison to those sleeping at home, even when accounting for time since stroke (Bakken et al., 2011). This provides further support for the notion of hospitals being places that do not promote healthy sleeping. Actigraphy studies have also found that stroke survivors during the acute phase of stroke (up to 15

days since hospital admission) display increased WASO than when tested at a 6-month follow-up (Bakken, Kim, Finset & Lerdal, 2012). However, these studies only included data collected from 3 nights actigraphy recording and so the reliability of these results is difficult to confirm.

Although post-stroke sleep quality problems may be at their worst immediately after stroke, survivors at the chronic stage (> 6 months post stroke) also experience worse sleep when compared to healthy controls. One study found that in comparison to controls, stroke survivors at the chronic stage had a reduction in Actual Sleep Time (AST) and an increase in both Sleep Latency (SL) and sleep Fragmentation (Cavalcanti, Campos & Araujo, 2012) but this study had quite a small sample size (patients n=22, controls n=24) and data were analysed from just 5 night's actigraphy and so to test the reliability of these results, more research is needed on chronic stroke survivors' sleep. Falck et al. (2019) tested the difference in sleep quality between a cohort of 35 stroke survivors at the chronic stage and 35 age-matched controls with 7 nights of actigraphy. It was found that sleep Fragmentation and SE were significantly worse in the chronic stroke patients when compared to age matched controls. Falck et al.'s paper uses a larger sample size (patients n=35, controls n= 35) with a richer data set from 7 nights of actigraphy recording, making it a more reliable study. However, no comparisons were made between the objective and subjective sleep measures recorded and so it would be interesting for future research to investigate the relationship between these two measures.

Overall, the evidence from actigraphy studies suggests that stroke has a negative impact on sleep quality and although the severity of this impact is heightened in the early stages after stroke, the problems persist through to the chronic stage. Further research with a larger

number of night's actigraphy recording is needed, however, to increase the reliability of these results. Furthermore, comparisons between participants' subjective and objective sleep measures should be included in research to investigate the relationship between perceived and objective sleep difficulties.

Questionnaires

Sleep questionnaires are very commonly used in sleep literature, they provide a useful insight into the perception of sleep quality and are commonly used in screening for sleep dysfunction (Mollayeva et al., 2012). Many studies investigating sleep and stroke use questionnaire data as a measure of sleep quality, including a number of studies that have found that patients report their sleep quality as worse than controls (Chen et al., 2015; Jiang et al., 2013; Wu et al., 2016).

The reliability of subjective reports of sleep problems is somewhat tenuous as the overestimation of SL and underestimation of TST has been consistently reported in numerous patient populations including Primary Insomnia, Unipolar and Bipolar Depression, Chronic Fatigue and Chronic Pain groups (Harvey & Tang, 2012). This is described as "sleep misperception" (the inability to accurately perceive one's own sleep quality).

Given the prevalence of sleep misperception across different patient groups, it is important not to rely solely on subjective measures of sleep quality when assessing the difference in sleep quality between a patient group and healthy controls in order to disentangle whether an observed difference is based on an objective difference in sleep quality or whether it is due to the precariousness of individual's accuracy when reporting on their own sleep.

It is important to note, however, that even in cases where objective sleep measures show more optimal sleep patterns than subjective reports, individuals who perceive their sleep to be worse than it is often show the same symptoms of increased anxiety, arousal and cognitive deficits as those with objectively worse sleep (Harvey & Tang, 2012; Van Den Berg et al., 2008). Therefore, it is important to recognise the legitimacy of subjectively reported sleep difficulties as the perception of poor sleep can add to the negative symptoms associated with insomnia in the same way that objective poor sleep can. Therefore, an approach incorporating both subjective and objective measures of sleep is optimal in research comparing stroke survivors with controls.

Bakken, Kim, Finset, & Lerdal (2014) investigated the difference between subjective and objective reporting of sleep quality in 100 stroke survivors and found that although the two measures did not correlate during the acute phase (suggesting sleep misperception), a positive relationship was seen at >6 months post stoke. This suggests that inaccuracy in sleep perception early after stroke may improve during recovery. However, this study only recorded 3 nights of actigraphy data which, as previously discussed, is not a large enough number of nights to reliably report on sleep difficulty. Given the consistent findings of increased sleep misperception in other patient populations and the lack of a reliable number of night's recordings in this sleep misperception study, it could be argued that sleep misperception could still be seen at the chronic level of stroke, but more research would be needed to clarify the levels of sleep misperception in stroke survivors.

The Current Study

Given the role of sleep in consolidation of memory and the diminished quality of sleep reported by stroke survivors, understanding the relationship between sleep quality and

stroke could provide scope for developing interventions to improve outcomes. Therefore, the present study aimed to compare the quality of sleep between chronic stroke survivors and healthy controls using actigraphy and self-reported sleep questionnaires. Actigraphy was chosen as the objective measure because it has been shown to be a reliable measure of objective sleep quality and given the larger numbers needed to compare stroke survivors to controls, due to the heterogenous nature of stroke, actigraphy was chosen as a more feasible measure for larger participant groups. Additionally, it was feasible to use in the participants usual environment, rather than requiring the use of a sleep lab. The addition of a healthy control group allows for the investigation of stroke related differences in sleep quality at the chronic stage, rather than comparing different time points in recovery from stroke. Similarly, using both subjective and objective measures of sleep quality allows for analysis of both sleep difficulties and their perceived impact on the individuals.

The study aimed to investigate a) whether objective sleep quality differs between stroke survivors and healthy controls, b) the factors that may explain variance behind any differences in sleep outcomes and c) whether sleep misperception is greater in a group following stroke than in healthy controls.

It was predicted that participants in the stroke group would have a lower objective sleep quality than controls. Specifically, it was hypothesised that stroke survivors would have an increased Fragmentation Index (FI), reduced AST(%) and longer WASO in comparison to controls. These sleep measures were chosen given the usage of these measures in previous sleep studies. FI and WASO give good representations of general sleep disturbance and has been shown to be valid in comparisons between stroke survivors and controls in previous literature (Falck et al., 2019; Suh, Choi-Kwon & Kim, 2014). Although Sleep Efficiency (SE) is

reported in a lot of sleep literature (Gottlieb et al., 2019), it was not possible to do so in the present study as it was not possible to obtain accurate time measures for time in bed. Therefore AST(%) was used as it is the closest measure to SE but focusing solely on sleep time against wake, exclusive of time in bed.

It was also hypothesised that HADS scores, average daily activity, level of functional movement and sleep affecting medications would explain variance in sleep quality across participants. Finally, stroke survivors were hypothesised to show greater levels of sleep misperception than controls.

Methods

Participants

A total number of 113 participants agreed to take part in the study. After excluding participants who had fewer than 7 nights of sleep recording due to early removal of the actigraphy monitor or technical malfunction (n=13) a final group of 50 stroke survivors and 50 controls were used in data analysis. The stroke group included 31 males and 19 females, aged between 25 and 87 (mean age 61.8). The control group included 22 males and 28 females, aged between 20 and 83 (mean age 54.2) (See Table 2.1).

The study was approved by the National Research Ethics Service (11/H0605/12), and all participants gave written informed consent prior to participation. Participants were recruited using online advertisements shared on various social media websites as well as through poster advertising in the community, through the Cognitive Neuropsychology Centre database (University of Oxford) and through presentations at stroke user group

meetings. Participants from previous studies who had agreed to be contacted about future studies were also invited.

Materials

Sleep data was recorded over one week using the 'MotionWatch8', a light weight, tri-axial, water-proof wrist worn actigraphy (WWA) monitor (MW8; CamNtech, Cambridge, UK). Participants wore their WWA monitor for 7 days, day and night giving an estimated wear time for each participant as 168 hours.

Participants in the stroke group with unilateral motor weakness were asked to wear the WWA monitor on the unaffected hand for ease of distinguishing between movement and sleep. Participants in the control group were asked to wear the WWA monitor on their non-dominant hand, following standard protocol established in previous WWA validation studies (Crouter, Flynn, Bassett, & Crouter, 2015; Johansson, Ekelund, Nero, Marcus, & Hagströmer, 2015). Participants were asked to keep a sleep diary (see Figure 2.1) over the week of the study. They recorded, for each night, the time they tried to get to sleep, the time they woke up in the morning and a rating of the quality of their sleep on a 5-point scale from "Very Poor" to "Very Good".

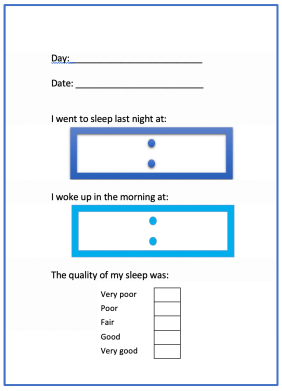

Figure 2.1 Example page from sleep diary.

Prior to the sleep recordings participants completed two questionnaires: The Sleep Condition Indicator (SCI) (Espie et al., 2014) and The Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983). The SCI is a short questionnaire comprised of 8 multiple choice questions used clinically to screen patients for insomnia, with higher scores indicating better perceived sleep. The HADS is a multiple-choice questionnaire made up of 14 questions used to assess levels of depression and anxiety, with lower scores indicating better perceived mood levels.

For participants in the stroke group, two upper limb motor assessments were also carried out, the Action Research Arm Test (ARAT) (Lyle, 1981) and the upper extremity section of the Fugl-Meyer Assessment (FMA) (Fugl-Meyer, Jääskö, Leyman, Olsson & Steglind, 1975). The ARAT is a test of upper limb function used to assess participants' ability to manipulate objects of differing size, weight and shape. The FMA is test of motor impairment and ability to make movements in and out of synergy.

Design

An independent groups, cross-sectional design was used for this study. Participants were either in the stroke or control group with sleep quality being used at the dependent variable assessed at one time point.

Procedure

Participants were invited in to our research centre for one session. After consent was taken, general information about participants was also collected including any medications currently being taken. Participants in the stroke group were also asked about date of stroke, type of stroke and lesion location, if known.

Participants then completed the ARAT, FMA, the SCI and HADS, as applicable. After all assessments had been completed, participants were given the WWA monitor and sleep diary. Participants were instructed to wear the actigraphy monitor solidly for one week, and record the times in the sleep diary over the 7 nights, and were provided with an envelope to send back the materials at the end of the week. Previous research has shown that the reliability of sleep actigraphy improves significantly when comparing 7 nights to 3 in patient groups, (Van Someren, 2007). In the case of the present study, 7 nights was chosen to improve the reliability of the research but also to not be too demanding for the participants given the patient population being investigated.

Actigraphy Parameters

Actigraphy data were sampled at 50Hz (with filtering at 3–11Hz) and in the present study were recorded using 30s epochs, given that the analysis algorithms used in the Camntech software have been validated for sleep at 30s epochs (Oakley, 1997).

Raw data was downloaded using MotionWare software (Camntech Ltd) and the sleep period each night was manually selected using motion activity level and reported times of 'trying to sleep' and 'wake up' from the sleep diary. Any missing data from a sleep period can be manually selected and will be removed from the epoch averaging. However, in the present study we excluded participants altogether if they had any missing data and so the data presented are from 100 complete data sets.

The MotionWare algorithm estimates periods of specifically low activity as 'sleep' and periods of specifically high activity as 'wake' over the night sleep duration. Similarly,

'immobile' and 'mobile' periods are calculatd from the low and high activity during the day. Although actigraphy has been shown in the past to overestimate low activity periods as sleep, the use of sleep diaries to set the sleep period has been shown to significantly reduce this overestimation bias (de Souza et al., 2003). Average activity counts are averaged over the course of the 30s epoch and each epoch is categorised accordingly. From the counts of sleep, wake, immobile and mobile counts a number of measures are produced to describe the sleep quality.

For this study AST(%) (percentage of the total sleep time spent in sleep), WASO (Total time spent in wake from sleep onset to final wakening) and FI (the sum of the percentage of 'Mobile' time and the percentage of 'Immobile' bouts lasting <1 minute) were included in the main analysis to assess sleep quality, using the mean values over the 7 nights. Average daily activity was also used in analysis as a potential factor explaining variance in sleep quality. This is a measure of the amount of movement over each 30s epoch totalled and averaged for each 24-hour period.

Statistical analysis

Comparisons of the sleep quality measures were run between the stroke and control groups, while controlling for age using analysis of covariance (ANCOVAs). For the stroke group only, a regression analysis was run with average daily activity, scores the HADS, ARAT and FMA, and sleep-affecting medications as predictor variables with each sleep quality measure as the dependent variable. Medications were classified as either inducing/ aiding sleep, having no effect on sleep or reducing sleep (and scored +1, 0 or -1 respectively). Where participants were taking multiple medications, the scores were combined to generate a total score, with positive scores being classed as inducing sleep, 0

scores classed as no effect and negative scores classed as reducing sleep. Finally, subjective and objective measures of sleep were compared using Pearson correlations between SCI scores for subjective measures with the actigraph outcomes as objective measures. Correlations were then compared between groups with Fisher's exact test. All statistical analysis was done using SPSS (version 24, IBM inc). Although multiple sleep measures were considered, no correction was made for multiple comparisons due to limited power.

Results

Participant Demographics

Table 2.1 shows the distribution of behavioural and stroke related characteristics for the participant groups. The stroke group was significantly older than the control group (independent samples t-test: $t(90) = -2.32$, $p = .023$) and so age was controlled for in all analyses. No significant difference was found in a Chi square test between groups on sex ($p = 0.071$).

Table 2.1. Participant characteristics and behavioural measures.

Variable	**Stroke *(n=50)***	**Control *(n=50)***
Age (years) * *(M, SD)*	61.82, 13.67	54.2, 18.78
Sex *(Male: Female)*	31: 19	22: 28
Time Since Stroke (months) *(M, SD)*	61.66, 50.23	N/A
Hand Affected *(Left, Right)*	33, 17	N/A
SCI * *(M, SD)*	20.88, 7.65	24.46, 6.16
HADS * *(M, SD)*	10.6, 5.58	7.04, 4.88
Average Daily Activity (motion units) * *(M, SD)*	63.71, 27.35	76.42, 27.52
ARAT *(M, SD)*	27.08, 22.13	N/A
FMA *(M, SD)*	36.54, 21.25	N/A

Abbreviations: M = Mean, SD = Standard Deviation, SCI = Sleep Condition Indicator score, HADS = Hospital Anxiety and Depression score, ARAT = Action research arm test score, FMA = upper extremity Fugl Meyer assessment score. * significant difference between groups, $p < 0.05$.

Differences between groups

One-way ANCOVAs were run on AST(%), WASO, FI and SCI between the two groups, controlling for age. Stroke survivors showed significantly increased WASO ($F(1, 97) = 4.44$, $p = .038$), FI ($F(1, 97) = 5.58$, $p = .02$) and SCI ($F(1,97) = 6.63$, $p = .012$) (See Figure 2.2). However, no differences were found between the groups on AST(%) ($F(1, 97) = 3.2$, $p = .077$).

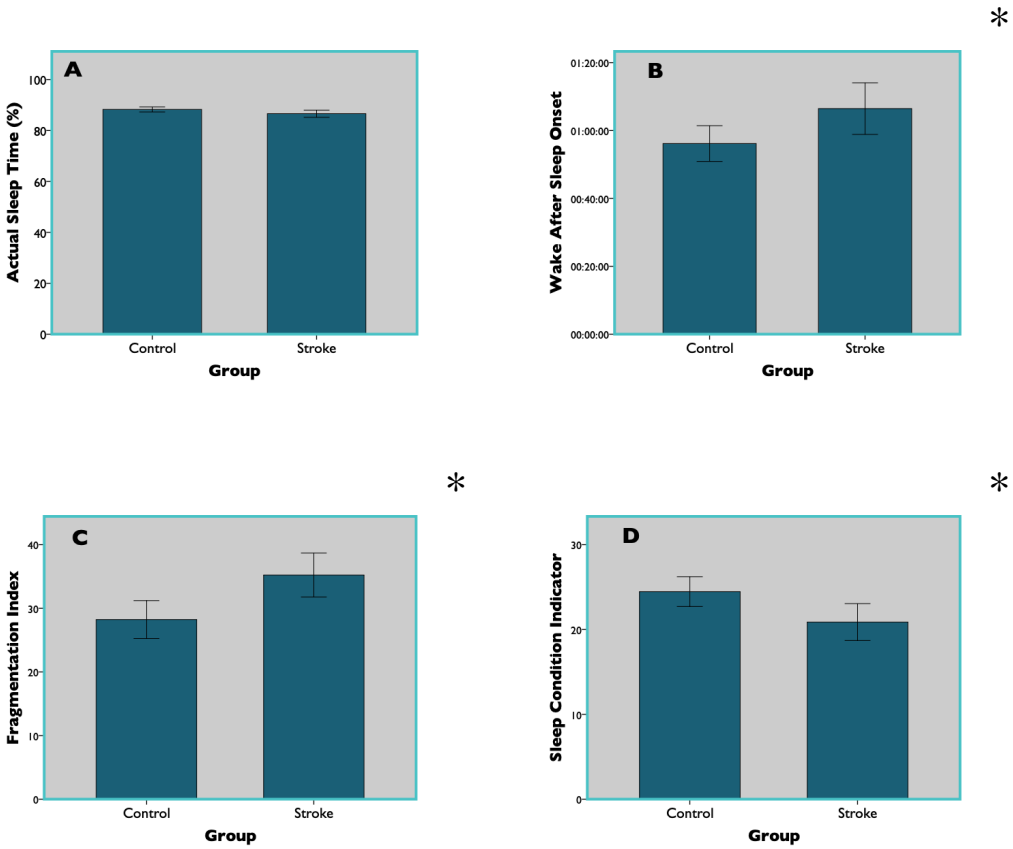

Figure 2.2 One-way ANCOVAs between groups on different sleep quality measures controlling for age. A) Difference in AST(%) between groups, B) Difference in WASO between groups. C) Difference in FI between groups. D) Difference in SCI between groups. * significant difference between groups, $p < 0.05$.

Factors Affecting Sleep

Three multiple regression analyses were run on the stroke group's sleep outcomes. Focussing on FI, WASO and SCI. Scores on the HADS, ARAT and FMA as well as average daily activity and sleep-affecting medications were used as the set of predictors. None of the covariates were found to significantly explain the variance in Fragmentation Index: $F(5, 43) = 0.87$, $p = .507$, $R^2 = .092$. HADS, ($p = .425$), ARAT ($p = .223$), FMA ($p = .265$), average daily activity ($p = .436$), medications ($p = .171$).

Similarly, the variables also did not significantly explain variance in WASO for the stroke group: $F(5, 43) = 0.9$, $p = .489$, $R^2 = .095$. HADS ($p = .77$), ARAT ($p = 0.626$), FMA ($p = .312$), average daily activity ($p = .645$), medications ($p = .541$).

Finally, the regression analysis was significant for SCI scores within the stroke group: $F(5, 43) = 2.78$, $p = .029$, $R^2 = .244$. HADS score was the only variable that significantly predicted the variance in SCI (HADS ($p = .003$), ARAT ($p = .698$), FMA ($p = .909$), average daily activity ($p = .919$), medications ($p = .35$)).

Sleep Misperception

Correlations were run between the subjective sleep scores from the SCI and the objective sleep measures for both groups (See Figure 2.3). No correlations were found between subjective and objective sleep measures in the control group; SCI and FI: $r(47) = -0.064$, $p = .658$, SCI and WASO: $r(47) = -0.09$, $p = .529$. Similarly, no correlations were found between subjective and object sleep measures in the stroke group; SCI and FI: $r(47) = -0.11$, $p = .44$, SCI and WASO: $r(47) = -0.002$, $p = .988$.

Further analysis showed that the correlations between SCI and FI and SCI and WASO were not significantly different between groups ($p = .453$ and $p = .582$ respectively, Fisher's exact test). This suggests no difference in sleep misperception between groups.

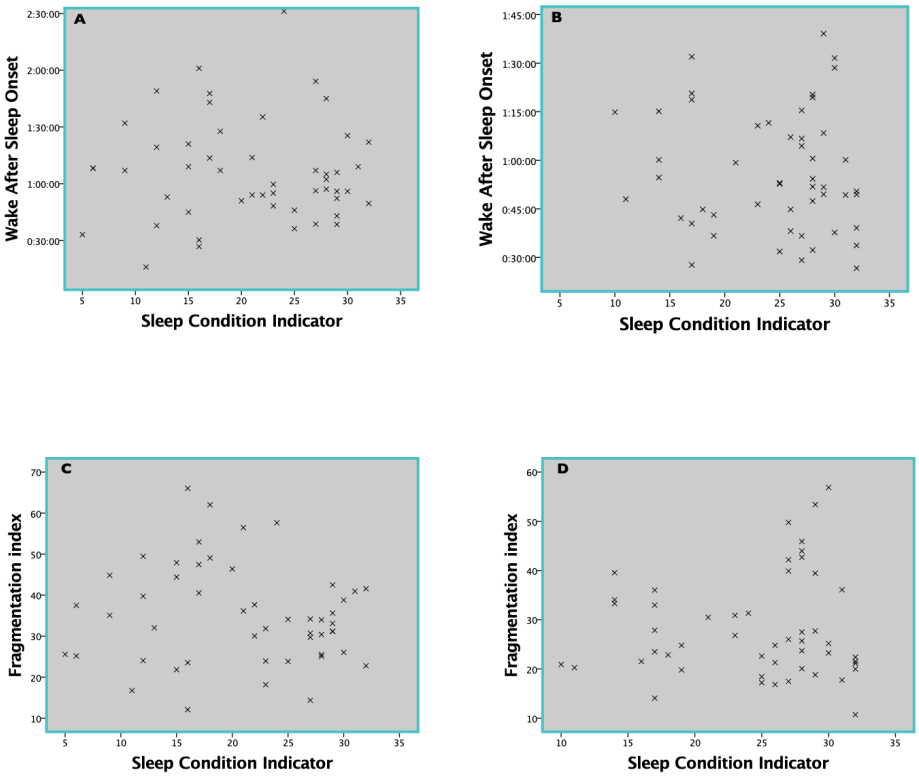

Figure 2.3 Correlations between subjective and objective sleep measures in both groups. A) SCI with FI in stroke group. B) SCI with FI in control group. C) SCI with WASO in stroke group. D) SCI with WASO in control group. No correlations were significant.

Discussion

The present research provides support for previous literature showing differences in sleep quality measures between stroke survivors and controls (Baglioni et al., 2016). Both WASO and FI were significantly different between groups, with stroke survivors showing more disrupted sleep. This indicates that during a typical night's sleep, stroke survivors are spending more time awake and having a larger number of short sleep periods between the time of sleep onset and final wakening. Subjective sleep quality as reported on the SCI was also significantly lower for stroke survivors. Cohen's d calculations revealed medium to large effect sizes for each sleep measure (WASO = 0.45, SCI = 0.52, FI = 0.62) suggesting

that the increased FI and WASO in stroke survivors could be significantly impacting on their quality of life, given the relationship between healthy sleep and well-being (Li et al., 2018; Walker, 2009).

No differences between groups were found in AST(%), but this measure was approaching significance, trending towards controls having a higher percentage of their night spent asleep than stroke survivors. So potentially a difference may be found with a larger sample size. Nonetheless, the differences found with WASO and FI suggest that stroke survivor's sleep is more disrupted than healthy controls, regardless of age. This could suggest that normal sleep cycles are being disrupted and could therefore alter the amount of REM sleep received. This would be in line with previous research showing that stroke survivors have reduced REM sleep and spend more time in lighter stages of sleep (Bassetti, & Aldrich, 2001; Terzoudi et al., 2009).

The regression analysis did not find that any of the variables significantly predicted the variance in objective sleep outcomes for stroke survivors. HADS scores significantly predicted subjective sleep quality which would be expected given that depression/ anxiety levels have been shown to influence sleep quality (Espie, 2002; Harvey, 2002). However, amount of daily activity and sleep-affecting medications have all also been shown to influence sleep quality (Hartescu, Morgan & Stevinson, 2015; Legros & Bazil, 2003). Although scores on the ARAT and FMA have not been directly related to reduced sleep quality, research into reduced mobility in Parkinson's patients has shown that patients with reduced bed mobility also have reduced SE (Louter et al., 2013) which suggests a general link between mobility and sleep quality.

It is interesting in this case that none of the other recorded variables were found to be significant predictors of the difference in objective sleep quality as it suggests that there might be something specific about stroke that is responsible for the change to normal sleeping more so than other behavioural/ medicinal factors. It is also likely that although all of these variables may be influencing different elements of sleep, no single variable is strong enough to be the driving factor for the difference in sleep disturbance between people.

This leads to the question of whether there is a separate variable responsible for the reduction in sleep quality or whether there is something about stroke that might influence each aspect more globally? Given that stroke directly affects the structure of the brain it would follow that an analysis of stroke lesioned brains and sleep outcomes would be worth investigating.

Interestingly, no correlations between subjective and objective sleep measures were found in either the stroke group or the control group. The lack of correlation in this case means that participants were neither reporting their sleep quality accurately when compared to objective measures, nor were they reporting their sleep quality as being the complete opposite to what the objective measures suggested. This would suggest that both groups had inconsistencies between their subjective and objective sleep quality recordings. Crucially, even though participants' subjective ratings were not completely to the contrary of the objective measures, they were not accurately perceiving their sleep quality.

This could be due to the older age range of participants in comparison with other studies, as previous research has shown that sleep misperception tends to increase with age (Van Den Berg et al., 2008). However, the study by Van Den Berg et al. (2008) included

participants aged 55 and older (with a mean age of 68.5) and another study into sleep misperception including a participant cohort with a mean age of 58 found that estimates of subjective sleep quality were accurate (Maconi et al., 2010). The average age of the participants in the present study is closer to that of the Maconi et al., study (2010) which would suggest that age might not be the factor responsible for the lack of correlations between objective and subjective sleep seen here.

The measure of subjective sleep quality used in this analysis was the total score on the SCI which covers a number of areas relating to sleep such as: sleep onset time, sleep disruption, the influence of poor sleep on daytime functioning and the duration of sleep problems. Whereas, the objective sleep quality measures only really address sleep disruption and so the two variables may not be accurately comparable and a lack of correlation could be more representative of the lack of relatedness of the chosen sleep measures. Therefore, further analysis using just the scored responses to questions relating to sleep disruption in comparison to objective measures of sleep disruption, could more accurately assess sleep misperception within this cohort.

Given the importance of sleep on consolidation of memory (Sutherland & McNaughton, 2000), and the increase in sleep disturbance within the stroke group, it follows that treatment should be targeted to the group in order to aid with skill learning during rehabilitation. In order to correctly target treatment for sleep difficulty it is important to work out what is influencing the problem. As previously stated, many factors can impact normal sleep functioning and given that none of the individual predictors in the regression analysis significantly predicted the difference in sleep, a more holistic approach to treatment might be necessary when treating this group.

Chapter 3: Investigating the Neural Correlates of Poor Sleep Following Stroke

Introduction

A large body of research has focused on the neural underpinnings of poorer sleep in older adults and people who experience insomnia, but very little work has been done into how stroke can affect sleep, despite the common complaints of poorer sleep among stroke survivors (Kim et al., 2015). Given the importance of good quality and regular sleep, understanding what might be driving poor sleep is key in working out how best to improve it.

A number of brain regions have been shown to be related to sleep functioning. The circadian rhythm is widely reported to be controlled by the suprachiasmatic nucleus within the hypothalamus (Takahashi, Hong, Ko & McDearmon, 2008). Beyond the function of circadian rhythm, the hypothalamus and thalamus more generally have been linked to sleep function through the regulation of arousal-controlling neurotransmitters, such as Gamma-Aminobutyric Acid (GABA) and serotonin, allowing for normal transitions between sleep and wake (Brown, Basheer, McKenna, Strecker & McCarley, 2012). The basal ganglia have also been implicated in controlling aspects of wakefulness with lesions to the basal ganglia causing increased sleep fragmentation (Qiu, Vetrivelan, Fuller & Lu, 2010). This illustrates the breadth of regions associated with sleep functioning, which also suggests that damage to a number of areas of the brain through stroke could interrupt the normal processes of healthy sleep. It is possible that disruption to the specific sleep-associated brain regions

could drive the disruption in the stroke group. However, given the heterogeneity of stroke lesion locations, large sample sizes are needed to investigate this relationship.

Similar to the non-imaging research on the subject, imaging research on the relationship between sleep and stroke has focused on diagnosable sleep disorders. One study looking at the relationship between RLS and the location of the stroke lesion (Lee et al., 2009a) found that of 17 patients that presented with RLS, 16 had subcortical strokes suggesting a link between brain region and the diagnosis. Furthermore, the basal ganglia were the most commonly affected area within the 17 patients, with 59% having basal ganglia lesions, 24% had pontine lesions. Researchers suggested that the damage to subcortical regions involved in motor control and the sleep-wake cycle had led to the development of RLS. This provides support for the notion of lesion location being responsible for disruption to certain sleep processes.

Studies investigating Sleep Disordered Breathing (SDB) in stroke populations have found conflicting evidence. Fisse et al. (2017) found that of the 142 participants studied, there was no link between lesion location and presence of SDB (with 59% of the cohort exhibiting SDB). They concluded, however, that those with higher risk factors for SDB prior to the stroke were more likely to have a related disorder afterward. Conversely, Brown et al. (2014) found that of 355 ischemic stroke participants, those with brainstem infarcts were significantly more likely to have SDB than those with lesions elsewhere. Given the heterogeneity of stroke lesions, larger sample sizes are needed to reliably assess the link between location and outcome. Therefore, Brown et al.'s study could be argued to have stronger validity suggesting that damage to the brainstem is related to the onset of SDB.

Surprisingly, given the high prevalence of reported difficulty sleeping after stroke (Duss et al., 2017) there is very little imaging research into the relationship between stroke and sleep quality. This is very important as targeted interventions aimed at improving sleep for stroke survivors would be enhanced by knowledge of how lesions affect sleep processes.

Although there is currently a lack of research into the effect of stroke lesions on sleep function, there has been a large body of work looking at the brain of older adults with poorer sleep and insomnia patients. Previous neurological research looking at ageing and sleep difficulties have found varying relationships between brain regions and sleep difficulties. One common trend appears to be the link between worsened sleep quality and cortical atrophy. Spira et al. (2016) found that a faster rate of cortical thinning in frontal areas was associated to sleep abnormalities by either reducing sleep periods to less than 7 hours or significantly increasing the amount individuals were sleeping. Further research by Lim et al. (2016) found that in a group of 141 older adults lower cortical grey matter volume (GMV) in the lateral orbitofrontal cortex and inferior frontal gyrus pars orbitalis was associated with greater sleep fragmentation as reported on a subjective sleep questionnaire. Lower GMV was also found in the dorsolateral prefrontal cortex and middle cingulate cortex in a cohort of 113 older adults in relation to higher sleep fragmentation measured by 7 nights of actigraphy (Li et al., 2018). Similar results were found in a study of 290 older adults (Del Brutto et al., 2016), in which self-reported lower sleep quality was associated to higher global cortical atrophy.

Overall, investigations of people who experience insomnia and older adults have shown trends of reduction in cortical/ GMV volume in relation to lower sleep quality. Stroke, however, is not part of healthy ageing and, although related to increased prevalence of

insomnia (Leppävuori et al., 2002), is neurologically independent to insomnia. Therefore, separate research into the relationship between brain structure in stroke survivors who experience poorer sleep quality is needed to uncover how stroke affects sleep. The present study aims to investigate the relationship between neurological structure and sleep quality within a stroke cohort. Studies investigating lesion location in relation to sleep measures need very large sample sizes, given the anatomical differences in lesions even within the same brain region. Given the current study's limited sample size, analysis focused on global measures of grey matter and lesion volume following findings from studies of older adults showing higher cortical atrophy in relation to poorer sleep quality.

Methods

Participants

15 participants (13 male, 2 female) aged between 41 and 86 (mean 65.5) with a stroke at least 6 months prior to participation (mean 77.66 months) were recruited to a separate MRI study focused on improving motor rehabilitation after stroke. Participants completed a series of MRI scans as part of the procedure of the study and so the T1-weighted anatomical scans collected from each participant were used for data analysis in the present study.

Inclusion criteria for the MRI study were: single stroke, at least 6 months prior to participation, unilateral motor weakness as a result of the stroke whilst also being able to complete a baseline task which involved a grip and release of the affected hand. Participants were excluded if they were: unable to give informed consent, unsafe to be scanned at 3.0 Tesla (such as having ferromagnetic implants or metallic implants that pose a heating risk

i.e. overlapping cardiac stents), unable to attend a minimum of five sessions, or if they had another neuropsychiatric condition.

The study was approved by the National Research Ethics Service (ref 14/LO/0020), and all participants gave written informed consent prior to participation. Participants were recruited through the Cognitive Neuropsychology Centre database (University of Oxford), online advertisements, poster advertising in the community and through presentations at stroke user group meetings.

All participants also took part in study 1, and so 7 night's sleep actigraphy data was obtained for each participant. Prior to consenting to the MRI study, 12 participants had completed study 1 and three participants completed study 1 upon completion of the MRI study. The T1-weighted images acquired closest to the actigraphy recordings were used in analysis in the present study. An average of 15 weeks elapsed between the sleep recording and T1 scan with a range of 1 – 65 (however, there were only three cases of elapsed time that exceeded 10 weeks).

MRI Parameters

In this cross-sectional study, anatomical MRI scans (T1-weighted) were acquired on a 3.0 Tesla Siemens MAGNETOM scanner. 192 1mm axial slices with a voxel size of 1mm isotropic were obtained with Repetition Time (TR) = 1900 ms, Echo Time (TE) = 3.97 ms, Inversion Time = 904 ms, flip angle 8° and Field of View 192 x 192.

Data Analysis

MRI data were analysed using the FMRIB Software Library (FSL; www.fmrib.ox.ac.uk/fsl) to look at the relationships between lesion and grey matter volume (GMV) with the objective sleep measures obtained in study 1 (AST(%), WASO and FI).

3D Lesion masks for the T1-weighted images were created manually using 'fslview' and 'fslstats' was then used to calculate total lesion volume. T1-weighted images with lesions in the left hemisphere (n = 5), and the corresponding lesion masks, were flipped along the x axis using 'fslswapdim' so that lesions masks could be collated onto the same hemisphere for the group mask.

Brain tissue volume, normalised for subject head size, was estimated with FSL SIENAX (Smith 2001, Smith 2002). SIENAX starts by extracting brain and skull images from the T1-weighted image (Smith et al., 2002). The brain image is then affine-registered to MNI152 space (Jenkinson & Smith, 2001; Jenkinson, Bannister, Brady & Smith, 2002) (using the skull image to determine the registration scaling); this is primarily in order to obtain the volumetric scaling factor, to be used as a normalisation for head size. Next, tissue-type segmentation with partial volume estimation is carried out (Zhang, 2001) in order to calculate total volume of brain tissue (including separate estimates of volumes of grey matter, white matter, peripheral grey matter and ventricular CSF). Individual lesion masks were then removed from the segmented images using 'fslmaths' to calculate GMV excluding lesioned tissue.

A group lesion mask was created by warping the individually created lesion masks into standard space using FNIRT (Andersson, Jenkinson & Smith, 2010). The lesions were then collated into a group lesion with 'fslmaths'. The group lesion was then warped back into

subject space for each participant using the inverse transformation matrix. These masks were then removed from the individual participant's segmented images to calculate GMV in the tissue that was collectively unaffected by the stroke lesion.

Lesion volume, GMV for whole brain and GMV group-lesion removed scans were correlated using Pearson correlations to the sleep measures investigated in study 1: FI, WASO and AST(%), controlling for age. For details on how the sleep quality values were obtained, see pages 19-22.

Results

Participant characteristics, lesion volume and measures of GMV for each participant are shown in Table 3.1.

Table 3.1. Distributions of participant characteristics, Lesion Volume and GMV excluding individual and group lesions

Participant	Sex	Age	TSS (mo)	Hemisphere Affected	Lesion Volume (cm^3)	GMV Excluding Lesion (cm^3)	GMV Excluding Group Lesion (cm^3)
1	M	62	118	R	56.72	660.07	544.44
2	F	74	34	R	95.95	522.53	461.03
3	F	54	229	R	2.68	603.63	487.81
4	M	86	46	R	12.62	591.23	412.59
5	M	83	72	L	51.77	606.69	458.76
6	M	41	97	L	68.91	625.09	528.32
7	M	84	126	R	0.38	643.45	474.27
8	M	60	7	L	4.56	693.45	553.98
9	M	64	10	R	7.26	665.03	532.38
10	M	57	105	L	2.16	697.59	554.13
11	M	61	85	R	39.06	665.00	557.31
12	M	60	21	L	133.81	646.43	556.51
13	M	64	42	R	4.71	634.62	482.73
14	M	59	96	R	23.58	712.85	581.99
15	M	74	67	R	39.81	661.46	531.49

Abbreviations: TSS = Time Since Stroke, GMV = Grey Matter Volume, mo = months.

Figure 3.1 shows the distribution of lesions across participants. The most commonly affected areas were subcortical, only one participant had a cerebellar lesion. The inclusion of 2 lacunar strokes explains the presence of small lesion areas in the contralateral hemisphere.

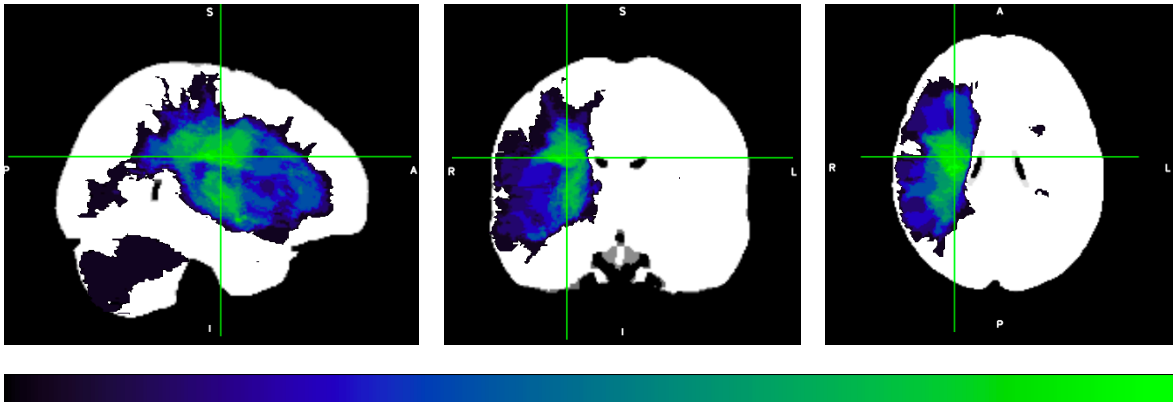

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Figure 3.1. Distribution of lesion location across subjects overlaid on MNI Brain Mask. Lighter areas indicate multiple lesions in the same anatomical space (colour bar indicates that the highest number of lesions found in same anatomical space was 9). MNI Coordinates: 33, -11, 24.

Lesion Volume and Sleep

No correlations were found between lesion volume and any of the sleep measures, controlling for age: FI $r(12) = -.118$, $p = .687$, AST $r(12) = .057$, $p = .847$, WASO $r(12) = .072$, $p = .806$. (See figure 3.2 A-C)

Grey Matter Volume and Sleep (individual lesion excluded)

No correlations were found between grey matter volume (excluding individual lesion) and any of the sleep measures, controlling for age: FI $r(12) = .062$, $p = .835$, AST $r(12) = -.098$, $p = .74$, WASO $r(12) = .06$, $p = .838$. (See figure 3.2 D-F)

Grey Matter Volume and Sleep (group lesion excluded)

No correlations were found between grey matter volume (excluding group lesion) and any of the sleep measures, controlling for age: FI $r(12) = .059$, $p = .842$, AST $r(12) = .039$, $p = .894$, WASO $r(12) = .075$, $p = .799$. (See figure 3.2 G-I)

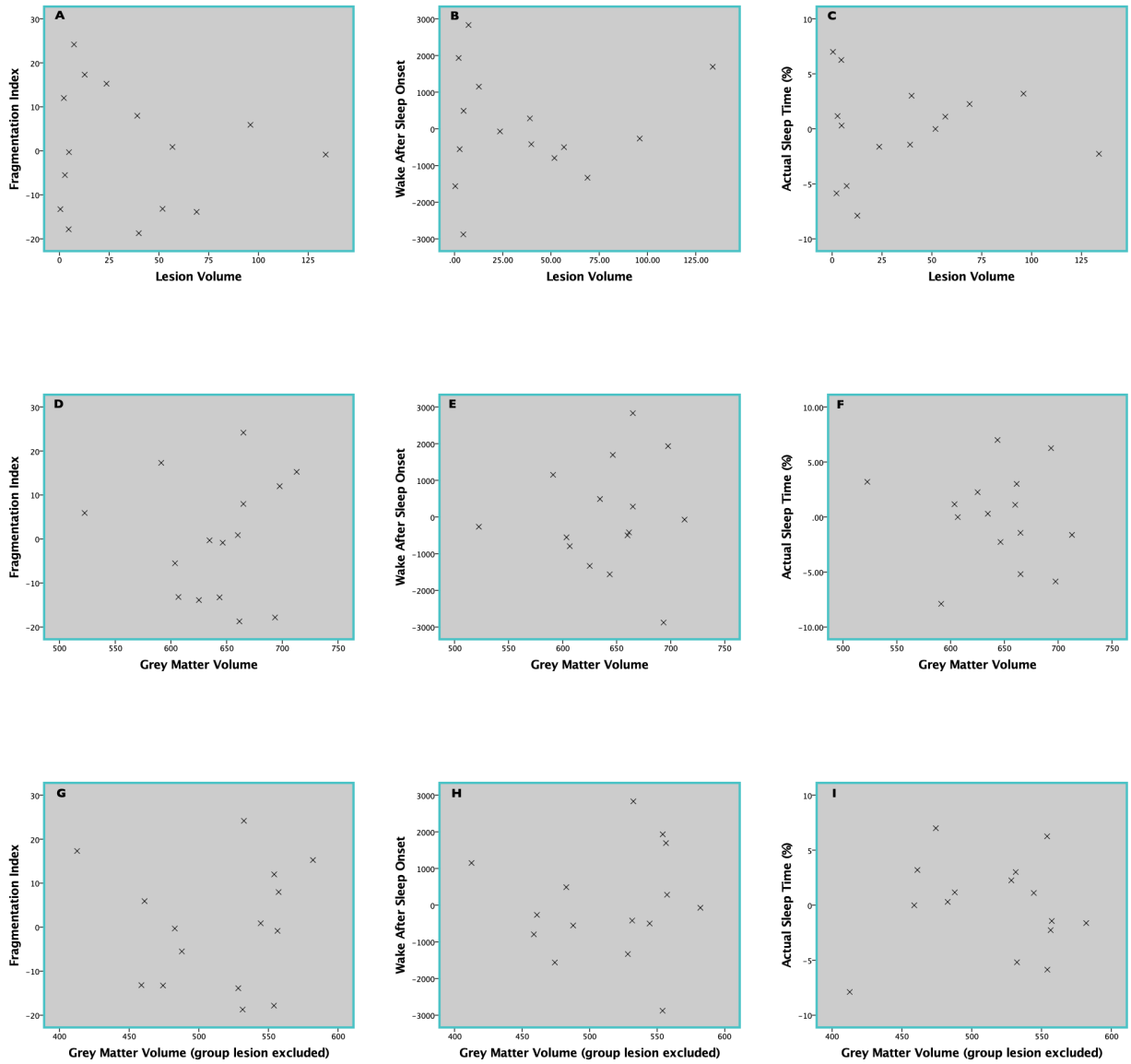

Figure 3.2. Partial correlations between sleep outcomes and measures of cortical volume, controlling for age. A) Correlation of FI with lesion volume. B) Correlation of WASO with lesion volume. C) Correlation of AST with lesion volume. D) Correlation of FI with GMV. E) Correlation of WASO with GMV. F) Correlation of AST with GMV. G) Correlation of FI with group lesioned GMV. H) Correlation of WASO with group lesioned GMV. I) Correlation of AST with group lesioned GMV. There were no significant correlations.

Discussion

The current study found no correlations between any of the sleep and cortical measures. The null results could be a result of the heterogeneity of the participants and the small sample size, however it also could be that there is no relationship between the measures of grey matter and lesion size with sleep quality in this population. The measures of grey matter were quite global measures of cortical structure and therefore might be too general to be connected with the process of sleep.

Similarly, lesion volume is quite a general measure of neural damage. Investigating lesion location in relation to sleep difficulty, may be a more appropriate measure, given the literature linking certain locations to sleep function. However, this would require a much larger sample size than was possible here, given the heterogeneity of lesion locations in a general stroke cohort.

It is not possible to rule out a link between sleep quality and lesion location in the present study. Past evidence has shown a link between RLS and subcortical damage and SDB and brainstem damage in stroke (Brown et al., 2014; Lee et al., 2009a). Previous research has linked the suprachiasmatic nucleus to the regulation of the circadian rhythm and other subcortical regions such as the basal ganglia with regulating sleep-wake periods (Qiu, Vetrivelan, Fuller & Lu, 2010; Takahashi, Hong, Ko & McDearmon, 2008). It would be reasonable therefore, to suggest that damage to particular regions of the brain could impact normal sleeping.

As all participants in the present study had motor related issues following stroke, there are difficulties in disentangling whether sleep disturbance is related purely to the stroke or

whether motor deficits specifically impact sleep. Previous literature suggests that both motor impairment and brain lesion could separately impact sleep quality. Difficulties with mobility have been linked to increased sleep difficulty in older adults without stroke (Stenholm et al., 2010). This could suggest that the impact of a motor cortex stroke reducing mobility is what leads to the sleep difficulties regardless of neurological damage. However, subthalamic lesions have also been implicated in inducing insomnia (Marquez-Romero, Morales-Ramirez & Arauz, 2014) independent of causing motor problems. Therefore, it seems that mobility deficits and damage to the brain could impact sleep separately, but further investigation of lesion location and motor deficits on sleep quality is needed to properly understand this relationship.

Given the research into older adults with poorer sleep it would seem that there is a general relationship between reduced GM/ WMV and poorer sleep (Del Brutto et al., 2016). Hence, the present study hypothesised that a reduction in GMV due to stroke would be related to poorer sleep quality. However, stroke is not a part of healthy ageing and so the change in GMV after stroke is not directly comparable to that of older adults and could be following a different mechanism which does not affect sleep as a consequence, which could explain the null results in the present study. Furthermore, the lack of a control group in this study means that it is not known whether the GMV measures would differ to those of a healthy older cohort and so any relationship identified could not have been directly attributed to the stroke lesion.

Literature focusing on insomnia has often found links between the presence of insomnia and larger amounts of cortical arousal. When looking at participants with insomnia, Winkelman et al. (2008) found that, in comparison to controls, participants with primary

insomnia had a 30% reduction in GABA, an inhibitory neurotransmitter responsible for reducing cortical excitability. Hyperactivity was also found in a cohort of participants with insomnia and SDB, specifically within the salience network and the insula (Khazaie et al., 2017). Similarly, an MRI resting-state study explored the differences between brain networks in insomnia groups compared to controls and found higher rates of spontaneous fluctuations in regional brain activity was found for the insomnia group (Li et al., 2016). It could therefore be worth investigating stroke survivors' resting state functional MRI data in relation to sleep in future studies.

There were several limitations in the MRI metrics used in the present study. As lesion volume was used as a correlation measure, it would have been beneficial to have a T2-FLAIR scan of each participant so that the lesions could be masked more sensitively thereby increasing the accuracy of the volumetric measurements. Furthermore, when studying the relationship between the brain and sleep, measures of white matter through DTI would be worth acquiring given previous literature showing a connection between white matter abnormalities and sleep disorders insomnia and SDB (Li et al., 2016; Kumar et al., 2014).

Although the small sample size of the present study meant that significant relationships between neurological values and sleep outcomes were perhaps unlikely, the present study can perhaps rule out the likelihood of differences in sleep outcomes measured in study 1 being mainly due to differences in lesion volume or GMV amongst participants.

Chapter 4: The Feasibility of the Digital Cognitive Behavioural Therapy Programme 'Sleepio' for a Population of Stroke Survivors

Introduction

Chapter 2 demonstrated that stroke survivors have impaired sleep quality compared to healthy controls. Given the evidence showing the benefit of sleep on consolidation of memory and long-term health, sleep interventions should be targeted towards stroke survivors to aid consolidation of skill learning from rehabilitation therapies and also to reduce the risk of further health problems for survivors in the chronic stage.

Cognitive Behavioural Therapy (CBT) is now recommended as the standard primary treatment for insomnia (Qaseem, Kansagara, Forciea, Cooke & Denberg, 2016), and has shown success in helping the recipients to improve sleep quality (Savard, Simard, Ivers & Morin, 2005; Wagley, Rybarczyk, Nay, Danish & Lund, 2013). However, as traditional CBT involves repeated sessions delivered one-to-one, in face-to-face meetings between a patient and therapist, this type of therapy would not currently be feasible to meet the population demand for stroke survivors experiencing sleep difficulties, given the size of this group (Kim et al., 2015).

Providing CBT to a wide group of people has been attempted through the dissemination of self-guided CBT books, shown to be effective by Varley, Webb & Sheeran (2011), CBT over the phone (Bastien, Morin, Ouellet, Blais & Bouchard, 2004) and group therapies (Koffel, Koffel & Gehrman, 2015). While these methods have all shown success, they still do not provide the scale needed to address the demand, given that phone-based CBT and

group sessions still require time from a trained professional. The only medium here with the potential for the scaling needed would be self-guided CBT books, however, meta-analyses investigating the efficacy of this form of therapy concluded that the benefits gained from this type of therapy had small to moderate effect sizes (Farrand & Woodford, 2013; Van Straten & Cuijpers, 2009). Therefore, a new solution is needed in order to provide CBT to the number of people who would benefit from it, while keeping the effectiveness of traditional CBT.

Digital CBT (dCBT) programmes offer a novel route to providing the magnitude of CBT needed. dCBT programmes are designed to mimic traditional CBT on a digital platform through the usage of previously recorded advice on how to deal with specific problems that can be offered to different groups experiencing that problem. dCBT programmes have been shown as effective methods for treating insomnia. A meta-analysis of 15 trials testing the efficacy of dCBT programmes for insomnia found that the programmes were highly effective in improving sleep efficiency, total sleep time and reducing scores on the Insomnia Severity Index (Seyffert et al., 2016). Furthermore, there were no significant differences between the effect sizes on those measures between traditional face-to-face CBT and the dCBT programmes. This suggests that dCBT programmes could be the route to meeting the demand for CBT whilst maintaining the efficacy of traditional therapy.

Sleepio® (Espie et al., 2012) is a dCBT programme for insomnia. The programme is a totally automated CBT programme that has been shown as an effective dCBT for improving sleep in cohorts of people who experience insomnia (Cheng et al., 2019; Luik, Kyle & Espie, 2017; Miller et al., 2018). However, it has not been studied in a cohort of stroke survivors.

In order to study the effectiveness of this programme in a cohort of stroke survivors it is first necessary to establish how feasible it is for this population to use the programme in its current form. Many stroke survivors experience long term functional difficulties with movement, speech and cognition, therefore a computerised programme may need to be adapted in certain ways in order to accommodate these difficulties, both in the forms of the programme's interface and the type of advice offered to the users.

The present study therefore aimed to investigate the feasibility of Sleepio to be used by community dwelling, chronic stroke survivors. The specific considerations for the feasibility were:

1. Whether or not participants experienced any adverse events by using the programme
2. Whether participants were able to complete the programme and if there were any specific barriers to completion of the programme or its elements
3. How many days beyond the 6-week minimum it took participants to complete the programme
4. The general experience participants had while using the programme.

Methods

Participants

Participants were recruited through presentations at stroke user group meetings as well as by contacting participants from previous studies who had expressed an interest in other research studies. Inclusion criteria were: at least 18 years of age and >3 months post stroke with an interest in improving their sleep. Exclusion criteria were: current, frequent travel between time-zones and current ongoing shift work. A total number of 11 participants (6

male and 5 female) agreed to take part in the study out of 20 contacted. Participants were aged between 41 and 78 with a mean age of 63.18.

Of the 11 recruited to the study, 6 have completed the study at present, and so main analysis was done on the post interview responses of those participants. However, baseline data for all 11 participants was used in basic quantitative analysis. The study was approved by the University of Oxford's Medical Sciences Interdivisional Research Ethics Committee (R61184/RE001), and all participants gave written informed consent prior to participation.

Design

This study followed a mixed methods design. Quantitative and qualitative results were both included in analysis to identify patterns in qualitative reporting related to quantitative trends.

Procedure

Participants had 2 face-to-face visits at the beginning and end of the study which took place either at our centre at the John Radcliffe Hospital in Oxford or in their homes (based on participant preference). In the first visit, after taking informed consent, participants completed the SCI and the Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005). Then, audio recordings were started as participants were introduced to the Sleepio programme. Audio was recorded for qualitative analysis of responses during the baseline session and the follow-up interview, using an encrypted iPhone 8 and Macbook Pro. Two recordings were obtained to reduce the risk of technical issues corrupting a session. Once the quality of the Macbook recording had been confirmed the audio from the phone was deleted. Audio for the baseline and post sessions were transcribed by the researcher.

Baseline Session

Participants were encouraged to speak openly at all times during the recording, giving any opinions that came to mind following the "Thinking Aloud" Protocol (Lewis, 1982). Firstly, participants watched a 2-minute video giving a brief overview of the Sleepio programme (Sleepio, 2013). Following this, participants created an account with Sleepio using a code to give researchers viewing access to their account for the purpose of tracking progress.

Each participant then completed the full sign up to the programme formed of a questionnaire approximately 10 minutes in length. This questionnaire goes through the details of a typical night over the previous month covering attempted and actual sleep times, nightly routine and lifestyle. From this, the programme generates specific advice for participants for the sessions. Although the sessions follow the same structure and general content for every user, there are a number of bespoke responses and suggestions made based on this initial questionnaire and the daily sleep diary (see Appendix 1).

Following the completion of the set-up questionnaire, participants were asked to complete the first session of the programme. This covers some introductory concepts and familiarises users with the physical display and layout of the programme's features. Once the session had been completed, participants were asked for their initial thoughts on the programme and they were allowed some time to get used to the software and investigate the sleep diary page of the programme. The programme is available to be used via web browsers and also as an apple app and so, participants who had a preference to use an iPhone over a computer/ laptop were given the opportunity to familiarise themselves with the app display so that they would be able to use it on that device at home.

The structure of the Sleepio programme follows that users are asked to keep a daily sleep diary and complete weekly sessions of dCBT roughly 15-20 minutes in length, led by digitally animated guide 'the Prof'. Although the Sleepio programme is six-weeks in duration, sessions become available one week after completion of the previous session. Therefore, when sessions are not completed on the day they become available they delay the release of the subsequent sessions. The number of days participants were overdue to complete the sessions were recorded for each week.

During the programme

Participants were advised that they would be contacted by the researcher on a weekly basis to check on progress and for opinions on the programme (see Appendix 2). The weekly questions were designed to explore any issues that participants may have been experiencing so that they could be tracked over time and addressed in the final interview. The 4th session of the programme advises users to restrict the amount of time they sleep each night for one week, in order to boost the quality of sleep in subsequent nights. The weekly questions asked after participants had completed the 4th session, also included the SCI to track any large changes to their sleep quality after a week of sleep restriction.

Follow-up interview

Once participants had completed the 6th session of the Sleepio programme they were invited in for a final interview to discuss their experiences of using the programme. The interview was a semi-structured design with a number of pre-determined questions (see Appendix 3) aimed to assess the programme's ease of usage. Unstructured questions were also asked to encourage participants to elaborate on points they made during the weekly

question checks or if they mentioned elements of usage that had not been previously addressed by the structured questions.

Analysis

Pearson correlations were run on the amount of time participants took to complete the programme with age, MoCA and SCI scores at baseline.

Qualitative data were analysed using a reflexive thematic analysis approach as outlined by Braun & Clarke (2006). This method involves the process of finding patterns within the data by identifying common threads and similarities between the experiences of participants and constructing themes from these commonalities. Additionally, in the present study, an inductive approach was used, meaning that themes were data driven and not predetermined based on an existing theoretical framework.

Once the researcher had been sufficiently familiarised with the data, codes were generated from participants' responses identifying important elements brought up in the interviews directly related to the feasibility of use of the programme. Once the codes had been collected they were grouped into larger themes of common experiences reported by multiple participants. These themes were then analysed to explain the wider story of why stroke survivors had the specific experiences of using the programme that they reported.

Results

Quantitative analysis

Table 4.1 shows the distributions of cognitive and sleep scores, as well as the total number of overdue days for the Sleepio sessions. The table shows a general trend for improvement

on the SCI across the duration of the programme. The variation between participants' programme duration is discussed below.

Table 4.1. Participant demographics, distributions of cognitive and sleep scores across the duration of the programme.

Participant	Age	Sex	MoCA	SCI at Baseline	SCI at Midpoint	SCI at Post	Total Days Overdue at Completion
1	54	F	27	9	16	16	12
2	41	M	26	28	31	31	8
3	54	F	25	9	12	22	13
4	78	F	24	31	32	31	11
5	76	M	10	30	NC	NC	NC
6	70	M	29	17	26	28	30
7	60	F	26	16	18	18	20
8	78	M	25	23	23	NC	NC
9	72	M	26	18	NC	NC	NC
10	53	M	24	12	9	NC	3
11	59	F	28	13	27	NC	1

Abbreviations: MoCA = Montreal Cognitive Assessment (higher values indicate better cognition), SCI = Sleep Condition Indicator (higher values indicate better sleep quality), NC = Not completed at time of writing.

Figure 4.1 shows the trend in overdue session days across the duration of the programme, starting from session 2, which was the first session to become available after the baseline session. The general trend is that initially, participants had longer periods without accessing

the available sessions but as the course continued they became closer to accessing the sessions on the day they became available.

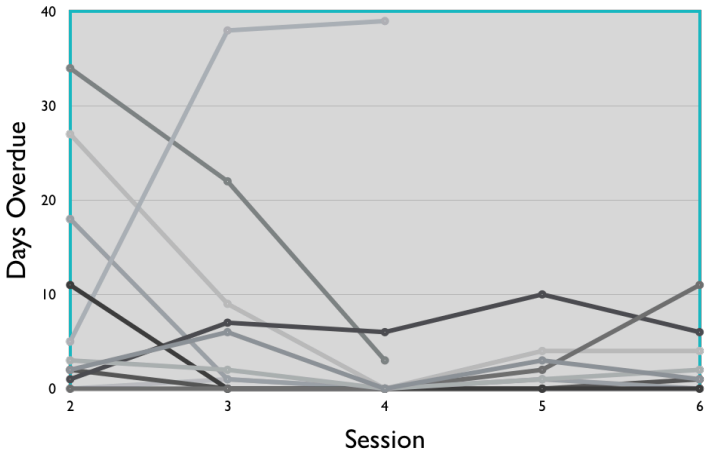

Figure 4.1. Days overdue over the duration of the Sleepio programme.

Correlations of cognition and sleep with time taken to complete programme

There was a high variability in the amount of overdue days each participant acquired over the duration of the programme. Correlations were run on the total number of overdue days with measures of cognition and subjective sleep quality to investigate the relationships between delayed completion of the programme and factors that could influence engagement.

As the trend was for earlier sessions to take longer to complete than later sessions, an average of the number of days overdue (ADO) was used in analysis as well as the total number of days overdue (TDO) (up to current point in programme). A significant correlation was found between age and TDO r = .67, p = .024, however age was not significantly correlated to the average number of overdue days r = .60, p = .053 (see Figure 4.2 A&B).

The baseline scores on the SCI were not significantly correlated with TDO r = .31, p = .362 or ADO r = .31, p = .359 (see Figure 4.2 C&D). Similarly, no relationship was found between MoCA scores and TDO r = -.35, p = .293 or ADO r = -.45, p = .163 (see Figure 4.2 E&F).

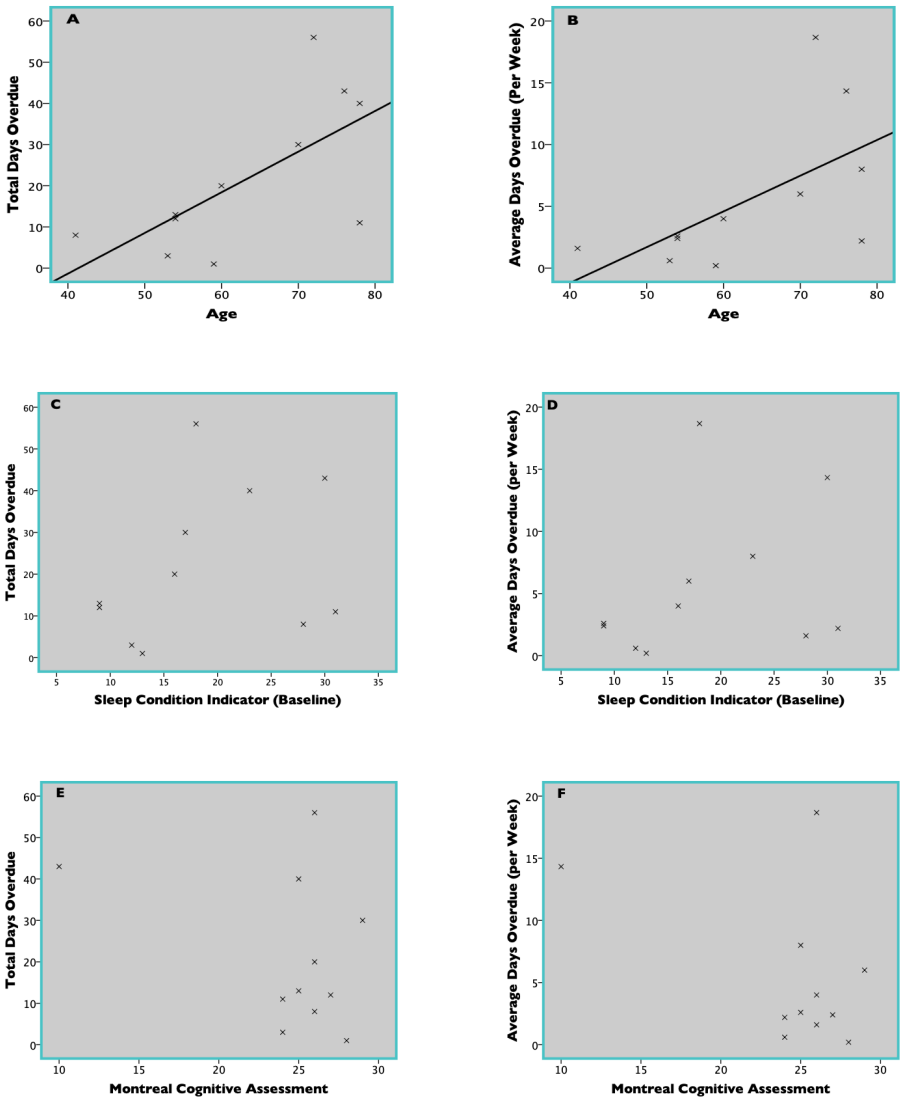

Figure 4.2. Correlations between overdue days and measures of age, subjective sleep and cognition. A*) Age with TDO B) Age with ADO C) Baseline SCI with TDO D) Baseline SCI with ADO E) MoCA with TDO F) MoCA with ADO. (Abbreviations: TDO = Total Days overdue, ADO = Average Days Overdue, SCI = Sleep Condition Indicator, MoCA = Montreal Cognitive Assessment. * significant correlation, $p < 0.05$).

Qualitative analysis

Reflexive thematic analysis (Braun & Clarke, 2006) revealed four main themes in relation to the feasible usage of the Sleepio programme by stroke survivors, shown in table 4.2.

Table 4.2. Main themes and corresponding sub-themes for post interview responses.

Themes	Sub-themes
Physical Accessibility of the Programme	Initial difficulty navigating programme
	Disparity between platforms used
	Stroke related accessibility
Impractical Advice	
Positive Engagement with the Programme	
Negative Engagement with the Programme	

Theme 1: Physical Accessibility of the Programme

Sub-theme 1: Initial difficulty navigating programme

The Sleepio programme is available via webpage on a computer or as an application available to Apple product owners. The modalities used by participants in the present study varied in that some used only one modality while others used both the website and the iPhone application.

The issue of physically accessing the programme was raised in the interviews. Although all participants who attended the post interview session had completed the programme successfully, there were elements of usage that were consistently found to be difficult. Most notably, participants consistently struggled to find the prompt to start the first session that

became available after the baseline which was often expressed as a problem realising that there was a new feature to the programme:

> **P1** *"It didn't say "click here" you know "you've got through another week click here" it just says "continue" on a space that you don't usually use … it's assuming a lot that someone should just assume that you know without a prompt."*

Multiple participants experienced a delay in completing the first available session (as shown in Figure 4.1) but the reasoning behind the delays were different across participants. P4 expressed this early delay as a result of her inexperience with working computers generally:

> **P4** "*I'm not very good with computers. Once I'm set up I'm fine but before that I'm a bit confused you know."*

As a result, her first session was left unopened for 11 days as the prompt given by the researcher to "continue to the next session" did not match the exact wording on the button to use to access the session:

> **P4** "*You said "continue session" but it was "visit the prof" and once I'd found it, it was fine."*

The set-up of the programme was also challenging for P4, given her inexperience with internet programmes and digital technology more generally. She did find that she was able to complete the programme without difficulty after the baseline session and finding the access to future sessions, but expressed the difficulty that would have occurred without one-on-one help in finding and setting up the programme:

> **Researcher** *"Do you think that if you'd just been told about it but hadn't been given any instructions…"*
> **P4** *"No it would have been more difficult then"*

This could mean that a future version of the programme would need to contain further instructions for less technologically familiar users.

Sub-theme 2: Disparity between platforms used

Other participants found that the first session was harder to find due to the difference in the presentation of the webpage and app, being initially familiar with only one medium of the programme, finding the access point to the sessions on a second platform was not immediately obvious:

> **P7** "*I loaded it straight up on my iPad, it isn't there at all so you don't even know you're supposed to be doing it.*"

P7 described the fact that she had not noticed the button used to access the sessions in the iPad version as it was "greyed out" in comparison to the green button used on the webpage version:

> **P7** "*I didn't really even notice it because when you first get it you press everything to see what it does (laughs) and that didn't do anything and then whenever I then looked at it, it was always grey and I couldn't do anything with it.*"

Although this issue was mainly seen at the beginning of the course, 6 out of 11 participants needed to be given extra guidance in finding the access to the sessions in order to continue. This guidance varied from simply telling participants that a session should be available to sending screenshot images with the access point to the sessions highlighted to help participants find it. Therefore, it is difficult to know whether all participants would have been able to complete the programme without additional help.

The initial session of the programme takes the user through the layout of the platform but this is only on one modality. When a second platform is used (in this case the app version)

there is no tutorial on where to find the programme's content and as the layouts are different, many participants had difficulty navigating the second platform. This became an issue, given that participants often expressed preferences for using two modalities for different aspects of the programme, whether related to the preference for easier usage or because of the reduced focus associated with phone usage:

> **P7** *"I found the iPad easier for the registering my sleep in the morning because it's just easy and it's directly right there. The following the Sleepio programme… it was easier just to sit there in front of the laptop. Didn't have to prop it up."*

> **P3** *"I wouldn't look at the sessions on my phone… I just feel like if I'm sitting up properly I've got a coffee or a glass of water I'm focussing on my laptop but if I've got my phone I'm usually slouched and not concentrating as much."*

Participants also spoke of modality preferences being related to symptoms of stroke. P1 expressed a difficulty in sitting upright to use a laptop in comparison to the ease of using a phone in any position:

> **P1** *"So even if I had a better working computer I would still rather read the articles on the phone… I just don't like sitting at the computer basically and also anyone who's got a physical disability probably suffers more from sitting."*

P6 mentioned the difficulties of using smaller devices requiring more precision in usage following a reduction in motor control after stroke although he did not use the app version of the programme:

> **P6** *"I'm not very good on the phone… and that may be related to the stroke but I'm not very good at it because you have to be quite precise where you're putting your finger"*

Given the stroke related preferences in usage, it was important for both mediums to be fully available to users. However, the app does not contain the full range of features that

the web-based programme does. This means that users choosing to use the phone exclusively were often unaware of the extra features available to them online:

> **P7** *"I was using it on my iPad to begin with, and it wasn't then until we had the conversation where you said "there should be these extra options" that I then plugged into my computer… the actual laptop and there were all these extra things going on."*

> **Researcher** *"So, was there mention of the Sleepio community page?"*
> **P2** *"No"*

Therefore, some users did not have access to the full range of the Sleepio course tools, given the modality they chose to use to access the programme.

Sub-theme 3: Stroke related accessibility

Many of the participants involved in the study had experienced ongoing mobility difficulties since their stroke. Specifically, one sided weakness leading to the functional usage of only one hand. It was discussed at the post interview whether there had been any difficulty in the physical usage of the programme, for example, through the requirement of manipulating a phone or laptop with two hands. All participants expressed that they had not encountered any issues with physical difficulty in using the programme, and many reported the physical ease of using the programme, despite mobility problems:

> **P1** *"I've got a nimble thumb and am very happy using it… there was nothing problematic with the app specifically, it was easy to use… an iPhone with the keyboard one-handed which is sort of how I trained to get online one-handed"*

> **P2** *"I have only one hand, sadly, but everything that I could do, could be done with one hand."*

> **P3** "*Yeah I'm pretty good at typing everything on the computer with one hand. No there was nothing that I couldn't do because I had the stroke or because I had mobility problems."*

P4 *"No nothing that I couldn't cope with it. It was fine."*

The physical operation of the programme, on either medium, was not a problem for the participants regardless of motor difficulty after stroke. No element of the programme needed the usage of two hands, which is a benefit to many stroke survivors. However, aside from the physical aspect of using the programme, there was an issue with accessing some of the written parts of the programme.

P2 encountered difficulty with the length of the initial questionnaire given his aphasia. He experiences tiredness after reading large amounts of text, which was found at the initial questionnaire during the baseline session. Beyond this, he reported noticing that although the sessions were largely audio driven, the daily sleep diary (see Appendix 1) did not have an accompanying audio:

> **P2** *"Personally I would like to see all audios so the… what's it called? "Think about the typical night of the last month". It was readable but not speaking…So I could read that but some people can't."*

Although he reported little difficulty with shorter amounts of reading, he identified the potential difficulty for stroke survivors with more severe aphasia:

> **P2** *"My aphasia isn't so bad with reading and writing… for little phrases, but because sometimes when it says "turn the screen portrait, landscape to keep going"… possibly that isn't as useful for aphasic people."*

Therefore, although the programme seems to be easily used by stroke survivors with motor difficulties, survivors who experience aphasia might have a more difficult time using the programme.

Theme 2: Impractical Advice

Perhaps the most common theme that emerged from the data was the problem of content not being feasible for a stroke survivor. Almost all of the participants reported advice given by the programme to not be suitable for them based on their outcomes from stroke. The most commonly reported advice was regarding napping. The programme suggests that naps during the day should be avoided to benefit nightly sleep. However, participants consistently reported that their decision to have a nap was based on a greater need for sleep, given experiences with fatigue:

> **P1** *"Many stroke survivors, might have a problem with fatigue, I know I do. So, there were never any questions about whether you'd had a nap in the day"*

> **P3** *"I was trying not to but if I sit down for any more than 10 minutes I sort of nod off if I'm just sitting doing nothing. And I find that really hard to fight… that could be the stroke more than anything else"*

> **P6** *"After a stroke you do get more tired. I notice it, I can't concentrate for so long and I, very often I have to have a little snooze during the day which others do as well. And this tends to say "oh don't do that" … So, I'm not sure if that's necessarily a good advice."*

> **P6** *"Since the stroke you suddenly, really, suddenly are burdened with tiredness. You just can't do anything, you have to stop."*

The programme is not designed specifically for stroke survivors and therefore fatigue is not something that is explicitly considered in the sessions which many participants noted the programme not addressing:

> **P1** *"I just didn't feel it was really aware of, of the sort of living situation that people with disabilities have"*

> **P7** *"I get tired in the afternoon… I know you're not supposed to sleep during the day but with the condition I have unless I have a rest sort of… and then it's like pressing the rest button for me. If I don't, it's just this murky evening."*

> **Researcher** *"And was that something you found the programme didn't take into account?"*
> **P7** *"No, it didn't at all."*

As well as neglecting the experience of fatigue, the programme also offers some advice for sleep improvement that was not totally practical for this cohort. One piece of advice suggests that those lying awake in bed struggling to sleep should get out of bed and go to another room and wait until tiredness sets in again, and then return to bed. It was brought up by several participants that this was not a mobility friendly piece of advice:

> **P3** *"I'm just worried about being a bit too wobbly in the middle of the night and, you know, if I start walking down the stairs I am a bit groggy and with my mobility problems I don't really want to start moving around the house."*

Similarly, the programme suggests users to move items around in their room to aid sleep but P1 pointed out that this is another mobility demanding task, saying of the suggestion to move items within the room:

> **P1** *"Actually it might not be within your control."*

Finally, it was recommended to Sleepio users that when struggling to fall asleep in the first instance, there are some relaxation techniques to try in order to aid this. One in particular is known as Progressive Muscle Relaxation (PMR) which involves systematically tensing and relaxing different parts of the body. One common outcome from one sided weakness post stroke is to have the affected hand be in a constant state of tension with it being very difficult to relax:

> **P1** *"So I can tense and then yeah I mean it is a problem getting it to relax"*

Participants who were experiencing this explained that PMR is not necessarily a feasible relaxation technique as tensing an affected side of the body can reduce the likelihood of

subsequently relaxing it, or even lead to pain. P3 explained that activating her affected hand leads to a lasting tension:

> **P3** *"That's quite hard to do, it's like your left side doesn't work, you can't really do it… that's the worst thing I can do is to try and activate it because it just switches on permanently."*

She also described stretching out the affected hand as being a way to aid in the relaxation but suggested that doing this close to a sleep time would not be totally beneficial:

> **P3** *"Well it could be good to stretch, I need to stretch my arm and hand as opposed to tense it… But not in the middle of the night."*

Including impractical or unfeasible advice to users signals that the programme was not designed for them, which can lead to users feeling less connected to the programme, or feeling that the course might not be for them. Participants expressed that when this type of advice was mentioned in the course it led to reduction in their engagement with the programme.

Theme 3: Negative engagement with programme

The Sleepio programme takes a minimum of six weeks to complete and requires users to fill in a sleep diary. The level of engagement participants felt with the programme was commonly raised. One aspect of the engagement that was experienced by many participants was the aspect of feeling isolated from the programme through the content not being stroke friendly, as outlined in the theme above. With the design of the programme being to cater advice to individual users based on their questionnaire and diary input, at times when advice was not well suited to the individual, the disconnection was felt quite strongly. P1 described this disconnect with the programme when advice was given that was not stroke friendly:

> **P1** *"I mean, I sort of lost faith in the whole thing. I continued to do my recording because as I said it was a good process for me just to do the recording but it felt they'd lost me."*

This was a specifically difficult piece of advice for her and the isolation felt from not having the advice catered towards her almost made her feel like not continuing with it:

> **P1** *"I mean my motivation did drop definitely… it would have dropped out."*
> **Researcher** *" So even with that sort of… motivation to improve your sleep, the advice on moving around that would switch you off a bit?"*
> **P1** *"Yeah… like they weren't talking to me"*

This was a common trend that participant's noticed hearing advice that didn't apply to them which was frustrating:

> **P6** *"The way they spoke as if most people's problems was thinking about not sleeping that's not my case. I can't sleep because my mind's active on thinking about completely different things"*

> **P3** *"I found the sessions to listen to him a bit irritating because he was a bit patronising and a bit condescending… I know how to relax in bed, I do not start thinking of what I've got to do and all the worries or anxiety I don't have that, so I know I don't suffer from that. So I didn't really need that advice of what to do."*

This advice also led to the perception of the duration of programme feeling longer or having a higher demand:

> **P3** *"Thought it was a bit of a long time I think, some of the sessions were a bit too long… you could have made them shorter, or just done maybe 4 sessions, I think 6 was too like… this week's session, I just couldn't be bothered to do it."*

> **P3** *"There was just too much information in all the sessions and some of it applied to me and some of it didn't"*

P3 mentioned the feeling of sessions feeling like they became longer towards the end due to the fact that not all of the information in them were relevant to her. Once she had perceived the relevant advice to become reduced, her engagement with the programme

started to lessen. A similar experience was had by P1 who explained that the repetition of the sleep diary over the course of the programme became more difficult:

> **P1** *"I got slightly flippant by the end because it's like the same question for 30 days in a row… just a bit tedious to be asked the same and not asked for any elaboration or anything"*

She went on to say that had the diary given an option to elaborate on the box categories that can affect sleep times (see Appendix 1) the diary would have felt less demanding towards the end:

> **P1** *"Because as soon as you're asked for your own opinions it's like it's not just ticking boxes, it's like you're engaging with it"*

The notion of the demand of the programme was something that was discussed by most participants. Given the frequency of reporting and completing sessions, a number of participants described difficulties finding the time to complete elements of the programme given other responsibilities. P2 explained that balancing parenting with doing the sessions as they became available was not always doable:

> **P2** *"My kids were with me on the first week, but they didn't give me enough time because it's fairly long session about half an hour"*

The demand of the programme was also brought up by P6, having not had a phone app version of the programme available to him (as he did not own an iPhone) he was using a pen and paper to record his sleep times and then later inputting them to the programme via a laptop (as recommended by The Prof). This increased the perceived demand of the programme due to the dual recordings and subsequently led to delays in completing the online diaries, and by extension, the sessions.

> **P6** *"To have a laptop beside your bed is not ideal so I remembered to note in a notebook and then at some point, usually a week later, by the time I got round to it, transfer it to a laptop."*

He described the delays in completing the diaries as being related to combination of general busyness, but also the extra work involved with doing it:

> **P6** *"When I was really busy I, you know, to find time sitting, doing it on the computer when I should be doing over things. But again, if it was only once I was doing it rather than twice it probably would've been alright."*

When asked if remembering to complete the diary would have been easier if an app version had been available to him, he suggested that it would have been better:

> **P6** *"I suppose if you were picking up your mobile phone you might remember whereas a bit of pen and paper is…"*

Suggesting that making the app more widely available could help with the overall engagement in the programme by reducing the demand associated with completion. Generally, participants did not explore the additional elements of the programme beyond the diary and weekly sessions, such as the library articles and community groups. This was mostly attributed to a feeling of the additional elements being perceived as extra work or taking up too much time:

> **P3** *"No I didn't go into the chat rooms and all that thing, he did mention it but I thought "oh if I start doing that it's going to take forever""*

> **P6** *"If I'd had more time, I might have done."*

But P4 mentioned that her lack of exploration of the programme was due to not feeling confident enough with the computers to explore beyond what she had been shown in the baseline session, despite the introduction session including information on where to find

these extras, it appears these instructions were not detailed enough for someone who is generally unfamiliar with online programmes:

> **P4** "*I didn't dare look at the computer… I'll stick to what I know…cause with computers I'm a little bit, you know… I'm not clever enough, it goes wrong, it goes wrong."*

This suggests that previous experience with digital technology might be required to access the full breadth of the programme. There was also a connection made by several participants in that the level to which they were willing to follow the advice and engage with the programme was directly the perceived severity of their sleep problem.

> **P1** *"I didn't find them hugely useful but I guess it's not that I feel I need radical changes or that I'm so worried about my sleep that I'll do whatever it takes"*

> **P2** *"Because I haven't got a sleep problem, as such… so if I had a sleep problem I would be more likely to engage with it more."*

> **P6** *"I think if I was having a real problem sleeping then it might have been worth it but I don't."*

This suggests that even when advice is useful and feasible, the perceived demand of implementing that advice was weighed against the potential benefit that could be gained from following it. P3 likened these types of advice to dieting:

> **P3** *"It's a little bit like being on a diet, you know what you're supposed to be doing and you know what you're not supposed to be doing but it doesn't mean that you listen to the advice always… But when you do listen to the advice it's positive"*

Interestingly, even though the comparison to dieting suggests that implementing the advised changes is difficult, she expressed positivity in resulting from the advice. This was similar to many other participants, who found positive experiences from completing the programme.

Theme 4: Positive engagement with programme

A common experience with the programme was the feeling of positive and active engagement connected to the advice being effective. In contrast to feelings of disconnect to the programme when advice did not seem personal or feasible, when advice was shown to work, participants expressed feeling much more positive towards the programme and motivated to stick to it. P3 explained that even though there had been some elements of the programme that hadn't felt relevant to her, experiencing a good night's sleep made her feel engaged with the course:

> **P3** *"All it took was for one good night sleep and then I was just "Oh my god I've had a good night's sleep" and then I was motivated"*

> **P3** *"When I hit the 90 I was really pleased because I thought "I'm doing it right now, there's something I'm doing right" and I can continue to build from that."*

In spite of other problems, with the programme's content, seeing her own results reflected back gave the positive reinforcement needed to keep going with the programme. The effectiveness of the advice was mentioned by several others on the course:

> **P6** *"Well it cured a number of things it suggested it would"*

> **Researcher** *"Would you say there's been a change in the quality of your sleep?"*
> **P7** *"Latterly, I would say"*

In conjunction with the effectiveness of the advice, it was commonly reported that participants enjoyed the course, either due to the educational nature of the programme or through being able to track their progress:

> **P1** *"It was quite good for me to record my, my patterns of sleep… It was really nice actually to get into a routine and just by recording it you were aware of what the system was."*

> **P1** *"I mean I was also amazed actually my efficiency was quite high sometimes it was like 80-something… so actually it made me feel you know, quite pleased about it"*

> **P2** *"It's good to have a view of what you're actually sleeping like"*

> **P4** *"No problem at all, very informative actually, good ideas, very good ideas… I enjoyed the whole lot. I really enjoyed it, it was very good… in fact I miss it now I don't do it anymore."*

P4 in particular reported great enjoyment from the programme. It is interesting also that P4 did not describe herself as having a sleep problem, but was very interested with the programme regardless. She repeatedly expressed enjoyment at the educational aspects of the programme, even when the advice was not directly relevant to her, stating that she would definitely recommend it to others struggling with their sleep.

Similar to the increased motivation when advice was effective. Participants reported a low demand involved with the programme in relation to their enjoyment of using it:

> **P1** *"Because it wasn't demanding I was quite happy to do it"*

> **P2** *"Found using the programme was quite easy…it wasn't too demanding,"*

Participants reported the daily usage of the programme as quickly becoming part of their routine when it was easy to do so. Participants who were filling in their diaries immediately after waking in the morning (usually because they were using the app which was quickly accessible) did not feel that the sleep diary was demanding as it was more of a routine activity:

> **P3** *"The sleep diary wasn't a problem at all… It's just one of those other apps you check in the morning."*

P4 *"Part of my routine. Out of bed and do it right away."*

P1 *"This is not onerous, it's like two minutes of your time"*

This would suggest that improving the ease at which participants can use the programme will increase engagement. Another level of positive engagement discussed by participants, was the sensation of feeling more in control of their sleep problems just by nature of being on the programme. P7 mentioned the feeling of being in control being related to the act of recording her sleep and being able to watch the progression over time

P7 *"It reassured me when I saw things that I thought weren't getting better, getting better. So it's that letting you know that actually the things you're doing are helping… if you're having trouble it makes you feel a bit more in control of what's happening to you."*

Similarly, P1 reported the positivity of simply recording the sleep diary over the course of the programme which she thought would also benefit others:

P1 *"Would I recommend it to someone who has problem sleeping? Yeah actually I think I would… it could help and just by the recording I think that's a benefit"*

A sentiment echoed by P7, who reported on the benefit of being able to monitor the input over the course of each week:

P7 *"You can see the scale of what you've been doing and that kind of thing so… I'm naturally a monitor so I like to measure and see things."*

Although the programme may not have been specifically set up with stroke survivors in mind, every participant reported enjoyment from the programme on some level, and many who had reported difficulty sleeping prior to taking part expressed that completing the course had been beneficial and so even with the elements of the programme that were

more difficult or less relevant, many participants were still happy with their involvement with the programme. A feeling well expressed by P3:

> **P3** *"No I'm really happy I did it, I didn't find it too difficult to do and my motivation was to get better sleep… and it worked."*

Discussion

Adverse Events

There were no specifically reported adverse events by any of the participants. The closest difficulty reported came in the discussions of the 'sleep restriction'. This is considered to be the only element of the programme that comes with a warning that users can experience heavy drowsiness during the days of this week. In the present study, when experiencing greater daytime tiredness, participants generally discontinued the sleep restriction. A couple of participants who did not adjust their sleep schedules in accordance to the advice given in the programme explained that their engagement with advice was proportional to their perceived sleep problem. Meaning that some participants did not feel their sleep problems were bad enough to warrant participating in a week of sleep restriction.

> P6 "*I think if I was having a real problem sleeping then it might have been worth it but I don't."*

Completion of programme and its elements

This relationship between cognition and programme completion, was raised by P7. She mentioned that the nature of her stroke means that information is often needed to be repeated more than once in order to make it memorable.

> P7: *"And I think with strokes, personally anyway, telling me once isn't enough."*

This sentiment was echoed by P6 who mentioned going back into sessions on a few occasions to recap on certain points:

> P6 *"I did go back to one of them from the library, one of the previous sessions because I wanted to recap on it because… it was the relaxation one I couldn't remember quite the order it did things in."*

Suggesting that the initial session was not enough to allow some to remember when the sessions would become available. However, no correlation was found between MoCA scores or TDO/ ADO and so this may not have been as strong a predictor for difficulty as age.

One solution that seemed to arise from the interviews would be further instructional content to help novice users navigate the programmes more easily, or a more obvious prompt when the sessions become available such as a pop-up message after logging in. However, it is worth noting that the Sleepio programme offers users the option of being sent email reminders for when new sessions would be available, but as this is an optional feature, most participants in this study did not choose to have reminders sent to them.

Participants who were using the app versions of the programme found the technology easy to navigate and required very little assistance during the set-up at baseline, but this was largely due to their previous experience with the devices being used. There were, however, some difficulties between usage of both mediums given the difference in layouts and available content. A tutorial guide that could be watched at any time for each medium the programme is available on, might help to make both versions equally easy to use regardless of which medium was used during the initial session which contains the navigational instructions.

No physical issues associated to operating the programme were identified by participants. The addition of audio accompaniment to all written sections of the programme would help to make the programme slightly more suitable for stroke survivors with language difficulties, which could benefit wider usability of the programme as prevalence of aphasia in stroke patients has been shown to be at 12% in the chronic stage (>6 months) but a larger 44% reporting speech as abnormal (Wade, Hewer, David, & Enderby, 1986) and so an audio feature, in addition to text, could benefit a large group of potential users. Otherwise, the current layout and design of the programme was easily usable by all. This was largely due to there being no restrictions to any aspect of the programme requiring the use of two hands, of which, many of the cohort did not have functional usage.

Participants frequently reported advice not being personalised enough and that specific bits of advice were not particularly stroke friendly, causing potential drop out from future users. One of the most frequently mentioned pieces of advice was the instruction to leave the bed when unable to sleep. This was regarded by a number of participants as not being feasible for them. The advice is based on the idea that if an individual spends a lot of time struggling to sleep in bed, they create an association with their bed as a place where sleep does not occur, and leaving the bed during periods when not sleeping can help to break this association. This advice could potentially be adapted to be more stroke survivor friendly by advising users to sit on the edge of a bed, if leaving the room is not feasible. More research is needed to test if this technique is as effective, but if the advice is adaptable to include users with reduced mobility and still effective, this could mean that a more disability conscious version could be created without having to sacrifice the amount of advice available in the programme.

Days Overdue

A significant relationship was found between age and total days overdue on the Sleepio programme. It could be suggested that the older members of this cohort may have had less experience with the platforms the programme was on and this led to the difficulties in initial usage. Participants with less familiarity with the technology could have been less likely to explore the programme, as mentioned by P4 when she stated that she wouldn't explore other elements of the programme saying "*… I'll stick to what I know".* It could, therefore, be the case that older participants may have been less likely to find the access to the initial sessions through individual exploration of the programme.

As the significance of this relationship was lost when looking at the mean number of overdue days, it seems that the difficulty with accessing the sessions was only the case early on in the course of the programme. Once participants had located the access point to the weekly sessions, there was a reduction in the number of days they were overdue. On average, participants were 12.25 days overdue for completion, compared to an average of 8 days overdue shown in past studies on Sleepio with insomnia (Espie et al., 2012). Considering that a number of participants were not included in this average in the present study due to not completing the programme in time for inclusion in the analysis, this can be considered as a low estimate of average days overdue across the whole cohort. This could suggest that beyond age, this population in particular had difficulty with completing the programme or perhaps more specifically, locating the access point to the second session. Most participants reported delays in accessing new sessions simply in not realising that another session was available:

> **P1** *"It didn't say "click here" you know "you've got through another week click here" it just says "continue" on a space that you don't usually use … it's assuming a lot that someone should just assume that you know without a prompt."*

Therefore, a clearer access point to the new CBT sessions could improve completion efficiency in users following stroke.

Given the need for participants to complete the programme in order for the discussion of feasibility to take place for the current study, the researcher eventually aided a number of participants with finding access to the sessions. This means that there is a possibility that the participants who required further help would not have managed to access the next session before their account access had expired.

P5, who has not currently completed the programme, delayed the completion of sessions 2 and 3 to the point where programme access expired (standard access lasts for 10 weeks). It is worth noting that this participant also had a MoCA score suggesting large cognitive difficulties, which implies that higher cognition may be related to easier completion of the programme, and it might not be feasible for users with lower cognition to use the programme without additional guidance, not currently given by the programme.

<u>Experience of programme usage</u>

There was a consistent trend that participant's engagement with the programme and perception of demand was related to their enjoyment and sleep improvement. Many participants reported the programme feeling more difficult as the course progressed, with sleep diary questions becoming more demanding based on the medium participants were using. However, when asked about their overall enjoyment and engagement with the

programme, all participants reported positive experiences with the programme with many participants also reporting noticeable improvements in their sleep quality.

This could be due to the purpose of the programme being to improve sleep, and so until an individuals' sleep is perceived as improving, the tasks required by the programme can seem more demanding as the results have not been experienced yet. This was outlined by P3's comment stating that the improvement in sleep sparked motivation to continue:

> **P3** *"All it took was for one good night sleep and then I was just "Oh my god I've had a good night's sleep" and then I was motivated"*

Overall, it appears that the Sleepio programme is generally feasible to be used by most stroke survivors in its current form. Tt is enjoyable and has even been reported as being effective in improving sleep quality. However, stroke survivors with more severe cognitive and language problems after stroke may not be able to use the programme in its current form. In addition, the issues of advice that does not consider physical disability and the difficulties in initially accessing the CBT sessions, could put stroke survivors at a higher risk for dropout or incompletion of this programme.

So although the programme is feasibly usable there are a few areas which could benefit from a small modification:

Navigation Aids:

- As many participants struggled with finding the session 2 button, having a pop-message reminder upon logging in would help to reduce this issue
- Having a tutorial guide available on the app would help show users where to find resources when using a second modality. Furthermore, including a list of resources on the app that can only be accessed via the desktop version could increase user engagement when only using the phone.

Advice:

- Napping: Considerations of fatigue should be included with this advice. Adapting the advice to suggest aiming naps to be between 2-3pm and for 10-15 minutes where needed would add an allowance for fatigue and be in line with the natural increase of drowsiness caused by the circadian rhythm (Milner & Cote, 2009)
- Leaving the bed when not sleeping: Advise users with limited mobility to sit up on their beds rather than leaving the room as a way of breaking the association between the bed and insomnia without requiring large amounts of mobility.
- Progressive Muscle Relaxation: Advice to avoid using an area or side of the body that is prone to prolonged tension could be implemented with this advice in order to accommodate for users with hemiparesis or chronic pain.

Chapter 5: Conclusions

For this thesis, three studies were run, all on the topic of sleep quality following stroke with the aim of answering:

1. Is sleep quality impaired after stroke?

2. Does variation in sleep quality in stroke survivors relate to variation in brain structure?

3. Could a current digital Cognitive Behaviour Therapy (dCBT) programme for sleep be feasibly used by stroke survivors?

The first study established that sleep quality is impaired in community dwelling, chronic stroke survivors. A larger number of wakenings and an increase in total WASO was found for stroke survivors in comparison to controls. This finding is further to support to research establishing a link between lower sleep quality and stroke (Falck et al., 2019). However, a causal relationship was not able to be established with this study as participants were only tested once after stroke. Establishing whether stroke is causing sleep problems rather than exacerbating pre-existing problems could benefit the development of sleep improvement programmes for stroke survivors.

The second aim of the thesis was to investigate one of the possible factors influencing the reduction in sleep quality for stroke survivors. No relationships were found between either lesion volume and sleep quality or measures of GMV and poorer sleep. Although the small sample size of this study can limit the validity of the results, it would appear that neither lesion volume nor GMV are significant influencers of poor sleep quality at the chronic stage. It is perhaps more likely, that poor sleep after stroke would be due to lesion location, or disruption of cortical pathways, given the connection to regions in the brain responsible

for controlling sleep functioning (Takahashi, Hong, Ko & McDearmon, 2008). Perhaps the best route for investigating this link would be through the use of big data such as the UK Biobank. By comparing the lesions of a large sample of stroke survivors with measures of sleep quality, connections between lesion location and sleep quality could be more reliably identified. Furthermore, given the longitudinal nature of this cohort, causal links between sleep quality and stroke may also be determined.

The third and final aim of the thesis was to investigate the feasibility of the Sleepio programme. Given the wide availability of the programme and previous efficacy research showing Sleepio to be beneficial to multiple cohorts, including insomniacs (Luik, Kyle & Espie, 2017), Sleepio could be a useful programme to use in benefitting stroke survivors with poorer sleep.

Although all participants interviewed at the post session were able to complete the course, there were a number of difficulties associated in doing so, specifically in relation to outcomes after stroke. Difficulties with navigating the programme initially and not being physically able to implement advice from the programme mean that stroke survivors may not be able to optimally engage with the programme in its current form. However, many participants still reported improvements to their sleep quality after finishing the programme and so there is still reason to suggest that this programme could be used in improving sleep after stroke.

Given the results from study 1 suggesting that elements of sleep quality are impacted by stroke, the focus of future research should be in optimising treatments for poorer sleep within this cohort. As no specific neural correlates have been established between stroke

lesions and sleep quality, treatments directly targeting brain functioning (such as using medications to reduce cortical arousal, as offered to insomniacs) may not be the best avenue to explore without further evidence establishing a relationship.

The Sleepio programme offers a holistic approach to improving sleep that is based on previously tested advice which has shown to be effective in improving sleep (Espie, 2012). Following the results from the third study showing that the programme is widely usable within a stroke cohort, efficacy studies with this patient group could provide evidence for the programme's use in improving sleep quality. If the programme is shown to be effective, offering the course to stroke survivors in the early phases of stroke could be specifically beneficial given the evidence showing sleep problems being more prevalent and severe during the acute phases of stroke (Bakken, Kim, Finset & Lerdal, 2012).

However, as other symptoms of stroke are also commonly more severe during the acute phases of stroke, before rehabilitation therapy has started, another version of Sleepio, specifically designed for adults with disabilities, could worth developing. By adapting parts of the advice, including more detailed instructions for using the programme, as well as introducing audio options for the written parts of the programme, a secondary version of the programme could be a widely dispersible solution to improving the sleep of stroke survivors at any stage of recovery.

By providing sleep improvement resources to stroke survivors in earliest stages of recovery, the optimisation of all therapies, through improved consolidation of memory, could potentially lead to greater recovery from stroke in all aspects of function. Furthermore, stroke survivors in the chronic phase of recovery would also benefit from

sleep improvement programmes, both to increase general well-being, but also to reduce the risk of further health problems. By targeting sleep in both the early and later stages of stroke, recovery could be continually improved for survivors and lead to a significant increase in quality of life.

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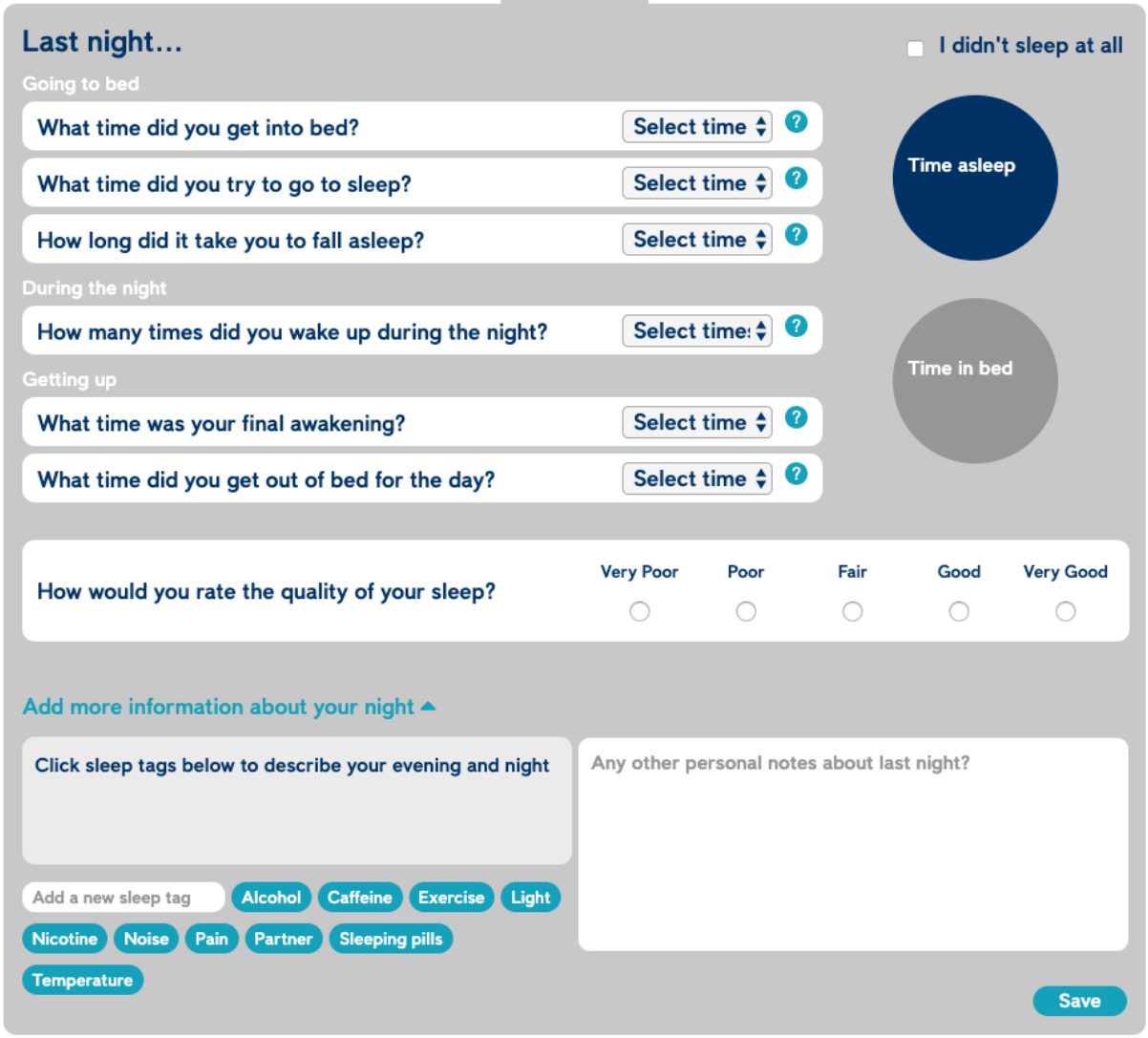
Appendixes:

Appendix 1. Sleepio Sleep Diary



Appendix 2. Weekly Questions:

How are you finding the sessions?

How are you finding keeping the diary?

(From week 2 onwards): Have you made any changes suggested by the programme?

Does the weekly session schedule suit you?

How difficult are you finding it to keep up with the programme (scale of 1-10 1=Very Easy, 10=Very Difficult)?

(End of Week 3): Complete SCI with participants

Appendix 3. Final Interview Questions:

How did you find using the Sleepio programme?

Was there anything you found particularly difficult?

Did you find it easier to use the phone or laptop/ why did you use the modality you used?

Were you able to remember all the different times asked for in the diaries? Did you find it difficult?

How motivated were you to stick with the programme?

Do you feel like it helped? Have you noticed a change?

Did you learn anything new about the way we sleep?

What was your favourite thing about the programme?

What was your least favourite thing?

Were any problems you found with the programme related to your stroke, difficulty using the programme/ difficulty remembering to complete the sessions?

Would you suggest anything to change within the programme to make it better or easier to use?

Did you use all the functions: diary, checklist etc. if so, were they easy to use/ helpful? If not, why not?

Did you use the library articles or community?

Were you able to implement any of the changes?

Do you have anything else you would like to talk about that we touched on, or do you have any questions for me?