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The Effectiveness of Background Noise During a Sleep Deprived EEG: a Randomised Control Trial

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The effectiveness of background noise during a sleep deprived EEG: A randomised control trial



**A thesis submitted to the Dublin Institute of Technology as a
requirement for the award of Masters in Philosophy**

(MPhil)

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Abstract

Introduction

Sleep Deprived Electroencephalogram's (EEG's) are usually carried out routinely in dedicated children's Hospitals as they have been shown to increase the yield of the study. However, despite sleep deprivation being successfully carried out prior to the EEG the patient may fail to fall asleep. Various techniques have been developed to enhance sleep, such as the use of "white or background noise". This study examined the use of background noise during the sleep portion of the EEG in comparison with a control group.

Methodology

This was a randomised control trial with two interventions (two different types of background noise) and a control group (no noise). There were 202 patients enrolled in the study over a two year period and randomly allocated to each group. They were given forty minutes for the sleep portion of the test and if still awake after forty minutes, this was noted as a "fail to sleep". The study was performed in the Neurosciences centre, Our Lady's children's hospital.

Literature Review

The literature review was carried out after the study commenced which highlighted that as well as the use of white noise during sleep, the use of music as another technique was also frequently used to enhance sleep. Also emphasized were the various confounding factors that were present in this type of study and therefore this thesis attempted to address these issues and endeavoured to control for these influences so as not to affect the results.

Results

Initial results examining the three groups in terms of the data distribution showed that there was little difference in relation to whether the participants fell asleep or not or the time taken to fall asleep. This was also the case when further statistical analysis was performed.

However a trend was noted between group B (CD noise) and C (No noise) which was statistically significant at $p=.037$.

Further data was obtained regarding sleep showing that 91% of the participants fell asleep regardless of the allocated group. It was also noted that 15% of patients only had abnormalities in sleep.

Conclusions

In relation to the data on arousals, this information should be interpreted with caution as correlating peak noise was not measured, in order to determine if the noise was the cause of the arousal or not. There were also little differences between the groups on the other outcomes measured however there may be small differences between the CD noise and the control group as somewhat more participants fell asleep when using the CD noise. Further studies need to validate these results, particularly across various departments under strict controlled settings in order to eliminate the confounding factors outlined in this thesis.

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Chapter 1

Introduction

1.1 Background

An electroencephalogram (EEG) records the electrical activity of the brain and is primarily used as an aid in the diagnosis of epilepsy. Epilepsy is the recurrence of stereotypical, unprovoked seizures.

Unfortunately it is known that in approximately half of these patients that were clinically diagnosed with epilepsy, a routine, waking EEG does not show any abnormalities (DeRoos et al. 2009). Gibbs and Gibbs were the first to describe the relationship between sleep and epilepsy in 1947 which found that sleep may activate clinical seizures as well as abnormal discharges on the EEG which is seen in patients that are liable to seizure (Aneja & Gupta 2005). Sleep has been found to activate both focal and generalised discharges on the EEG in about one third of all patients with clinical epilepsy (Kotagal & Yardi 2008).

1.1.1 Sleep Deprived EEG's

Sleep deprived EEG's involve the patient being fully or partially deprived of the sleep the night prior to attending for the EEG, and are encouraged to fall asleep during the test. The American Electroencephalography society guidelines and technical standards state that in paediatrics, sleep recordings should be obtained whenever possible (Anon 1994), as sleep or the act of sleep deprivation has been noted to increase the diagnostic yield of the study, especially in children. For this reason, some Neurophysiology departments choose to sleep deprive all paediatrics patients the night prior to the test in order to provide the best chance of achieving sleep during the investigation.

1.1.2 Use of Pharmacology for sleep induction in EEG

As well as the use of sleep deprivation prior to the EEG, pharmacological agents such as chloral hydrate or benzodiazepine's can be used as sedatives in order to induce sleep. This is not only during an EEG but also throughout other investigations such as Computed Topography (CT) or Magnetic Resonance Imaging (MRI) however this method is controversial. In recent years various literatures have noted adverse reactions to these medications, most commonly nausea, vomiting and restlessness (Loewy et al. 2005). A

survey was conducted of 80 children that were administered Chloral hydrate during a hospital stay, however the parents commented on side effects including sleepiness, unsteadiness, hyperactivity, poor appetite and vomiting (Kao et al. 1999). Chloral Hydrate can also obscure the EEG by causing an increase in faster frequencies up to 30Hz which can alter the EEG interpretation in some children. Melatonin can also be used for co-operation and sleep induction during the EEG and is a hormone which regulates the sleep wake cycle and its synthesis relies on environmental cues, for example light. As melatonin in this case would be used on a one-off basis for the patient it would be unlikely to cause any side effects. However various articles have reported side effects such as diarrhoea and agitation in some children using chloral hydrate (Loewy et al. 2015), and the long term effects of melatonin are unknown and may affect the hormone and normal growth and development (British National Formulary BNF for Children 2014-15).

1.1.3 The use of White noise for sleep induction

Hospitals are noisy places and it can be difficult to facilitate natural sleep in children attending for an EEG whether they are sleep deprived or not. Sleep in a hospital environment is particularly problematic without the use of the aforementioned pharmacological agents together with the growing demand for efficient handling and management of patients within the service (i.e. avoidance in spending a considerable amount of time trying to obtain sleep) and the ever increasing hospital waiting lists.

White noise is a noise which covers the entire range of human hearing (20-20,000 Hz) (Forquer & Johnson 2007), and there has been a considerable amount of research into white noise and its use in improving sleep. Variations of white noise are also available such as “pink noise” which is defined as a “white noise that has been equalized differently which is a less high pitched sound but with the same masking qualities as white noise” (Kawada & Suzuki 1993).

Some EEG departments within a hospital environment have attempted using these alternative measures with some using a form of background or “white” noise in combination with partial sleep deprivation to enhance the chances of obtaining sleep in children referred for an EEG. Anecdotal experiences within these departments have found it to be favourable. However this concept of background noise facilitating sleep in patients during EEG has not been evidence based, particularly not within this type of population and indeed some formal

studies of so-called “white noise” have shown no benefit in its routine use (Zimmer et al. 1993).

1.2 Research Aim and study Objectives

As a considerable amount of research has gone into the use of music for sleep induction, there was minimal recent research performed on the use of white noise. As well as this, there seems to be few high quality studies, randomised control trials with large sample sizes performed recently on white noise and sleep. This study aims to address this gap in the literature. In doing so by comparing the use of white noise with a control group with no noise in a paediatric population during a sleep deprived EEG.

1.2.1 Aim of study

The main aim of the study is:

“To investigate if any background noise is helpful in facilitating sleep in a hospital setting during a sleep deprived EEG. This allows us to evaluate the clinical value of background noise as a cost-effective, non-pharmacological, risk-free method to be used during an EEG.”

1.2.2 Research objectives

- To analyse and understand why it is important to achieve sleep during EEG’s particularly in a paediatric population;
- To critically analyse the previous literature on the use of background noise/white noise/music in sleep induction either at home or most relevantly in a noisy hospital setting
- To analyse the results using Statistical Package for the Social Sciences (SPSS);
- To discuss the results along with the limitations of the study;
- To draw conclusions and make recommendations for future research.

1.3 Conclusion

The structure of this paper is as follows:

1.3.1 Chapter 1 – Introduction

This section has given a brief introduction to the paper, which detailed the aim and objectives of the paper and the layout that the paper will follow.

1.3.2 Chapter 2 – Physiology of sleep

This chapter examined firstly the physiology of sleep including a brief description on early and modern research surrounding sleep together with various features that make-up sleep and how these are recognised within these diagnostic investigations.

1.3.3 Chapter 3 - Electroencephalogram

The basic concepts of EEG were discussed including how an EEG is recorded, what type of data is collected and why it is the current “gold standard” investigation (Mcgonigal et al. 2002) in the diagnosis of epilepsy.

1.3.4 Chapter 4 – Study Methodology

In order to understand how white noise affects this specific population a large cohort of patients were enrolled in a randomised control trial which was considered to be the most appropriate method. This section outlines how the patients were selected, the sample size that was deemed suitable, the protocol that was used to obtain the data and the statistical analysis that was used to obtain the results.

The analysis of the data was conducted with the aid of SPSS software, which allows large amounts of data to be analysed relatively quickly. Statistical analysis approaches, such as chi-squared testing (similar to the methodology adopted by Lowery et al 2005) will be adopted. Further descriptive statistics (for example standard deviation) and non-descriptive statistics (for example relationship testing) will be employed in the analysis.

1.3.5 Chapter 5 – Literature Review

The literature review was carried out after the study commenced which highlighted that the use of music as another technique used to enhance sleep was noted to be equally as successful in this area. However it was felt that at this stage in the study it was not appropriate to add another intervention. The available literature was critically analysed, taking note of any future recommendations for further studies on this topic in order to fill the gap in the research that has already been produced.

1.3.6 Chapter 6 – Data Analysis

The data describing the patient demographics were displayed here in table form in this chapter in order to give an overview of the differences between the groups studied. In addition to this, the data was analysed to determine:

- If the data was normally distributed which in turn would decide what type of statistical analysis would be performed in chapter 7.
- To inspect any outliers that may be due to manual error input into the SPSS program or data that may possibly be excluded from the results as they may skew the outcome.

1.3.7 Chapter 7 – Results

This section will outline and bring together the results identified from the study along with graphs, tables and charts to aid explanation. Firstly the main results of the study for the three outcomes measured are noted followed by the results and data established on the sleep survey carried out.

1.3.8 Chapter 8 – Discussion

This section will deliberate the findings from the SPSS data as well as identifying limitations namely, only participants being referred for an EEG were included in the study, therefore no adults were involved and there were no children with learning difficulties or developmental concerns included and therefore caution should be taken on the generalizability of these results to other populations.

1.3.9 Chapter 9 – Conclusions and Future Recommendation's

Conclusions from the main outcomes and secondary outcomes were summarized in this chapter along with the conclusions from the sleep survey also performed from the data collected. Future recommendations were based on the sample examined and it may be better to look at different cohorts of patients or perhaps gain baseline data from the same individuals to benchmark the intervention against as a control group. Furthermore there was no qualitative data collected on the preference of the noise used as it is suggested that there was a relationship between the degree of liking a sound and relaxation (Iwanaga & Moroki 1999)

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Chapter 2

Physiology of Sleep

2.1 Introduction

This chapter aims to examine the underlying physiology of sleep in regards to the research provided in the literature, however some of which still remain as theories and will remain unknown. In order to proceed further it is vital to understand the fundamentals of sleep. How is sleep regulated? Why do we need to sleep? What keeps an individual awake?

Early researchers dating back to 350BC began to understand the concept of sleep and began to further investigate the underlying changes in the physiology of the brain during this state of quiescence. Certain developments in technology in the 1900's are allowed sleep to be standardised and to more accurately classify sleep. This chapter will attempt to outline how sleep can be better understood; going back to theories in early research to more standardised and now understood elements of sleep from more recent research.

Sleep disturbance is a common problem affecting all ages in the modern society. For example infants and toddlers often have difficulty settling or staying asleep throughout the night or adolescences may display parasomnias such as sleep walking or excessive daytime sleepiness (Stein et al. 2001). There have been pharmacological and non-pharmacological treatments developed in order to address problems getting to sleep and problems staying asleep. These techniques were examined to determine their efficiency and whether they could be an alternative to pharmacological agents and to compare risks and adverse side effects of each.

2.2 Historical perspective

2.2.1 Early history of sleep

Aristotle 350BC describes sleep as “a seizure of the primary sense organ, rendering it unable to actualise its powers” (Papachristou 2014).

In 1584, a book written by Thomas Coogan continued to put forward Aristotle's initial theory on sleep that the body's blood would retreat back into the organs which was why sleeping bodies felt “cool” to the touch (Healthy Sleep 2008). A German psychiatrist Wilhelm Criesinger noted eye movements during dream states in 1868. In 1900, Sigmund Freud

published his infamous book “The interpretation of dreams” in which he theorised at how dreams could be interpreted to detect the psychological insights of that person (Dream Research 2015).

However it was in 1913 when a French scientist Henri Peiron (1881-1964) authored a book called “Le probleme physiologique du sommeil”, which was one of the first to look at sleep on a physiologic basis (Morrison 2014).

2.2.2 Moderate research in sleep

Modern research dates back to the early 1930’s after the discovery of EEG in 1929 by Hans Berger a German psychiatrist (Šušmáková 2004). Sleep for once could be understood from a neurophysiological standpoint and it was here that Hans noted a difference between the electrical activity of the brain in wakefulness and sleep. It was however Dr Nathaniel Kleitman (1895-1994) who is considered the “father of American sleep research”, who gave a great contribution to sleep research, most prominently in the discovery of Rapid Eye Movement (REM) sleep. He was a co-discoverer of REM sleep in 1953, which was one of the major findings of sleep research in the 20th century (Gottesmann 2013). He also divided Non Rapid Eye Movement sleep (Non-REM) into four stages, ranging from the lightest sleep stage, stage 1, to the deepest, stage 4 (K. Susmakova 2004).

In 1968 Rechtschaffen and Kales standardised methods for scoring sleep into Non-REM and REM sleep. A reclassification of these sleep stages was later carried out in 2007 by the American Academy of Sleep Medicine (Iber et al. 2007) to ‘W’ (Wakefulness), Stage N1-3 (Non-REM) which N3 incorporates stage ‘3 and 4’ and ‘R’ for REM sleep.

2.3 Sleep stages

Sleep is divided into two sections: Non-REM sleep and REM sleep (See figure 2.1). One cycle of Non-REM and REM lasts from 90-100 minutes with ~4-5 cycles during one night in a normal adult (K. Susmakova 2004).

2.3.1 Non-REM sleep

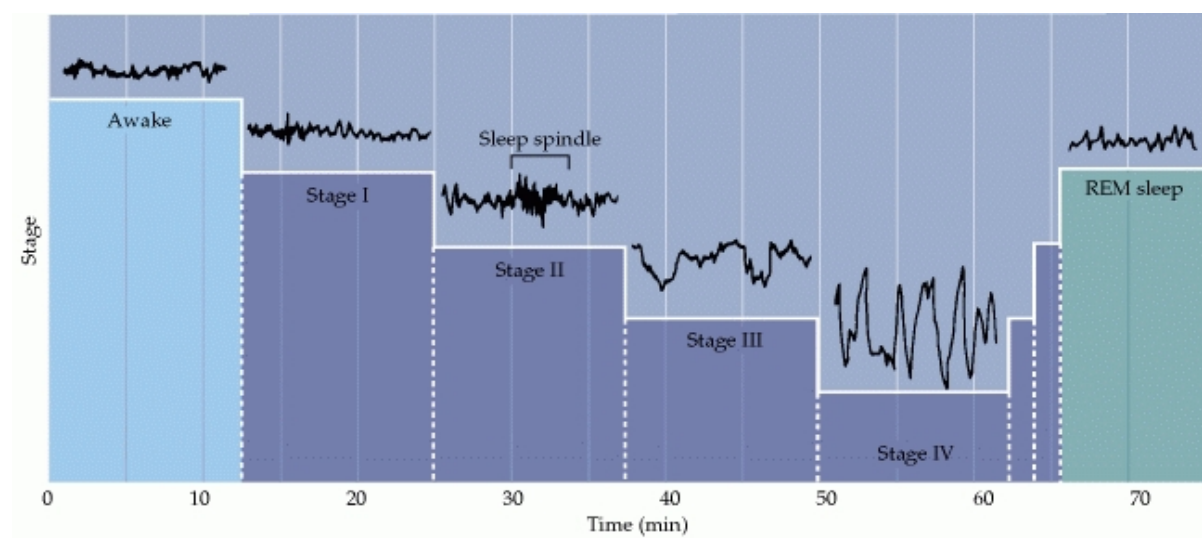
Non-REM sleep makes up 75-80% of total sleep time (Lee-Chiong 2005). Stage 1 is marked by the disappearance of the main dominant rhythm called the “alpha rhythm” which is usually seen at 8-13Hz when the patient is alert and awake. The electromyography (EMG) or muscle activity decreases and accompanied by slow rolling Eye Movement on the electro-

oculograph (EOG). Stage 2 sleep comprises ~45-50% of NREM sleep, with the appearance of “sleep architecture” such as sleep spindles and k-complexes which are described further in chapter 3. Stage 3 and 4 occupy ~15-20% of NREM sleep (Lee-Chiong 2005) and together are known as “slow-wave sleep” with increasing amounts of slower frequencies as sleep progresses.

2.3.2 REM sleep

REM sleep occupies ~20% of total sleep time (Lee-Chiong 2005) and occurs ~60-90 minutes after sleep onset. The EMG activity is intermittently increased during this stage with twitching of chin and limb movements with otherwise muscle atonia accompanied by visible rapid eye movements. Physiologic changes such as irregular heart rate and respiration is also observed. REM is also the sleep stage known for dreaming with vivid dream recall reported in ~80% of arousals from this sleep stage (Carskadon & Dement 2011).

Figure 2.1 showing the sleep cycle during 70 minutes of sleep



Purves, D et al (2001)

2.4 Function of Sleep

The meaning and understanding of why we sleep or why we need to sleep has been one of the great unsolved theories of modern research. We know that sleep is one of the great mechanisms that our body uses to fight infection and to maintain our good health. For example, the human growth hormone is secreted during deep sleep, enhancing the synthesis of bone and the formation of red blood cells (K. Adam et al 1984).

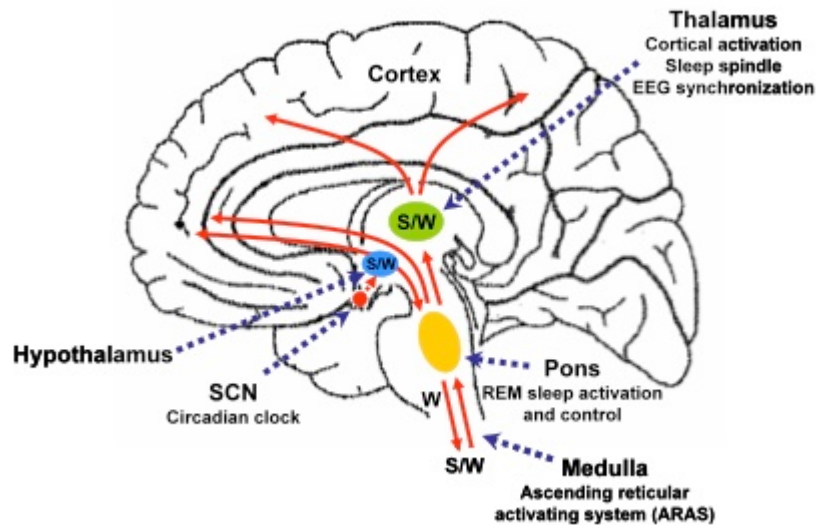
Examining the effects of even several days of sleep deprivation resulted in an increase in mortality also causing an increase in cardiovascular events (Kato et al. 2000). Partial sleep deprivation over a fortnightly period was found to result in a significant accumulative deficit in cognitive performance on various tasks (Van Dongen et al. 2003). In addition to this further studies on rats show that after chronic sleep deprivation resulted in death after 2-3 weeks (Lee-Chiong 2005). Several theories have been put forward to explain the purpose of sleep, from energy conservation or regulation of emotions to memory and learning (Šušmáková 2004). Other studies have suggested thermoregulation as a possibility as the previously mentioned study on rats (Lee-Chiong 2005) showed a drop in body temperature, however there are no widely accepted theories at present.

2.5 Neurobiology of sleep

Sleep is generated by activation of the pre-optic area of the anterior hypothalamus (See Figure 2.2). This in turn inhibits wake-promoting centres with the help of a neurotransmitter called γ -aminobutyric acid (GABA) (Šušmáková 2004) and thereby turning off arousal systems during sleep. The sleep generating systems including neurons in the pons (See figure 2.2) switch from NREM to REM sleep throughout the night and send outputs to the lower brainstem and spinal cord to assist with muscle atonia (Colten et al. 2006).

Wakefulness is generated by ascending arousal systems from the brainstem that activates parts of the forebrain to maintain wakefulness (See figure 2.2). These involve two pathways: the first activates part of the thalamus and the second originates in the upper brainstem which control neurotransmitters such as norepinephrine, serotonin, dopamine, and histamine. These neurotransmitters enter the hypothalamus where they pick up inputs from nerve cells. Together with further additional inputs from the forebrain (acetylcholine & GABA) these inputs enter the cerebral cortex, activating the nerve cells, preparing them for interpretation of incoming sensory information (Colten et al. 2006).

Figure 2.2 showing hypothalamic and brain stem sleep activation



Pace-Schott EF et al (2002)

2.6 Models of sleep Regulation

There are three different models/processes of sleep regulation, (1) Homeostatic process (2) Circadian rhythms and (3) Ultradian process, all contributing to achieve optimum sleep wakefulness.

The homeostatic process controls the amounts of sleep and wakefulness a human achieves to maintain optimum homeostasis. An indicator that homeostasis is in operation, is the amount of slow wave sleep (SWS) observed, which is stage 3 and stage 4 sleep. This stage or stages of sleep occur more so in the first part of the night, decreasing as sleeps progresses. Studies have shown that this SWS increases after a night of sleep deprivation thereby enhancing the optimum level of this type of sleep in order to maintain homeostasis.

The Circadian rhythm is dependent on the effects of environmental factors or external events within a 24 hour period. Its form within the brain is called the Suprachiasmatic nuclei, located in the hypothalamus (Lee-Chiong 2005). This is linked with the retino-hypothalamic tract, thereby making light the main dominant input for the circadian rhythm.

These two processes are closely linked as the circadian rhythm impacts on the homeostatic need to sleep, e.g. increased alertness in the early evening, even after a sleepless night (Lee-Chiong 2005). The Ultradian process alters the variations from NREM to REM sleep during the night (Lee-Chiong 2005).

2.7 Sleep inducing Techniques

2.7.1 Pharmacological Treatments

Sleep disorders may be a result of aging, environmental stressors; psychiatric illnesses such as anxiety disorders are also present in children with developmental issues. Due to these causes, sleep disorders can be long-standing and therefore may require persistent drug treatment.

Benzodiazepines are a group of drugs used in order to induce sleep in various sleep disorders. Drug names within this group include diazepam, temazepam or zolpidem etc. These drugs act on the benzodiazepine site of the GABA complex to increase the frequency of chloride channel openings therefore increase inhibition of nerve impulses. Barbiturates more commonly provide sedation which generally can last up to 12hrs and include phenobarbital and pentobarbital etc. Benzodiazepines have been noted to be quite successful in the induction of sleep, particularly associated with an increase in sleep duration (Holbrook et al. 2000).

However there were adverse side effects reported such as dizziness, light-headedness and daytime drowsiness. Diphenhydramine, which is an antihistamine, was used successfully to treat children with sleep problems (Russo et al 1976) and performed significantly better than the control group. However various other studies have found that these drug treatments are of limited value in the treatment of chronic sleep disorders.

2.7.2 Non-Pharmacological Treatments

Recent research has noted the emergence of new alternative therapies in the treatment of sleep disorders and sleep induction among other psychological disorders such as depression etc. Varieties of therapies were trialled in the literature:

- Progressive Muscle relaxation

The participant is instructed to sit comfortably in a chair and asked to purposely tense a muscle and relax it and to use this routine at bedtime which has been shown to be helpful. The theory is that this increases the awareness of muscle tension and has been found to decrease perceived stress and anxiety and thereby improving sleep (Lee et al. 2012).

- Cognitive Behavioural Therapy (CBT)

CBT involves the “identification and modification of dysfunctional automatic thoughts and behavioural experiments aimed at breaking the vicious cycle of the symptoms and their consequences” (Speckens et al. 1995). EEG analysis along with subjective measures has validated the use of CBT in improving the quality of sleep (Cervena et al. 2004).

A study in 2003 concluded that during tapering of benzodiazepines in older people alongside the use of CBT was superior to tapering alone and the long-term effects were felt for up to one year post therapy (Baillargeon et al. 2003).

- Background noise

The use of noises such as music or white noise has been theorised to help in enhancing sleep however the reasons why this is the case, are not fully understood. Theories have been put forward such as that it masks any sudden “peak” noise, for example a door banging that may rouse the sleeper thereby increasing the quality of sleep. A habitual effect may be the cause as once the sleeper gets used to the sound they associate it with sleep, for example in conditioning young children. This study has examined this technique further in the literature review in chapter four.

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Chapter 3

The Electroencephalograph (EEG)

3.1 Introduction

The electroencephalograph (EEG) is a recording of the electrical activity of the brain (Binnie et al 1982). This electrical activity can be obtained via scalp electrodes. The EEG was first discovered in 1929 by the German Neuropsychiatrist Hans Berger (1841-1941) during his determination to attempt to understand more about psychiatric illness. It was from 1924 to 1929 that Berger obtained a sustained amount of recordings showing an alpha rhythm. An alpha rhythm includes frequencies within 8-13Hz and is the main dominant rhythm in the EEG that is present in waking on eye closure in neurologically normal adults. Prior to 1929 a physician named Richard Caton (1841-1926) became interested in the electrophysiological phenomena using a galvanometer and a beam of light concluding that currents pass through a multiplier when electrodes were placed at two sites (Jellinger 2011).

In this chapter the basics of EEG are examined, how the signals are generated from the cortex and how these signals differ with state change (wakefulness transitioning to sleep) with EEG examples. The association between the EEG and the waveforms in patients with epileptic seizures became clear soon after the discovery of EEG. In 1935 Gibbs demonstrated a specific 3 per second pattern during a “petit mal” attack or an event where the individual appears vacant for a short time which we now know as “absence seizures” (Smith 2005). In this chapter we intend to look further into the contributory factors of the EEG, also examining how various activation procedures during the EEG, particularly focussing on sleep, can be an important factor in the diagnosis and classification of different types of epilepsies.

3.2 The Origin of the EEG and Basic EEG standards

3.2.1 EEG Signals

Neurons can generate time-varying electrical currents when activated. These are generated by transmembrane currents at a cellular level. The neurone is depolarised which is mediated by sodium/potassium voltage dependent ionic changes. This is a rapid change in membrane potential from a negative to positive potential and the nerve impulse is generated followed quickly by returning to a negative potential and propagates along the nerve axon.

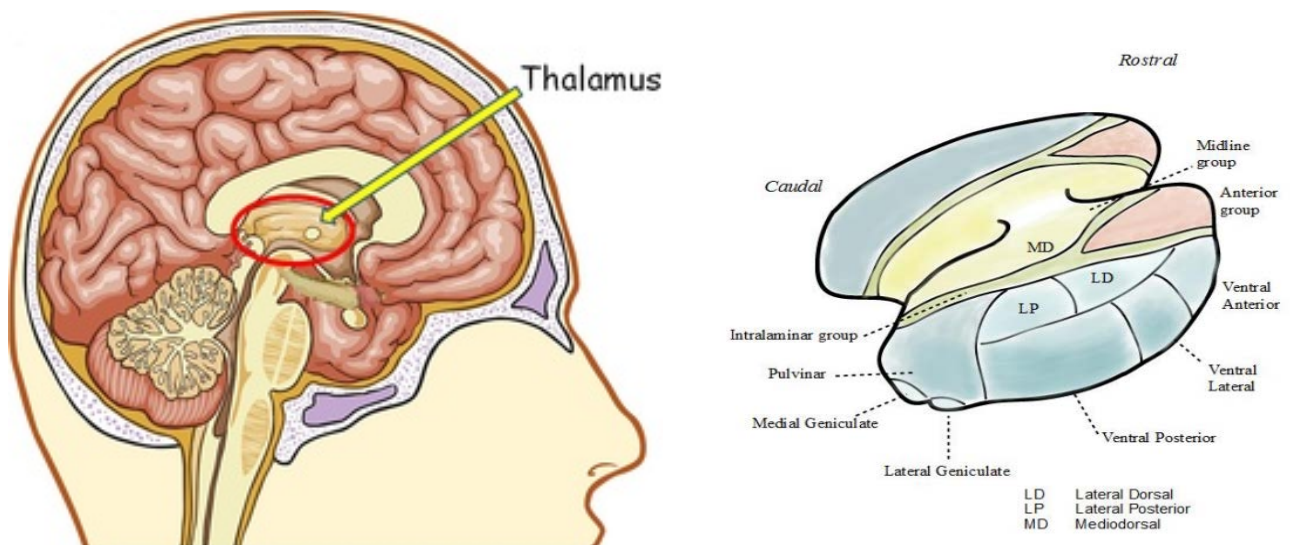
There are also slower post-synaptic potentials such as excitatory post synaptic potentials (EPSP's) and Inhibitory post-synaptic potentials (IPSP's) which change the potential to positive and negative inwards in the cell respectively. However the neurons that mainly contribute to EEG activity are those that form "open fields" i.e. pyramidal neurons which are present in the cortex of the brain. When these nerve cells are activated by the described impulses generated with a degree of synchrony, coherent electrical/magnetic fields are generated. These are alike to current dipoles which can be detected at a small distance by electrodes (Lopes, F et al 2010).

The EEG signals are comprised of a summation and synchronisation of thousands of excitatory and inhibitory pyramidal cell post-synaptic potentials (PSP) generated from the cerebral cortex of the brain. In addition to PSP, intrinsic changes in cell currents produced by activation of ionic channels could possibly contribute to the generation of EEG potentials. The scalp electrodes record the potential differences of these PSP in the cell membranes of cortical neurons. Two scalp electrodes could be at different voltage levels and record this difference. The amplitudes that are detected are dependent on surrounding anatomy and vary with the physiological state of the brain and the age of the person. For example if the patient had a vascular insult (i.e. stroke) the surrounding brain tissue would be damaged and therefore the amplitudes of the EEG would be lower over the affected area.

Tissue such as scalp, skull, brain and cerebral-spinal fluid (CSF) between the above generating cells and the scalp recording electrode creates an "electrical volume conductor", which is what changes the amplitude and morphology of the waveform.

The dorsal thalamus (located deep in the brain) is considered the main sub-cortical EEG generator where the thalamic nuclei is thought to interact with the cortex to produce the synchrony of the EEG rhythms or PSP during waking and sleeping states (Olejniczak 2006).

Figure 3.1 showing location of Thalamus in the brain and the dorsal thalamus



Neurophysiologic Basis of EEG (2006)

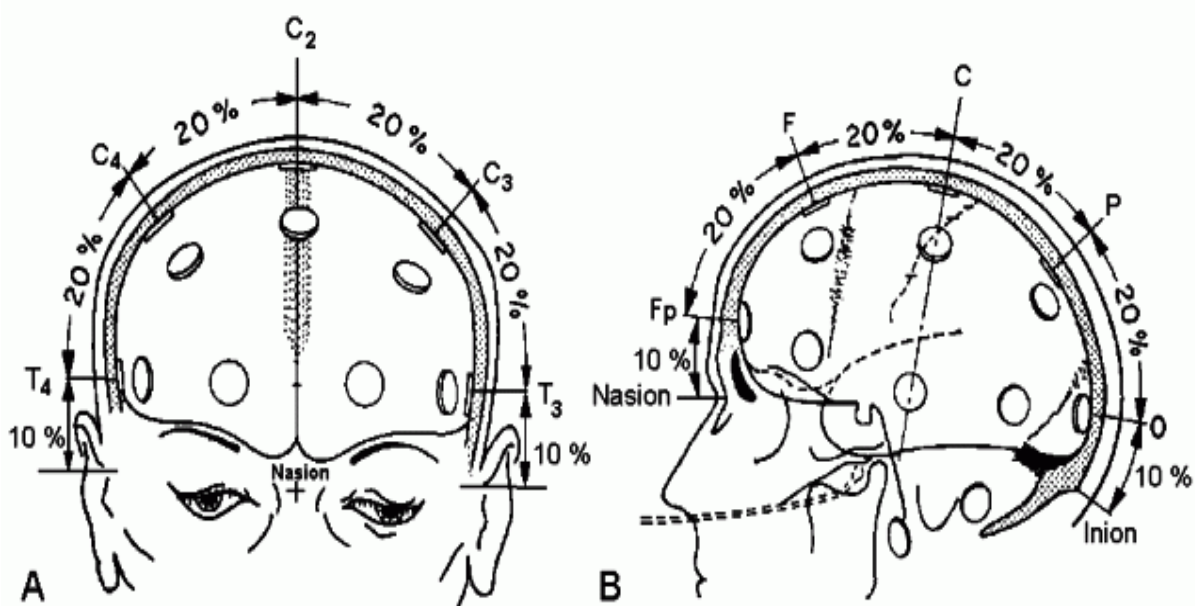
*Massachusetts institute of Technology
(1998)*

3.2.2 Electrode Placement

The international 10-20 system (Figure 3.2) of measurement is based on definable anatomical landmarks and is used in order to ensure equal electrode distance and to standardise these measurements between EEG departments. The patients head is measured with a tape measure and marked lightly with a china graph art pencil prior to electrode set-up.

Figure 3.2 showing the international 10-20 system of measurement

Staalhemel - responsive environment for brainwaves (2009)

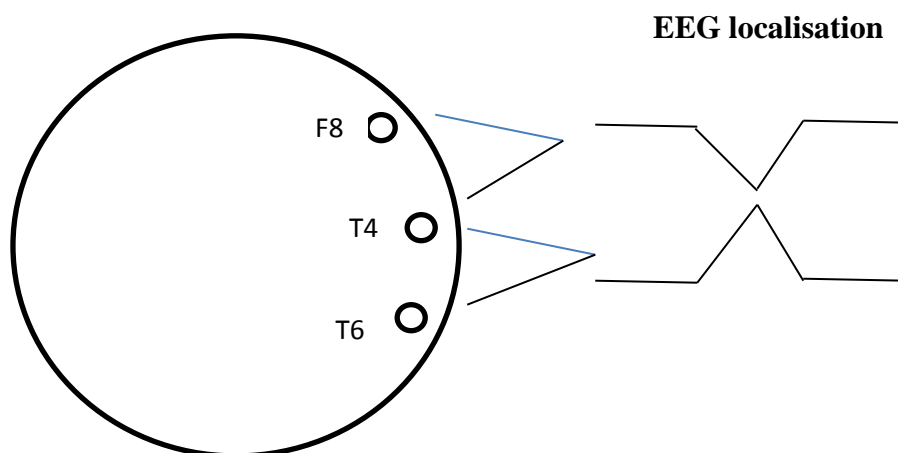


3.2.3 Electrode Channels, impedance and montaging standards

A minimum of $5k\Omega$, which is the resistance value between the electrode and the scalp, should be used for electrode impedances which are achieved by using a scarifying scrub on each placement prior to applying silver chloride electrodes. The full 21 channels of simultaneous EEG recording are encouraged and no less than 8 recording channels is accepted, except the case of premature babies with small head circumferences according to the international federation of clinical neurophysiology (Nuwer et al. 1999). A channel displays the potential difference between a pair of electrodes (Binnie et al 1982) and is one line of EEG with two electrodes plugged into an amplifier.

There are two different ways of analysing the EEG activity. The bipolar method can show minor differences between two electrode sites and a simple way to localise a maximal field due to phase reversal which is also unaffected by the amplitude of the surrounding background rhythms. The word phase refers to the waveform that begins in one direction. As the EEG is looking to detect areas of negativity phase reversal can attempt to localise an abnormality (See figure 3.3) The referential method localises abnormalities by amplitude however this can be difficult if the surrounding background frequencies are quite high in amplitude. Both Bipolar and referential montages must be used as it markedly modifies the EEG signals. These both have advantages and disadvantages to view certain abnormalities but both should be analysed to gain the maximum amount of information from your EEG.

Figure 3.3 – A head stamp of the layout of EEG electrodes showing an area of negativity at T4 which is located over the right temporal portion of the brain.

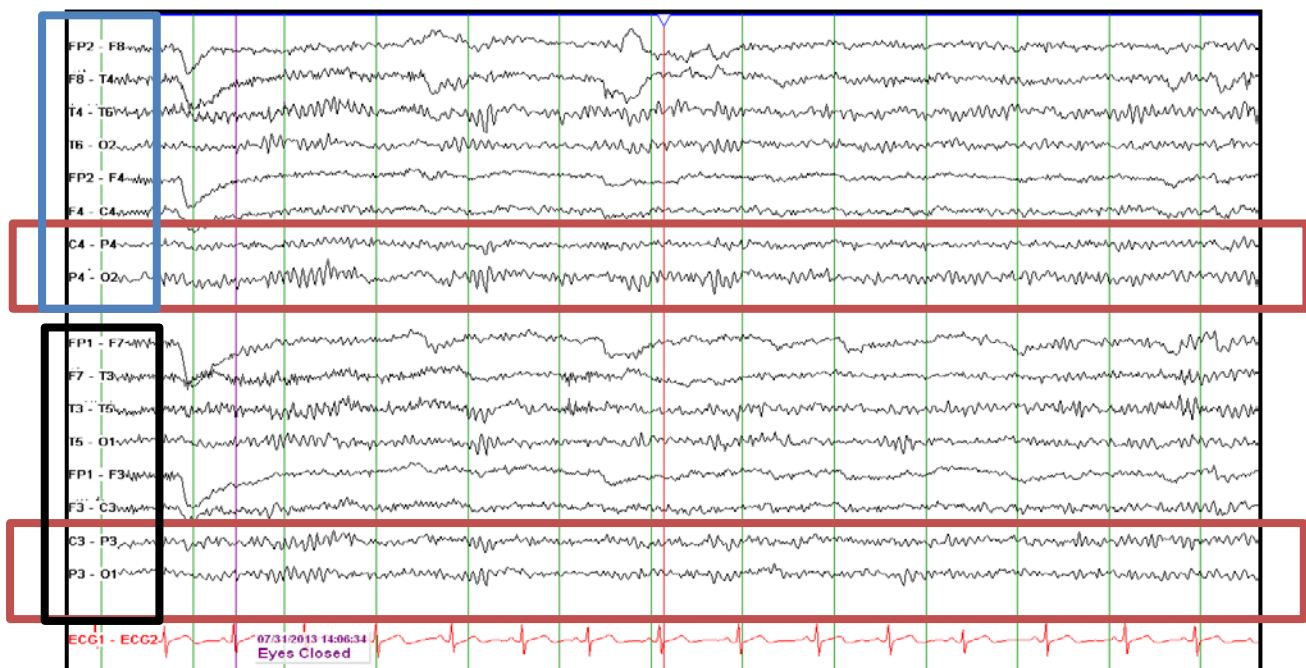


3.3 The Normal waking adult EEG and sleep staging

3.3.1 Normal waking EEG (adult)

A normal waking adult EEG should have a responsive and symmetrical alpha rhythm at 8-13Hz on eye closure at amplitude of 40-100 microvolts located maximal over central and post-central regions (Figure 3.4 – See red outlined area). This can be accompanied by mild amounts of theta activity at 7Hz however is it more notable in a paediatric or adolescent's EEG. Faster frequencies within the beta bandwidth at 14-30Hz can be noted in small amounts. Varied amounts of muscle activity (>30Hz) can be seen depending on how relaxed the patient is.

Figure 3.4 showing an example of the waking background seen during an EEG – Each electrode is referenced to another and this is located down the left side of the page. The Letters represent the underlying lobe of the brain (e.g. F= Frontal lobe) and the numbers given represent the hemisphere (e.g. Left = odd – black box, Right = even – Blue box).

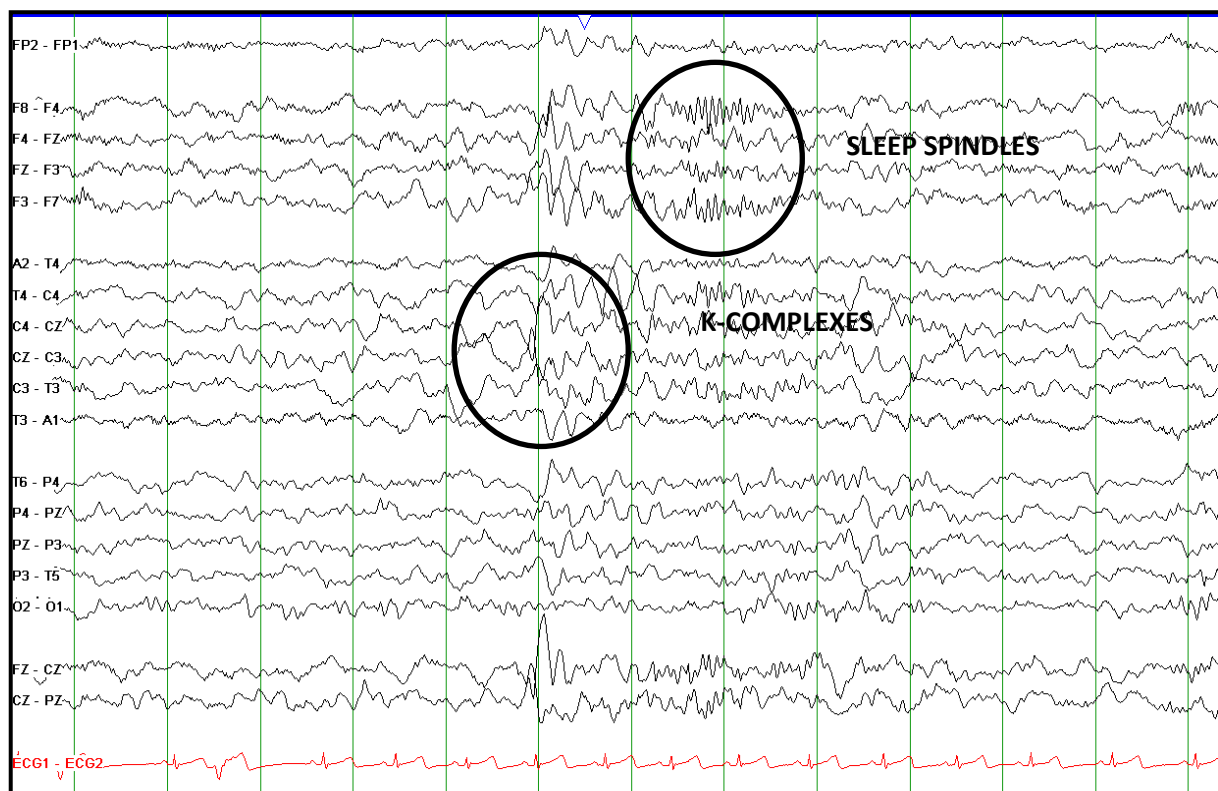


3.3.2 Non-REM Sleep

Non-REM sleep occurs when there is an altered transmission at the thalamus whereby sounds/noises etc. from the environment are inhibited from the cerebral cortex. As already mentioned in chapter two, Non-REM is divided into four stages: Stage one is early sleep or drowsiness, which is comprised of slowing of the background frequencies together with a

disappearance of the previously described main dominant (alpha) rhythm. This is accompanied by slow lateral eye movements and a relative reduction in muscle activity as the patient starts to relax. Stage two (figure 3.5) is a more definitive and less subjective sleep stage with prominent sleep architecture such as “sleep spindles” which are made up of faster frequencies at 12-14Hz over the vertex (otherwise known as CZ in the 10-20 system of measurement used in EEG). Vertex sharp waves and “k-Complexes” are also observed (figure). Stage three and four (deep or delta-wave sleep) can be difficult to distinguish from one another. They show a further increase in the amount of background slower delta activity, increasing in amplitude as sleep progresses. The American Academy of Sleep Medicine (AASM) altered the scoring methods of the Rechtschaffen and Kales rules whereby N1-N3 is used to describe stages 1-4, with N3 denoting both stage three & four combined .

Figure 3.5 showing Non-REM sleep (N2/stage 2 sleep).



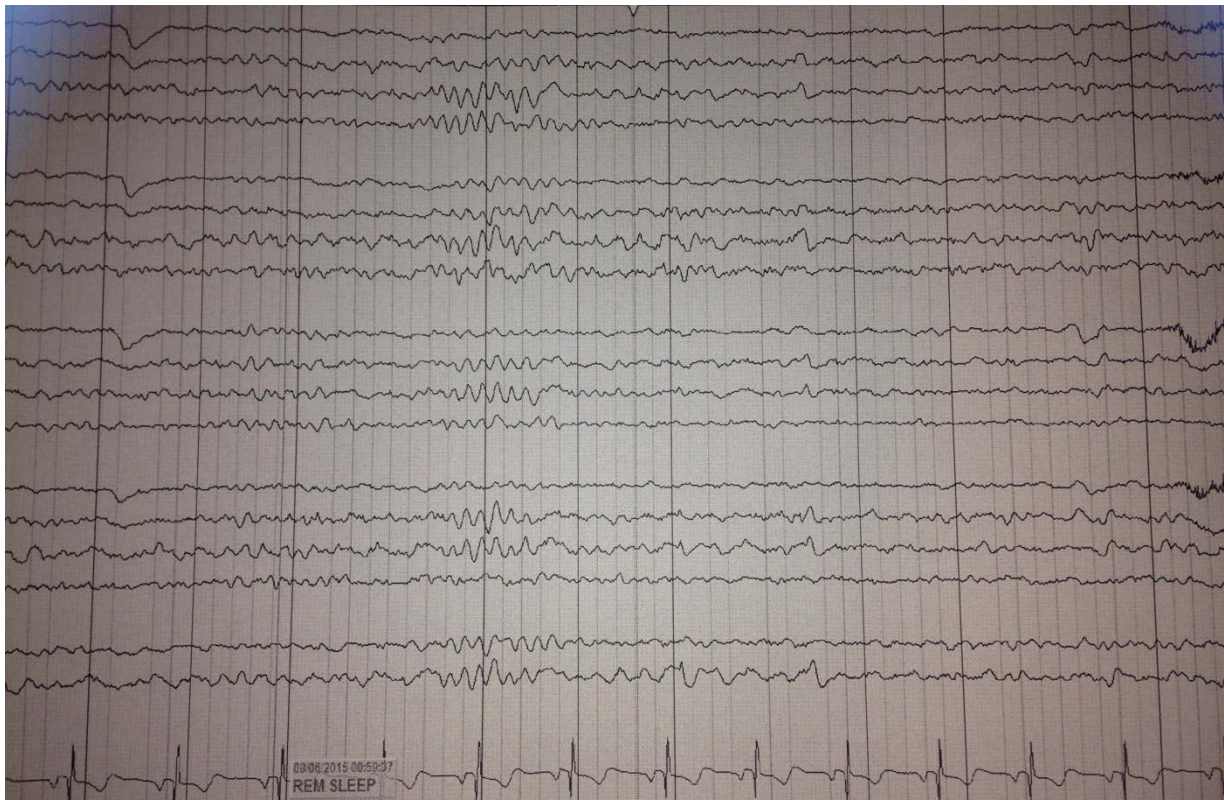
3.3.3 REM Sleep

REM sleep or “Rapid eye movement” is a state of “active” sleep where the EEG appears to have similarities to the waking EEG background (Figure 3.6). The EEG is dominated by low

amplitude faster frequencies within the theta-alpha bandwidth (5-10Hz). This is accompanied by rapid eye movements and irregular breathing.

REM sleep is most commonly known as the state in which you dream. A study by Dement and Kleitman et al (1957) found that 80% of people after arousal from REM sleep were able to recall vivid dreams.

Figure 3.6 showing REM sleep



3.4 The EEG and Epilepsy

3.4.1 Seizures types and epilepsy

Epilepsy is defined as the tendency to have recurrent, unprovoked stereotypical seizures. Approximately five people in every 100 will have an epileptic seizure at some stage in their life (Epilepsy action 2015).

A seizure occurs when there is a sudden, abnormal burst of electrical activity within the brain. Clinical Seizures can be divided into two types:

- Partial
- Generalised

Within these two seizure-types each can manifest itself very differently. For example a partial seizure may involve a sudden interruption in awareness of their surrounding environment. They may become unresponsive accompanied by changes in facial expression or include autonomic features such as colour change, sweating or a change in heart rate. This type of seizure can also be sub-divided into simple and complex partial seizures. In simple partial seizures one can remain completely alert and responsive during a seizure, possibly accompanied by either twitching of the limbs, for example a simple motor seizure or “jacksonian march”. In complex partial seizure one can experience a feeling of déjà vu and loss of awareness of the individual’s surrounding’s.

A primary generalised seizure can cause the individual to lose consciousness followed by a stiffening of all four limbs with jerking movements followed by a period of confusion or excessive sleepiness post event. Occasionally the individual can be incontinent of urine or have may have bitten their tongue during the event. These also can manifest as brief myoclonic jerks of limbs (mainly upper) without any interruption in consciousness. One of the most common forms however are “absence seizures” which are commonly seen in childhood during which the patient may grow out of in adolescence, depending on the aetiology of the seizures. These involve a momentary loss of awareness and clinically a vacant stare is noted, lasting from 10-20seconds after which the patient is usually unaware the seizure has occurred with no symptoms post event.

Seizures can be idiopathic in that there is no known cause. Cryptogenic meaning there is a suspected but currently unknown cause and symptomatic, there is a known cause for the seizure (i.e. stroke or space occupying lesion).

It must be noted though that the current National Institute Clinical Excellence (NICE) guidelines for an EEG referral is to perform an EEG only to support the diagnosis of epilepsy when the clinical history suggests that the seizure is likely to be of epileptic origin (Anon n.d. 2015).

3.4.2 EEG and the diagnosis of epilepsy

During an epileptic seizure, waveforms known as “spikes or sharp wave” components or “epileptiform discharges” are frequently noted. However as the individual may have only had a handful of seizures in the past the EEG is unlikely to capture an event during a routine twenty minute recording. Inter-ictal or in between discharges are noted on the EEG which

give a view that the patient may be at risk of having seizures due to these abnormal discharges, it can determine whether these are focal or generalised in nature in order to determine the best management or possibly aid in syndromic classification.

However, the EEG may also be normal in patients with definite seizure activity, as ~50% of patients that are clinically diagnosed with epilepsy will have a normal EEG (Smith 2005). There are several techniques used during the EEG in order activate these “epileptiform abnormalities” such as the act of hyperventilation. This involves the patient breathing deeper for ~three minutes which decreases the carbon dioxide level in the blood thereby causing the cerebral blood vessels to constrict which reduces the blood flow to the brain and lessens the availability of oxygen and glucose to the brain. Another activation routinely used is intermittent photic stimulation which can determine whether a patient may be photosensitive at certain flash frequencies that may trigger a seizure. Repeat studies are also used to increase the yield however this increases the workload for the EEG physiologist and the yield is decreased to 10% by the fourth repeat recording (Salinsky et al. 1987). The activation procedure yielding the largest (up to 80%) is the use of sleep deprivation prior to recording the EEG, which may be fully or partially sleep deprived. Some dedicated children’s hospitals chose to partially sleep deprive all the patients attending the department for an EEG and aim to capture a period of sleep during the study.

3.5 Conclusion

This chapter outlined the basics in EEG including the origin of, how the EEG is utilised (i.e. activations procedures) in order to elicit the best yield from the investigation, and the basic types of seizure along with how the EEG can aid in the diagnosis and management of epilepsy. The following chapter will describe how the proposed study was carried out prior to commencement and outlining the main aims that this study attains to achieve.

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Anon, Epilepsies: diagnosis and management | guidance | Guidance and guidelines | NICE.

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Neurophysiologic Basis of EEG (2006)

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Date:27/02/2015

Massachusetts institute of Technology (1998)

<http://www.braincoretherapy.com/wp-content/uploads/2014/01/Neurophysiologic-Basis-of-EEG.pdf>

Date visited: 27/02/2015

Staalhemel - responsive environment for brainwaves (2009)

<http://www.staalhemel.com/page/2>

Date visited: 27/02/2015

Epilepsy action - Epilepsy facts, figures and terminology (2015)

<https://www.epilepsy.org.uk/press/facts>

Date visited: 27/02/2015

Chapter 4

Study Methodology

4.1 –Patient selection

All patients referred to the Neurosciences Centre, Our Lady's Children's Hospital, Crumlin, Dublin for an outpatient routine EEG between September 2013 and February 2015. Patients between the ages of 3 and 17 were offered the opportunity to enrol in the study if they fulfilled the inclusion criteria.

4.1.1 Inclusion and exclusion criteria

The patients included were:

- Normal development or patients with mild learning difficulties were also included
- No presence of on-going sleep disturbance or sleep disorder

Patients excluded were:

- diagnosis of ADHD or ASD
- diagnosed with sleep-related disorders such as narcolepsy or sleep apnoea
- habitual users of background noise were excluded.

This was based on information given on each referral form. Age-appropriate information leaflets for the parents/guardians and patients who were recruited for the study were sent by post along with the EEG appointment letter. It should be noted however, that based on the patient selection, the results of this study cannot be generalised to adults or children with ADHD or moderate-severe learning difficulties.

4.1.2 Ethics

The study was approved by the Hospitals Ethics Committee and informed consent was obtained from parents/guardians and assent forms were collected from all patients (See appendix 1-5).

4.2 Study Design

4.2.1 Study Protocol

This is a randomised, physician blinded control trial of two interventions and one control condition. Prior to performing the EEG each participant was randomised to one of three groups. Group A and B were the intervention groups consisting of a slightly different low-pitched humming noise at ~40dB and Group C was the control group, no noise. Ideally the control group would be a baseline recording of the same individuals present in groups A and B however this was not practical as firstly it would add extra stress to the individual and their families and secondly the department running the study had on-going waiting list pressures. These groups are described in table 4.1.

Table 4.1 showing three groups

Group	Condition	Outcome
Group A	Intervention	Mechanical White Noise
Group B	Intervention	Recorded White noise (Played on a CD Player)
Group C	Control	No noise (Silence)

Further questions were asked to the family on arrival to the department, such as

- Does the patient take any medications that may affect the results?
- Do they use melatonin regularly?
- Have they had a nap on the way to the hospital?

All aspects of the EEG were carried out routinely. All patients coming to have an EEG in the department were partially sleep deprived (~4hrs of sleep deprivation) in order to further increase the chances of obtaining sleep. This was the same for the study and the exact amount of sleep deprivation compared with the patient's normal hours of sleep was recorded as the sleep deficit (See appendix 6). An initial baseline EEG was carried out along with any activation procedures (hyperventilation and intermittent Photic Stimulation) before the patient was placed supine on the bed. Lights out was annotated on the tracing as the room was darkened, the sound was switched on if in intervention group (Placed 1.5m away from

the patient) and the Clinical Physiologist left the room to analyse the data at a nearby review station. It was the parents/participants preference on whether or not the parent stayed in the room. Forty minutes from lights out was timed and if the patient failed to sleep during this time it was recorded as a fail to sleep. The EEG duration could be prolonged if there was a clinical need to achieve sleep regardless of the study. Ideally the participants would be blinded to the study however due to the nature of the intervention this was not possible.

4.2.2 Sample size

Due to the limited impact of this study on the participants, the study was able to obtain a large sample size (>200 participants) and therefore create accurate results compared to smaller sizes.

4.2.3 Statistical Analysis

Both categorical and continuous variables were present in the data and therefore different statistical tests were performed. Both parametric and non-parametric tests were used. Chi-squared tests were used for categorical variables, with Mann Whitney-u tests also carried out. A P value of < .05 was accepted as statistically significant.

4.3 Electroencephalograms

All EEG's were performed using 25-channel digital recording on Xltek system with Neuroworks software. Silver chloride electrodes were placed according to the 10-20 system of measurement. EEG's (including sleep parameters) were analysed by a Clinical Paediatric Neurophysiologist.

4.4 Equipment used

The computer software used for performing the statistical analysis was SPSS for Windows version 22. Microsoft Excel 2010 software was also used for some of the graphs produced.

Xltek Equipment (EEG32) was used to perform the EEG's with Neuroworks software. The noise from the intervention groups was produced with an old, out of use GOMCO suction machine and this was recorded onto a CD and played on a CD player for the second intervention (See appendix 14, 15 and 16 for equipment specifications).

4.5 – Data Collection

After all EEG's were performed and interpreted by the Clinical Neurophysiologist (during which there was allocation concealment), one researcher extracted the data from the patient

study forms to an excel spread sheet, such as group, age, appointment time etc. (See appendix 2). The consultant will mark when the sleep portion begins (N1) and the prospective stages after this. He also has marked if there were any arousals present during the sleep portion.

4.5.1 Randomisation Technique

The aim was to generate comparable intervention groups which are alike, in order to eliminate selection bias, known or unknown confounding factors and to provide accurate testing of the interventions and work well for large sample sizes (Suresh 2011). This study used “simple” randomisation techniques which consisted of three groups written on three pieces of paper chosen from an opaque pot.

4.5.2 Analysis of sleep stages

The data was analysed by the consultant Neurophysiologist after the EEG was completed. This entailed annotating the EEG in regards to the sleep stages along with annotating arousals that occurred during the EEG. Firstly, the sleep stages obtained were to be annotated on the EEG during later review. This can be a subjective process and therefore the data was analysed by the same person throughout the study and therefore could be standardised and was also blinded to the group allocation. As mentioned in chapter 3, in sleep there is Non-REM and REM sleep. As the entire sleep portion of the investigation lasts no longer than ~60 minutes, stages within the Non-REM portion of sleep are only identified. All Non-REM sleep stages were annotated as shown in the examples below (figures 4.1-4.4) using the revised AASM scoring system.

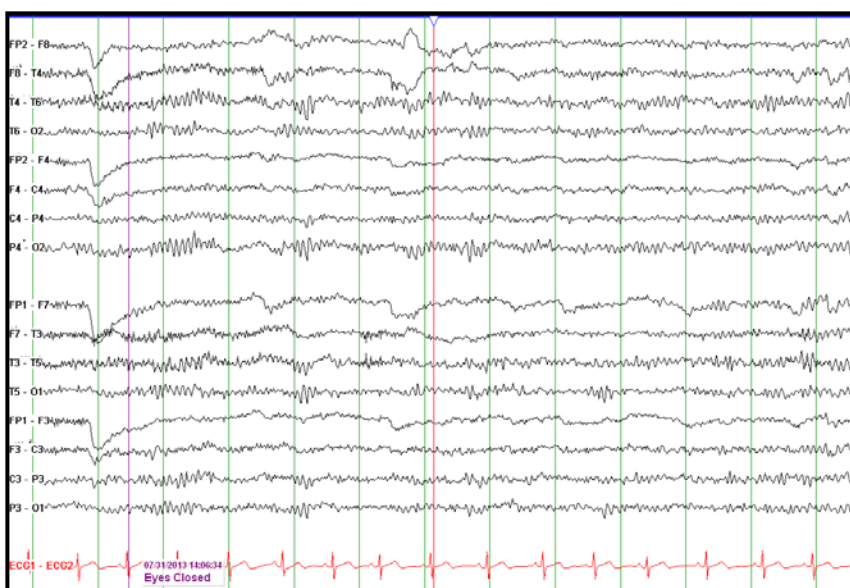


Figure 4.1 showing an example of the waking background seen during an EEG.

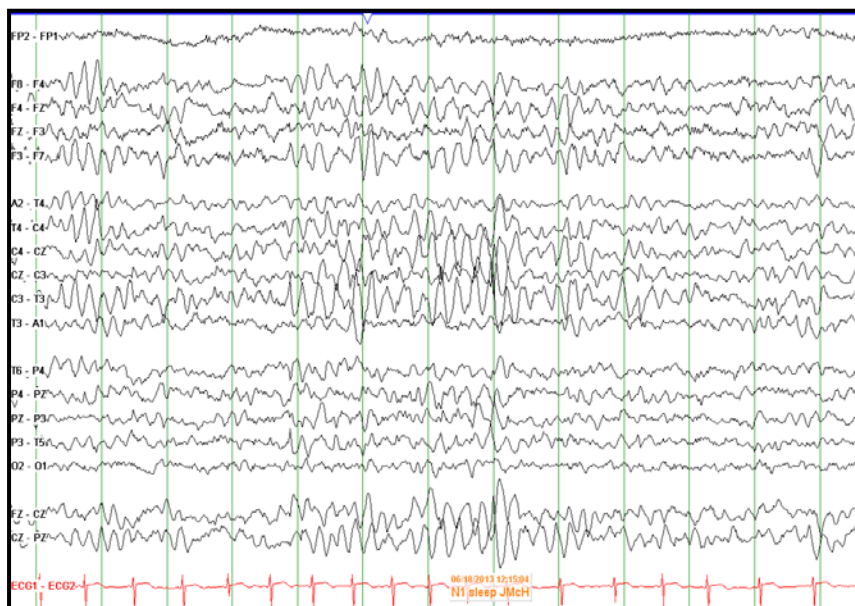


Figure 4.2 showing N1 sleep marked by the consultant Neurophysiologist

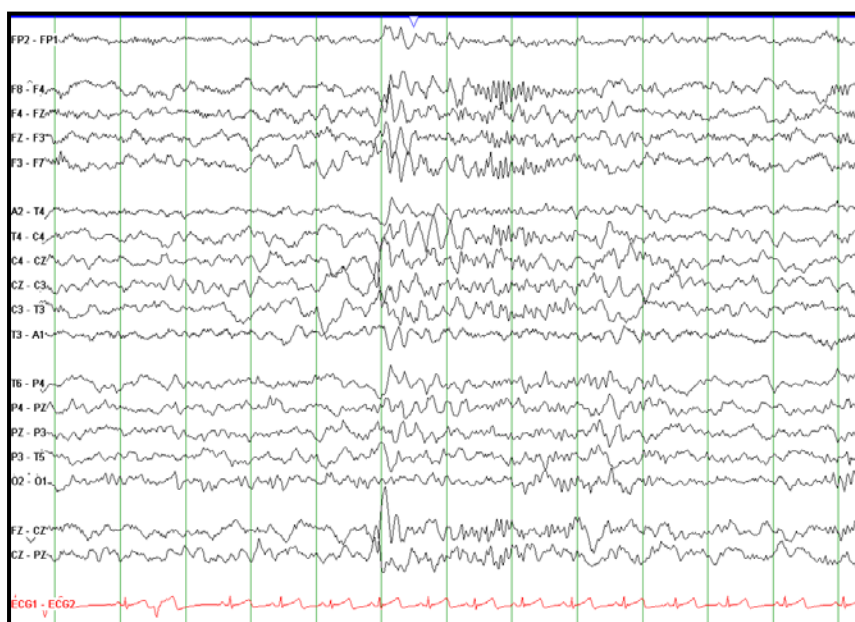


Figure 4.3 showing N2 sleep (Sleep onset).

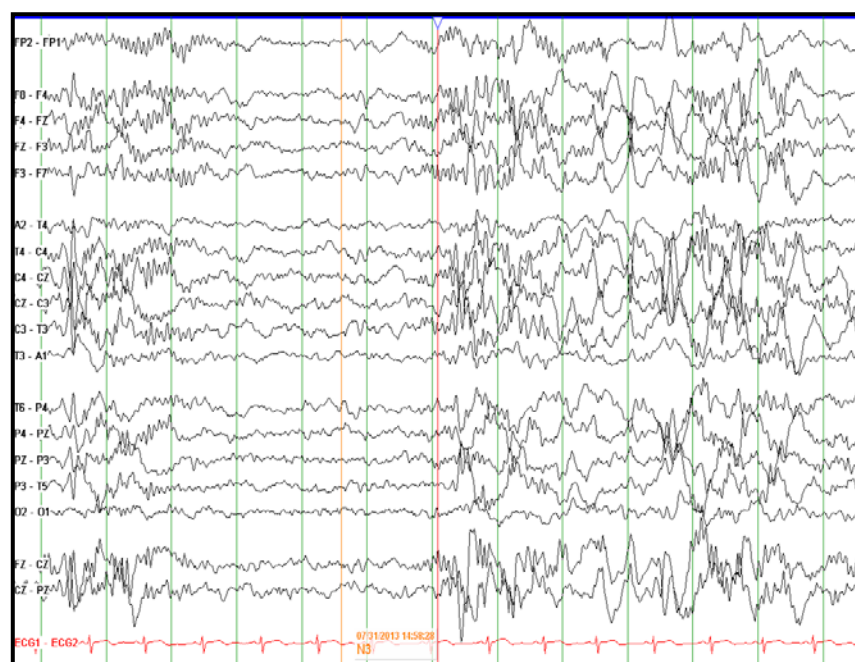


Figure 4.4 showing N3 sleep (combination of Stage 3 & 4 sleep)

4.5.3 Data collection for “Sleep vs. no sleep between each of the three groups”.

A time interval of 40 minutes after the room was darkened was allowed for the physiologist to wait for sleep to occur. Forty minutes was the time used as this is how long the Clinical Physiologist would allow for the sleep portion of the study. If the patient did not fall asleep during this time it was noted in this study as a “fail to sleep” for this outcome. However the study would always be prolonged if it was deemed clinically necessary.

4.5.4 Data collection for “Time taken to N2 sleep in all three groups”.

The onset of Sleep was discussed with the co-investigators of the study and it was decided collectively that sleep onset was best to be defined as N2 or stage 2 sleep. N2 sleep was used as sleep onset, as firstly, it was a deeper sleep stage and therefore N2 sleep was easier to define as often patients can drift between drowsiness and N1 sleep and therefore marking N1 sleep appeared to possibly be more subjective. This stage was used as the already mentioned sleep architecture known as “sleep spindles” (See in figure 4.3) were mostly very easily identified in all ages. Even though N1 sleep was annotated, in this study the patient was not defined as asleep until N2 sleep was observed.

4.5.5 Data collection for spontaneous arousals from sleep in each group

Spontaneous arousals were also identified by the Consultant Neurophysiologist along with where in sleep they tended to occur and compared these scores in each of the three groups. An arousal was characterised by “an abrupt shift in EEG frequency, which may include theta, alpha and/or frequencies greater than 16Hz but not spindles, subject to the EEG arousal scoring rules” (Bonnet et al. 1992).

4.6 Main aims and outcomes

This study examines:

- Sleep success rates across all three groups
- Secondary outcomes of the study included:
 - The time taken to achieve N2/stage 2 sleep across the groups
 - Comparing the numbers of arousals present in each group
- Survey on sleep in paediatric EEG’s within a dedicated children’s Hospital

- Sleep success
- Duration of study
- Time to achieve sleep
- EEG Abnormalities captured

4.7 Null Hypothesis

The Null hypothesis is:

“Background noise does not influence sleep during a sleep deprived EEG”

4.8 Conclusion

This methodology section aimed to scrutinize all aspects of this trial, from the study protocol to the statistical analysis used, in order to fill any gaps present in the published literature such as the lack of quantitative analysis using modalities such as EEG or PSG or the recurrence of smaller sample sizes in the review. The following chapter looks at the literature published on this area and has further revealed areas requiring further research or more accurate protocols etc.

4.9 References

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Chapter 5

Literature review

5.1 Introduction

As mentioned in chapter one, Some EEG departments within a hospital environment have tried alternative measures of attaining sleep with some using a form of background or “white” noise (a low pitched hum) in combination with partial sleep deprivation to enhance the chances of obtaining sleep in children referred for an EEG. Anecdotal experiences within these departments have found it to be favourable. However this concept of background noise facilitating sleep in patients during EEG has not been evidence based. The main aim of this literature review is to determine if any background noise is helpful in facilitating sleep in general, whether at home or more relevantly in a hospital setting. This allows us to evaluate the clinical value of background noise as a cost-effective, non-pharmacological, risk-free method to be used during an EEG.

5.2 Methodology

5.2.1 Study selection criteria

Studies chosen for this review were obtained from key works such as **“Sleep”, “background noise”, “Electroencephalography (EEG)”, “white noise”, “music”, “Arousals” and “Epilepsy”**. A survey was undertaken on the methodological qualities of the articles to determine if it was appropriate to use them in this review.

All studies published with background noise and sleep in the title and were in the English Language between 1985 and present were analysed for relevancy.

5.2.2 Search strategy

All available medical electronic databases were searched primarily **MEDLINE, CINAL, SCIENCE DIRECT and PUBMED CENTRAL** to identify studies relevant to the research question, in English Language, and had free access to full-text. The studies were identified using an advanced search method, and analysed for their relevance. Figure 5.1 shows a flowchart of the overall electronic search strategy used.

Hand and author searching was also to be conducted in order to find any further papers. A recent article in 2005 (Greenhalgh 2005) emphasized the importance of using various searching methods in undertaking a literature search and therefore after identifying key articles that related to the review question, the reference lists of these key articles were to be analysed. In addition to the studies already collected, many of the key articles already found were to be examined to determine if further articles were written by similar groups of authors, and would therefore introduce additional studies to this review.

Figure 5.1 Electronic Database Flowchart

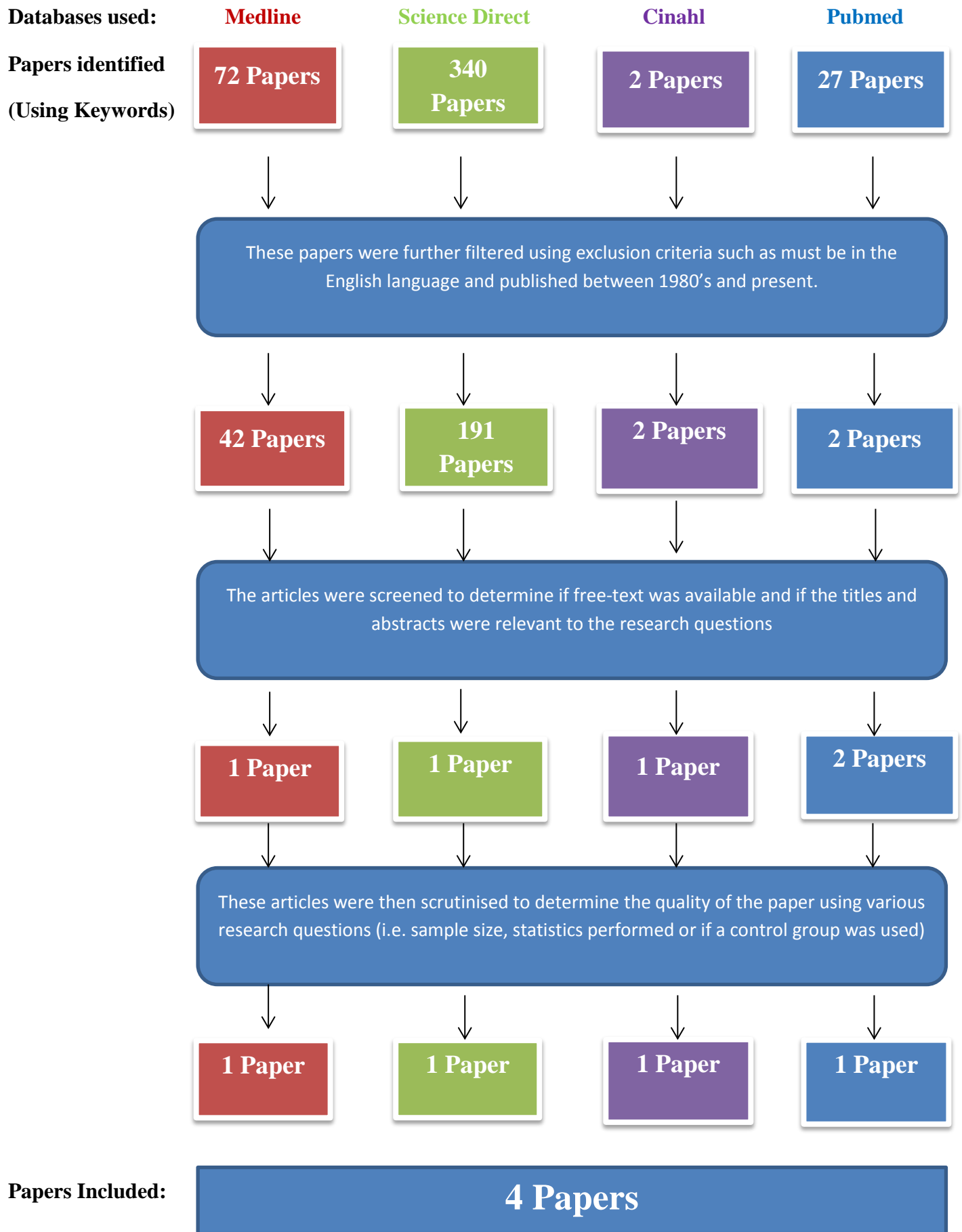


Figure 5.1 showing Number of Papers located and selected using an Electronic Database Search Strategy

Four hundred and forty-one papers were initially identified through electronic databases. Of these, Four hundred and thirty-seven were excluded mostly on the basis of irrelevance towards the research question and the unavailability of free-text. The remaining four papers were included in the review together with a further ten papers found by other searching means. Eight of these fourteen papers had “white noise” and “sleep” in the title and therefore were classified as our core articles. However, six papers were on the use of music or another type of background noise but were felt to also be relevant to our research as a similar alternative therapy. A total of fourteen papers were included in this review.

5.3.1 Research Quality of articles

Before proceeding with each paper, the validity of these articles were evaluated to ensure that the results were relevant to our research question and if the research methods were of adequate quality. These results were divided into two groups, represented in Table 5.1 and 5.2. These studies included a total of 379 participants. The participants involved in these studies varied from neonates (36-41 gestational age, which is the time from conception to birth) and new born babies (2-7days) up to 80 years of age. There was equal gender distribution throughout most of the populations. Weight can have an effect on sleepiness and therefore the slightly older patients in one paper were noted to have a BMI of $<26\text{kg/m}^2$, however this was generally not mentioned or seemed not to be controlled in the remaining studies. Mean sample size was 25 participants. The duration of the intervention varied from 5 minutes during a single one-time session to an on-going study using the intervention at bedtime and naps lasting up to 10 weeks. The type of intervention used was either white noise or music. The sound levels of both treatments varied from 50-100 Decibels with some articles failing to quote the spectral band of the white noise. The exception to this was one study which used pink noise at 60dB. The music chosen was mostly classical music which was a mixture of either standardised for every participant or a personal preference was given for the type of music and the sound level, to be adjusted by the individual participant. Other music was “monochord sounds” which is an ancient stringed instrument or “delta-embedded music” which pulsates at 0.25-4Hz (Picard et al. 2014). One study made use of the hospital’s music therapist which played “live music” to the children during a sleep deprived EEG.

Table 5.1 Articles examining the use of white noise in sleep

Study	Total (n)	Country	Treatment	Measure	Control condition	Intervention duration	Dwelling and Population	Result
Spencer et al 1989	40	UK	White Noise (67-72.5dB) between a spectral band of 500Hz to 9KHz	Sleep onset defined as "state of Quiescence"	Silence	Six minutes	Neonates 2-7 days old in their own cot	Sixteen Babies (80%) fell asleep with white noise in 5 minutes. Five babies (25%) fell asleep within 5 minutes with no noise.
Forquer and Johnson 2008	4	USA	White Noise at 75dB	Sleep Diaries detailing No. of night waking's, times and length of naps etc.	No Control	Ten Weeks	13 Months-two years (Normal Development) – Own home	Two out of three children showed reductions in night waking's. Parents seemed comfortable with white noise and would recommend it.
Zimmer et al 1993	22	USA	White Noise at 100dB to foetus in-utero	Foetal Heart rate, movements recorded by mother and if state were active or quiet.	Silence	Five Minutes	Foetus at 36-41 gestational age	No significant difference in parameters between control and intervention.
Forquer and Johnson 2007	4	USA	White Noise at 65-70dB	Sleep diaries, PSQI and Sleep Hygiene self-test	No Controls	Four Weeks	College Student (mean age 19yrs)	All students showed a decrease in sleep latency and night waking's during treatment, however one person's night waking's returned after the treatment was discontinued. All were comfortable with white noise and would recommend it to aid sleep problems.
Ogata, S 1995	8	Japan	Classical Music and simulated white noise at 88dB	Self-report questionnaire	No Control	Twenty-one Minutes	Ages 20-27years	Changes in EEG frequency were noted toward both sound conditions.
Kawada, T et al 1993	4	Japan	Pink Noise at 60dB	PSG	Baseline figures for the same participants were used for control group - Silence	N/A	19-28years	There were no statistical differences in sleep latency found in group A. Similar findings for other groups were found however the Noise group achieved sleep in 13.5mins compared to control in 23mins however this was no statistically significant.
Stanchina, M et al 2005	8	USA	White Noise (1-22.05KHz) at 62dB	PSG	Same participants were used for control group - Silence	Three Nights (Baseline, ICU Noise and ICU noise with white noise)	18-65 (BMI<26kg/m2)	Total Sleep time was similar across conditions. Stage 1&2 increased during noise night but not white noise night. Stage 3&4 decreased in noise night but not white noise night. Arousals increased in noise night but returned to baseline during white noise night.
Knight, R 2014	3	USA	Circadian rhythm management, Positive bedtime routines, white noise (50-75dB) and graduated extinction	Gilliam autism rating scale and daily sleep diaries	No Controls	Two Months	Children at 4-5years with Autistic spectrum disorder (ASD)	All children showed some improvement in night waking's and overall the behavioural treatment package was effective in reducing sleep latency and frequency of night waking's.

Table 5.2 Articles examining the use of Music in sleep

Study	Total (n)	Country	Treatment	Measure	Control condition	Intervention duration	Dwelling and Population	Result
Tan,L.P et al 2004	86	USA	Standard “sedative” classical music on CD for 45minutes at naptime and bedtime	PSQI	Silence	3 Weeks	Elementary school children	Subjects who received background music had greater sleep efficiency and duration than those in the control group. No significant differences were observed for perceived sleep quality, sleep disturbance, daytime dysfunction and sleep latency.
Piccard. L et al 2014	20	Canada	“Delta embedded” music pulsating at 0.25-4Hz	FIQ and Jenkins sleep scale scores	No controls	4 Weeks	Patients with fibromyalgia from a pain management clinic	Subjective sleep quality showed significant improvement however there was no significant effect on pain.
Lee. E et al 2012	40	Germany	Monochord Sounds 34mins	EEG and SAI	No controls	18 Weeks	Patient undergoing chemotherapy	Reduction in anxiety and improvement in physical and psychological states during chemo with an almost gradual decline in anxiety as the treatment progressed however there were no significant differences between the two groups.
Olishar. M et al 2011	20	Melbourne	Standard Classical music at 50-55dB	Amplitude integrated EEG	Environmental noise (ICU Noise)	20mins	Neonatal ICU (32<weeks gestation)	80% in intervention group showed reduction in amplitude in quiet sleep after music exposure. More mature sleep wake cycles were seen in those subjects exposed to music compared to controls.
Lai, H et al 2006	60	Taiwan	Patient selected sedative music of daily 45min sessions at bedtime	PSQI Epworth sleepiness scale	Silence	3 Weeks	Older Adults (60-83yrs)	Statistically significant improvement of total sleep quality score and 5/7 PSQI components (P=0.04-0.01).
Loewy, J et al (2005)	60	USA	Music or Chloral Hydrate	EEG	No Controls	30mins	1 Month-5yrs	97.1% of children subjected to music therapy completed the EEG recording successfully compared with 50% of the children using chloral hydrate which was statistically significant. Children were described as “easily awakened” in the music group compared to the chloral hydrate group. The mean time to sleep was 23 mins with music as opposed to 32mins in chloral hydrate but was not statistically significant.

Nine out of the fourteen papers used subjective tools for the measurement of sleep quality such as sleep diaries on daytime naps, bedtimes, sleep latency and night waking's with most using the Pittsburgh sleep quality index (PSQI) which examines the quality and pattern of sleep. Other measures included sleep surveys, absence of foetal movements, foetal heart rate accelerations or basic observations such as one paper who defined sleep as "a state of quiescence with eyes closed and regular breathing" (Spencer et al. 1990). Five papers used standard EEG, amplitude-integrated EEG or polysomnography (PSG) to determine features of sleep and sleep stages. These methods were standardised, using the 10-20 system of measurement while also using the *Rechtschaffen and Kales* sleep classification (Iber et al. 2007) which further standardised the stages in sleep.

All studies included some flaws or limitations. For example, most papers failed to acknowledge if the testing examiner or results analyst were blinded to the outcome or clinical information, and therefore bias towards one intervention was possible. In this type of study it was difficult to blind the participants to the intervention allocated.

Overall statistical analysis was well described with all papers using a significance value as $p < 0.05$, however some sample sizes from various studies were too small to perform any accurate statistical data. All studies were approved by their local ethics committee while also gaining prior consent from participants before the study commenced.

5.3.2 The impact of white noise on sleep

Eight papers were selected that were the most relevant to our study and were the "core articles" for this review. Firstly, the participants involved in these studies varied from neonates (36-41 gestational age) and new born babies (2-7days) up to 65years of age. Out of these eight papers two of the studies used a control group. One paper used a different set of participants for the control group and the other used baseline data from the same participants to produce the control data. One out of eight articles showed statistical significance between the intervention and control groups however kawada and Suzuki (1993) showed improvements to one or various area of sleep such as perceived sleep quality, sleep latency etc.

As already mentioned white noise has been speculated to have an effect on sleep. These eight papers all used some form of white noise, in a range of 60-100 decibels of a sound level. Only two papers state the spectral frequency of the sound as 1-22.05 KHz frequency

blend (Stanchina et al. 2005) or 500Hz-9KHz (Spencer et al. 1990). The population studied was also varied between the papers, for example one paper included participants that only included college students at 19 years of age from the same institution and another used studied children with autistic spectrum disorder (ASD). The clinical diversity of the articles was also quite large considering some participants suffered from fibromyalgia and another study examined patient's under-going chemotherapy and therefore pooling the data from this review was deemed inappropriate as the effect of the intervention could be dependent on the patient's condition. See table 5.1 for summary of article characteristics.

Confounding factors were not always accounted for, however factors such as prohibiting alcoholic and stimulant beverages and drug ingestion prior to the study commencement or standardising illumination and temperature if the study was performed in laboratory was noted on a few occasions. Undertaking hearing tests prior to the experiments was only accounted for during three of the articles. If the study was not conducted in a laboratory, compliance with the study protocol was an issue if they were required to control their intervention (i.e. turning on white noise at night and off in the morning or accurately completing the sleep diaries). One study allowed the analysts to validate interventions and sleep diary entries with the use of videotapes (Forquer & Johnson 2005).

Forquer and Johnson (2005) had multiple confounding factors as the participants were toddlers of 13-23months which were particularly profound as the study had a small sample size and the absence of a control group and therefore no statistical data was conducted. Factors such as weaning from daytime naps, feeding measures (breast fed, bottle fed etc.), parental attachment and the use of comforters are extremely variable at this age. However through their study criteria they did eliminate some aspects such as excluding children who slept beside the parents or those who used some form of white noise already.

Spencer et al (1989) conducted a study on 40 normal neonates aged from 2-7 days old to determine if a group of babies exposed to white noise (N=20) had an effect on sleep in comparison to a control group (N=20). A sound level ranging from 67-72.8dB was used at 12-20inches away from the baby's head. The results showed that out of 20 neonates 16 (80%) fell asleep within 5mins of exposure to white noise. This is in comparison with the control group where only 5 babies (25%) fell asleep with no noise. In other words more than 3 times as many babies fell asleep with white noise than without it. These results were comparable with a study of 4 toddlers (aged 13-23mths) who showed resistance in going to

sleep at night and frequent night waking's. Three out of four toddlers were sleeping better at the end of treatment with continuous white noise however problems did represent in one toddler after the white noise was discontinued (Forquer & Johnson 2005).

An experiment was performed to examine the effect of white noise on unborn foetus' (Zimmer et al. 1993) in order to produce a "quiet foetal state". This state is desired when performing invasive intrauterine procedures. Twenty-two healthy pregnant women at 36-41 gestational ages would have a sound device located on their abdomen playing white noise for 5mins at a sound level of 100dB in order to attempt to bring on a "quiet foetal state". Foetal heart rate variability, heart rate accelerations and foetal movements were measured. However the results showed no significant difference in parameters between control and intervention groups.

The remaining three articles in this group all showed improvements when using white noise. Kawada & Suzuki (1993) used a variation of white noise called "pink noise" which was defined as "the correction of white noise by making sound pressure level of each frequency band to be constant". The results found that there were no statistically significant differences in sleep latency (measured using EEG) found between the four participants. However looking at the individual average sleep latencies in white noise groups (13.5mins) and control groups (23mins) there is a substantial difference of 58.7% or a 9.5min shortening of the sleep latency in using steady pink noise. Other studies used sleep diaries and sleep quality surveys to investigate night waking's and sleep latencies. In one particular study of this nature, even though all college students (N=4) did portray improvements in their sleep when using white noise, however again, there were no statistical analysis performed. A group of eight participants were exposed to ICU noise alongside white noise in comparison with their baseline results. It was found that the addition of mixed frequency white noise increases arousal thresholds in normal individuals exposed to ICU noise. It was hypothesized that the white noise reduces the difference between background noise and peak noise (Stanchina et al. 2005).

5.3.3 The impact of music or other background noises on sleep

In searching for those papers that included the use of white noise in sleep, an abundance of further studies were uncovered on the use of music in sleep and relaxation and were also felt to be relevant and were therefore included in this review. A total of six studies were incorporated into the review from 2006-2014, three being randomised control trials. Out of

these six studies, four showed statistically significant differences between the intervention and control groups, between two interventions groups (i.e. progressive muscle relaxation and monochord sounds), or comparing the intervention to baseline results. However all studies showed some form of improvement regarding sleep (i.e. sleep latency).

The types of music used included mainly classical but also used was “delta-embedded music” which pulsates regularly at 0.25-4Hz, lullaby music and monochord sounds which is an ancient stringed instrument. One of the articles looked at the psycho-physiological effects of music on the human brain in order to attempt to understand why music may cause a state of relaxation and aimed to develop a control group instead of using only silence (Ogata 1995).

The populations were very specific in each of the studies with different age groups. For example one study looked specifically at neurologically healthy new-born babies at $32 \leq$ weeks gestational age that were admitted to the neonatal intensive care unit (NICU). Other populations were comprised of patients with fibromyalgia (36-56yrs), patients undergoing chemotherapy, elementary school children (11yrs) and children with ASD (Knight & Johnson 2014).

Most participants were not given a choice of music in any of the studies however in some they were instructed to adjust the audio volume to their personal preference. Two papers used EEG/ amplitude EEG while others used PSQI surveys etc. The majority of the papers were looking at the long-term effects of music on sleep and therefore the study duration ranged from 3-18 weeks apart in comparison to the one-time sessions used to evaluate a musical effect on the sleep of neonates in NICU (Olischar et al. 2011). See table 5.2 for summary of article characteristics.

A study found that subjects who received the background music had greater sleep efficiency than those in the control group however there were no differences in the groups in perceived sleep quality, sleep disturbance, daytime dysfunction and sleep latency (Tan 2004). However a review by Lai, H et al (2006) examined sleep quality in older adults with the use of music found that out of 7 PSQI components, there were statistically significant improvements of total sleep quality scores ($P=0.04-0.01$). However in those participants who had an on-going condition causing anxiety or sleep problems showed opposite effects. Those patients with fibromyalgia had showed significant improvements in sleep quality but no significant effect on pain whereas those patient’s under-going chemotherapy ($N=20$) showed a gradual decline in anxiety however there were no significant differences in those exposed to music and those

using progressive muscle relaxation (N=20). This shows that the effect could be dependent on the condition. These two groups were not compared to control groups and subjective measures were used. In addition to this, the study by Piccard, L et al (2014) admitted that without controls and the use of more accurate measures (i.e PSG/EEG) there was the possibility for the placebo effect. There was also no control for medication effects, which for fibromyalgia can include drugs such as anti-depressants and pain relievers and therefore may have affected the results.

A study by Olishar, M et al (2011) showed that all neonates demonstrated a continuous background and sleep-wake cycling (SWC) and showed that more mature SWC was seen in those exposed to music compared to controls however there were no further studies for direct comparison. None of the researchers reported any adverse effects. Lastly, an article by Loewy et al. 2005 was very relevant to our study as it utilised two different interventions during an EEG. They compared the use of live music (played by a music therapist) to using the drug chloral hydrate (a hypnotic - British National Formulary - BNF 2015) during EEG testing. The results indicated that 97.1% of children subjected to music therapy (N=33) completed the EEG recording successfully compared with 50% of the children using chloral hydrate (N= 24), and this was statistically significant. Children were also described as “easily awakened” in the music group compared to the chloral hydrate group. The mean time to sleep or sleep onset latency was 23 minutes with music as opposed to 32minutes with chloral hydrate but was not statistically significant. All confounding variables were accounted for in this study such as “the absence or presence of a caregiver” which was analysed separately and found that the difference in the two groups was not statistically significant (P=0.920) and therefore did not affect the results.

5.4 Discussion

The current study identified a total of 14 experimental studies for review to evaluate the effectiveness of white noise and/or music on sleep. The results demonstrated the efficiency of both white noise/music in improving various aspects surrounding sleep (total sleep time, sleep latency, reduction in wakening’s etc.) in a variety of medical conditions, environments and age ranges. Despite no statistical differences found in the use of white noise in sleep (partly due to the lack of performing statistical analysis due to small sample sizes), notable improvements were documented which would be profound in certain environments (i.e. hospitals). For example, in the use of pink noise in sleep (Kawada & Suzuki 1993), the time

taken to fall asleep was almost half (mean difference 9.5minutes) in comparison to the control group. This reduction in the time taken to achieve sleep would be helpful for instance in a dedicated EEG sleep laboratory where healthcare professionals would welcome techniques in improving the time taken for patients to fall asleep. This could not only reduce the duration of the test and thereby the anxiety and stress caused to the patient but increase the amount of patients seen on a daily basis and in turn reduce hospital waiting lists. Spencer et al (1989) also agreed with this as 80% of babies (2-7days old) could also fall asleep within 5 minutes with listening to white noise compared to 20% of babies in the control group.

The mechanism by which white noise affects sleep was not made clear in any of the literature included in this review however it was speculated that white noise increases the baseline noise level and therefore can appear at a similar or higher sound level thereby reducing the difference between background noise and an abrupt environmental noise (Stanchina et al. 2005). Another hypothesis included a habitual effect on the subject following repeated exposure to the stimulus, or that white noise may induce and keep an individual asleep by masking environmental noises that cause an arousal from sleep (Forquer & Johnson 2007). A study analysed brainstem auditory evoked potentials (BAEP), which can be used to assess conduction through the brainstem and auditory nerve pathways, found that the peak latency (P300) increased during wakefulness and listening to background noise (Salisbury et al. 2002). This therefore suggested that background noise had a masking effect. It is also recommended by the American Clinical Neurophysiology society (American Clinical Neurophysiology Society 2006) that during this procedure, the contralateral/non-stimulated ear must be masked by white noise at 60dB to eliminate cross-over responses and inaccurate testing.

More recent research appears to have been dedicated to the use of music to enhance sleep with six papers included in this review. The results showed statistically significant differences in at least one area of sleep in all studies. A psychophysiological theory was derived stating that sleep quality can be improved by relaxing the body with “sedative” music which has been shown to decrease noradrenaline (Gerra et al. 1998) which has also been associated with sleep onset.

The main type of music used was classical music; others used “sedative” music however the exact type of sounds used was rarely described in the articles. Certainly, from the results of this review it seems that music does have an effect on sleep however it does not answer the

question of the type of music that should be implemented. A psychologist Dave Elliot found that the most relaxing music, according to volunteers taking part in anxiety studies had certain features such as 90 beats/minute or that the piano and strings were the most preferred instrument (Elliott et al. 2011). However it was noted that some of these studies allowed the participant to choose their preferred type of music and may have enhanced the results of that study. On reflection, most of these researchers concluded that the degree of liking the music was not considered or monitored which may have impacted on the results, and many would recommend giving the participant the facility to choose their preferred music.

With most of these studies convenience sampling was used for example “elementary school children” or patients with “fibromyalgia” and therefore this limits the ability for generalisation. Although direct comparisons with other studies may not be appropriate, it is noted that over various age ranges and a broad range of medical conditions (i.e. fibromyalgia, oncology patients), at least one area of sleep was improved and therefore could be effective regardless of the participant, surrounding environment or medical condition.

An explanation for non-significant results could be due to familiarity with the music or the increased ability to relax during each treatment administration. Overall using music before and during sleep was viewed to have a positive effect.

In this review, a number of other study characteristics emerged that may have a confounding effect on the intervention used and the overall study results.

5.4.1 Participants

Due to limited articles, there were no age selection criteria for this review. The participants were aged from 2days old to 83 years (Lai & Good 2005) however the majority of the articles examined participants either from 2days to toddlers to young children up to 5yrs and also adults from 19yrs to 28yrs of age. The clinical diversity of the participants was also varied as some participants were neonates within an intensive care environment and others were oncology patient’s under-going chemotherapy at the time. However there seems to be a positive general consensus which would mean that the intervention may be independent of any underlying medical conditions or developmental issues and possibly allowing us to generalise the results among many populations. However a specific review on the use of music on children with autism and special needs stated that additional studies were needed before treatment effectiveness could be determined (Simpson & Keen 2011).

5.4.2 Administration of intervention

The review included a mixture of articles where the intervention was implemented at home or at a specified laboratory within a hospital setting. The participants who had their treatment at home could have been subject to many more variables (i.e. environmental noise and/or in compliance with the study protocol) out of the investigators control. However this also could have had a positive effect as mostly people are more relaxed in their own environment and may therefore enhance the effect of the intervention.

5.4.3 Investigators

Very few of the investigators made reference to the training and understanding in administering music or white noise as an alternative therapy. As mentioned in the results, only one article made use of a music therapist with “live music” on patients (4weeks-5yrs of age) attending for a sleep deprived EEG. This highlights that more research should be examined into the administration of these alternative therapies and possibly utilising them during procedures as a distraction technique to alleviate stress in a hospital setting as well as trying to demonstrate its effect on sleep. This also poses the question on the deliverance of the intervention to the participants on whether it is more effective if the sounds are produced “live” or whether it’s delivered at a specific sound level etc.

Confounding variables of differences in traits of those individuals administering the intervention cannot be ruled out as only one article controlled for this allowing a variety of music therapists, physicians and healthcare professionals taking part in the study (Loewy et al. 2015)

5.4.4 Study Analysis

Analysis of the outcome of studies varied from mostly a lack of objective verification with the use of questionnaires/surveys or sleep diaries in order to determine sleep quality such as the PSQI in nine out of fourteen studies. Only five studies supported their outcomes with the use of EEG or PSG. Analysis using these methods allowed accuracy and definitive measurement on countless variables such as:

- Number of Arousals
- Where in sleep these arousals occur
- Sleep onset latency

- Duration of sleep stages
- EEG frequency components
- Total sleep time
- Depth of sleep achieved

Other means of measurement can be subjective, for example an individual may not have been aware of exactly how many arousals were present throughout the night or may feel that they have had longer sleep than the true total sleep time and therefore it is difficult to determine a “quantifiable effect” on sleep. Wolfson et al (2003) found that for a student survey performed, the reported total sleep time in students at weekends were significantly greater than actigraphy analysis therefore allowing room for significant error in analysis of results.

Correlation with EEG has been proven to be beneficial in terms of relaxation studies which have shown a significant increase in slower frequencies, which are usually associated with drowsiness, seen during meditation (Lee et al. 2012).

As stated above, arousals can be an indicator of the quality of sleep achieved however not all of these studies monitored the arousal rate. Some studies examined night waking's however this can be difficult to accurately monitor without objective verification (EEG/PSG). It is well established that arousals increase in frequency with age and it is difficult to determine if an arousal was due to noise disruption or some unexplained factor having an influence on sleep and therefore can be an inaccurate variable to use.

5.4.5 Blinding

The Hawthorne effect can be a major influence on the results of these studies and may explain non-significant improvements as the subject is aware of their participation in the study and obviously blinding is difficult. For example, in the study by Tan et al (2004) the control group also showed improvements in sleep as well as the intervention group making there no significant differences between the two groups and the Hawthorne effect may explain this. Other potential bias include the failure to blind the data collector which in most instances was not practical or treatment bias in that the administrator was the same throughout the studies giving rise to potential bias of personality traits of that individual.

5.4.6 Review Limitations

This review had some methodological limitations. The most obvious factor alluded to above was that none of the studies were double-blinded as this is almost impossible as the nature of the study included an intervention that is obvious to the participant (i.e. sound vs. no sound). The number of studies present in this review could have been increased if more free-text articles were available to the researcher. Within the studies available most had small sample sizes, particularly those examining the use of white noise (N=93) in comparison to music (N=286), and therefore statistical analysis was not performed by a number of these (See table 5.1).

5.5 Conclusion

In terms of potentially harmful factors in the use of music and white noise, there have not been any reported contraindications stated in the literature so far. In fact, from this review, the use of these alternative therapies has mostly had a beneficial and positive affect in comparison with silence or the use of pharmacological agents in all ages and across a broad range of medical conditions.

As already mentioned in the review limitations, there has been very few randomised control trials with adequate sample sizes in the use of white noise/music, and these studies have difficulties controlling for the ample confounding factors that are often present in research of this nature. For this reason, the results should be interpreted with caution. More standardised research is needed in this area in order to determine if in fact white noise or music has a calming or inducing factor for sleep regardless of these influences (environment, caretakers, age, time of day, medical condition etc.). It is also important to determine if a particular type of sound, noise level or spectral frequency of white noise and/or music is the more effective also with the use of a larger population. The “gold standard” for the analysis for these findings should include accurate sleep measurement with the use of EEG or PSG alongside questionnaires/surveys to determine the patient’s personal experience of the intervention.

While various studies have been dedicated to examining a variety of alternative measures used surrounding sleep, the most recent and best quality research leads towards the use of music during sleep. Furthermore there is few, up to date research of adequate quality in the use of how white noise, and most importantly the different types and spectrums of white noise are used in various settings. This study attempted to research this gap in the literature

by endeavouring to determine the efficiency of a particular form of white noise in obtaining sleep during a non-invasive EEG investigation within a hospital setting. In doing so, this will be challenging a well held belief within the EEG department that white noise can be effective in this environment in order to achieve sleep.

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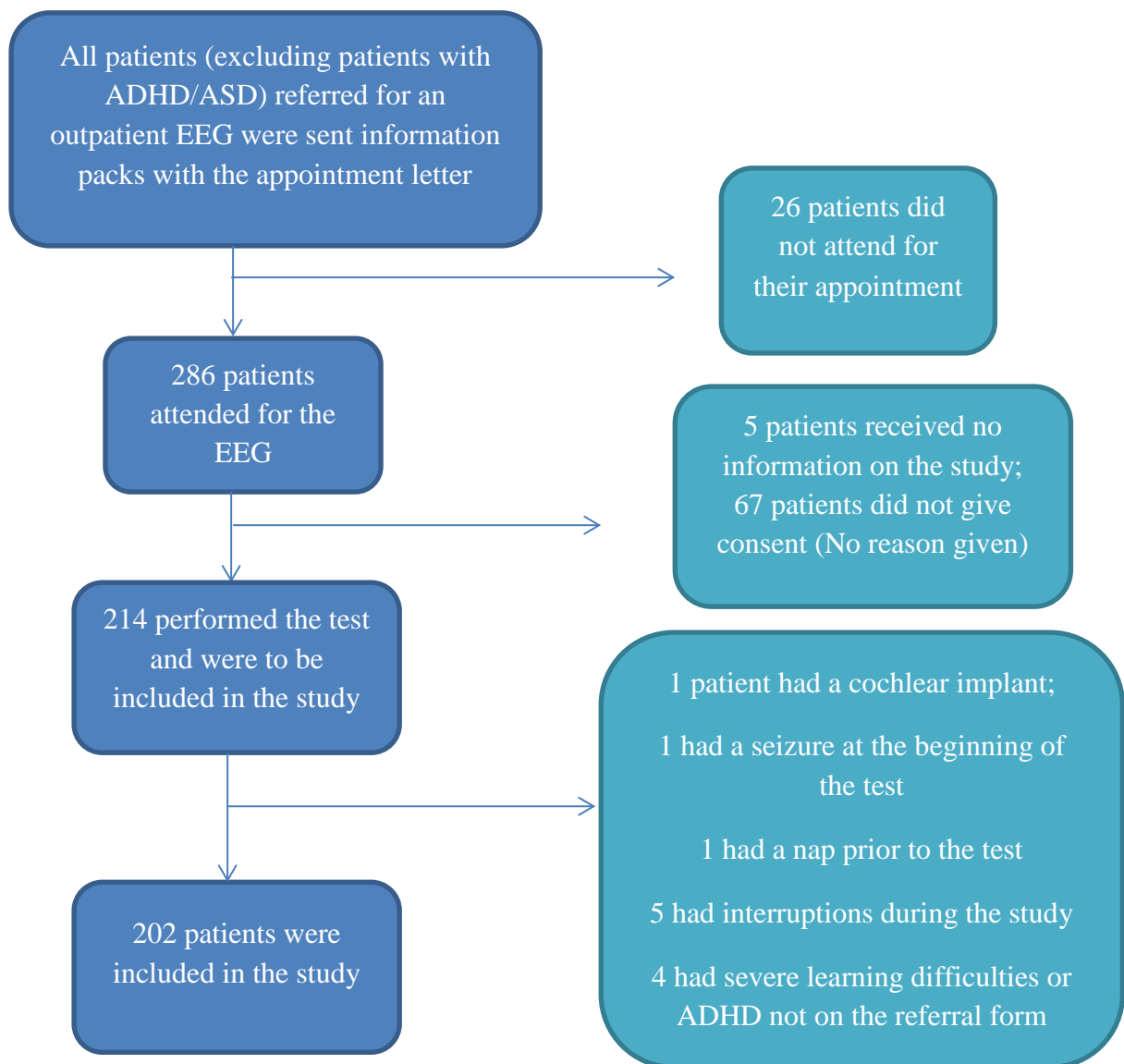
Chapter 6

Data collection and analysis

6.1 Introduction

This chapter outlined how the data was collected from the study defining and standardising certain details such as the specific markers for sleep onset in the study. This data was then analysed to determine the distribution using the statistical package SPSS in order to determine the type of statistics test to use for each outcome variable.

Figure 6.1 showing a flowchart of participant enrolment process.



6.2 Participants Enrolment

All patients referred for an outpatient EEG were enrolled in the study with some excluded if they were diagnosed with ADHD/ASD. Figure 6.1 shows the process of how the participants were included in the study and any that were excluded for various reasons.

6.3 Data analysis

Prior to embarking on further statistical techniques, the data collected was analysed using descriptive statistics to determine (1) the patient demographics across the three groups (2) examine the types of variables present (Categorical and/or continuous), (3) investigate the data to determine if it is normally distributed in order choose the correct statistical methods and lastly (4) to highlight any possible outliers in the data that may skew the results.

6.3.1 Participant Demographics

To further control for possible differences in distribution of background characteristics (age, gender, sleep deficit etc.) between the groups, t tests and χ^2 tests were used. The tests determined whether the variables were unevenly distributed between the three groups. The results are shown in Table 6.1 (See appendix 7-13). All variables showed a p value of $>.05$ and therefore there were no statistical significant differences between the three groups. The lack of difference between these factors across the three groups suggests that none of them acted as a confounding variable. The study was conducted within a two year period. Eight different clinical physiologists and one consultant Neurophysiologist participated in the study.

Table 6.1 showing patient demographics distributed between the three groups

Background Characteristic	Group A (Compressor) N = 70	Group B (CD) N = 70	Group C (No noise) N = 62	P = <.05
Age	Mean 10.2yrs SD 3.369	Mean 10.5yrs SD 3.517	Mean 9.9yrs SD 3.366	.652
Gender	M = 15.85% N =34 F = 16.94% N = 36	M = 21.31% N = 40 F = 15.85% N = 30	M = 13.11% N =27 F = 16.94% N =35	.298
Parent/guardian P = Present A=Absent	A = 31 P = 39	A = 24 P = 46	A = 29 P = 33	.296
Average hours of sleep deficit	Mean = 2.83 SD 1.351	Mean =2.89hrs SD 1.399	Mean = 2.89hrs SD 1.356	.737
Room used	1 = 30 2 = 40	1 =31 2 = 39	1 = 21 2 = 41	.426
Appointment Time	10am – 8 ppl 11.30am – 23ppl 2pm – 33ppl 3.30pm – 6ppl	10am – 4 ppl 11.30am – 26ppl 2pm – 36ppl 3.30pm -4ppl	10am – 8 ppl 11.30am -15ppl 2pm – 35ppl 3.30pm -4ppl	.483
Season	Winter = 33 Summer =37	Winter = 31 Summer = 39	Winter = 28 Summer = 34	.942

6.3.2 Type of variables

Categorical Variables

An example of a Categorical variable was “gender” which is shown in Table 6.2.

Table 6.2 shows the distribution of Males and Females taking part in the study

M/F

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Male	101	50.0	50.0	50.0
	Female	101	50.0	50.0	100.0
	Total	202	100.0	100.0	

Continuous Variables

An example of a continuous variable assessed was “age” which was analysed across the three groups and produced histograms, Q-Q plots and boxplots as shown in figure 6.2-6.7.

Histograms were used to display the distribution of age across all three groups with a normal distribution curve superimposed. The actual shape of the distribution could be seen for each group and the distribution seems to be reasonably normally distributed. This can also be seen with the normal probability plots (figures 6.3, 6.5 & 6.7). This shows the observed values for each score plotted against the expected value from the normal distribution. A box plot was also generated again showing the distribution of age across the three groups. This shows that SPSS software considered that there were no outliers in age and the line across middle is the median which is similar in each group (Pallant, J 2001).

Figure 6.2 Histograms showing age distributions across group A (Compressor).

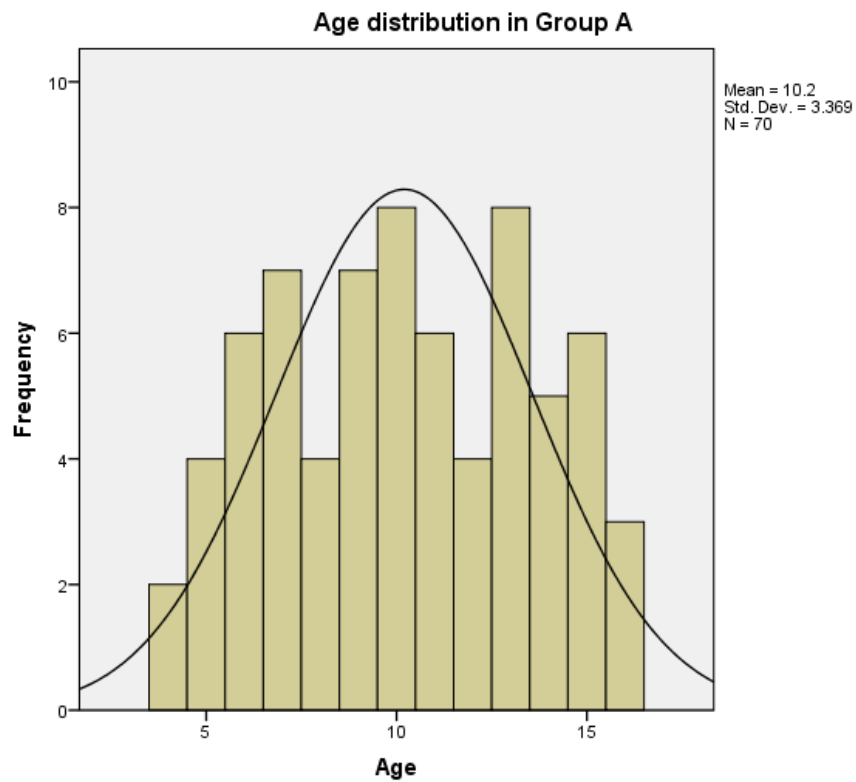


Figure 6.3 Q-Q Plots showing age distributions across group A (Compressor).

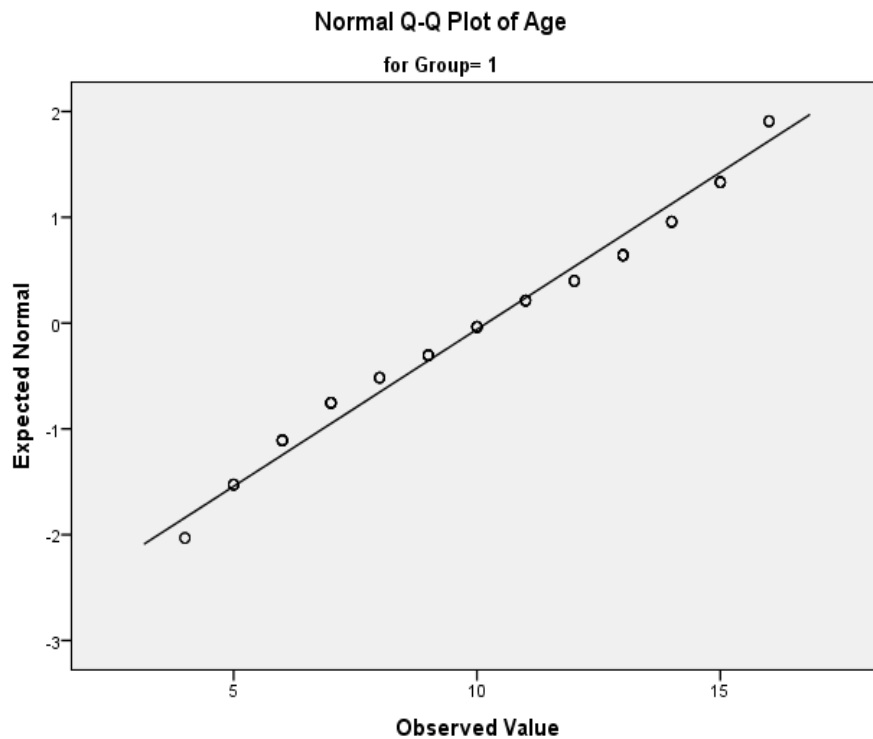


Figure 6.4 Histograms showing age distributions across group B (CD player).

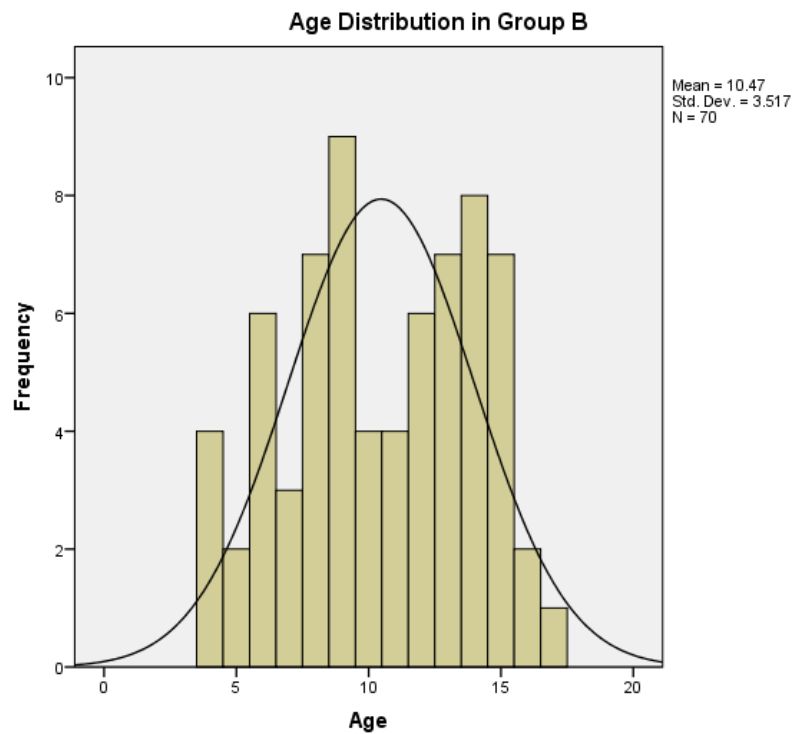


Figure 6.5 Q-Q Plots showing age distributions across group B (CD player)

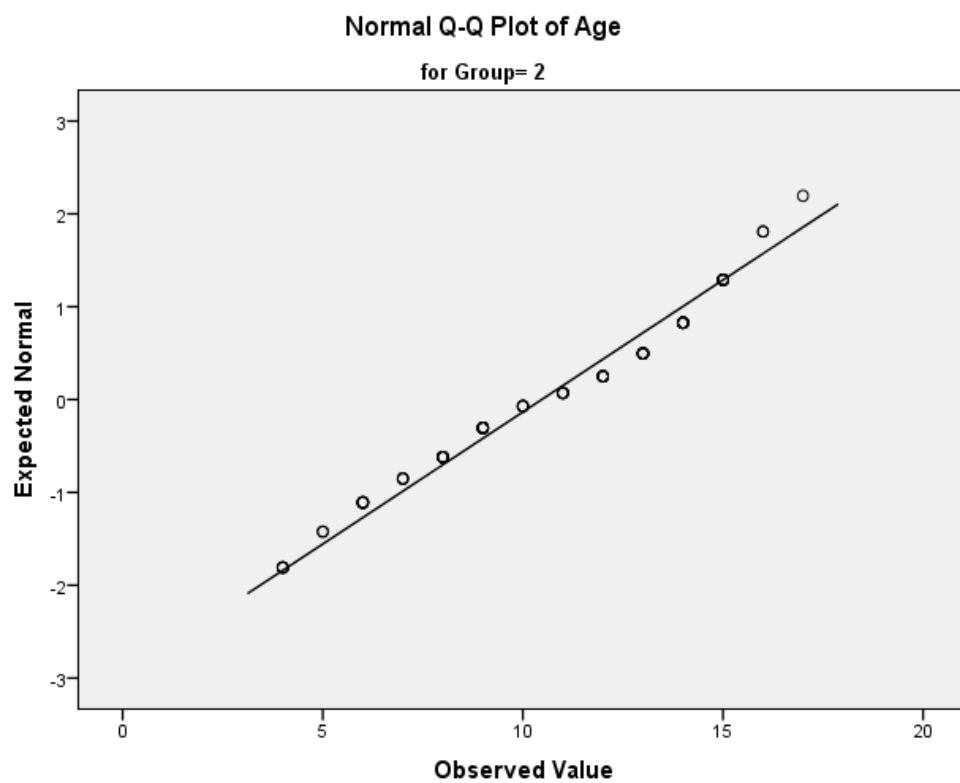


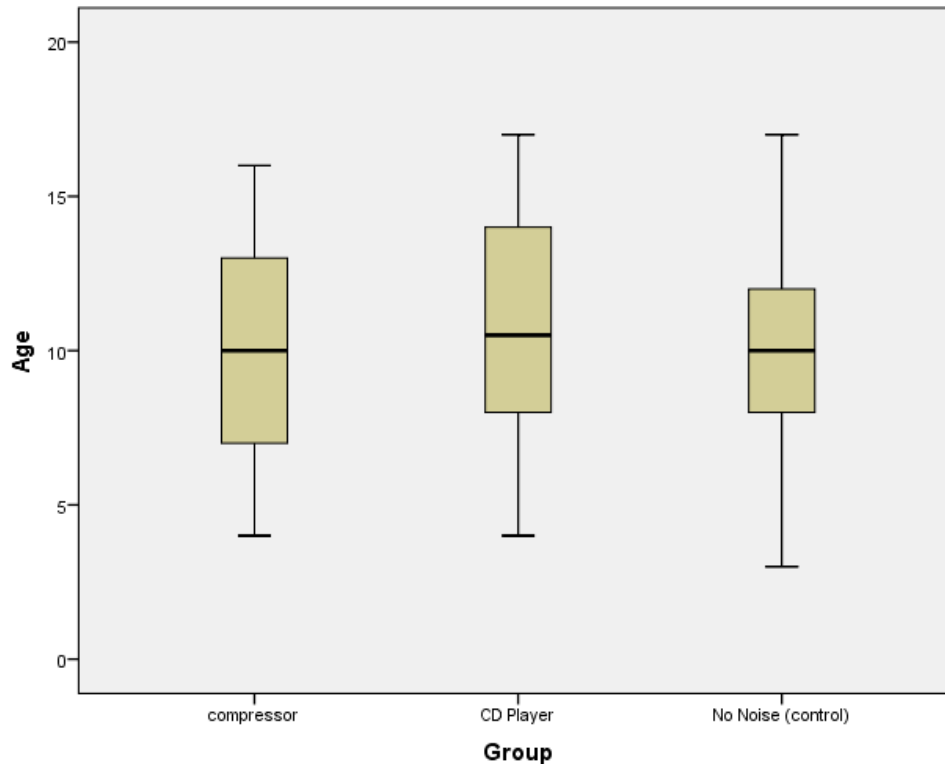
Figure 6.6 Histogram showing age distributions across group C (No Noise)



Figure 6.7 Q-Q Plots showing age distributions across group C (No Noise)



Figure 6.8 Boxplot showing age distributions in each group.



Further boxplots were performed in order to determine if there are true outliers within each group when comparing with a main outcome such as the time taken to fall asleep. It is also to examine if there has been a manual error input of the data or most importantly if it is a true value should this be included in the statistical analysis in chapter 7. In figure 6.9 the variable “time taken to fall asleep” in all three groups was analysed by a boxplot. This shows eight outliers and one extreme outlier. Further analysis was performed on these outliers to determine firstly if the outlier’s score is genuine, and if so, should it be removed from the data? When performing statistical analysis on this outcome it was decided that the data should be statistically analysed with and without the outliers in order to test if the data skew’s the results of the study. This was performed and they did not affect the outcome result when further statistical analysis was performed and therefore were included in the overall analysis (See Appendix 22).

Figure 6.9 Boxplot showing the time taken to fall asleep across the three groups

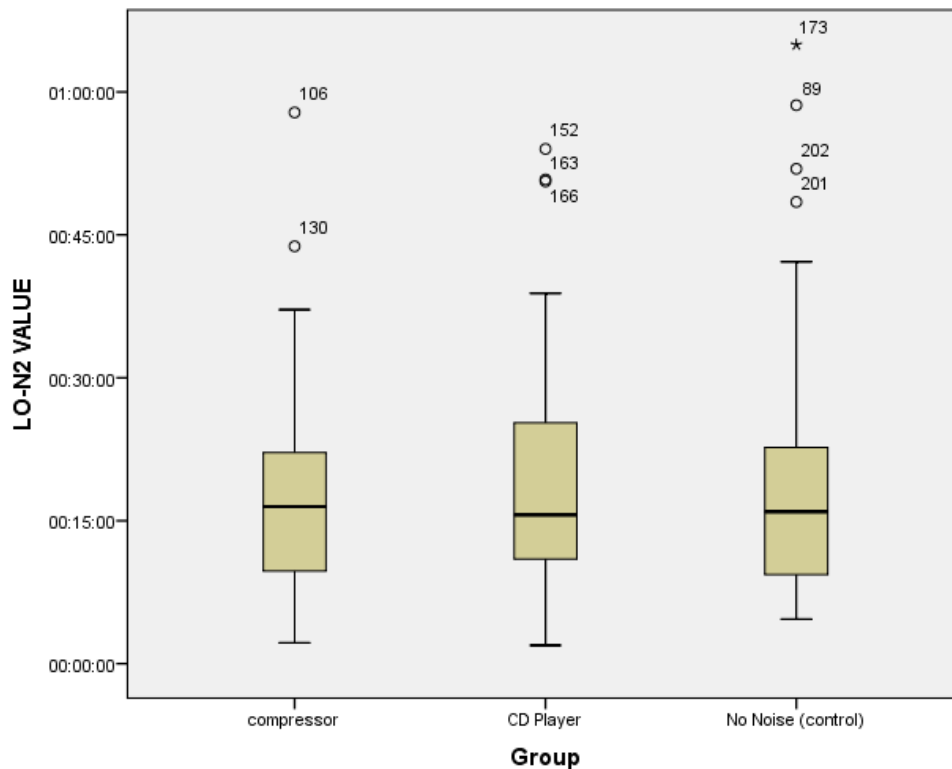


Table 6.3 showing number involved in above boxplot (Figure 6.9)

	Group	Cases					
		Valid		Missing		Total	
		N	Percent	N	Percent	N	Percent
LO-N2 VALUE	A – Air Compressor	60	100.0%	0	0.0%	60	100.0%
	B – CD	68	100.0%	0	0.0%	68	100.0%
	C – No Noise	55	100.0%	0	0.0%	55	100.0%

The above descriptive statistics were performed for a number of other variables tested within the study to determine mainly if they were normally distributed, also to examine if there were any outliers with the variables measured that may skew the results and to manually check for errors in data entry. These are shown in appendix 4.

6.4 Conclusion

This chapter demonstrates how the data was initially analysed and to examine the characteristics of the sample used. The next chapter further explores the statistical analysis used for each outcome in order to determine if there were any relationships between the variables measured.

6.5 References

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Chapter 7

Results

7.1 Introduction

This chapter is dedicated to outlining the results obtained in this research project. This not only includes examining the main aims of the study, but also addressing any other additional information collected from the data acquired.

The results section is divided as follows:

- Main aim of the study - comparing the sleep success rates across all three groups
- Secondary outcomes of the study examining (1) the time taken to achieve N2/stage 2 sleep across the groups and (2) Comparing the numbers of arousals present in each group
- Survey on sleep in paediatric EEG's within a dedicated children's Hospital. This included:
 - Sleep Success
 - Duration of the study
 - Time to achieve sleep
 - EEG Abnormalities

7.2 Main results

7.2.1 Sleep vs. no sleep across the three groups

The main aim of the study was to compare the two intervention groups which encompassed two different types of background noise and a control group which administered no noise, in terms of sleep success rates between the three groups. A χ^2 cross-tabulation was performed to explore the relationship between these two categorical variables (See table 7.1). The value of interest is the Pearson chi-square = **4.664**, **df = 2**, **p = .097** which is greater than the significance value of $<.05$ and therefore our result is not significant. In other words the proportion of participants that fell asleep and/or did not fall asleep is not statistically different throughout the three groups. The minimum expected count is 8, which means we have not violated the assumption, as all the expected cell sizes are greater than 5.

Table 7.1 showing χ^2 cross-tabulation with sleep success rates (Sleep Vs. no sleep) across the three groups			
	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi-Square	4.664^a	2	.097
Likelihood Ratio	5.109	2	.078
Linear-by-Linear Association	.081	1	.776
N of Valid Cases	202		
a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 8.			

Although there were no statistically significant results noted between the three groups, it was noted that they reported a trend ($p < .10$). A post hoc analysis was carried out and a relationship was found between groups B (CD) and C (No noise). The results are shown in table 7.2 and show $\chi^2 = 4.370$, $df = 1$, $p = .037$ and therefore these results are statistically significant. This means that there is a significant difference in the proportions of participants that did not fall asleep in groups B ($N = 5$) and C ($N = 12$) or, in other words, more people failed to sleep in group C (control group).

Table 7.2 showing χ^2 cross-tabulation with sleep success rates (Sleep Vs. no sleep) across groups B and C <u>only</u>					
	Value	Df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	4.370^a	1	.037		
Continuity Correction ^b	3.349	1	.067		
Likelihood Ratio	4.447	1	.035		
Fisher's Exact Test				.041	.033
Linear-by-Linear Association	4.337	1	.037		
N of Valid Cases	132				

7.2.2 Time taken to achieve sleep

The amount of time taken to achieve N2 or stage 2 sleep was a second variable of interest. This continuous variable was analysed in order to evaluate the differences in means between

the three groups. The mean time to achieve N2 sleep only in those participants that achieved sleep (N=183) was compared across the 3 groups A, B and C and is noted in table 7.3. The comparison in mean times to achieve sleep was not found to be clinically meaningful and was not statistically significant. This was also the case for the time taken to achieve N3 sleep (See table 7.4)

Table 7.3 showing means and standard deviations of time to achieve N2/N3 sleep across all three groups.

Variable	Group A	Group B	Group C
Time to achieve N2 sleep (Sleep onset latency)	N =58 Mean 16min 45s SD 08:29 min	N = 65 Mean: 17 min 29s SD 09:21 min	N = 50 Mean 15min 22s SD 08:00 min
Time to achieve N3 Sleep	N = 56 Mean 26 min 11s SD 11:57 min	N = 59 Mean 26min 07s SD 11:59 min	N = 43 Mean 22min 45s SD 12:18 min

In the initial analysis of the data (See section 7.3, figure 7.6), the distribution of the population of those participants that reached N2 sleep was not deemed to be normal. Non-parametric testing was performed with the use of the Mann-Whitney U test (See table 7.4). This showed that the significance level was not lower than .05; therefore the results were not significant.

Table 7.4 showing Mann-Whitney U Test comparing time to N2 sleep across all groups

	Comparing Group A & B	Comparing Group A & C	Comparing Group B & C
Mann-Whitney U	1962.500	1604.000	1739.000
Wilcoxon W	3792.500	3144.000	3279.000
Z	-.370	-.258	-.666
Asymp. Sig. (2-tailed)	.711	.797	.505

7.2.3 Arousals in sleep

This outcome examines if arousals were present or absent during the participants' sleep which is looking at the quality of sleep achieved. This was considered to be a relevant variable as this ultimately tests the hypothesis that this white noise masks the effect of peak noise levels in order to avoid arousals from sleep in the noise groups A and B in comparison

to group C (no noise). A χ^2 cross tabulation was performed which is shown in table 7.5. The $\chi^2 = .401$, $df = 2$, $P = .818$ which means that the results are not significant.

<i>Table 7.5 showing chi-square comparing relationship between arousals and three groups</i>			
	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	.401^a	2	.818
Likelihood Ratio	.401	2	.818
Linear-by-Linear Association	.116	1	.733
N of Valid Cases	183		

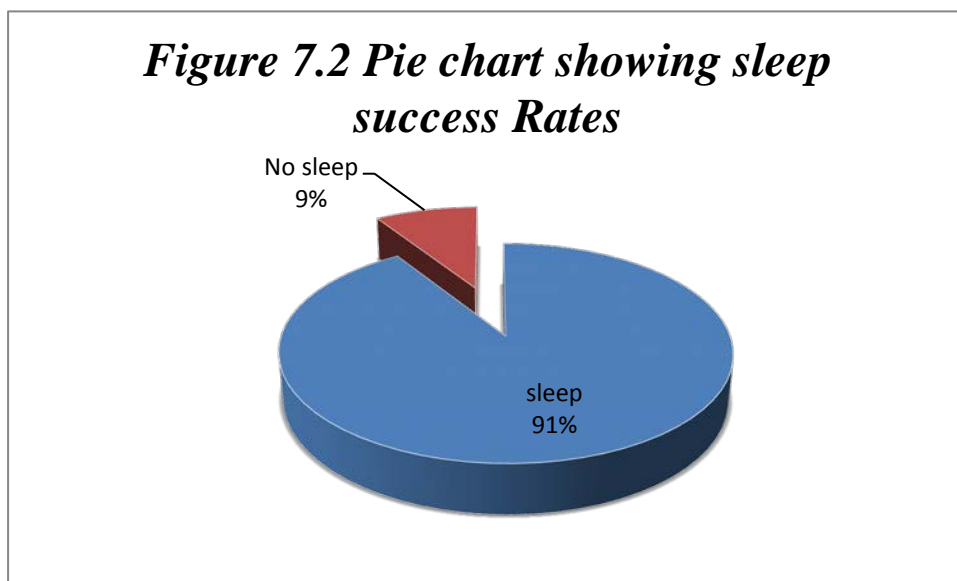
7.3 Survey on sleep in paediatric EEG's in OLCHC

In addition to the above results, further valuable information can be produced from this study and used as an audit to evaluate the current practice and protocols within this department. The following survey examined several different aspects of the investigation:

- Sleep success
- Duration of study
- Time to achieve sleep
- Abnormalities present in waking and sleep

7.3.1 Sleep success

Firstly it was noted that there was particularly high success in obtaining sleep in the 183 that fell asleep (See Figure 7.2). Out of the 202 participants, 91% achieved N2 sleeps which for the purpose of this study was to reduce subjectivity of sleep stages; this was defined as the sleep onset marker.



7.3.2 Duration of study

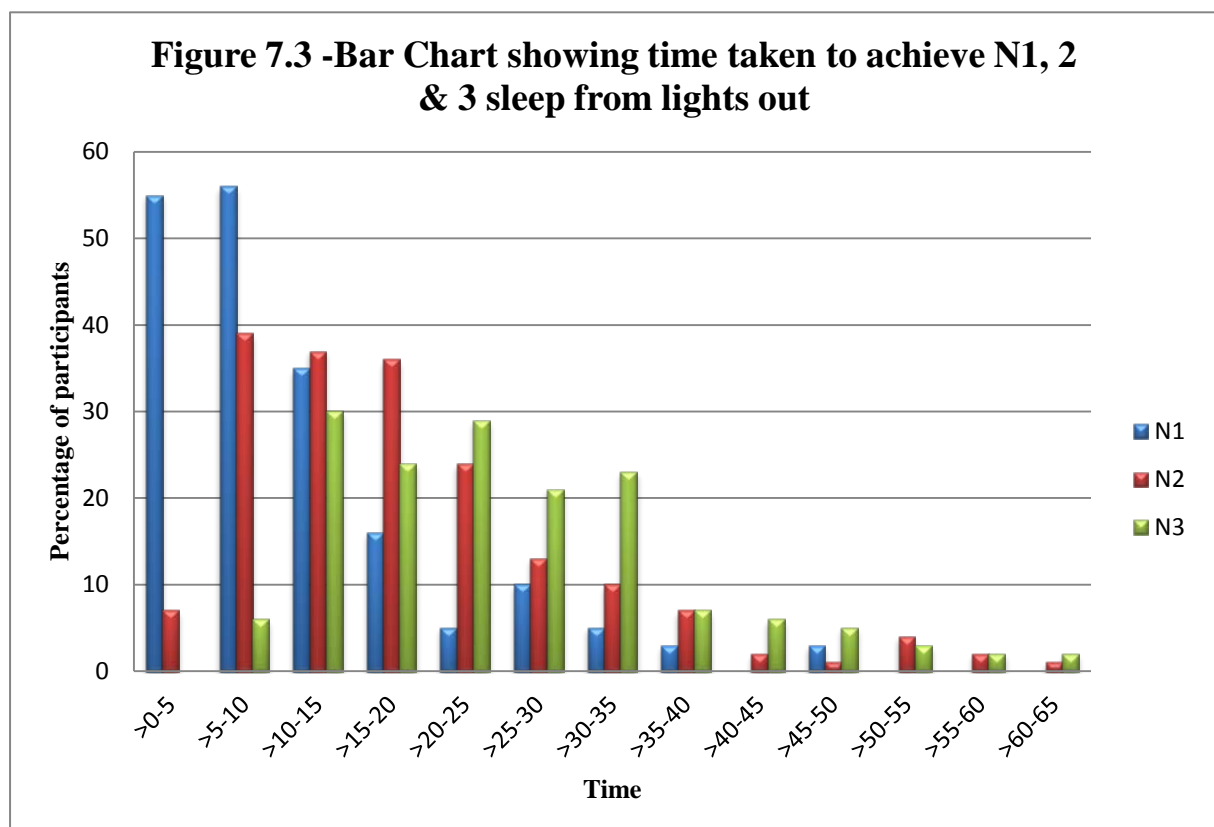
The duration of the EEG's are dependent on the local protocol used within each department and is also dependent on the specific needs and patient variety of the department. As this department's protocol attempted to achieve sleep during the EEG, the standard "60 minute time slot" is prolonged to 90mins to allow for this. However this can be flexible depending on the individual's referral reason as sleep may be a clinical necessity. The first 30 minutes

of the study is spent setting up the patient and recording a baseline study (this may take longer depending on co-operation from the patient) and therefore the remaining 60 minutes are allotted for sleep.

The average duration for the sleep portion of the study from “lights out to lights on”, which signalled the end of the study, regardless if sleep was obtained or not was **41 minutes 12s** and therefore well within the allotted 60minutes appointment slot.

7.3.3 Time to achieve sleep

The time taken to achieve each sleep stage (N1-3) was noted in groups of five minutes and is illustrated in figure 7.3. It is important to achieve all stage of sleep (N1-3) during the EEG, and staff were encouraged to obtain, in particular N2 & N3 sleep. Figure 7.3 shows that out of those participants who fell asleep, the majority of them achieved N1 sleep within 20minutes, N2 sleep within 25minutes and N3 sleep within 35minutes.



Similar data configuration can also be illustrated by finding the upper and lower limits of normal in order to determine the time taken to achieve N2 sleep by the majority of participants. Figure 7.4 shows a histogram exhibiting skewed distribution of data and

therefore the Log^{10} of this data was converted and shown in a further histogram (See Figure 7.5) which shows a normal distribution curve. This was converted to the Log^{10} in order to determine the upper and lower limits of normal in terms of the shortest and longest times taken to fall asleep. This normally distributed data was then used to determine the upper and lower limits of normal within this population to two standard deviations and is shown in Figure 7.6. The times to N2 sleep were converted and are demonstrated in table 7.6.

Figure 7.4 a histogram of the time taken to fall asleep showing the data skewed

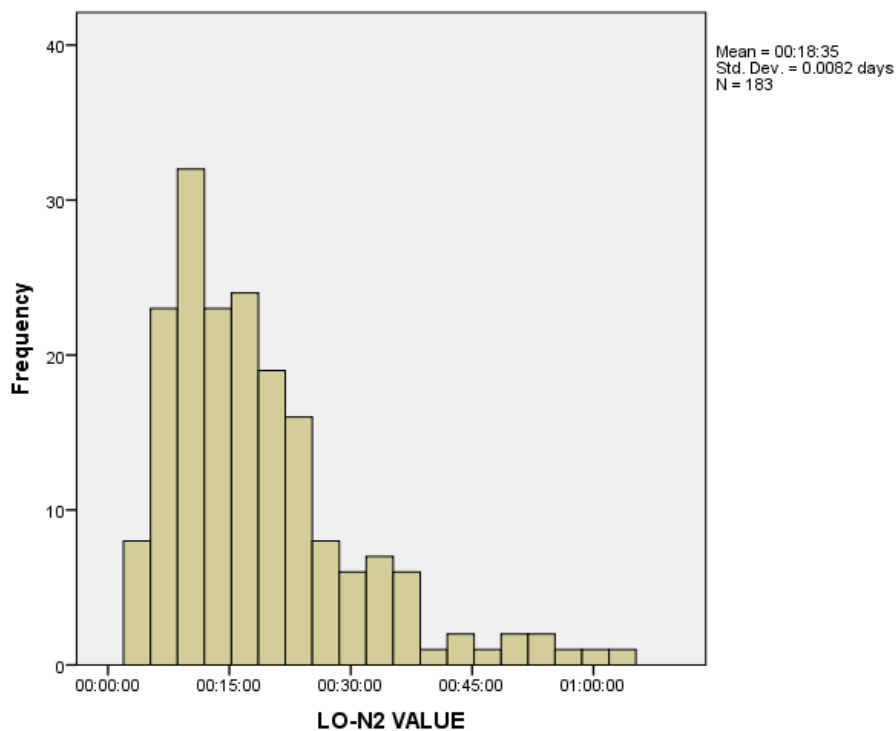


Figure 7.5 showing a histogram of the Log_{10} of figure 7.4 (Time to N2 Sleep)

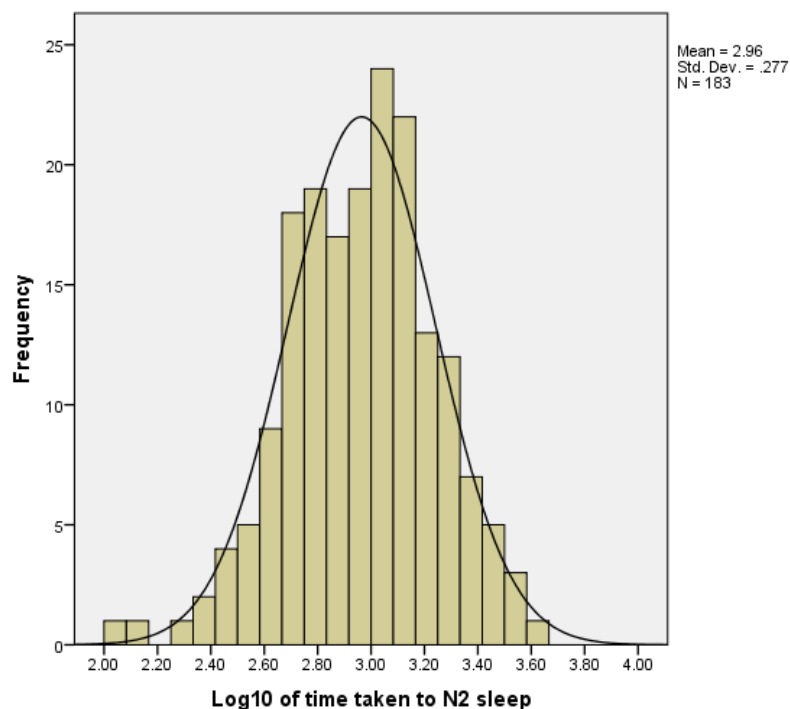


Figure 7.6 showing the upper and lower limits of normal in the time taken to achieve N2 Sleep

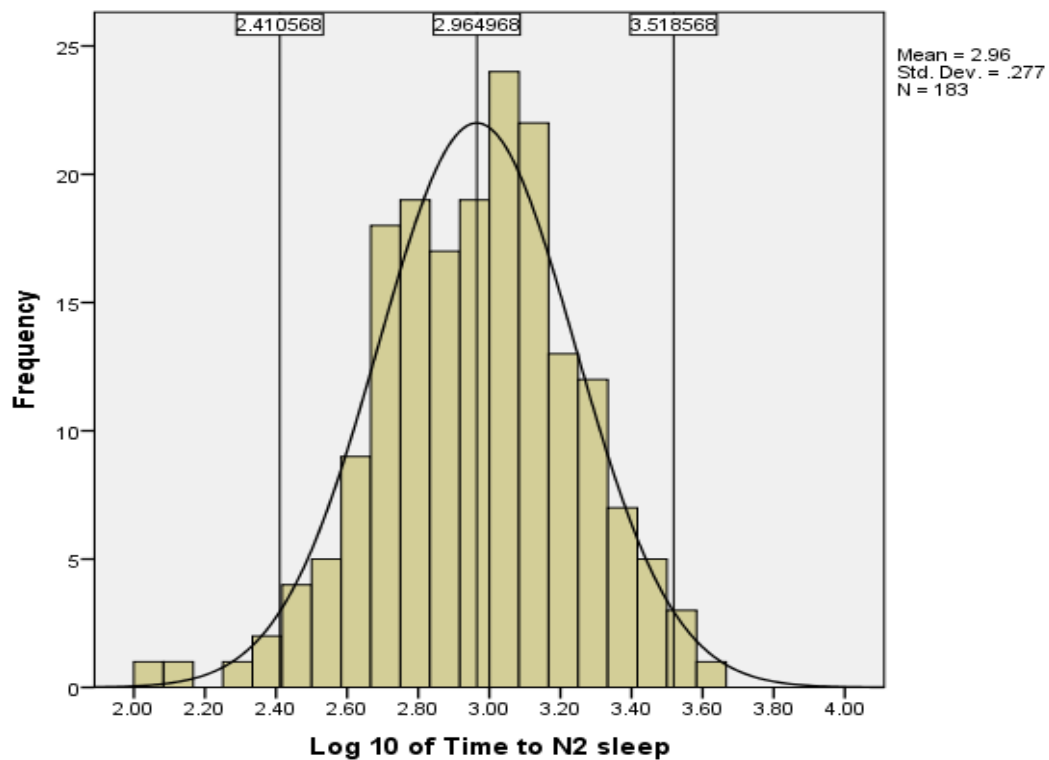


Table 7.6 Log 10 converted to Inverse Log (i.e. original time to achieved N2 sleep)

Limit	Log 10 Value	Converted to original Time (Inverse Log)
Lower	2.410568	4 Minutes 20 Seconds
Mean	2.964568	18 Minutes 35 Seconds
Upper	3.518568	61 Minutes 36 Seconds

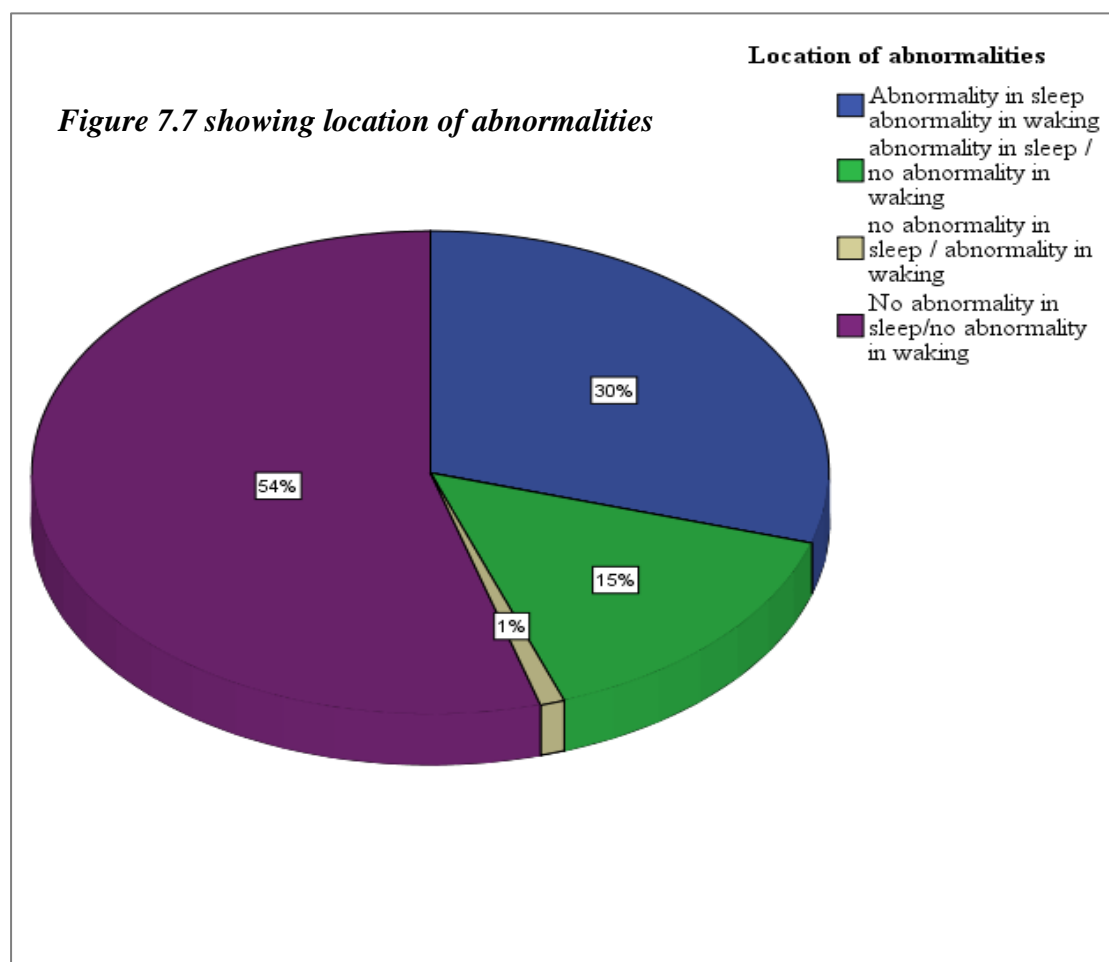
7.3.4 EEG Abnormalities

The abnormalities captured during the tracing were analysed on the basis of whether they were present or not, where they appeared during the tracing (i.e. in sleep or in waking) and if they were more likely to appear in a specific sleep stage.

The abnormalities obtained were sorted into four categories:

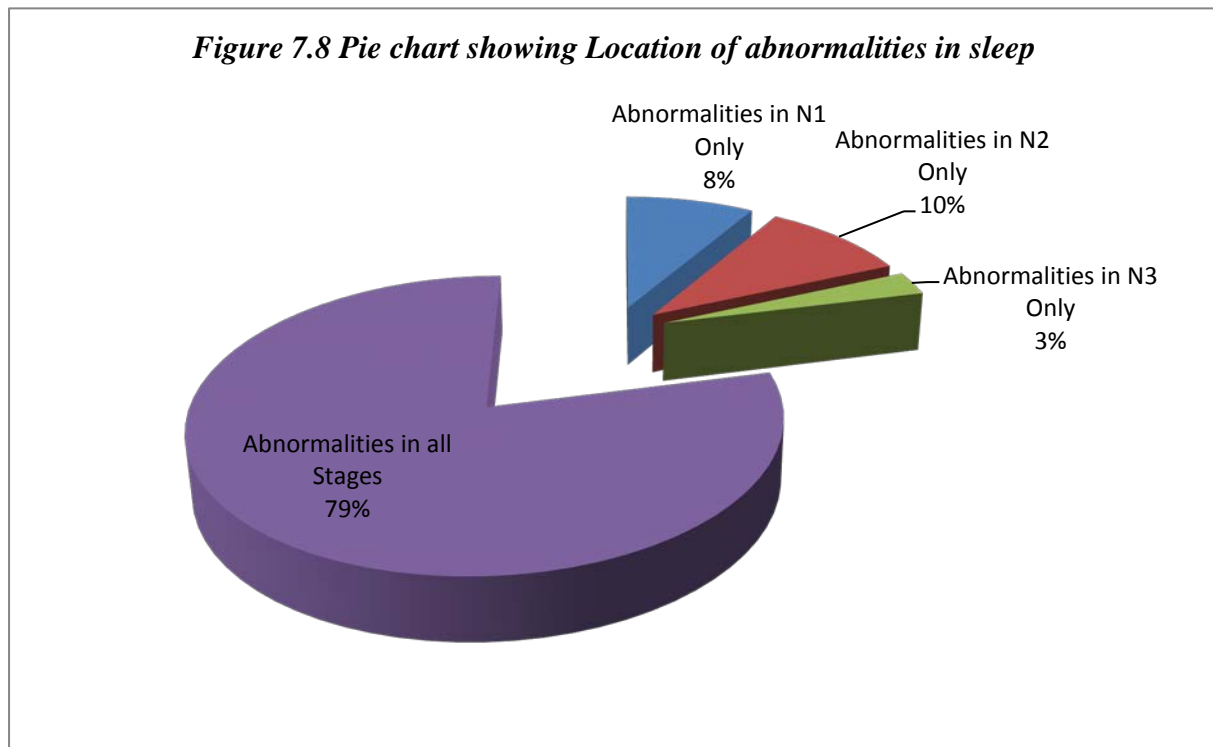
- (1) Abnormalities present in sleep; Abnormalities present in waking
- (2) Abnormalities present in sleep; No abnormalities present in waking
- (3) No abnormalities present in sleep; Abnormalities present in waking
- (4) No abnormalities present in sleep; No abnormalities present in waking (Normal)

Figure 7.7 demonstrates that out of the people that achieved sleep (N = 183), 54% or over half of the patients had a “normal” result (category 4), 30% had abnormalities in both waking and in sleep (category 1) and most importantly, 15% only had abnormalities evoked by sleep (category 2). It should be noted that the category 2 participants had on average 3.2 hours of sleep deficit.



In addition to the above pie chart, further information could be added in relation to which sleep stage in particular these abnormalities occurred. Figure 7.8 shows the location of abnormalities in sleep. The majority of participants (79%) who had abnormalities, they were evoked by all sleep stages. The remaining sections of the pie chart display those participants

who showed abnormalities in only that sleep stage. It was noted that only 3% of participants displayed abnormalities only in N3 sleep and therefore one could deduce from this that with the majority of patients that do not have a positive results in N1-2 sleep, N3 sleep would be unlikely to add any further information to the investigation.



7.4 Conclusion

This chapter has addressed the main aims of the study together with additional information that may also be of some value to the day-to-day routine of an EEG department. These results may also be helpful in the monitoring of protocols and procedures that are used on a daily basis i.e. duration of study. This is required in order to identify and build on acceptable standards within the EEG department in order to improve standardisation and to comply with national guidelines.

The results of this thesis have been presented in this chapter. In order to reject or accept the Null hypothesis outlined in chapter 5, the results outlined here will be deliberated and discussed in chapter 8.

Chapter 8

Discussion

8.1 Introduction

This study was conducted in order to determine if the protocol of using background noise during a routine EEG promotes sleep. In this randomised control trial, participants were assigned to either one of two intervention groups that involved listening to two types of background noise or a control group with no noise. The main aim of this study was to evaluate the effectiveness of background noise as an aid to encourage sleep during a sleep deprived EEG.

8.2 Interpretation of main study outcomes

Three hypotheses were tested in this study:

1. A higher number of participants will fall asleep in the intervention groups compared to the control group.
2. Participants will fall asleep faster in the intervention groups compared to the control group.
3. Participants will have fewer arousals in sleep when compared to the control group.

The results of the study indicate that the use of white noise at a sound level of 40-50db may influence sleep in paediatrics during a sleep deprived EEG. This was statistically significant between groups B which was white noise played by a CD player and group C which was the control group with no noise. There were no statistically significant results identified with the other outcomes measured (Time to N2 sleep and arousals in sleep). No side effects were reported throughout the study.

To strengthen the validity of the results certain confounding variables were be considered. This study included an abundance of possible confounding factors to consider. Table 6.1 shows the patient's demographics of the study outlined in chapter 6 which lists several factors that may differ between the participants, these include:

- Age
- Gender

- Parent/guardian present or absent in room
- Average hours of sleep deficit
- Room used
- Appointment Time
- Season

There were no statistically significant differences between the three groups and therefore theoretically these factors should be controlled for and not affect the results. However, other confounding factors that may also have had an impact on the results was the temperature within the room, however this was not measured, and the body mass index (BMI) of the participants although this would be more relevant to an adult population. These patients were also at various stages in their diagnosis. For most, it was their first presentation of possible clinical seizure activity with a possible impending diagnosis of epilepsy and therefore there was a certain amount of understandable stress surrounding the families participating. The Clinical Physiologists performing the tests could have caused some bias towards a group however there were seven in total and therefore bias can be eliminated due to multiple professionals.

In terms of potentially harmful factors of the white noise, there were no contraindications reported in the literature so far. There have been mostly positive experiences noted from parents and participants themselves. A study examining sleep problems in children with ASD used a behavioural package in order to aid sleep which included the use of continuous white noise. A social validity survey indicated that the mothers believed that the treatment improved their children's sleep, recommending the treatment to other parents (Knight & Johnson 2014). This study did not enquire whether the participants or the parents/guardians favoured the white noise or disliked it which may be useful in future research. However on a few occasions the parents commented that they also found the noise soothing and admitted to the scientist that they also fell asleep during the study. In terms of the staff within the department, they all reported anecdotal evidence of the effectiveness of background noise since its implementation over fifteen years ago.

Various assumptions were made as to why white noise or background noise may be useful in influencing sleep. The first is that white noise may increase the baseline noise level which would be greater than a total increase in the peak noise level (i.e. banging door), thereby reducing the difference in noise levels making arousal from sleep less likely. Conversely, in

this study there were no statistically significant differences in sleep arousals across the three groups and therefore the results of this study do not correlate with the existing literature. Caution should be taken in this interpretation as in this study there was the absence of measure of the peak noise to correlate with an arousal and therefore the analyst could not determine whether this arousal was due to a peak noise or some intrinsic stimuli causing the arousal. Also, the study did not measure the quantity of arousals present in one study but whether or not arousals were present overall and therefore this was not an accurate representation of arousals numbers of the participants. The literature shows that the use of both white noise and music showed a decrease in night wakening's. These studies tended to be over a longer term, performed over several weeks and may have been due to the habitual effect of white noise (Stanchina et al. 2005). A comparative study (Stanchina et al. 2005) on arousals over three consecutive nights (comprised of a night at baseline, the following night with noise and lastly listening to white noise) which showed decreased arousals with white noise, however our study had no previous comparative data from the same individuals as the control group data was a different set of participants.

There were no statistically significant differences between the sleep latency across the three groups. Studies examine sleep onset latency showed that using "pink noise" reduced the sleep latency by 9.5minutes (Kawada & Suzuki 1993), also showing a reduction of 9 minutes when comparing music to using chloral hydrate however neither of these results was statistically significant (Loewy et al. 2005).

In summary, the main strengths of the study was its design which uses the gold standard research technique of a "randomised control trial", a large sample size of 202 participants and the use of EEG analysis as a quantitative measurement of sleep and EEG outcome.

In regards to our survey on paediatric sleep; this allowed us to examine sleep behaviour and to determine the diagnostic usefulness of sleep in paediatric EEG in a sizeable cohort of participants. Out of the 202 participants, 91% achieved N2 sleep (which for the purpose of this study and to reduce subjectivity of sleep stages; this was defined as the sleep onset marker). These figures are quite high although these are excluding children with learning difficulties (ADHD/ASD), and therefore are not entirely applicable to the general population. It would also be useful to compare these figures to other dedicated children's hospitals. The results looked at the presence or absence of epileptiform abnormalities in waking and sleep and showed that the proportion of abnormal or diagnostic EEGs increases significantly, in

particular for the focal and generalized epilepsy group. This concluded that the proportion of focal epilepsy increased more than two-fold and the proportion of intermittent generalised discharges by a factor of five in sleep. This is in keeping with the literature published (Smith 2005, Binnie et al 1996) on how important sleep can be to increase the yield of the test. Other articles (Gilbert et al. 2004) have examined the theory that may be the actual act of sleep deprivation that was causing an increase in epileptiform discharges in waking however our studies showed that 15% failed to show any discharges in waking (average sleep deficit of 3hrs) which were evoked by sleep.

In terms of where these abnormalities are likely to appear in sleep, 97% of IEDs manifest by N2 sleep, with a small minority in N3 sleep only and therefore the study could recommend to attempt to achieve N1 and N2. However based on the results of this study it seems that N3 sleep may not add any further information to the study. Examining the time taken to fall asleep, as mentioned in chapter 7, the majority of these participants fell asleep between ~4minutes and 1 hour and therefore this allows ~90minutes to be scheduled for the study which allows ~15mins to apply the electrodes (with good patient co-operation) and 15minutes for a baseline study which is the current protocol in the department.

8.3 Limitations

There are some limitations to this study. Firstly, the study is limited to children with normal intelligence as children with ASD and ADHD were excluded from the study therefore the results cannot be generalized to other populations with special needs. Studies have suggested that children with behavioural disabilities experience higher rates of sleep problems with children with ASD having the highest prevalence (Polimeni et al. 2005). Therefore if the results from this study could be replicated using participants from this population, this may aid not only sleep during the EEG but may increase relaxation for the general successful completion of the study, regardless of whether sleep was achieved or not. As this study was also a purely paediatric population it is again unable to generalise towards an adult population. On a similar matter, the use of convenience sampling during this study has also added some drawbacks, as the participants were outpatients being referred for an EEG. Therefore unfortunately concrete conclusions cannot be drawn from the results and again cannot be compared with the general population.

Another limitation to the study which may have led to the results not being significant, is the fact that the parents or children were randomised to each group however it may have been

helpful if they were given a choice in the sound that was used or if the study had measured the degree of liking of the sound as some participants and parents did informally comment that it wouldn't be their most preferred sound. Previous studies have shown significant correlations between the degree of liking for music and relaxation (Stratton and Zalonowski 1984) which can be related to sleep onset (White 1992) as they show similar changes in the circulation of norepinephrine in the body during these times (Tan 2004). An article looking at the effect of music on sleep (Gerra et al. 1998) had a psychophysiological theory that sleep quality can be improved by relaxing the body with sedative music. An article demonstrated that in a cohort of patients receiving chemotherapy (a highly anxious environment), monochord sounds reduced anxiety after every visit (Lee et al. 2012).

These significant results could be due to other factors related to the study design. As mentioned in the methodology, the participants were asked to sign an assent form after being given an age-appropriate information leaflet. The participants were therefore very much informed of the study and therefore this may have given rise to the "hawthorn effect" which may have influenced the results, however as the study were dealing with children as young as three years of age, their participation in the study may not have been fully understood. This may also explain why such high sleep success rates were also present in the control group however this is difficult to say with the absence of baseline data prior to commencing the study. Obtaining baseline data was thought not to be feasible due a number of reasons including staff reductions, increasing waiting lists and was not practical for the participants and their parents/guardians as many of them were travelling from a longer distance. The participants were also not blinded to the intervention due to the nature of the study; however the researcher that produces the results was blinded to the group allocation to exclude any bias during analysis of results.

In addition to the above limitations, medication effects on the participants were also considered, however although none of the children were on sedatives, a considerable amounts may have been on other medication such as anti-epileptic drugs (AED's) however this was not measured. The side-effects that come with AED's include weight gain, confusion, unsteadiness and most importantly daytime sleepiness (epilepsy research), and this may have had an impact on the results and again exhibits the inability to compare the results of the study to the general population as a large majority of the participants may have been on AED's.

8.4 Conclusion

Generally the above results suggest that this background noise used may influence sleep during a sleep deprived EEG in paediatrics which can be compared to other literature already published, although it is important to note that some of the articles reviewed did not submit quantitative analysis of certain aspects of sleep, with a proportion of them using surveys and questionnaires to determine the outcomes.

In regards to other variables measured, there was no relationship between the noise and the sleep onset latency or whether or not arousals were present in sleep. This was interesting to note as several of the articles were therefore conflicting, be that statistically proven or not, between white noise and a reduction in arousal levels. This is also one of the theories of how white noise is believed to improve sleep, in that it masks the surrounding noises in order to reduce arousal from sleep. However this study, in hindsight failed to accurately measure this outcome and the results of this variable should be interpreted cautiously.

8.5 References

Articles

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Chapter 9

Conclusions and Future recommendations

9.1 Introduction

The following chapter outlines conclusions from the results and findings from the SPSS data collected and on the data presented in our analysis of sleep. Also, any possible changes or issues that were addressed in this thesis that should or may be amended during any future research performed in similar areas were noted.

9.2 Conclusions

White noise may be useful in order to influence sleep during a sleep deprived EEG in paediatric participants however it remains unclear as to why this is the case. Our study was unable to prove the hypothesis that white noise masks unwanted noise in the surrounding environment and therefore produce less arousal from sleep, however as mentioned in chapter 8 this interpretation should be taken with caution as the measurement of arousals was not correlated with the environmental peak noise. There are various limitations to this study as outlined in chapter 8; however it was one of the largest sample sizes compared with the literature examined, using accurate quantitative information from EEG data on the measurement of a brief portion of sleep. This study also provided the local department with a survey on their current protocols which may be revised in order to improve general patient care and efficiency within the EEG department.

In conclusion, the use of background noise during a sleep deprived EEG in paediatrics may be a cost-effective alternative to avoid the use of pharmacological agents or the addition of further repeat studies in order to achieve sleep.

9.3 Future Recommendation's

This study has already answered vital questions, mainly validating the protocol of the EEG department in using white noise for the sleep portion of the study. Although this is the case, in regards to other recommendation's and for future research there are various areas that should be examined. These include:

- Replication of this study across other departments of similar populations (i.e. other dedicated children's hospitals) in order to validate the significant results.
- Duplicated and performed on children with autistic spectrum disorder or attention deficit hyperactivity disorders to determine if this strategy may also be useful with this population; given that we excluded these types of patients from our study and physiologist may agree that it is more likely that these patients will be more difficult in terms of obtaining sleep.
- Request the parents/guardians or the participants themselves to possibly choose a preference of music/ background noise to listen to (however it is usually the protocol to not highlight to the child that they need to sleep as this may cause anxiety towards the child)
- The terminology of white noise which is "random noise with a uniform frequency spectrum over a wide range of frequencies" (Dictionary.com 2015). This should be addressed in regards to the "frequency spectrum" as often the term white noise is used very broadly and the actual frequency of the noise was not described.
- Use of a sound meter to record peak noise and correlate these with an arousal to determine true arousals within the noise and no noise groups.
- Other alternative measures need to be examined in order to make these tests as anxiety-free as possible, such as progressive muscle relaxation or cognitive behavioural therapy. Enlisting the help of a play therapist may also be of use if appropriate.

Further research in general should be carried out in order to research different alternative therapies to utilise during these invasive and non-invasive investigations in order to make them as stress-free for the patient and their parents/guardians.

9.4 References

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Glossary of Terms

Absence Seizures

A type of generalised seizure causing a brief interruption of consciousness, where the patient appears to stare vacantly and is most common in childhood. The EEG shows an abnormal 3Hz spike and slow wave discharge pattern over both hemispheres.

Activation Procedures

Procedures used in the EEG to elicit abnormalities that ordinarily would not be present. These include:

Hyperventilation – Asking the patient to deep breathe for 3 minutes causing a reduction in carbon dioxide in the blood, thereby causing a constriction of cerebral blood vessels

Intermittent Photic Stimulation – Showing the patient a flashing light at intermittent frequencies (1-50Hz) to determine any photosensitivity.

Sleep Deprivation – A patient is fully or partially deprived of sleep the night prior to attending for the EEG. The patient will be encouraged to sleep during the test which may increase the yield of the study.

Alpha Rhythm

The main dominant rhythm in the EEG, which occurs at 8-13Hz and is seen over posterior regions of the head upon eye closure.

Anti-epileptic Drugs (AED's)

A group of drugs used to treat seizures

Arousals

An abrupt shift in EEG activity from the sleeping background which may include delta, theta or sometimes alpha activity with an increase in muscle

Assent Forms

An age appropriate consent form signed by the participant (Under 18 yrs) to say they have been fully informed of the study.

Attention Deficit Hyperactivity Disorder (ADHD)

A condition involving restlessness, short attention span or impulsive behaviour, ranging in severity

Autistic Spectrum Disorder (ASD)

A variety of disorders consisting of difficulties with social interaction, communication, thought or behaviour and sensory problems. These can range from mild to severe.

Benzodiazepine

A group of drugs used as anxiolytics and hypnotics, e.g. Temazepam or Diazepam

Beta Activity

Electrical brain activity within 13-30Hz and can be seen bilaterally or over anterior regions.

Brainstem Auditory Evoked Potentials

Can be used to assess conduction through the brainstem and auditory nerve pathways

Cerebral-Spinal Fluid (CSF)

A clear fluid found in the brain and spinal cord

Chloral Hydrate

A sedative and hypnotic and is used for treating sleep disorders

Circadian Process

Denoting a biological rhythm or cycle of ~24hrs

Clinical Physiologist

A healthcare professional which performs studies to do with the brain and spinal cord such as EEG's, Nerve conduction studies (To determine conditions affecting peripheral nerves and the spinal cord) and Intra-operative monitoring

Computed Topography (CT)

A form of x-ray examination constructing 3D images of body structures.

Cryptogenic

A condition where the cause is yet unknown

Decibels

Can be used to measure sound level

Electrodes

A solid conductor of electric current through which a current enters or leaves

Electroencephalogram (EEG)

Measures and records the electrical activity of the brain.

Electromyography (EMG)

A recording of muscle activity

Muscle activity on the EEG is at a frequency of >30

Epilepsy

The recurrence of unprovoked, stereotypical seizures.

Epileptiform Discharges

Abnormal electrical activity in the brain present on the EEG. May be “generalised” and affect the whole of the brain or they could be “focal” and only affect certain areas.

Fibromyalgia

A chronic rheumatoid condition characterised by fatigue, stiffness and joint pain

Foetal

Between the embryonic state and birth

Galvanometer

An instrument for detecting electrical current

Gamma-amino butyric acid (GABA)

An amino acid found in the central nervous system, mainly in the brain where it is used as an inhibitory neurotransmitter.

Gestational Age

The age from conception to birth and is measured in weeks

Hertz (Hz)

The unit of frequency

Homeostatic Process

Internal systems of the body are maintained at equilibrium despite changes in the surrounding environment.

Idiopathic

A condition with no known cause

Impedance (*In EEG*)

The contact resistance between the electrode and the patient's scalp

Magnetic Resonance Imaging (MRI)

An imaging technique based on emission of electromagnetic waves from the body when the patient is placed in a strong magnetic field and exposed to radiofrequency radiation.

Melatonin

Natural hormones which can help regulate wake and sleep cycles

National Institute for health and Care Excellence (NICE) Guidelines

Provides quality and care standards for healthcare professionals

Neonate

An infant less than four weeks old

Neurophysiologist

A physician specialising in the physiology of the central nervous system which performs studies such as Nerve conduction studies, Electromyography (Recording muscle activity) and reporting on EEG's.

Neurophysiology

The study of chemical and physical changes within the nervous system.

Non- Rapid Eye Movement (Non-REM)

This is comprised of four stages of sleep (encompassing slow wave sleep) which is seen from sleep onset.

Peak Noise

A sudden increase in noise intensity

Pittsburgh Sleep Quality Index (PSQI)

Used to measure the quality and patterns of sleep in adults

Polysomnography (PSG)

A multi-parametric test used in the study of sleep

Post-synaptic potentials (PSP)

A temporary change in the membrane potential of a post-synaptic membrane which can initiate or inhibit an action potential.

Rapid Eye Movement (REM)

A stage of sleep that usually occurs ~90minutes after sleep onset. Is the sleep stage associated with dreaming.

Seizure

A sudden, abnormal burst of electrical activity within the brain.

Sleep Architecture

Describes features of sleep on the EEG which distinguishes the stage of sleep.

Sleep Deprived EEG

A patient is fully or partially deprived of sleep the night prior to attending for the EEG. The patient will be encouraged to sleep during the test which may increase the yield of the study.

Sleep onset latency

The length of time taken to transition from wakefulness to sleep

Spectral Frequency

Describes how the variance of data is distributed over the frequency domain of which it is encompassed

Statistical Package for the Social Sciences (SPSS)

Used in research for statistical analysis of results

Symptomatic

A condition where its cause is known

The international 10-20 System of measurement

This is a measurement technique used in EEG departments worldwide for electrode placement. This technique allows for equidistance between electrodes and standardisation between departments.

Theta Activity

Electrical brain activity within 4-7Hz and is seen in temporal and posterior regions.

Ultradian Process

Denoting a biological rhythm or cycle that occurs more frequently than once in 24hrs.

White Noise

A noise which covers the entire range of human hearing (20-20,000Hz).

APPENDICIES

APPENDIX 1 – PARENTAL CONSENT FORMS



Consent Form

The use of a sound generator on enhancing sleep during a routine EEG

Please tick the appropriate answer:

	Yes	No
I confirm that I have read and understood the study information leaflet attached.	<input type="checkbox"/>	<input type="checkbox"/>
I understand that participation in this study is entirely voluntary and that I may withdraw my child at any time.	<input type="checkbox"/>	<input type="checkbox"/>
I understand that my child's identity will remain confidential at all times.	<input type="checkbox"/>	<input type="checkbox"/>

I(Parent/Guardian) give informed consent for my child..... to participate in this research study lead by the Neurophysiology Department.

.

Signed.....

Date.....

To be completed by co-Investigator

I the undersigned have taken the time to fully explain to the above parent and child, the nature of the study. I have answered any queries or questions that they had prior to the study.

Signed.....

Date.....

APPENDIX 2 – PARTICIPANT (AGE-APPROPRIATE) ASSENT FORMS



Children's Assent Form (<8Years)

(To be read by parents if appropriate)

We would like you to read the information booklet given to you. If you would like to take part in our project please sign your name below. You do not have to take part in this project if you do not want to. If so, we will not use any of your information for our project. We always try to make the test fun and as easy for you as possible. Your parents (Mum and Dad) /guardians have been told about our study and have agreed that you may take part in it, if you are happy to do so.

If you sign this paper it means you have read about our project and would like to be in the study.

Signature of child

Questions are welcome!

APPENDIX 3 – PARTICIPANT (AGE-APPROPRIATE) ASSENT FORMS



Children's Assent Form (8-11Years)

We would like you to read the information booklet given to you. If you would like to take part in our project please sign your name below. You do not have to take part in this project if you do not want to. If so, we will not use any of your information for our project. We always try to make the test as enjoyable and easy for you as possible. Your parents (Mum and Dad) /guardians have been told about our study and have agreed that you may take part in it, if you are happy to do so.

I _____ have read about the study from the information booklet given to me and would like to take part in the project during my test today.

Signature of child

Questions are welcome!

APPENDIX 4 – PARTICIPANT (AGE-APPROPRIATE) ASSENT FORMS



Assent Form (12-14Years)

The use of a sound generator on enhancing sleep during a routine

EEG

Please tick the appropriate answer:

	Yes	No
I confirm that I have read and understood the study information leaflet attached.	<input type="checkbox"/>	<input type="checkbox"/>
I understand that participation in this study is entirely my own choice and that I may change my mind at any time.	<input type="checkbox"/>	<input type="checkbox"/>
I understand that my identity will remain confidential at all times.	<input type="checkbox"/>	<input type="checkbox"/>

I (Your Name) give informed consent to take part in this project performed by the EEG Department.

..Signed.....

Date.....

To be completed by co-Investigator

I the undersigned have taken the time to fully explain to the above parent and child, the nature of the study. I have answered any queries or questions that they had prior to the study.

Signed.....

Date.....

APPENDIX 5 – PARTICIPANT (AGE-APPROPRIATE) ASSENT FORMS



Assent Form (15-17Years)

The use of a sound generator on enhancing sleep during a routine EEG

Please tick the appropriate answer:

	Yes	No
I confirm that I have read and understood the study information leaflet attached.	<input type="checkbox"/>	<input type="checkbox"/>
I understand that participation in this study is entirely voluntary and that I may withdraw at any time.	<input type="checkbox"/>	<input type="checkbox"/>
I understand that my identity will remain confidential at all times.	<input type="checkbox"/>	<input type="checkbox"/>
I (Your Name) give informed consent to participate in this research study lead by the EEG Department.		

.

Signed.....

Date.....

To be completed by co-Investigator

I the undersigned have taken the time to fully explain to the above parent and child, the nature of the study. I have answered any queries or questions that they had prior to the study.

Signed.....

Date.....

APPENDIX 6 – Clinical Physiologist Study form

Compressor Study Form

General

Patient Name:..... Study Date:.....

Appointment Time: Group :.....

Age:..... Scientist (Initials):.....

Male	<input type="checkbox"/>	Female	<input type="checkbox"/>
Room 1	<input type="checkbox"/>	Room 2	<input type="checkbox"/>

How many hours of sleep will the patient usually acquire per night?

.....

How many hours of sleep did the patient have the night prior to the study?

.....

Did the patient have a nap prior to the study?

No	<input type="checkbox"/>
Yes	<input type="checkbox"/>

Does the patient use Melatonin Regularly?

No	<input type="checkbox"/>
Yes	<input type="checkbox"/>

Study Information

Did you need to enter the room after lights out?

1 Yes, I stayed in the room	<input type="checkbox"/>
2 No	<input type="checkbox"/>
3 I entered the room once or more	<input type="checkbox"/>

Did the parent/Guardian stay in the room after Lights out?

No	<input type="checkbox"/>
Yes	<input type="checkbox"/>

Where there any unintended interruptions after Lights out?

No	<input type="checkbox"/>
Yes	<input type="checkbox"/>

Was Melatonin used during the EEG?

No	<input type="checkbox"/>
Yes	<input type="checkbox"/>

If the patient did not sleep after 40 minutes, was there another sound source introduced?

CD player	<input type="checkbox"/>
Compressor	<input type="checkbox"/>

APPENDIX 7 - Statistical analysis on confounding variables across three groups
Distribution of room used throughout the three groups

A chi-square for independence correlation was used to determine if there is a difference in the room used across the three groups.

			Group			Total
			compressor	CD Player	No Noise (control)	
Room Used	Room 2	Count	40	39	41	120
		Expected Count	41.6	41.6	36.8	120.0
	Room 1	Count	30	31	21	82
		Expected Count	28.4	28.4	25.2	82.0
	Total	Count	70	70	62	202
		Expected Count	70.0	70.0	62.0	202.0

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	1.706 ^a	2	.426
Likelihood Ratio	1.727	2	.422
Linear-by-Linear Association	1.037	1	.309
N of Valid Cases	202		

There were no statistically significant differences between the distributions of the room used throughout the three groups.

APPENDIX 8 - Statistical analysis on confounding variables across three groups
Distribution of seasons throughout the three groups

A chi-square for independence correlation was used to determine if there is a difference in the seasons across the three groups.

			Group			Total
			compressor	CD Player	No Noise (control)	
Season	Summer	Count	37	39	34	110
		Expected Count	38.1	38.1	33.8	110.0
	Winter	Count	33	31	28	92
		Expected Count	31.9	31.9	28.2	92.0
Total		Count	70	70	62	202
		Expected Count	70.0	70.0	62.0	202.0

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	.120 ^a	2	.942
Likelihood Ratio	.120	2	.942
Linear-by-Linear Association	.056	1	.813
N of Valid Cases	202		

There were no statistically significant differences between the seasons at the time of the test throughout the three groups.

APPENDIX 9 - Statistical analysis on confounding variables across three groups
Distribution of whether the parents were present or not throughout the three groups

A chi-square for independence correlation was used to determine if there is a difference in the whether the parents stayed in the room or not across the three groups.

			Group			
				CD Player	No Noise (control)	
Parents after Lights out	No	Count	31	24	29	84
		Expected Count	29.1	29.1	25.8	84.0
	Yes	Count	39	46	33	118
		Expected Count	40.9	40.9	36.2	118.0
Total		Count	70	70	62	202
		Expected Count	70.0	70.0	62.0	202.0

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	2.433 ^a	2	.296
Likelihood Ratio	2.457	2	.293
Linear-by-Linear Association	.055	1	.815
N of Valid Cases	202		

There were no statistically significant differences between whether the parents absent or present throughout the three groups.

APPENDIX 10 - Statistical analysis on confounding variables across three groups
Distribution on the sleep deficit throughout the three groups

A one-way ANOVA was used to determine if there is a difference in the mean scores in the sleep deficit across the three groups.

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
compressor	60	2.73	1.287	.166	2.40	3.07	0	6
CD Player	68	2.90	1.416	.172	2.55	3.24	0	9
No Noise (control)	55	2.91	1.418	.191	2.53	3.29	0	7
Total	183	2.85	1.370	.101	2.65	3.05	0	9

ANOVA

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	1.158	2	.579	.306	.737
Within Groups	340.558	180	1.892		
Total	341.716	182			

There were no statistically significant differences between the sleep deficits throughout the three groups.

APPENDIX 11 - Statistical analysis on confounding variables across three groups
Distribution of the appointment times given throughout the three groups

A chi-square for independence correlation was used to determine if there is a difference in the appointment times given across the three groups.

Crosstab

			Appointment Times				Total
			10am	11.30am	2pm	3.30pm	
Group	compressor	Count	7	20	27	6	60
		Expected Count	5.6	19.0	31.1	4.3	60.0
	CD Player	Count	4	25	36	3	68
		Expected Count	6.3	21.6	35.3	4.8	68.0
	No Noise (control)	Count	6	13	32	4	55
		Expected Count	5.1	17.4	28.6	3.9	55.0
Total	Count		17	58	95	13	183
	Expected Count		17.0	58.0	95.0	13.0	183.0

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	5.486 ^a	6	.483
Likelihood Ratio	5.700	6	.458
Linear-by-Linear Association	.354	1	.552
N of Valid Cases	183		

There were no statistically significant differences between the appointment times given throughout the three groups.

APPENDIX 12 - Statistical analysis on confounding variables across three groups
Distribution of males and females throughout the three groups

A chi-square for independence correlation was used to determine if there is a difference in the gender distribution across the three groups.

			M/F		Total
			Male	female	
Group	compressor	Count	29	31	60
		Expected Count	30.2	29.8	60.0
	CD Player	Count	39	29	68
		Expected Count	34.2	33.8	68.0
	No Noise (control)	Count	24	31	55
		Expected Count	27.7	27.3	55.0
Total	Count	92	91	183	
	Expected Count	92.0	91.0	183.0	

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	2.423 ^a	2	.298
Likelihood Ratio	2.430	2	.297
Linear-by-Linear Association	.214	1	.644
N of Valid Cases	183		

There were no statistically significant differences between males and females throughout the three groups.

APPENDIX 13 - Statistical analysis on confounding variables across three groups
Distribution of age throughout the three groups

A one-way ANOVA was performed in order to determine if there are significant differences in the mean age scores across the groups.

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
					Lower Bound	Upper Bound		
compressor	60	10.25	3.438	.444	9.36	11.14	4	16
CD Player	68	10.53	3.551	.431	9.67	11.39	4	17
No Noise (control)	55	9.95	3.440	.464	9.02	10.88	3	17
Total	183	10.26	3.470	.257	9.76	10.77	3	17

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	10.382	2	5.191	.428	.652
Within Groups	2181.028	180	12.117		
Total	2191.410	182			

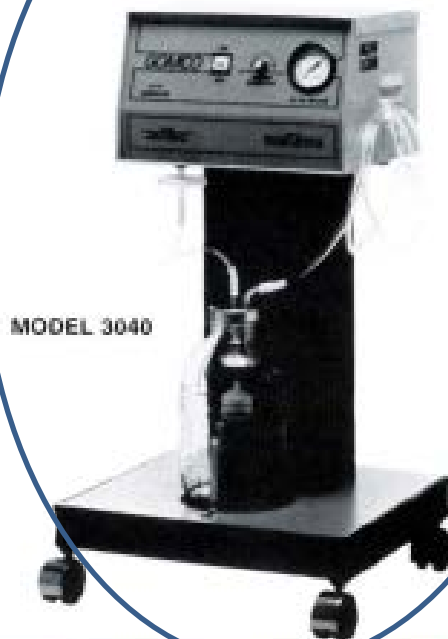
There were no statistically significant differences between ages throughout the three groups.

APPENDIX 14 – GOMCO

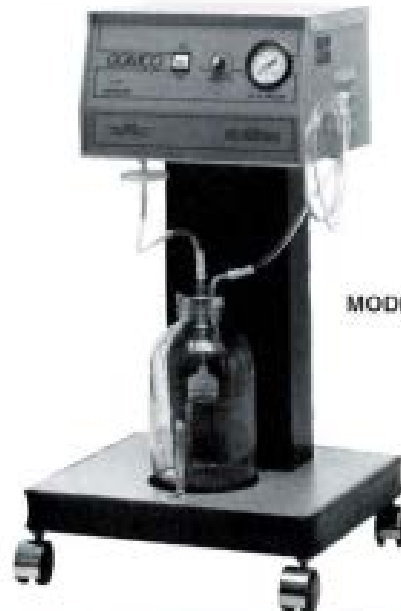
This is the GOMCO mobile aspirator model number 3040 used in the study. This was an out of use piece of equipment from another department with was electrical safety tested yearly by the EEG department and used routinely as a noise generator.

MOBILE ASPIRATORS

Models 3040, 4042



MODEL 3040



MODEL 4042

MOBILE ASPIRATORS – Gomco® stand-mounted units offer dependable, easy to regulate suction for hospital use. Stands include 3" non-marking casters, handy cord storage, chemical resistant stainless steel top, compact stand design, new float shut-off assembly, graduated one-gallon glass collection bottle or 2100 ml disposable canister, bacteria filter to help prevent fluid and aerosol contamination, and a hospital grade plug.

Suction systems are equipped with an easy-to-read gauge, calibrated in both inches Hg and mm Hg, and a suction regulating valve. These models also include illuminated on/off switches.

MODELS 3040/4042 – These units feature an insulated hidden motor and a durable stainless steel top. Model 3040 features a 1/8 horsepower diaphragm motor, and is UL listed and CSA certified. Model 4042 utilizes a 1/10 horsepower rotary compressor motor, and is UL listed.

MODEL	COLLECTION BOTTLE	MOTOR	COMPRESSOR	VACUUM RANGE	FLOW RATE	DIMENSIONS HxDxW	SHIPPING WEIGHT
3040	Glass	1/8 hp	Diaphragm	0-22 in. Hg	28 lpm	33 x 17 x 18 in.	70 lbs.
3041	Disposable			0-559 mm Hg		84 x 43 x 46 cm	32 kg
4042	Glass	1/10 hp	Carbon	0-25 in. Hg	30 lpm	33 x 17 x 18 in.	75 lbs.
4043	Disposable		Rotary Vane	0-635 mm Hg		84 x 43 x 46 cm	34 kg

APPENDIX 15 –Portable CD Player

(Brand - Groov-E Boombox Portable CD Player with AM/FM Radio Blue)



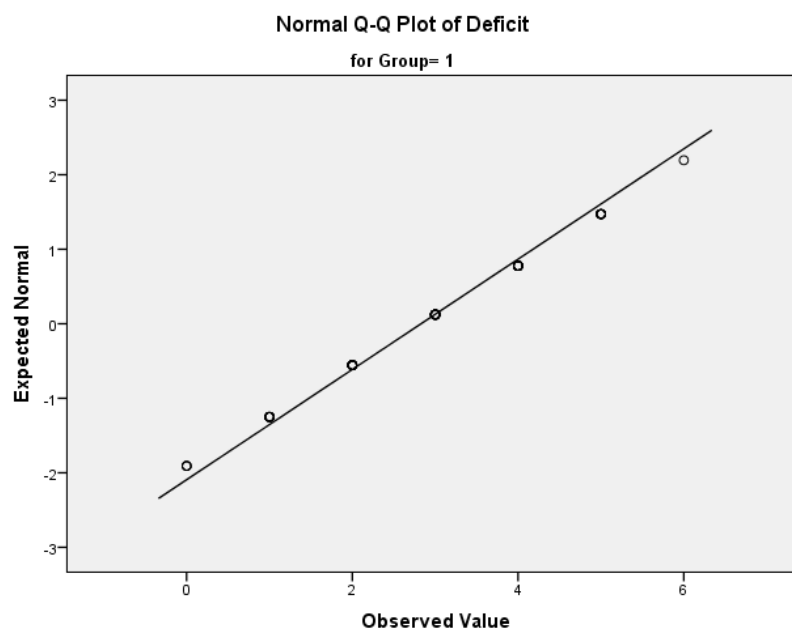
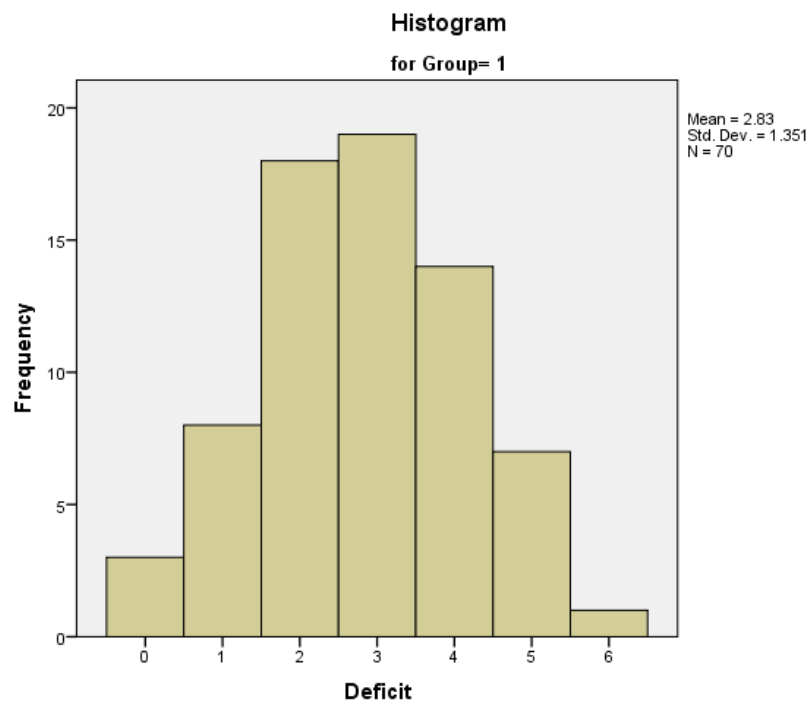
This was the CD player used for Group B to play the mechanical white noise recorded from the GOMCO suction machine in appendix 15, which was developed as another intervention for use in the study.

Specifications

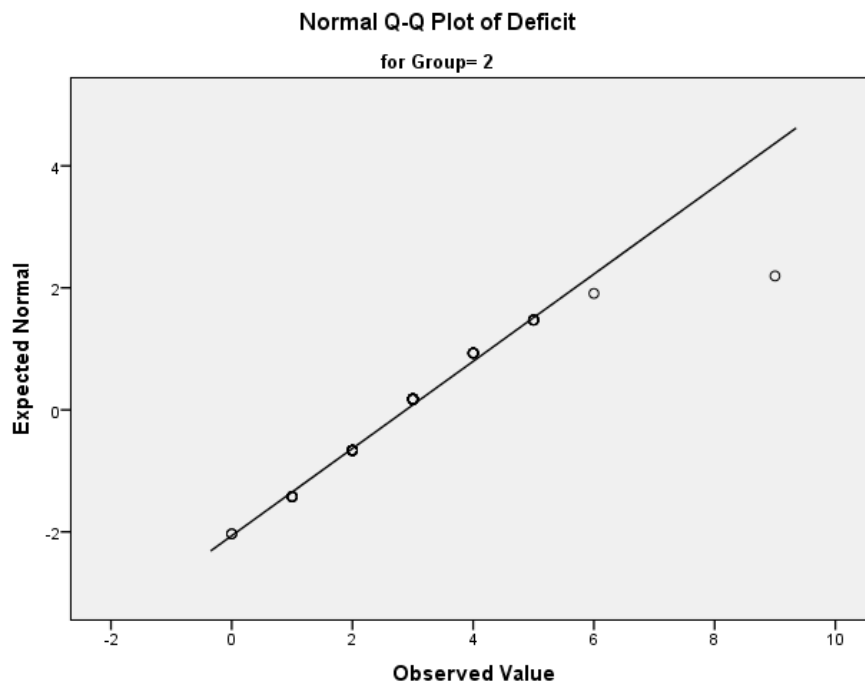
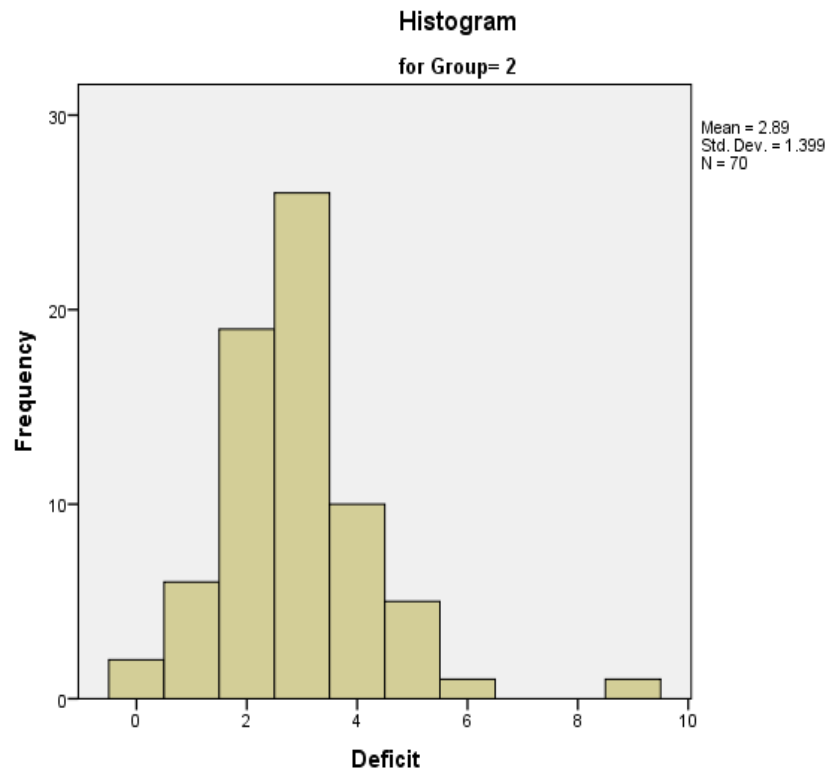
- CD/CD-RW compatible with AM/FM radio
- Built-in carrying handle
- 3.5mm auxiliary input

APPENDIX 16 – Descriptive Statistics

Distribution of Sleep deficit group 1

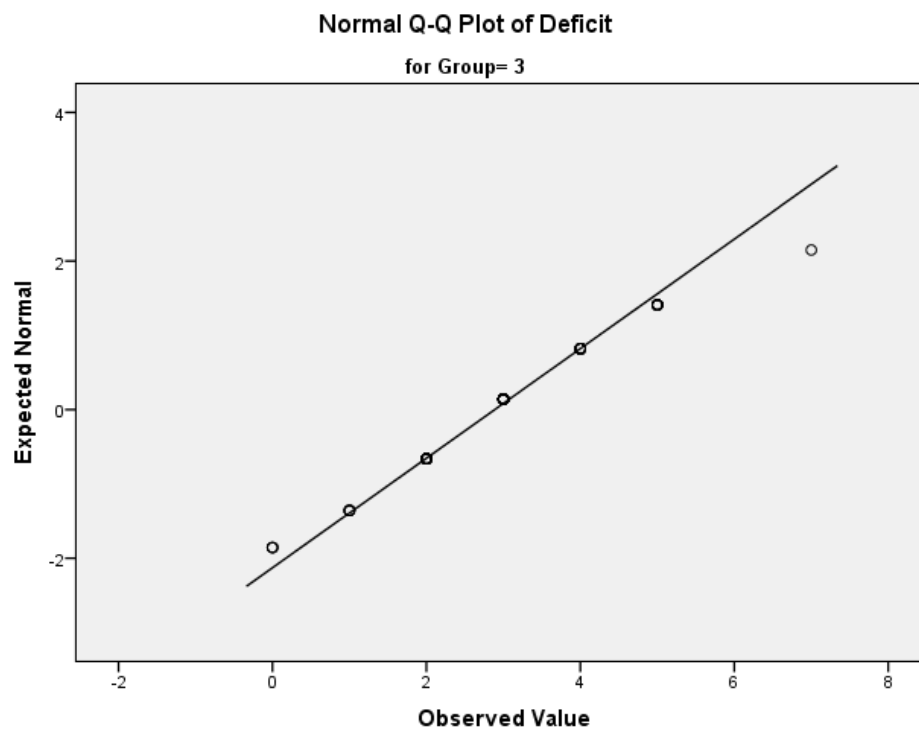
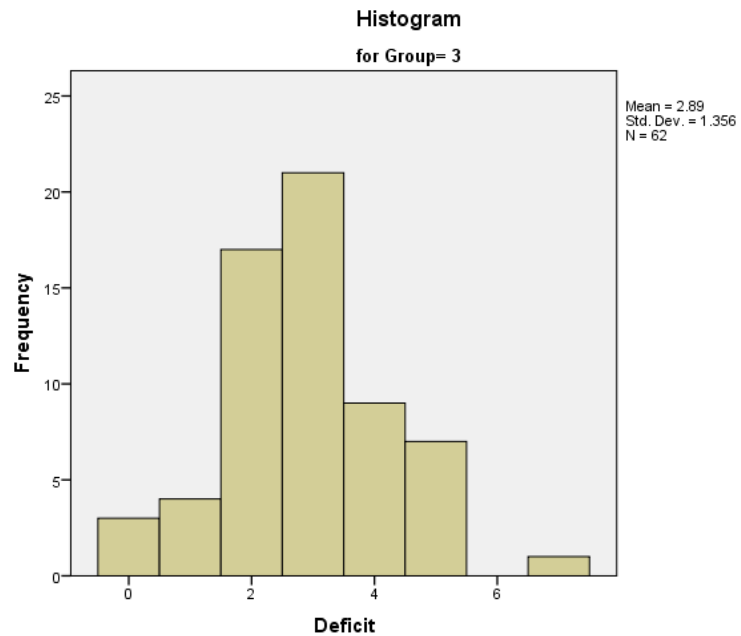


APPENDIX 17– Descriptive Statistics
Distribution of Sleep deficit group 2

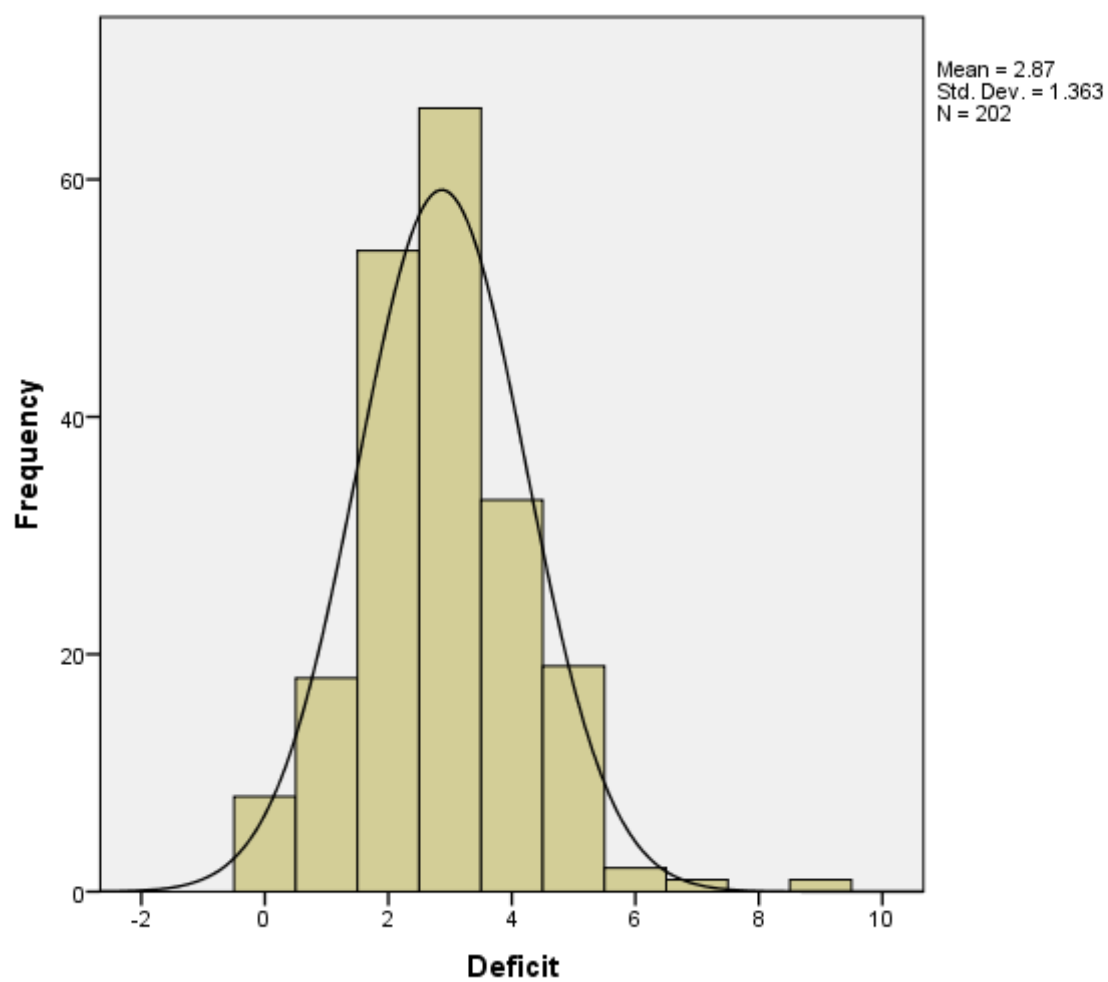


APPENDIX 18 – Descriptive Statistics

Distribution of Sleep deficit group 3



APPENDIX 19– Descriptive Statistics
Distribution of Sleep deficit across all groups



APPENDIX 20 – Boxplot of time to N2 sleep showing outliers

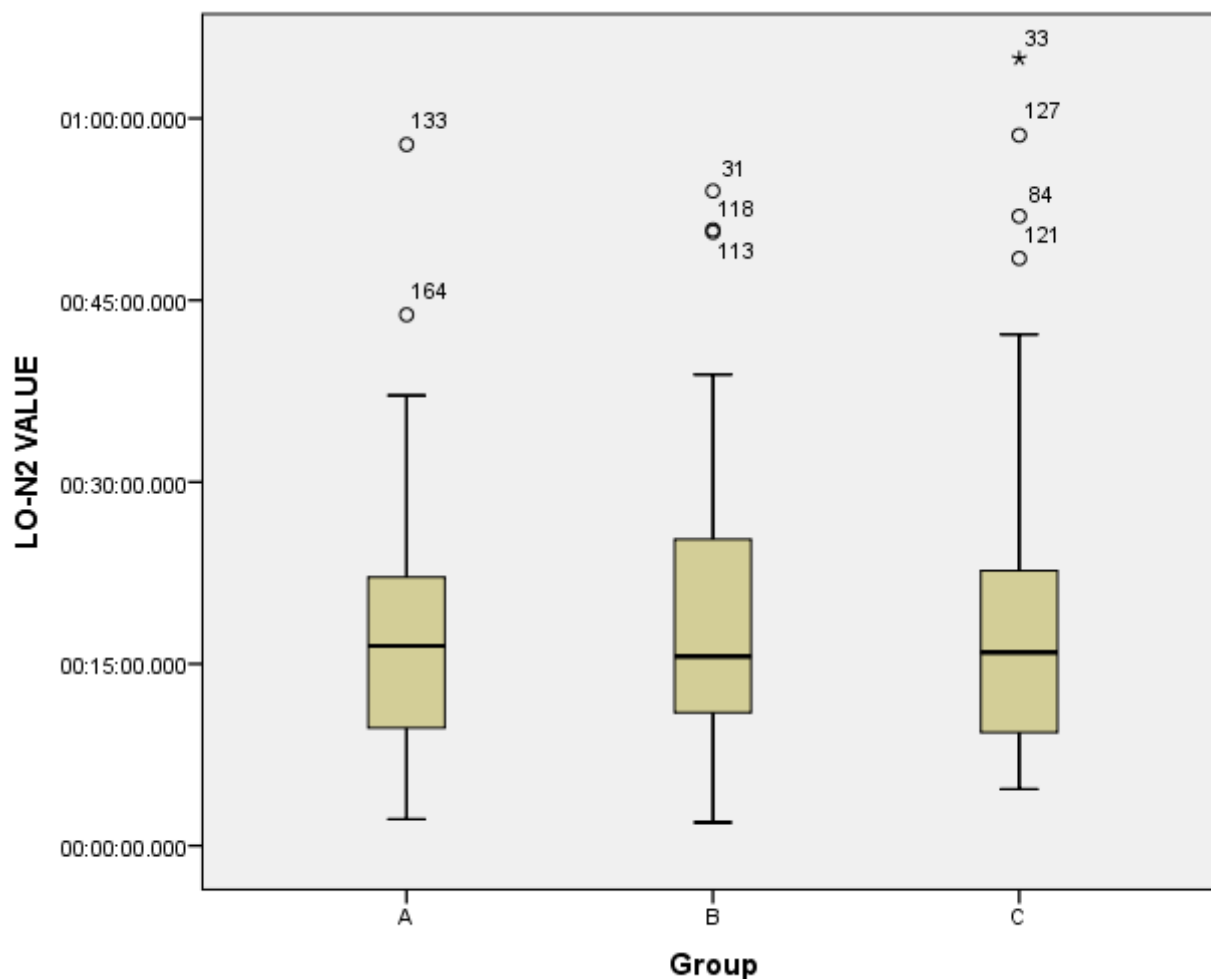


Table showing numbers of cases included in the above boxplot

	Group	Cases					
		Valid		Missing		Total	
		N	Percent	N	Percent	N	Percent
LO-N2 VALUE	A	60	100.0%	0	0.0%	60	100.0%
	B	68	100.0%	0	0.0%	68	100.0%
	C	55	100.0%	0	0.0%	55	100.0%

This boxplot shows only the patients that fell asleep however there are outliers and one extreme outlier.

**APPENDIX 21 – Mann-Whitney U tests of “time to N2 sleep compared all groups” –
With outliers removed**

Comparing Group A & B

Table showing Those who fell asleep (With Outliers in boxplot removed)				
	Group	N	Mean Rank	Sum of Ranks
LO-N2 VALUE	Group A Mechanical White noise (Suction machine)	56	60.31	3377.50
	Group B CD Player	66	62.51	4125.50
	Total	122		

Test Statistics	
	LO-N2 VALUE
Mann-Whitney U	1781.500
Wilcoxon W	3377.500
Z	-.342
Asymp. Sig. (2-tailed)	.733

Comparing Group A & C

Table showing Those who fell asleep (With Outliers in boxplot removed)				
	Group	N	Mean Rank	Sum of Ranks
LO-N2 VALUE	Group A Mechanical White noise (Suction machine)	56	57.20	3203.00
	Group C No Noise (control)	54	53.74	2902.00
	Total	110		

Test Statistics	
	LO-N2 VALUE
Mann-Whitney U	1417.000
Wilcoxon W	2902.000
Z	-.568
Asymp. Sig. (2-tailed)	.570

Comparing Group B & C

Table showing Those who fell asleep (With Outliers in boxplot removed)				
	Group	N	Mean Rank	Sum of Ranks
LO-N2 VALUE	Group B CD Player	66	63.29	4177.00
	Group C No Noise (control)	54	57.09	3083.00
	Total	120		

Test Statistics	
	LO-N2 VALUE
Mann-Whitney U	1598.000
Wilcoxon W	3083.000
Z	-.971
Asymp. Sig. (2-tailed)	.332

Despite removing the outliers highlighted by the boxplot the results remained not statistically significant.