Abstract
Alzheimer’s disease, the most common form of dementia, is an increasing problem in Europe with projections of prevalence doubling by 2050. This neurodegenerative disease is characterised by gradual cognitive decline due to degeneration of neurons which ultimately leads to death. Currently no medications can stop the neuronal degeneration however some medications have been developed to decelerate the decline in cognitive abilities, called cholinesterase inhibitors. This research seeks to develop a greater understanding of the effects of cholinesterase inhibitors on sleep as this medication is known to act on sleep-promoting neurons in the brain. This interaction will be investigated by determining the patients’ sleep patterns before and after medication in comparison to healthy age-matched controls.

Introduction
Alzheimer’s disease (AD) has symptoms of disruption of the sleep-wake cycle which causes significant problems thought to lead to earlier institutionalisation. These sleep problems include fragmentation of sleep during the night and more frequent napping during the day. A reduction in acetylcholine at the synaptic cleft is thought to be involved in the memory impairments observed in AD. The diagram (right) shows the cholinesterase inhibitor, donepezil, binding to the cholinesterase enzymes to inhibit them from breaking down the acetylcholine in the synaptic cleft. This therefore increases the amount of acetylcholine, improving neural transmission and cognitive functioning. The cholinergic neurons affected by this medication are also known to be involved in sleep, especially rapid eye movement (REM) sleep initiation and maintenance.

Hypotheses and aims
Based upon previous research the following are predicted to be observed:
Improvement in cognition observed across cholinesterase inhibitor treatment; alterations in REM sleep, especially increased REM sleep; decreased occipital slowing ratio; decreased frontal delta and theta.

Study Design
Part A: aimed at 194 moderate AD patients, any cholinesterase inhibitor, questionnaires only.
Part B: aimed at 31 healthy age-matched controls and moderate AD patients specifically prescribed Donepezil, questionnaires, EEG, Actigraphy, CANTAB tests.
All patients complete assessments at baseline when drug-naive and again 9 weeks after medication initiation. Controls follow the same timeline.

Preliminary results
1. Participant Screening: Patients (n=6) and controls (n=6) were confirmed to not be different in terms of age, gender and chromosome (preference of time of day of activity)(p>0.05).
2. Sleep Characteristics: Despite not being significant, at baseline, trends indicate that patients had more naps, longer time asleep and more daytime dysfunction than healthy age-matched controls. After medication initiation, patients’ sleep became more dysfunctional in comparison to controls.

3. Circadian: Patient’s activity levels were lower and more fragmented during sleep than the control’s at baseline. After medication initiation, both the amplitude of the patient’s activity and their sleep period’s activity fragmentation increased. Actograms below display the patient’s and control’s activity at both assessments.

4. Sleep architecture: Contrary to predictions, the patient had a reduction in REM sleep after medication initiation. The patient’s REM density (the density of rapid eye movements) increased 4 fold after medication, much higher than the control’s.

5. Cholinesterase Inhibitor effectiveness: Patients scored lower on measures of memory and attention (e.g. reaction times were longer) than controls at baseline. Patients improved on most measures after medication initiation. Functioning scores were much lower for patients than controls at both assessments (p<0.05).

Conclusions
Preliminary conclusions suggest that patients have poorer sleep quality and cognitive measures than controls at baseline. Patients appear to improve in terms of cognition suggesting positive treatment response. On the contrary, patients’ sleep appears to become more dysfunctional after medication initiation. A novel finding so far is the reduction in REM sleep after medication initiation, the difference from previous findings may due to the timing of this assessment. Further longitudinal data collection will show whether these current trends will be observed in a larger sample. This study could add to the information currently known about ChEIs’ effect on memory by detailing their associated sleep symptoms possibly improving its effective prescription.

References

Acknowledgements
This work is supported by NIHR Biomedical Research Centre, Oxford, UK. The author would like to acknowledge the OPTIMA research nurses for their teaching and assistance with recruitment; the OXMAC clinic, Oxford; OBMH clinics and CMHTs for referrals. Furthermore the author would especially like to thank all the participants and their families involved with the study.