

# FINAL PROJECT REPORT

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***Name:***

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***Project Title:***

Effect of Obstructive Sleep Apnea on Microsleeps & Cerebral Blood Flow
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## Summary

Obstructive sleep apnoea (OSA) is associated with increased risk of hypertension, cardiovascular disease, stroke, and cognitive dysfunction. While it is well known that OSA leads to chronic periodic blood oxygen desaturation during sleep, in this study we also found an association between moderate-severe OSA and decreased cerebral blood flow when awake. This study also found a relationship between OSA severity and microsleep propensity. OSA is associated with a substantially increased risk of car accidents (injurious and fatal). Our research supports the hypothesis that this increase in car accidents is likely to be due to increased propensity for 'fall-asleep-at-the-wheel' events. Ultimately, this research aims to reduce OSA-related vascular and cognitive impairment, and microsleep-related deaths and injuries by providing evidence for the need for increased funding for OSA screening and treatment.

**Please copy the "Specific Objective(s)" statement, entered on your application form, in the space below.**

This research aims to answer the following questions:

1. Do people with Obstructive Sleep Apnea (OSA) ( $\geq 5$  events/h) have a higher propensity for microsleeps than age- and sex-matched people without OSA?
2. Is there a correlation between OSA severity and microsleep propensity?
3. Do people with moderate-severe OSA ( $> 30$  events/h) have a higher propensity for microsleeps than matched people without OSA?
4. Do people with mild OSA (5–30 events/h) have a higher propensity for microsleeps than matched people without OSA?
5. Do people with OSA have differences in cerebral blood flow (CBF) as measured via Arterial Spin Labeling (ASL) compared to matched people without OSA?
6. Is there a correlation between OSA severity and resting CBF?

**Briefly describe how successful you were in achieving the stated objective(s). If the objective(s) was not achieved, explain why that is the case and describe what you did manage to achieve.**

1. Do people with Obstructive Sleep Apnea (OSA) ( $\geq 5$  events/h) have a higher propensity for microsleeps than age- and sex-matched people without OSA?

Group	N	Mean age (range)	Mean ESS (range)	Mean microsleep (range)	Mean AHI (range)
Control	19	50.0 (41–81)	4.5 (0–9)	10.4 (0–116)	1.2 (0.0–4.9)
Mild OSA	11	55.1 (41–64)	6.3 (1–20)	14.6 (0–52)	10.0 (5.2–14.8)
Moderate-Severe OSA	8	59.0 (50–70)	6.5 (1–14)	52.3 (0–187)	30.0 (15.7–52.8)

There was no significant difference in microsleep propensity between controls and all people with OSA (mean  $10.4 \pm 26.8$  vs  $30.5 \pm 50.7$ ,  $p = .13$ ). Despite what appears to be a large mean increase in microsleep propensity in the OSA group (i.e., nearly 3 times as many), there were very large standard deviations of the mean in each group, indicating very large variability in microsleep propensity across both the OSA and control groups.

2. Is there a correlation between OSA severity and microsleep propensity?

There was a correlation between OSA severity (as defined by number of events per hour) and microsleep propensity ( $r = .33$ ,  $p < .05$ ). Again, it should be noted that there was very large variability in microsleep propensity across all three groups. For example, there were people in each of the groups who had no microsleeps – including  $n=2$  in the moderate-severe OSA group. While over half the control participants had no microsleeps, one of the control participants had 116 microsleeps. Thus, while there is a relationship between OSA severity and microsleep propensity, other factors are also very important (e.g., trait sleepiness). The importance of trait sleepiness on microsleep propensity and cerebral blood flow is something that we have noted in our previous research in healthy normally-rested and sleep-restricted participants (Innes et al., 2010; Innes et al., 2011; Poudel et al., 2011, 2012; Innes et al., 2013).

3. Do people with moderate-severe OSA (>30 events/h) have a higher propensity for microsleeps than matched people without OSA?

People with moderate-severe OSA had a higher propensity for microsleep than controls (mean  $52.3 \pm 71.8$  vs  $10.4 \pm 26.8$ ,  $t[25] = 2.25$ ,  $p = .03$ ).

4. Do people with mild OSA (5–30 events/h) have a higher propensity for microsleeps than matched people without OSA?

There was no significant difference in microsleep propensity between controls and people with mild OSA (mean  $10.4 \pm 26.8$  vs  $14.6 \pm 19.0$ ,  $t[28] = 0.46$ ,  $p = .65$ ).

5. Do people with OSA have differences in cerebral blood flow (CBF) as measured via Arterial Spin Labeling (ASL) compared to matched people without OSA?

Analysis of regional differences in cortical blood flow was undertaken. Covariates of no interest were included so that any differences between groups were over and above any differences in cortical blood flow due to age, sex, body mass index, drowsiness during ASL scan, or mean total grey matter CBF.

Following multiple comparisons correction there was no difference in regional cerebral blood flow between people with mild OSA and controls. However, controls had greater cerebral blood flow than those with moderate-severe OSA in 3 clusters:

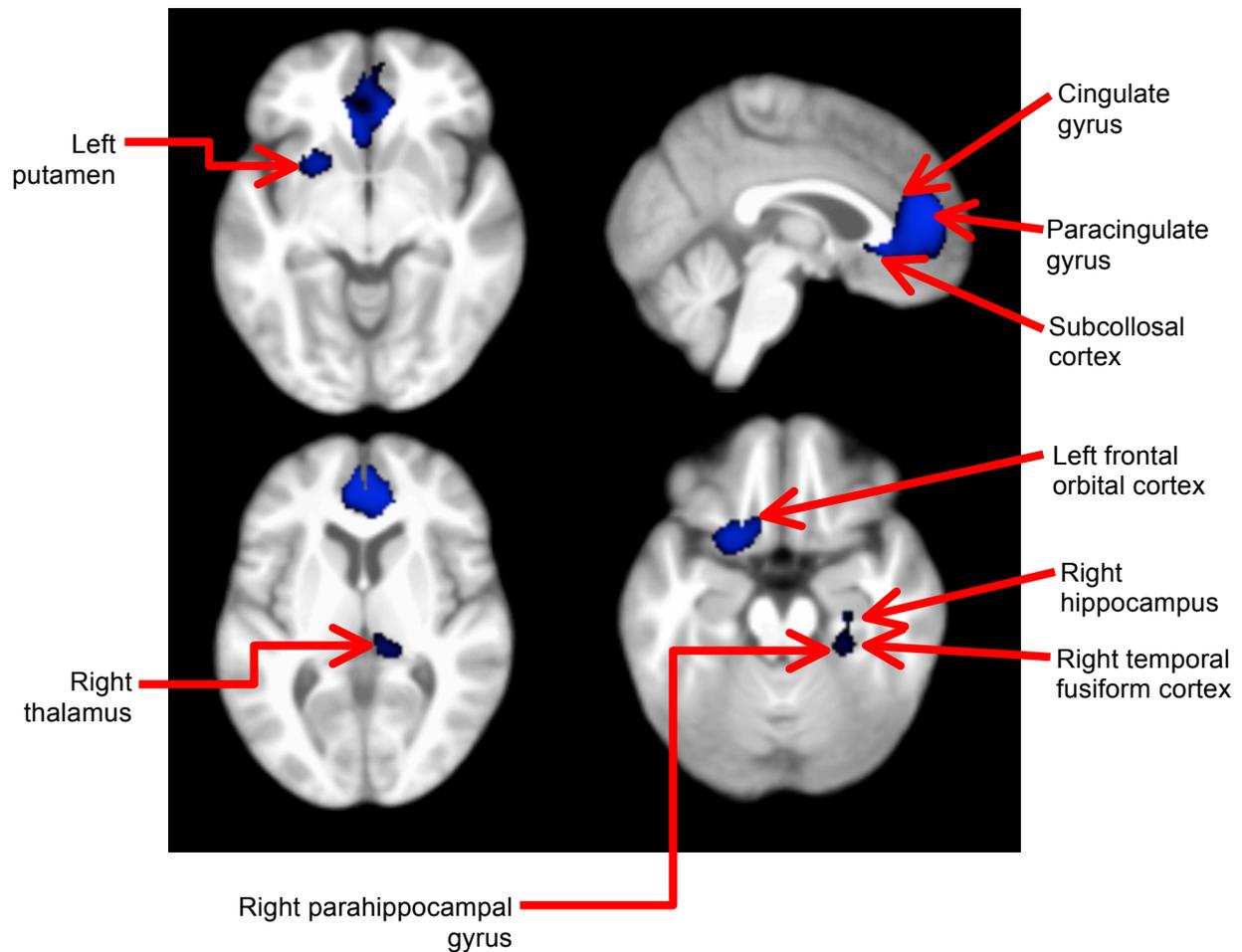
- Cluster 1 was a large cluster (5114 voxels) incorporating bilateral paracingulate gyrus, bilateral cingulate gyrus (anterior division), bilateral subcallosal cortex, left putamen, and left frontal orbital cortex.
- Cluster 2 (371 voxels) was a right lateralised cluster incorporating temporal fusiform cortex (posterior division), parahippocampal gyrus, and hippocampus.
- Cluster (291 voxels) was a right lateralised cluster located in the thalamus

Figure 1 (next page) shows the areas of decreased blood flow in people with moderate-severe OSA.

6. Is there a correlation between OSA severity and resting CBF?

There was a trend for a correlation between OSA severity (as defined by number of events per hour) and total grey matter CBF ( $r = .28$ ,  $p < .08$ ) but this just failed to reach significance.

**Figure 1. Brain regions showing decreased blood flow in people with moderate-severe OSA compared with controls.**



**Briefly describe any interesting outcomes which might not have been considered in your original objectives (if any).**

Many more people recruited to be healthy control participants turned out to have OSA than we had anticipated – especially those older than 50 years. Nine people originally recruited as controls were diagnosed with mild OSA and five were diagnosed with moderate-severe OSA. Although we excluded volunteers who had a previously diagnosed sleep disorder, those taking sedating or stimulating medications (including drinking 4 or more cups of coffee or tea per day), and those with unusual sleep schedules, we did not include an upper limit on self-reported excessive daytime sleepiness measure for our control group. We considered that if we had an upper limit sleepiness exclusion criterion for controls but not for people with OSA that this could add a false separation between our groups based on daytime sleepiness rather than OSA *per se*. That is, would we be able to determine whether the differences between

the groups were due to OSA or to increased sleepiness in the OSA group? Ultimately, only 2/37 people recruited as controls met the criteria for excessive daily sleepiness and those two people did have OSA. It is possible that these participants volunteered for the study as they had a suspicion that they may have OSA. Interestingly, 14/19 people who were diagnosed with OSA did not meet the criteria for excessive daily sleepiness either. This supports the findings of Weaver *et al.* (2004) who reported only a weak correlation between OSA severity and self-reported sleepiness.

People with severe OSA frequently reported other serious health conditions which could affect blood flow and drowsiness (either by themselves or due to medications to treat) and which excluded them from the study. People with severe OSA also frequently reported other sleep disorders such as periodic limb movements and central apnoea which also excluded them from the study. The findings of the study are thus limited to those people without other sleep disorders or serious health conditions and it is possible that there are more widespread and substantial changes in CBF in people with additional health conditions.

We are planning a longitudinal study investigating cerebral blood flow, microsleeeps, and cognitive function at baseline and following 6 months of Continuous Positive Airway Pressure (CPAP) treatment in people with moderate and severe OSA. CPAP works by blowing air into the pharynx and raising the pressure sufficiently to hold the airway open. CPAP treatment has been shown to have beneficial effects on vascular function. Amelioration of sleep fragmentation and excessive sleepiness can also improve attentional processes. However, cognitive dysfunction can persist even after compliant CPAP treatment and it is thought that the chronic intermittent hypoxia associated with long-term non-treatment of OSA may lead to permanent structural and chemical changes in the brain. Unfortunately, in New Zealand only those with the most severe OSA symptoms (e.g., ~25% of referrals to the Sleep Unit at Christchurch Hospital) meet the threshold for funded CPAP treatment while the majority of referrals remain largely untreated. Our proposed research study will determine whether CPAP treatment leads to improved cerebral perfusion and cognitive function in people with moderate or severe OSA or whether the decreased CBF that we have observed in our current study indicate permanent changes in function.

## REFERENCES

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