

EFFECT OF CPAP TREATMENT FOR OSA ON VISUAL PROCESSING OF DEGRADED WORDS

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Abstract

Background: In a previous uncontrolled study, CPAP therapy for OSA improved vision in patients with diabetic macular oedema.

Objectives: We have investigated whether the above improvement in vision (or visual processing) might have been due to reduced sleepiness, rather than a true improvement in retinal function.

Methods: Twelve normal control subjects, and 20 patients with OSA, were tested for their ability to recognise degraded words, using a computer programme that displays five-letter words, every four seconds, for ten minutes, with variable amounts of the bottom half of the word missing; the % of the word necessary to achieve correct identification on average half the time was 'hunted' (the test score). All subjects were tested twice, 2 to 3 weeks apart; the OSA group after the commencement of CPAP. The Epworth sleepiness score in patients was measured at the same visit.

Results: The test score at visit 1 was 26.7% for normal subjects, and 31.6% for patients with OSA. For visit 2, the test score was 25.0% for normal subjects, and 29.9% for patients with OSA. The groups showed a small and identical improvement over the trial period in the test score, of 1.7% ($p=0.01$ and $p=0.03$, normal and OSA groups respectively). The group with OSA experienced a drop in ESS of 7.5 (SD5.5) points following treatment.

Conclusion: The small and identical improvement in both groups suggests only a similar learning effect rather than any improvement due to reduced sleepiness.

Introduction

The WHO statistics suggest the number of adults with diabetes in the world is estimated to increase by 122% from 135 million in 1995 to 300 million in 2025 (1). Diabetic retinopathy, a microvascular complication of the diabetes, is emerging as one of the most important causes of blindness in people of working age in western countries.

Obstructive sleep apnoea (OSA) is the commonest form of sleep disordering breathing. In patients with type 2 diabetes, the prevalence of OSA is significantly increased at 17%, compared to 6% in a control population (2). Within the sub-set of patients with type 2 diabetes and diabetic macular oedema, there is an even higher prevalence of OSA, estimated at 54% (3).

In a study on men with type 2 diabetes, diabetic retinopathy was significantly more advanced in those with OSA, compared to those without (4). The research did not find a cause for these findings; however, it was suggested that in patients with OSA, the nocturnal episodes of repetitive hypoxia, surges in blood pressure, increased catecholamine secretion, and diurnal hypertension, might all be responsible.

Consequently it was proposed that if the nocturnal apnoea, desaturations, blood pressure surges, and arousals were abolished by the use of Continuous Positive Airway Pressure (CPAP), then this might arrest the progression of diabetic retinopathy, or possibly even reverse the visual deterioration.

In an uncontrolled proof of principle study (5), Mason et al identified a significant visual improvement of one line on the Logarithm of the Minimum Angle of Resolution (LogMAR, a test of visual acuity) in patients with OSA and diabetic macular oedema, following 6 months proven CPAP usage, compared with those who did not use their CPAP.

This was not a randomised controlled trial, and those patients who used their CPAP also experienced the expected improvement in sleepiness compared to those that did not use their CPAP, suggesting other potential hypotheses for the improvement in vision apart from a reversal of retinal damage. For example, there might be improved cortical visual processing, or even simply an increased enthusiasm for performing the LogMAR test.

We performed the following study with the aim to determine whether a reduction in sleepiness might cause an improvement in visual image processing, thus providing a potential alternative explanation for the improved visual acuity shown by Mason et al (5), rather than an improvement in retinal function.

Methods

Design

Intervention study, control subjects versus patients with OSA.

Subjects

All subjects were between 18 and 70. Twenty patients with newly diagnosed OSA, based on history, overnight respiratory polygraphy (VisiLab, Stowood Scientific Instruments, Oxford, UK) and an ODI of $>7.5/h$ and ESS >7 were recruited. All were set up on CPAP therapy. Twelve unmatched normal subjects were also recruited and both groups had visual processing testing at 0, and after 2 to 3 weeks. They did not have any known retinal pathology or visual impairment not corrected by glasses or contact lenses. Subjects were literate and none had a diagnosis of learning difficulty or had been taking psychoactive medications for mental disorders. Participants were not using recreational drugs.

Techniques

'Sleepy Eyes' computer program

A specially written computer program, aptly named 'Sleepy Eyes', was written. The programme aimed to simulate, in individuals with normal vision, the degraded vision of a patient with diabetic retinopathy and thus the requirement to process and interpret the image. The programme functions by displaying randomly selected 5 letter words written in capital letters (1.5 cms tall) on a separate screen for three seconds, followed by a one second break for ten minutes. The test starts with the top 50% of each letter of the word visible. The amount of all the letters of the word subsequently visible varies depending on how well the subject is performing; increasing correct word identification reduces the visible portion of the word making it harder to read, whilst deteriorating identification increases the visible portion making it easier to read (figure 1). Thus the individual's performance is 'hunted', centring on an average of half of the words being correctly identified. This is analogous to a hearing test that hunts the auditory threshold by increasing and decreasing the volume of the tones. This generates the 'test score', which is the % of the word needing to be shown for on average half to be correctly identified. Different word lists were used on the two test occasions to reduce any learning effect.

The Sleepy Eyes software generates a Microsoft Excel spreadsheet containing the 150 responses from the 10 minute test. From this, the last 100 values (equivalent to 6 minutes

and 40 seconds) were averaged. This gives a single value for the % of words visible that are being recognised correctly on average half the time.

Protocol

Participants were seated in a quiet, well lit room and positioned in such a way that they are unable to see the experimenter's laptop screen. Glasses or contact lenses were worn as usual. Subjects sat 1 metre in front of the second screen. The total test duration was 30 minutes. Subjects were tested for 10 minutes (test 1, practice, data not used), given a 10 minute break, and then retested for a further 10 minutes (test 2, the data used). .

Subjects were asked to read aloud the word displayed on the separate monitor. The tester entered (Y) or (N) on the laptop according to the correctness of the answer given by the subject. Each word was displayed for 3 seconds after which, should no answer be given, a (N) was automatically entered. There was a 1 second pause between each word where the screen was blank.

This protocol was approved by The South West Research Ethics Committee, number 12/SW/0154.

Data analysis

Statistical analysis was done using Student's *t* test, and Pearson's correlation analysis. A *p* value of 0.05 or less was considered statistically significant. The primary outcome was change over the trial period in the % of words visible that are being recognised correctly on average half the time; patients with OSA treated with CPAP, versus controls.

Results

12 young adult normal subjects (6 male and 4 female, age 34.2 SD 13.3, range 21 to 62), and 20 patients with OSA (17 male and 3 female), were tested at baseline (visit 1), and at 2 to 3 weeks (visit 2). The characteristics of the patients are shown in table 1. Three patients with OSA described themselves as being slightly dyslexic but performed similarly to the rest. The test scores are shown in table 2, and graphically in figures 2 and 3. Normal subjects at baseline were significantly better at the test than the patients, needing 5% less of the words to be visible for 50% recognition ($p=0.03$). There was a similar, statistically significant, improvement in test scores across the 2 to 3 weeks in both groups, with no difference between the groups ($p=0.98$). In the patients with OSA, there was a highly significant reduction in ESS of 7.5 points following CPAP (SD 5.5, $p<0.001$). There was no statistically significant correlation between the improvement in test score and the improvement in either ESS ($r = -0.05$, $p>0.01$, figure 4), or the CPAP compliance ($r = 0.09$, $p>0.01$).

Discussion

Normal subjects performed at baseline a little better than the patients with OSA, and we have no data to help explain why. The normal subjects were younger, drawn from friends of the experimenters, and were mostly professionals. Both the normal subjects, and patients with OSA treated with CPAP, showed a small but significant improvement in test score over the trial period. As the improvement is essentially identical in both groups, this suggests that the improvement is probably due to a similar learning effect, rather than the considerable reduction in sleepiness seen in the CPAP treated group. This is further supported by there being no correlation between the change in sleepiness score, and change in test score, in the OSA group, despite a significant and considerable reduction in sleepiness over the trial period of over 7 points on the Epworth Sleepiness score (ESS). Other studies looking at vigilance and cognitive changes after CPAP therapy for OSA have shown clear improvements in many dimensions, but these usually involve prolonged testing to amplify the effects of increased daytime sleepiness (6). The 10 minute duration used in our study was presumably too short to reveal these vigilance effects.

This study attempted to simulate degraded vision in normal subjects, using the idea of reducing the amount of a word visible. Alternative methods were considered, such as blurring, but these did not provide as clear or as precise a measurement as our approach. Subjects have to concentrate to try and recognise the word from the limited amount available and this should depend on enthusiasm and effort. To some extent this therefore recreates the problem of reading letters on a vision chart when visual acuity is reduced. However we accept that it is not the same, and different ways of trying to simulate the effects of macula oedema on vision might give a different result. In addition, our test period of 10 minutes is somewhat longer than usually taken to read a vision chart. However, if anything, this should have increased the chances of finding a difference between our normal subjects and patients with CPAP treated OSA due to their reduced sleepiness. Although three subjects used their CPAP for <3 h/night during the treatment period, the average was 4.8 h/night and produced a good improvement (and range of improvement) in ESS.

Thus, this study has not provided evidence to support the hypothesis that the improved visual acuity on the LogMAR chart, seen in the proof of principle study by Mason et al following CPAP therapy for OSA in patients with diabetic macular oedema (5), is likely to have been simply an 'artefact' of improved enthusiasm for reading the chart. A robust randomised controlled trial is therefore justified to establish if treating OSA with CPAP can truly improve visual acuity in patients with co-existent diabetic retinopathy.

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Tables

Table 1. Subject characteristics

17 Men, 3 women	Patients with OSA (20)		
	Mean	SD	Range
Age	50.7	12.9	21 – 75
Body Mass Index (kg/m ²)	38.0	8.6	28.3 – 55.6
Neck circumference (cm)	45.3	4.0	35.6 – 53.3
Epworth Sleepiness	15.3	4.1	8 – 22
Oxygen desaturation Index (events/h)	39.5	23.7	9.1 – 96.9
CPAP Compliance (h/night)	4.8	2.1	0 – 7.8

Table 2. Test score results

	Visit 1	Visit 2	Average change in test score	95% confidence intervals	p value
Normal subjects N=12 (SD)	26.7 (3.6)	25.0 (3.2)	-1.7 (1.9)	-0.58 to -2.80	P=0.01
Patients with OSA treated with CPAP N=20 (SD)	31.6 (8.1)	29.9 (9.3)	-1.7 (3.2)	-0.22 to -3.11	P=0.03

Figure legends

Figure 1 – An example of a test word used by the Sleepy Eyes programme where 50% of the word has been removed (lower word), and as seen by the researcher (upper word).

Figure 2 – Individual and mean (•) test score data on the normal subjects ($p=0.01$, $n=12$).

Figure 3 – Individual and mean (•) test score data on the patients with OSA, and treated with CPAP ($p=0.03$, $n=20$).

Figure 4 – Relationship between change in test score and change in ESS
($r = -0.05$, $p = 0.83$)