Effect of Continuous Positive Airway Pressure Treatment for Obstructive Sleep Apnoea on Visual Processing of Degraded Words

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Key Words

Continuous positive airway pressure · Visual impairment · Sleep apnoea · Type 2 diabetes · Diabetic maculopathy

Abstract

Background: In a previous uncontrolled study, continuous positive airway pressure (CPAP) therapy for obstructive sleep apnoea (OSA) improved vision in patients with diabetic macular oedema. **Objectives:** We 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, by means of a computer programme displaying 5-letter words every 4 s for 10 min, with variable amounts of the bottom half of the word missing; the percentage of the word necessary to achieve correct identification on average half the time was 'hunted' (the test score). All subjects were tested twice, 2–3 weeks apart; the OSA group after the commencement of CPAP. The Epworth Sleepiness Score (ESS) 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. At 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 $p = 0.03$ for the normal and OSA groups, respectively). The group with OSA experienced a drop in ESS of 7.5 (SD 5.5) 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.

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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 diabetes, is emerging as one of the most important causes of blindness in people of working age in Western countries.

TOUGH

TOUGH

Fig. 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).

Obstructive sleep apnoea (OSA) is the commonest form of sleep-disordered 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 subset 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 than in 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, Mason et al. [5] 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 of proven CPAP usage, compared with those who did not use their CPAP.

This was not a randomised controlled trial, and the 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 this study with the aim of determining whether a reduction in sleepiness might cause an improvement in visual image processing, thus potentially

attributing the improved visual acuity shown by Mason et al. [5] in their study to something other than an improvement in retinal function.

Methods

Design

This was an intervention study of control subjects versus patients with OSA.

Subjects

All subjects were between 18 and 70 years of age. Twenty patients with newly diagnosed OSA, based on history, overnight respiratory polygraphy (VisiLab, Stowood Scientific Instruments, Oxford, UK), an oxygen desaturation index (ODI) >7.5/h and an Epworth Sleepiness Score (ESS) of >7 points were recruited. All were set up on CPAP therapy. Twelve unmatched normal subjects were also recruited and both groups had visual processing testing at baseline and after 2–3 weeks. They did not have any known retinal pathology or visual impairment not corrected by glasses or contact lenses. All subjects were literate and none had a diagnosis of learning difficulty or had been taking psychoactive medications for mental disorders. No participants were using recreational drugs.

Techniques

'Sleepy Eyes' Computer Programme

A specially written computer programme, 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 capitals (1.5 cm tall) on a separate screen for 3 s, followed by a 1 s break for 10 min. The test starts with the top half of each letter of the word being visible. After this, how much of all the letters of the word is 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, but deteriorating identification increases the visible portion making it easier to read (fig. 1). Thus the individual's performance is 'hunted', aiming for 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 percentage of the word needing to be shown for on average half to be correctly identified. Different

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

Table 1. Subject characteristics

17 men, 3 women	Patients with OSA (20)
Age, years	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)
ESS	15.3±4.1 (8–22)
ODI, events/h	39.5±23.7 (9.1–96.9)
CPAP compliance, h/night	4.8±2.1 (0–7.8)

Values are mean ± SD (range).

Table 2. Test score results denoted as a mean ± SD

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

word lists were used on the 2 test occasions to reduce any learning effect.

The Sleepy Eyes software generates a Microsoft Excel spreadsheet containing the 150 responses from the 10-min test. From this, the last 100 values (equivalent to 6 min and 40 s) were averaged. This gives a single value for the percentage of words visible that are being recognised correctly on average half the time.

Protocol

Participants were seated in a quiet, well-lit room and were positioned in such a way that they were unable to see the researcher'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 min. Subjects were tested for 10 min (test 1 was a practice, i.e. data not used), given a 10 min break and then retested for a further 10 min (test 2, data used).

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

This protocol was approved by the South West Research Ethics Committee, No. 12/SW/0154.

Data Analysis

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

Results

Twelve young adult normal subjects, aged 34.2 years (SD 13.3 years and range 21–62 years) and 20 patients with OSA (17 male and 3 female), were tested at baseline (visit 1) and at 2–3 weeks (visit 2). The characteristics of the patients are shown in table 1. Three patients with OSA described themselves as being slightly dyslexic, but they performed similarly to the rest. The test scores are shown in table 2, figure 2 and figure 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 2–3 weeks in both groups, with no difference between them ($p = 0.98$). 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 ($r = -0.05$, $p = 0.83$; fig. 4) or the CPAP compliance ($r = 0.09$, $p = 0.71$).

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

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

Discussion

Normal subjects performed a little better at baseline than the patients with OSA, but we have no data to help explain why. The normal subjects were younger, drawn from among friends of the researchers 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 was 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 ESS or in test score in the OSA group, despite a significant and considerable reduction in sleepiness of >7 points on the ESS over the trial period. 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-min 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 how much of a word is visible. Alternative methods such as blurring

were considered, 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 that is visible 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 min was somewhat longer than is usually granted 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 3 subjects used their CPAP for <3 h per night during the treatment period, the average was 4.8 h per night and produced a good improvement (and range of improvement) in ESS.

Thus, this study has not provided evidence to support the alternative hypothesis that the improved visual acuity on the LogMAR chart, as observed following CPAP in the proof of principle study by Mason et al. [5], stemmed from an 'artefact' due to increased 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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