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Sleep apnoea and daytime function in the elderly—what is the impact of arousal frequency?

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Summary Arousals from sleep result in hyperventilation and hypocapnia that can lead to sleep apnoea. We have investigated whether sleep apnoea in the elderly is associated with more arousals compared with younger people. Additionally, the impact of arousals on daytime symptoms was noted. Four groups (n=11) of elderly (>65 years) and young (<39 years) apnoeic (EA and YA), and age-matched non-apnoeics (EN and YN) were studied. The arousal index (AI) and apnoea/hypopnoea index were determined from polysomnography. Sleepiness (Epworth Sleepiness Scale) and Quality of life (QoL, SF-36) were assessed. The mean (SD) AI was: EN 23.1 (7.6), EA 46.5 (8.8), YN 13.2 (6.6), YA 38.5 (12.1) events/h. AI was higher in the elderly (P=0.002) and in apnoeics (P=0.001); however, the increase in AI associated with sleep apnoea was not age dependent (P=0.73). The influence of sleep apnoea on sleepiness was similar in both age groups. YA but not EA reported reduced physical functioning (P=0.04), vitality (P=0.007) and general health (P=0.04) compared to non-apnoeics. We conclude that (1) the effect of sleep apnoea on arousal is no greater in the elderly compared to the young (2) despite similar levels of sleepiness, elderly apneoics perceive a reduced loss of QoL compared to younger patients.

Introduction

The frequency of brief cortical arousals from sleep increases with age.[1,2] This age-related increase in arousal frequency may be a contributing factor to the age-related increase in the prevalence of sleep apnoea.[3–6] Arousal from sleep leads to hyperventilation;[7] the associated hypocapnia and reduced central respiratory drive can result in a central apnoea. The observation that the elderly have a greater proportion of central apnoeas[4,6] supports the role of arousal in the age-related increase in apnoea. On the other hand, the increased prevalence of sleep apnoea in the elderly could be due to other factors such as congestive heart failure, and this might lead to more arousals. These counter arguments mean that it is difficult to discern cause from effect simply by comparing representative groups of young and elderly populations. In the present study, we aimed to examine more directly whether the impact of sleep apnoea on arousal frequency is age-dependent. To achieve this, we recorded arousals from sleep in groups of young and elderly subjects matched for (a) the absence and (b) the severity of sleep apnoea/hypopnoea; we also controlled for other potentially confounding factors such as body mass index (BMI) and co-morbidity.

The design of our study gave us an opportunity to pursue a secondary objective. It is established that sleep apnoea leads to an increase in daytime sleepiness in the elderly population.[8,9] Moreover,

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sleep apnoea has been found to contribute to a significant reduction in quality of life (QoL) measures in populations with mean ages of 48 and 63, years, respectively.[10,11] However, the differential effect of ageing on sleep apnoea-related daytime sleepiness and QoL has not been investigated. Consequently in the present study, we included measures of subjective indices of sleepiness and QoL in our matched groups of young and elderly subjects in an attempt to explore these issues.

We hypothesised that sleep apnoea would be associated with a greater increase in arousal frequency in the elderly, compared to that in the young. Such an increase in arousability would be consistent with the idea that ageing would be associated with a potentiation of sleep apnoea primarily via increased frequency of central apnoeas. We further hypothesised that sleep apnoea would have a greater impact on increasing daytime sleepiness and reducing QoL in elderly compared to younger people.

Methods

Subjects

Sleep and breathing were measured overnight in 44 subjects (four groups of 11 subjects—see below). Groups of elderly (>65 years) and young (26–38 years) patients with sleep apnoea (EA and YA) were recruited from local sleep clinics. The presence of sleep apnoea was defined as an Apnoea Hypopnoea Index (AHI) >10 events/h. EA and YA groups were matched for AHI ($\pm$6 events/h). For each of the patient groups, age-matched normal volunteers without sleep apnoea (EN and YN) were recruited from the general population. The absence of apnoea was defined as an AHI $<$6 events/h. All four goups were matched for BMI ($\pm$3 kg/m^2). All subjects had a forced vital capacity and forced expiratory volume in 1 s >80% of the predicted value.[12] None of the subjects had any neurological disease or any complaints of chronic pain, which might have influenced their sleep quality. The local ethics committee approved the experimental procedure, and subjects gave written informed consent.

Protocol

Subjects were asked to refrain from drinking alcohol or caffeine containing beverages for 4 h before the sleep study. They arrived at the laboratory 2 h before their normal bedtime and standard tests of lung function were performed. Each subject then completed questionnaires to assess subjective daytime sleepiness and QoL. Following this, overnight polysomnography was carried out; sleeping position was not restricted.

Polysomnography

Overnight measurements of sleep and breathing were made using a computerised data acquisition system (Jaeger Sleeplab 1000p, Jaeger, UK). Sleep was monitored using two electroencephalograms (EEG; C3-A2, C4-A1), two electrooculograms (EOG; left and right eye) and an electromyogram (EMG) of the submental muscle. Chest wall and abdominal movements were monitored using pneumotachobands. An index of airflow from the nose and mouth was recorded using a thermistor. Arterial oxygen saturation was estimated by using a finger pulse oximeter (Biox 3700e, Ohmeda, Boulder, USA). Tracheal sounds were recorded using a microphone positioned on the neck to the side of the trachea. Leg movements were recorded using an EMG positioned over the left tibial muscle.

The sleep stage was scored according to standard criteria[13] and brief cortical arousals defined using standard criteria.[14] The number of arousals was divided by the total sleep time to produce an arousal index (AI). Arousals were classified as: respiratory-related or periodic limb movement (PLM)-related, based on the presence of an apnoea/hypopnoea or PLM, or within 2 s of the arousal. If an arousal was found to be neither respiratory, or PLM-related it was classified as spontaneous. An apnoea was defined as a cessation of airflow for >10 s. A hypopnoea was defined as a >50% reduction in airflow for >10 s. The number of apnoeas and hypopnoeas was divided by the total sleep time to calculate the AHI.

Daytime sleepiness and quality of life

Daytime sleepiness was assessed using the Epworth Sleepiness Scale (ESS).[15] The ESS comprises eight questions to assess the chance of falling asleep, on a scale of 0–3, during eight daily situations. The responses to the questions are summed yielding a score between 0 and 24 with higher scores indicating greater sleepiness.

QoL was assessed using the Medical Outcomes Short Form-36 Health Survey (SF-36).[16] The SF-36 comprises 36 questions to assess health in eight domains: (1) physical functioning; (2) social functioning; (3) role limitations attributed to physical

problems; (4) bodily pain; (5) mental health; (6) role limitations attributed to emotional problems; (7) vitality; (8) general health perceptions. The responses to the questions in each domain are summed and transformed to scores which range from 0% to 100%. In all instances, a higher score is consistent with a more positive health status.

Statistical analysis

This investigation was designed as a controlled study, with age and sleep apnoea as controlled variables and arousal frequency and daytime function as outcome variables. Pre-study power calculations were performed to determine the sample size. Based on reported age-related differences in arousal frequency (1) a mean difference of 22 and standard deviation of 13, indicated that a sample size of 11 would detect similar differences in arousal frequency, between EA, YA, EN and YN, with 90% confidence and 0.05 power. Pre-study sample size calculations to determine differences in subjective daytime sleepiness in apnoeic compared to non-apnoeic subjects were based on previously reported work.[15] A mean difference of 5.8 and standard deviation of 3.4 yielded a sample size of 11, using 90% confidence and 0.05 power. We designed our study on these estimates.

For the AI, mean age, BMI, neck circumference, total sleep time, percentage sleep stages and AHI, the group mean data were compared using a two-way ANOVA with age (elderly and young) and disease status (apnoea and non-apnoea) as two between-group factors. For the ESS and SF-36 scores, group mean data were compared using non-parametric Kruskal–Wallis tests with the age/apnoea status (i.e. YN,YA,EN,EA) as the grouping factor. Evidence of statistical significance from this test was further explored with comparisons of pairs of groups using Mann–Whitney U-tests. In all cases, statistical significance was defined as $P<0.05$ in a two-tailed test.

Results

Subjects

Anthropometric data for all groups are shown in Table 1. There were no significant differences in age between the EN and EA groups or between the YN and YA groups. There was no significant difference in BMI between the elderly and young groups although BMI in apnoeics was significantly greater than in non-apnoeics ($P = 0.03$); EN*EA vs. YN*YA was not significant. The lower mean neck circumference in the YN group resulted in statistically significant differences with respect to age ($P = 0.04$), apnoea ($P = 0.03$) and EN*EA vs. YN*YA ($P = 0.03$).

Sleep characteristics

Sleep data are shown in Table 1. The total sleep time was not significantly different with respect to age, apnoea or their interaction. The elderly groups had significantly less stage II NREM sleep than younger groups ($P = 0.004$) and the apnoeics significantly less than the non-apnoeics ($P = 0.003$); EN*EA vs. YN*YA was not significant. Apnoeics had significantly less stage III/IV sleep than non-apnoeics ($P = 0.14$) although there was no effect of age; EN*EA vs. YN*YA was not significant. REM sleep was not significantly different with respect to age, apnoea or their interaction. As anticipated, the AHI was significantly higher in the

Table 1 Anthropometric and sleep characteristics.

	EN	EA	YN	YA
Age (years)	69.5±4.1	70.4±3.6	31.9±2.6	32.6±3.6
Male/Female	9:2	9:2	8:3	10:1
BMI (kg/m^2)	26.7±3.8	28.1±1.7	26.1±2.9	29.0±5.5
Neck circumference (cm)	40.6±4.3	40.7±2.6	35.6±4.4	40.8±4.1
TST (h)	5.4±1.2	6.4±0.6	6.1±1.2	6.2±1.3
Stage II NREM (% TST)	36.8±9.5	48.3±14.0	48.2±8.1	56.0±8.3
Stage III/IV NREM (% TST)	28.7±17.1	16.9±15.9	25.2±6.7	17.5±6.6
Stage REM (% TST)	16.2±4.6	15.6±7.2	19.1±4.3	15.4±6.6
AHI (events/h)	2.5±2.2	30.3±14.3	1.7±2.0	24.9±20.4

Values are mean ± SD. EN, elderly non-apnoeic; EA, elderly apnoeic; YN, young non-apnoeic; YA, young apnoeic; BMI, body mass index; TST, total sleep time; NREM, non-rapid eye movement sleep; REM, rapid eye movement sleep; AHI, apnoea/hypopnoea index.

apnoeic compared to the non-apnoeic groups ($P = 0.001$); however, this was not accompanied by any significant effect on EN*EA vs. YN*YA.

Arousal frequency

The mean AI data are shown in Fig. 1A. Consistent with previous studies we found that the elderly subjects had a significantly higher AI compared to younger subjects ($P = 0.002$), and not surprisingly that apnoeic subjects had a significantly higher AI than their non-apnoeic counterparts ($P = 0.001$). However the influence sleep apnoea on AI was not age dependent (i.e. EN*EA vs. YN*YA was NS).

The AI calculated from the number of spontaneous arousals is shown in Fig. 1B and likewise for respiratory-related arousals in Fig. 1C. There was no difference between the AI caused by spontaneous arousals in the elderly compared to younger groups ($P = 0.82$); however, this was not the case with respect to the respiratory-related AI ($P = 0.03$). The apnoeics had a higher AI, irrespective of whether it was calculated from spontaneous or respiratory-related arousals ($P = 0.05$; 0.001). The influence of sleep apnoea on AI calculated from either spontaneous, or respiratory-related arousals was *not* age-dependent (EN*EA vs. YN*YA, $P = 0.07$; $P = 0.19$ respectively). The AI calculated from the number of PLM-related arousals was small in the elderly group (EN: 2.2 (2.3); EA: 0.8 (1.4) events/h) and zero in the young group.

Impact of age and sleep apnoea on daytime sleepiness

ESS scores for all groups are shown in Table 2. Kruskal–Wallis analysis revealed that self-reported sleepiness was statistically significantly different across the four study groups ($P = 0.03$). Paired group comparisons showed significantly greater sleepiness only in the EA compared with EN group ($P = 0.009$).

Impact of age and sleep apnoea on quality of life

SF-36 scores for all groups are shown in Table 2. There were a statistically significant group effects for physical function ($P = 0.02$), general health ($P = 0.03$) and vitality ($P = 0.05$) perceptions. Paired group comparisons for these three indices revealed the following significant differences: physical function (EN <YN, $P = 0.005$; YA<YN, $P = 0.04$); general health (EN <YN, $P = 0.005$; YA <YN, $P = 0.04$); vitality (YA <YN, $P = 0.009$). No significant effects of apnoea on QoL indices were observed in the elderly subjects.

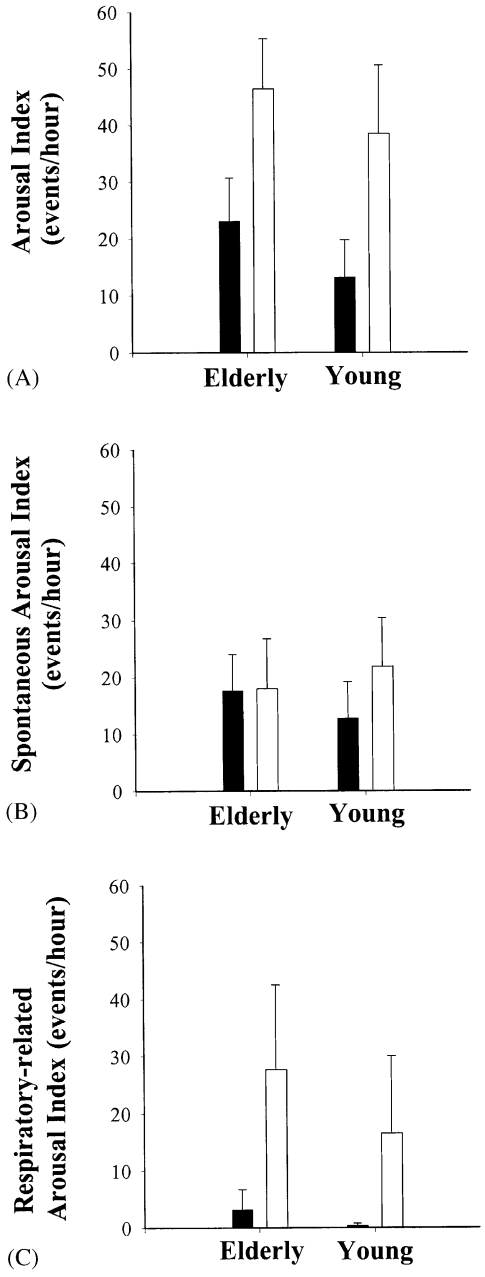

Figure 1 (A)Group mean ± SD Arousal Index for elderly (left) and young (right) non-apnoeic (filled bars) and apnoeic (open bars) subjects. (B) Group mean ± SD arousal index for arousals classified as spontaneous, determined for each group shown in A. (C) Group mean ± SD arousal index for arousals classified as respiratory-related, determined for each group shown in A. Note, that in the elderly the AI calculated from spontaneous and respiratory related-arousals does not add up to the total AI because a small number of arousals were periodic leg movement-related (EN: 2.2+2.3; EA: 0.8+1.4).

Table 2 Median (range) of scores from questionnaire data for elderly non-apnoeic (EN), elderly apnoeic (EA) young non-apnoeic (YN) and young apnoeic (YA) groups of subjects (n=11 for each group).

Group	ESS	Physical functioning	Role limits (physical)	Bodily pain	General health	Vitality	Social functioning	Role limits (emotional)	Mental health
EN	7 (1–12)	85 (10–100)	100 (0–100)	84 (24–100)	67 (57–82)	65 (40–85)	100 (75–100)	100 (0–100)	84 (36–100)
EA	13 (3–17)	90 (45–100)	100 (0–100)	84 (31–100)	70 (42–92)	55 (25–90)	100 (25–100)	100 (0–100)	76 (32–100)
YN	6 (3–13)	100 (90–100)	100 (75–100)	84 (72–100)	87 (67–100)	70 (50–85)	100 (63–100)	100 (10–100)	84 (60–92)
YA	12 (0–20)	95 (70–100)	100 (0–100)	90 (41–100)	67 (45–100)	55 (30–75)	87 (25–100)	100 (0–100)	80 (56–84)
P (K–W)	0.031	0.015	0.345	0.495	0.033	0.049	0.417	0.944	0.673
P (M–W)	0.009	0.005			0.005	0.009			
	(EN < EA)	(EN < YN)			(EN < YN)	(YA < YN)			
		0.04			0.04				
		(YA < YN)			(YA < YN)				

For ESS (Epworth sleepiness scale), higher scores indicate greater reported sleepiness. For the eight domains of the SF-36 quality of life scale, lower scores indicate lower reported health status. Statistical significance is shown by P-values with respect to Kruskal–Wallis (K–W) test for overall "group effect", and Mann–Whitney U (M–W) tests between group pairs, when K–W indicated statistical significance. All other paired comparisons were not significant.

Discussion

Our findings show that the impact of sleep apnoea on arousal frequency is not different between elderly and young people. Had we found that the elderly were more susceptible to arousal from sleep then this would have been consistent with arousal being a mechanism for the increased occurrence of apnoeas in this group. However, this was not the case and thus we found no support for this contention.

Subjective symptoms of daytime sleepiness were similar for elderly and young sleep apnoiecs (in fact only in the elderly was the effect of sleep apnoea on sleepiness statistically significant). Despite this, the young, but not the elderly apnoiecs had a reduction in QoL (physical functioning, vitality and general health) compared to their healthy counterparts. This suggests that although the perception of sleepiness is similar in both groups, in the elderly apnoiecs the more general effects of sleep deprivation, such as loss of vitality, are likely to be attributed to other mechanisms, e.g. the ageing *process* per se.

Impact of age on arousal frequency

In the present study we took care to match the AHI in the apnoeic and non-apnoeic groups, enabling us to conclude that the age-related increase in AI was likely to have been independent of sleep apnoea. However, in addition, we did not see a difference in the sleep apnoea-related increase in AI in the elderly compared to young, and thus found no support for the idea that increased arousability is the mechanism by which sleep apnoea (or more specifically its central component) could be potentiated in the elderly.

An alternative mechanism is that in the elderly, arousal from sleep produces a relatively large state-related change in upper airway mechanics. An age-related increase in upper airway resistance and a decrease in genioglossus and tensor palateni muscle activity during sleep has been reported in some,[17–19] but not all[20] previous studies.

The main findings of our study depend on a high reliability for the scoring of brief arousals. Previous investigators have suggested high inter-scorer reliability for the scoring of arousals using the ASDA criteria is hard to achieve;[21–23] however, others have reported better reliabilities.[2] In the present study all arousals were scored by one 'blinded' scorer, who had participated in a previous experimental setting in which 14 sleep experts from different sleep centres evaluated sleep recordings taken from ten obstructive apnoea

patients;[22] that study reported moderate agreement for arousal scoring (kappa=0.47). In the present study we assumed that any error in the scoring of arousals would have occurred randomly across the four study groups, and would not have systematically biased our findings.

Impact of age on daytime function

Numerous studies have documented that sleep apnoea is associated with an increase in sleepiness, measured subjectively and objectively.[24] In the present study we have shown the increased daytime sleepiness is not different in elderly apnoeic patients compared to young apnoeics. Therefore, although it is established that the prevalence of daytime sleepiness increases in the elderly,[8] our data suggest that this may be accounted for by an age-related increase in sleep apnoea, since when we controlled for AHI between our young and elderly groups there was no difference in sleepiness.

The subjective reporting of daytime sleepiness using the ESS has been shown to correlate well with sleep apnoea, as indicated by the AHI,[15] while other investigators have found no correlation with the AHI.[25] As an indicator of daytime sleepiness, the ESS has been well validated, including comparisons with objective sleep tendency as measured by the multiple sleep latency test.[26] Recent work has suggested that the ESS is a more sensitive and specific measurement of daytime sleepiness than either the multiple sleep latency test or the maintenance of wakefulness test.[27]

The comparable increases in sleep apnoea-related daytime sleepiness in the elderly and young groups were not reflected in the QoL scores. Compared to our non-apnoeic elderly subjects, the elderly apnoeic patients showed no significant reductions in physical functioning, vitality and general health perception scores on the SF-36 questionnaire. This was not the case for the young subjects where we found sleep apnoea to be associated with reductions in these domains. Although it has been argued that QoL measures may be useful in the evaluation of patients with sleep disorders,[28] our findings suggest that the value of such assessments as indices of sleep apnoea-related morbidity varies with age; thus they must be interpreted with caution.

In the largest study (n=5816) to address the association between SDB and QoL, high levels of sleep apnoea (AHI>30 events/h) were found to be associated with reductions in physical functioning, general health perceptions, vitality and social functioning. However, at lower levels of sleep apnoea, associations were only observed in the vitality domain.[11] In contrast, a further study, involving 737 participants, found even low levels of sleep apnoea (AHI=5) to be associated with reductions in physical functioning, social functioning, role limitations attributed to physical problems, mental health, vitality and general health perceptions.[10]

The lack of an association between sleep apnoea and physical functioning, vitality and general health perception in our elderly groups could be accounted for by the fact that our non-apnoeic elderly subjects had significantly reduced physical functioning and general health perceptions compared to non-apnoeic young people. This occurred despite the fact that our elderly non-apnoeic subjects were relatively fit with no co-related morbidity. The age-related reduction in physical functioning and general health perception scores in our relatively small group are similar to those recorded in a large sample (n=732) of older (55–64) male subjects.[29]

Clinical consequences of our findings

We conclude that sleep apnoea is not associated with more arousals in the elderly compared to younger people and that the age-related increase in sleep apnoea in this age group is likely to be due to other factors such as differences in upper airway mechanics. Differences in the subjective measurements of daytime sleepiness and QoL in the elderly, compared to young apnoeic patients, indicates the importance of asking specific questions when taking a clinical history in elderly people. We suggest that elderly apnoeic patients are able to accurately report specific symptoms of daytime sleepiness; however, more generalised changes such as reductions in physical functioning, vitality and general health perceptions are more likely to be attributed to the ageing process per se or other age dependent diseases.

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