

Cognitive Findings in Central Sleep Apnoea Syndrome

Abstract

We present the neuropsychological profile of a patient with central sleep apnoea syndrome. Performance was impaired on tests of short term memory and learning, verbal reasoning and processing speed, with borderline verbal fluency, but with relative preservation of language function. This pattern was suggestive of subcortical dysfunction, perhaps related to white matter cerebral metabolic derangements, as seen in other sleep apnoea syndromes.

Keywords: Cognitive function; Memory; Neuropsychology; Sleep apnoea

Sleep apnoea refers to temporary cessation of breathing during sleep, and is one form of sleep disordered breathing.^{1,2} Analysis of breathing patterns permits classification of three sleep apnoea syndromes: obstructive, in which cessation of airflow is associated with persistence of diaphragmatic and intercostal muscle activity (i.e. respiratory efforts); central, in which cessation of airflow is associated with no respiratory effort; and a mixed pattern.^{1,2}

Obstructive sleep apnoea-hypopnoea syndrome (OSAHS), the most common of these syndromes, may on occasion present with various neurological symptoms including excessive daytime sleepiness, blackouts, and headache, sometimes with features suggestive of raised intracranial pressure, and may be mistaken for narcolepsy, epilepsy, and idiopathic intracranial hypertension, respectively.³⁻⁵ Apparent intellectual decline which may be mistaken for dementia is also recognised to be a feature of OSAHS, which may improve after appropriate treatment of the underlying condition.⁶

Central sleep apnoea syndrome (CSAS) is much rarer than OSAHS. It may be associated with brainstem disorders (e.g. multiple system atrophy), neuromuscular or myopathic disorders, congestive heart failure, or be idiopathic. CSAS may reflect insensitivity of the respiratory centres with loss of automatic respiratory drive and hence inspiratory muscle effort.^{1,2} From the literature, it is not clear whether CSAS may be associated with cognitive impairment, as in OSAHS: it has been reported as a cause of confusion in the elderly,⁷ and of impaired daytime performance due to sleep fragmentation.⁸ Prior reports of neuropsychological assessment in CSAS have not been identified.

We report the neuropsychological assessment in a patient who proved to have clinical and investigative evidence of CSAS. The neuropsychological findings are compared with those in a typical case of OSAHS.

Case Report

A 52-year-old right-handed man presented to the Cognitive Function Clinic with a six-month history of difficulties with short term memory and concentration, lack of interest, and excessive daytime somnolence, symptoms which had required his wife to give him increasing assistance with activities of daily living. There was no complaint of headache or blackout. His weight had risen over a 4-year period by around 25 kilogrammes, and his collar size from 15.5 to 18 inches. He had been a snorer throughout his adult life.

Four years previously, he had presented with a 4-week history of headaches with progressive left hemiparesis and

left sensory and visual inattention. A right parietal enhancing lesion was seen on brain imaging which proved at complete excision to be a grade IV astrocytoma. Subsequent treatment included chemotherapy (lomustine, 6 cycles) and local radiotherapy (58 Gy in 29 sessions, fraction size = 2 Gy per session). There was a residual left homonymous hemianopia and left visual inattention. He remained on a small dose of steroid (dexamethasone 1 mg/day). Repeat brain imaging two years postoperatively showed no tumour recurrence.

On examination he was obese (114 kg; BMI 33 kg/m²). There was no asterixis, bounding pulse, or signs of heart failure; blood pressure was normal (130/70 mmHg) and he was normocapnic. There were no focal neurological signs other than the previously documented left homonymous hemianopia and visual inattention. Endocrine work-up showed no evidence of panhypopituitarism. His score on the Epworth Sleepiness Scale (ESS)⁹ was normal (3/24). Repeat MRI brain scan showed a right parietal defect from previous tumour resection, with no evidence of disease recurrence; a few small punctate high signal changes were evident in the white matter on T2-weighted imaging, thought to be of ischaemic origin; there was no brain atrophy or Chiari malformation.

Neuropsychological assessment was undertaken. The Mini-Mental State Examination¹⁰ score was 26/30 (serial 7's) and 27/30 (spelling), with points dropped for failing to follow the written instruction ('Close your eyes') and incorrect drawing of intersecting pentagons, failures possibly related to the visual field defect and visual inattention; five minute recall was normal (3/3). Using the Queen Square Screening Test for Cognitive Deficits,¹¹ he showed difficulty counting letters in an array, ignoring the left side of the page. Reading was also impaired, with the beginning of lines being missed, but there were no paralexias. Dot counting was impaired, but there were no problems reading fragmented letters or pictures. Object naming score was 9/10 but object recall was only 1/10. Verbal fluency for letter and category was satisfactory (C = 10 in 60 seconds; 17 animals, 12 musical instruments in 60 seconds).

Formal neuropsychological assessment using the WAIS-R¹² showed intellectual functioning in the impaired range. There was a 60 point verbal/performance IQ discrepancy in favour of verbal abilities. Factor index scores showed impaired performance on perceptual organisation and processing speed, with verbal comprehension and working memory at the lower end of the borderline range. Predicted premorbid fullscale IQ on the NART¹³ was 115, within the high average range. Hence there was pronounced generalised intellectual loss, with a decline in fullscale IQ of >50 points, particularly affecting non-verbal reasoning and processing speed. The general memory index was 70 (impaired). Performance was better on tests of auditory memory compared with recognition memory (low average). There were impairments in all aspects of short term memory and learning with particularly poor performance on working memory (attention and concentration) and delayed visual memory. Testing language with the Graded Naming Test¹⁴ he scored 17/30 (average). There were no word-finding or naming difficulties. Copy of the Rey figure was severely impaired, with clear left sided inattention. Performance was within the borderline range on both the Stroop Test and verbal fluency. On the Hospital Anxiety and Depression Scale,¹⁵ there was mod-

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erate anxiety (12) and mild depression (10).

Overnight pulse oximetry was unremarkable except for a brief period (< 30 minutes) of cyclic oxygen desaturations without corresponding heart rate arousals; these changes did not reach commonly agreed criteria¹⁶ for the diagnosis of OSAHS (i.e. Desaturation Index [DI] \geq 5). Mean oxygen saturation was 92% and lowest SaO₂ 84%. Because this relatively normal study failed to explain his excessive daytime somnolence, he proceeded to nocturnal polysomnography. This showed prolonged periods of periodic breathing without snoring. During these periods, typically four unobstructed breaths were followed by a pause for about ten seconds. These findings were in keeping with a diagnosis of CSAS.¹² There was no waxing and waning of the depth of respiration to suggest Cheyne-Stokes respiration. In the absence of signs of recognised causes, a diagnosis of idiopathic CSAS was made.

Discussion

This patient had pronounced cognitive impairment, affecting perceptual organisation, non-verbal reasoning, processing speed, and, to a lesser extent, verbal comprehension. There was poor performance on tests of short term memory and learning, particularly for visually presented information. Language was relatively well preserved. Hence, although impairments in visuospatial and constructional abilities

might be accounted for by the pre-existing left-sided inattention/right parietal pathology, the documented cognitive impairments suggested more widespread involvement which may be related to the diagnosis of CSAS.

Cognitive impairment may be a feature of OSAHS.⁶ In a typical patient (see ref. 3, case 2 for more details: weight 140 kg; BMI 40 kg/m²; ESS 18/24; DI > 60), neuropsychological assessment showed mild impairment of cognitive function, with slight reductions in verbal reasoning and verbal comprehension performance, poor performance on tests of short term memory and learning, reduced verbal fluency and mild attentional problems, whilst non-verbal reasoning, language, visuospatial and constructional functions were intact. These deficits show some overlap with those in our patient with CSAS, namely in short term memory and learning, verbal reasoning and processing speed, and attention. Such impairments are more typical of those ascribed to subcortical rather than cortical pathology, and might reflect white matter change, as seen in 'white matter dementias' such as multiple sclerosis. Cerebral metabolic impairments have been identified in OSAHS, using magnetic resonance spectroscopy, in association with white matter change.¹⁷

A possible confounding factor in the assessment of our patient was his previous brain tumour and its treatment. Cognitive decline in

patients with brain tumours may have many causes including the tumour itself, steroid therapy, mood disorder, and as a sequel to radiotherapy and chemotherapy.¹⁸ Many of these are highly unlikely explanations for our patient's cognitive problems: he had no evidence for tumour recurrence, his steroid dose was very low, and there was no significant mood disorder. The risk of cognitive deficits related to radiotherapy is known to increase with high radiation dose, large fraction and field size, and to be associated with diffuse white matter change and cortical/subcortical atrophy on brain imaging. Whilst we cannot entirely rule out radiotherapy as a contributor to the observed cognitive deficits, we think this unlikely because radiation dose and fraction size were modest (58 Gy at 2 Gy per session), the field size was local, and brain imaging showed only age-appropriate white matter changes and no atrophy. Focal radiotherapy is seldom a cause of cognitive impairment in patients with glioma.¹⁹

Despite the possible difficulties in interpretation, the key practical point to emerge from this study is the need to consider both CSAS and OSAHS as causes of cognitive decline, particularly when the profile is suggestive of subcortical/white matter, rather than cortical, pathology. The case also adds to the evidence that poor sleep per se may be a cause of cognitive dysfunction.²⁰

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