Nocturnal and respiratory disturbances in Steele–Richardson–Olszewski syndrome (progressive supranuclear palsy)

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Summary

Respiratory and sleep disturbances may be important causes of morbidity in Steele–Richardson–Olszewski syndrome but the frequency and character of nocturnal abnormalities remains uncertain. A prospective study of 11 patients with Steele–Richardson–Olszewski syndrome and age-matched control subjects was undertaken using clinical assessments, a structured sleep questionnaire, spirometry, static maximum inspiratory and expiratory pressures and nocturnal oximetry. The mean age of the Steele–Richardson–Olszewski syndrome patients was 63.2 (52–70) years and mean disease duration was 4.0 (2–6) years. There was moderate to severe motor disability in nine and mild to moderate dementia in eight. In the patients with Steele–Richardson–Olszewski syndrome the following abnormalities contributed to sleep disturbances significantly more frequently than in normal controls: depression, dysphagia, frequent nocturnal awakenings (usually associated with urinary frequency), immobility in bed, difficulty with transfers, impaired dressing and feeding. There was profound impairment of voluntary respiratory control whilst automatic and limbic control were well maintained. Nocturnal respiratory abnormalities were not present even in the most severely disabled. In Steele–Richardson–Olszewski syndrome sleep abnormalities are common; they relate to the cognitive, pseudobulbar and extrapyramidal disturbances and may therefore be amenable to symptomatic control.

Keywords: respiration, sleep, Steele–Richardson–Olszewski syndrome

Steele–Richardson–Olszewski syndrome (SROS) is a progressive, non-familial disorder beginning in middle or old age and characterised by a supranuclear ophthalmoplegia and at least two accompanying diagnostic features (box 1).^{1,2} Sleep disturbance is recognised as an important manifestation of SROS although, unlike idiopathic Parkinson's disease,^{3,4} the frequency, character and pattern of symptoms

SROS: diagnostic features

- supranuclear ophthalmoplegia + at least two accompanying diagnostic features:
- postural instability with falls backwards
- pseudobulbar palsy
- bradykinesia and rigidity
- frontal lobe signs (bradyphrenia, perseveration, forced grasping and utilisation behaviour),
- axial dystonia and rigidity

Box 1

due to such abnormalities remains unclear. Whilst there is a correlation between polysomnographic abnormalities and disease severity, the frequency and symptomatic significance of these disturbances of sleep pattern is uncertain. In idiopathic Parkinson's disease respiratory impairment is associated with upper airflow obstruction,^{5,6} reduced tidal volume,⁷ respiratory muscle weakness,^{6,8} restrictive defect due to respiratory muscle rigidity,⁹ abnormalities of central CO₂ sensitivity^{10,11} and impairment of voluntary control.¹² However, the pattern and severity of respiratory abnormalities in SROS are poorly described.

We undertook a study of consecutive patients with SROS and age-matched controls to estimate the frequency and character of sleep abnormalities and the incidence of nocturnal respiratory abnormalities.

Methods

We studied 11 patients with SROS fulfilling currently accepted clinical criteria¹ and eight age- and sex-matched control subjects. There was no history of lung disease that might have led to structural or functional pulmonary dysfunction.

The clinical details included duration, severity and clinical features of the SROS. The patients underwent cognitive assessment including the Beck questionnaire,¹³ MiniMental state examination¹⁴ and detailed psychometric assessment including the Wechsler Adult Intelligence Scales.¹⁵ A structured sleep questionnaire was used for interviewing the patient and their carer about sleep history and habit.¹⁶ Spirometry and static maximum inspiratory and expiratory pressures were routinely

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assessed in all patients.¹⁷ All patients were carefully instructed in the techniques and took several practice attempts at each manoeuvre. The patients were studied for one night in an isolated darkened room. Oxygenation was measured continuously using an Ohmeda 3700e pulse oximeter and transferred for subsequent computer analysis.¹⁸ The overnight baseline oxygen saturation (SpO₂) and the number of dips in SpO₂ > 4% lasting longer than 10 seconds were calculated and expressed per hour of recording.^{19,20} The presence of sleep was documented by the nurse observing the patient but polysomnography was not performed because of the severity of the underlying disability. Comparison between the patients and control group was made using χ^2 analysis. Values less than or equal to <0.05 were considered significant.

Results

Eleven patients with SROS (six male, five female) were studied with a mean age of 63.2 ± 6.6 (52–70) years and mean disease duration of 4.0 ± 1.2 (2–6) years. Eight healthy controls (five male, three female) with a mean age of 65.5 ± 6.8 (55–75) years. The clinical features at presentation are summarised in box 2. All the patients with SROS were aware of frequent falls associated with postural instability and a bradykinetic gait. Primitive reflexes included grasp, pout, palmo-mental and also imitation and utilisation behaviour. Two patients were independently mobile, three were mobile with aids, five required wheel-chairs and one was bed-bound. The mean Mini Mental score (*n* = 8) was 21.6 ± 7.5 (13–28) years but even those patients with higher values were noted to perform the tests slowly. Mean performance IQ was 88.4 ± 11.1 (77–101) and mean verbal IQ was 86.6 ± 10.6 (66–112). In the 10 patients in whom neuropsychological assessment was possible, nine showed generalised impairment of verbal and non-verbal memory, one impairment of non-verbal memory alone, five impairment of frontal lobe function, five difficulty in initiating tasks, slowness of execution, echolalia and perseveration, and two impairment of perception. There was evidence of moderate dementia in five patients, mild dementia in three and no dementia in three. There was clinical evidence of depression in

eight patients with a mean Beck score of 12.4 ± 6.2 with five scoring 16 or higher and three scoring six or below. Nine patients were receiving medication, these were sinemet (4), madopar (3), selegiline (2), amantidine (2), fluoxetine (1) and prothiadin (1). Responses to the sleep questionnaire were compared with a series of aged-matched controls. In the patients with SROS the following abnormalities were reported by nine or more patients and were significantly more frequent than in normal controls: depression, fatigue, dysphagia, frequent nocturnal awakenings (usually associated with urinary frequency), immobility in bed, difficulty with transfers, impaired dressing and feeding (box 3). The following abnormalities were more frequent in patients with SROS but did not reach statistical significance: hypersomnolence, reduced daytime alertness, daytime naps and a tendency to wake because of choking.

Spirometry and maximum inspiratory and expiratory pressure measurements were attempted in both patients and controls. The patients with SROS experienced extreme difficulties in performing the motor tasks of voluntary full inspiration and expiration and also forced inspiratory and expiratory manoeuvres. This seemed to be firstly because of a combination of cognitive impairment leading to difficulty understanding the commands and a particular problem being experienced in placing the mouthpiece between the lips (in the absence of any facial weakness) and in performing forced expiration to command. Secondly there was a profound slowness and perseveration in response to command and an inability to execute the complex motor manoeuvres despite adequate power, however, respiratory patterns did vary in response to emotional stimuli. It was therefore not possible to perform an adequate assessment of lung volumes or respiratory muscle strength. All the patients had a regular breathing pattern whilst awake with a mean baseline SaO₂ of 95% (94–97%). There were infrequent hypoxic dips of 4% below baseline in three patients but in none of these patients did the rate of hypoxic dips equal or exceed five/hour. The minimum saturations were 90%, 91% and 92%. Therefore, in all cases nocturnal oximetry was within normal limits.

Discussion

Previous polysomnographic studies in patients with SROS have shown that, with increasing

SROS: clinical features at presentation	
• falls	11
• bradykinetic rigid syndrome	11
• dysarthria	11
• supranuclear downgaze palsy	11
• dysphagia	9
• pyramidal signs	7
• primitive reflexes	7
• blepharospasm/apraxia of eyelid opening	6
• emotional lability	3
• tremor	1
<i>n</i>	11

Box 2

SROS: factors associated with nocturnal disturbance	
• depression	
• fatigue	
• dysphagia	
• urinary frequency	
• immobility	
• impaired dressing and feeding	

Box 3

disease severity, there is a reduction in total sleep time with large amounts of wakefulness interspersed throughout sleep, frequent early morning awakenings, prolonged latency of sleep onset and a progressive loss of the number and duration of episodes of REM sleep.^{21–25} Despite extensive and detailed polysomnographic studies there is no previous analysis of the frequency with which symptoms of nocturnal disturbance occur in SROS. Although insomnia is well described in SROS only four patients in the present series were aware of a difficulty in sleeping. However, patients were troubled by frequent nocturnal awakenings associated with urinary urgency and nocturia. Patients were also distressed by severe immobility due to rigidity, this led to difficulties in finding a comfortable position in which to sleep and difficulties with transfers out of bed. The rigidity also led to severe impairments of dressing and feeding which contribute to the overall morbidity of the condition.

Sleep-related behaviour disturbances are considered to be common during the latter stages of the disease.²¹ This was not a prominent feature in the present series in whom vivid dreams, nocturnal movements and disorientation were rare. This may be because the severe rigidity prevents dystonia or involuntary movements becoming manifest or because these abnormalities usually occur during REM sleep which is much reduced.

Previous reports of sleep-related respiratory abnormalities in SROS have suggested that obstructive, central or mixed apnoeas may occur but that these are mild and make only a minor contribution to sleep disturbance without contributing to respiratory insufficiency.^{25,26} In the present series nocturnal respiration was extremely well preserved with no significant sleep apnoea in any patient, regardless of the severity of disability. Although automatic respiration was apparently normal in this study there was a profound disturbance of voluntary (behavioural) control of respiration manifest as difficulty performing voluntary inspiration and expiration, breath holding and complex motor manoeuvres to command.²⁷ Behavioural control of respiration is mediated by rapidly conducting oligosynaptic pathways from the contralateral motor cortex descending with corticospinal and corticobulbar fibres in the lateral

Key points

- nocturnal disturbance is common and may be amenable to symptomatic treatment
- nocturnal respiratory insufficiency is rare
- there is a supranuclear impairment of ventilatory control (ie, disrupted voluntary control but well maintained automatic and limbic control)

Box 4

columns.²⁸ Selective interruption of voluntary pathways leads to a strikingly regular and unvarying respiratory pattern during which the patient is unable to take a deep breath, hold the breath, cough voluntarily or initiate any kind of volitional respiratory movements.²⁹ A related phenomenon of respiratory apraxia has been described in patients with Cheyne–Stokes respiration,³⁰ however, the respiratory pattern in this condition is not a true apraxia as the fixed pattern is obligate on abnormalities of central respiratory control and slowed circulation. The present series suggests that in SROS lesions of the corticobulbar pathways causing pseudobulbar palsy lead to a partial functional interruption of the behavioural pathways. The resultant supranuclear disturbances of respiration may cause severe motor retardation and impairment of the capacity to perform respiratory tasks to command. However, the apparent preservation of limbic ventilatory responses suggests that separate descending systems mediating emotional control were intact.³¹

The present study of 11 consecutive patients with SROS suggests that nocturnal abnormalities are common and relate to the severity of neurological disability and cognitive function (box 2). Nocturnal disturbance is usually associated with depression, fatigue, dysphagia, urinary frequency, immobility and impaired dressing and feeding. Nocturnal respiratory abnormalities are rarely symptomatic but the patients did show a supranuclear impairment of respiratory control manifest as a profound impairment of voluntary respiratory control whilst maintaining automatic and limbic emotional control of breathing.

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