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Daytime sleepiness and its relationships to fatigue and autonomic dysfunction in adults with spinal cord injury

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ABSTRACT

Objective: To determine the extent of daytime sleepiness in adults with spinal cord injury (SCI) and investigate the contribution of fatigue and autonomic function to sleepiness status.

Methods: Participants included 45 adults with SCI attending outpatient services or living in the community and 44 able-bodied controls. The Oxford Sleep Resistance Test (OSLER) was used to assess daytime sleepiness, while eye blink rate duration (electrooculography) and the Iowa Fatigue Scale assessed fatigue. Heart rate variability (HRV) was used to assess autonomic function. Survival analysis (Kaplan Meier) was used to estimate the rate of loss in participation in the OSLER task, as a measure of daytime sleepiness. Repeated measures ANOVA was used to determine HRV differences between groups. Regression analysis was used to establish factors that contributed to daytime sleepiness.

Results: Participants with high lesions ("T3 and above") had significantly increased daytime sleepiness. OSLER results revealed only 33% of those with high lesions remained awake during the task. Those with high lesions also had significantly reduced sympathetic activity while no differences in parasympathetic activity were found between groups. Lesion completeness had no effect. Standardized variation in heart rate, slow eye blinks, low frequency HRV and self-reported fatigue contributed to daytime sleepiness.

Conclusion: Neurological lesions at "T3 or above" have an increased risk of daytime sleepiness, impacting on independence in daily functional tasks and work performance. Autonomic imbalance alters cardiovascular control, affecting health and wellbeing. The interaction of these factors requires further investigation.

1. Introduction

Spinal cord injury (SCI) involves damage to the nervous system and spinal cord, caused by bruising or severing in a traumatic injury or non-traumatic causes, such as degeneration of the spine, infections or tumors [1, 2]. SCI results in many secondary conditions, including sleep disturbance (SD) [3], psychological disorder [4], chronic pain and fatigue [5], and disordered cardiac control associated with autonomic nervous system (ANS) imbalance/dysfunction [1, 6, 7]. In addition to paralysis and reduced mobility, secondary conditions contribute to greatly reduced quality of life [8].

Sleep disturbance in SCI has been comprehensively studied [3, 9, 10], with one form of SD, obstructive sleep apnea (OSA), estimated to range between 30 and 60% of those with SCI, especially in cervical and complete injuries [10]. Sleep disturbance involves difficulties getting to sleep or frequently interrupted sleep due to problems like obstructive sleep apnea, pain, and spasticity [9]. Daytime sleepiness is the propensity to fall asleep during the day and linked to problems such as reduced productivity [3, 9–11]. It is prevalent in tetraplegia and complete lesions, and sleep disturbance increases daytime sleepiness and vice versa [9, 10]. Chronic fatigue is also a substantial problem in adults with SCI [5, 8, 12] and defined as excessive chronic tiredness involving feelings of exhaustion and negative emotions, such as anxiety and poor mood [11]. It is the excessive and chronic nature of fatigue that distinguishes it from daytime sleepiness, or tiredness arising from daily physical and mental exertion [11, 12]. Further research is required to clarify relationships between daytime sleepiness and fatigue in SCI.

ANS dysfunction is generally more disordered in cervical and complete lesions [1, 6, 7]. Sympathetic preganglionic neurones for the heart are confined to the T1–T6 spinal segments, however, studies recording activity in cardiac postganglionic nerves, changes in cardiac

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activity and effects of electrical stimulation of nerves arising from different spinal cord segments (or from sectioning in anaesthetized animals), suggest that T1-T3 spinal segments, and particularly the T3 level, provide the major contributor to the cardiac sympathetic nerve supply in all mammals [13]. However, the exact topographic location and functional organization within the column of sympathetic neurones in the spinal cord pertaining to specific cardiac functions remains to be fully elucidated. In cervical and higher thoracic lesions (T6 and above), disruption of sympathetic nervous system (SNS) pathways may lead to various cardiovascular (CV) problems with persistent orthostatic hypotension and/or episodes of uncontrolled hypertension, referred to as autonomic dysreflexia [1]. Autonomic dysreflexia is a life-threatening problem involving unregulated blood pressure control, potentially resulting in fatigue, seizures, intracranial hemorrhage, and retinal detachment [1, 6, 7]. Lower thoracic lesions also have increased likelihood of uncontrolled hypertension and tachycardia [6, 7]. ANS dysfunction also has negative influences on respiratory control, thermoregulation, bowel, bladder and sexual function [6].

ANS dysfunction can be assessed by heart rate variability (HRV) [14–17]. Research generally finds reduced sympathetic activity (indexed by low frequency HRV) in tetraplegia compared to paraplegia and able-bodied controls [15, 16], while few differences have been found in high frequency HRV (mostly associated with parasympathetic activity) when at rest [15, 16]. Reduced autonomic modulation in SCI, indicated by lowered HRV, results in reduced capacity to regulate/balance the sympathetic and parasympathetic systems, with poor control of emotions and stress a possibility [18], and/or neuropathic pain [19]. Further, lowered HRV (especially reduced parasympathetic or cardiac vagal control) weakens a person's capacity to deal with stressful encounters [20, 21]. ANS imbalance is also related to sleep disorder in Parkinson's Disease [22], to daytime sleepiness in people with SD [23], and HRV has been used to detect daytime sleepiness [24].

Daytime sleepiness is a major problem for people with SCI, and factors that increase its occurrence and severity are rarely investigated. Therefore, the purpose of this study was to investigate connections between daytime sleepiness, fatigue, and ANS dysfunction in SCI. The aims of this study were: (a) determine extent of daytime sleepiness and fatigue in adults with SCI and definite disrupted CV control (lesions at “T3 and above”); (b) examine HRV in SCI; and (c) explore factors that contribute to daytime sleepiness in adults with SCI. Based on the research discussed above into sleep disturbance and autonomic imbalance in people with SCI, it was hypothesized that (i) participants with “T3 and above” lesions would have the highest propensity for daytime sleepiness and fatigue; (ii) participants with high lesions would have substantially reduced sympathetic activity, and (iii) multiple factors would contribute to daytime sleepiness, such as fatigue, HRV, risk of sleep apnea, hours slept the night before and body mass index (BMI).

2. Methods

2.1. Study participants

Included 46 adults with SCI and 46 able-bodied (AB) controls. One participant with SCI did not complete the study leaving 45. Recruitment sources included a SCI rehabilitation unit outpatient clinic, contacts in the community, and advertisements in SCI consumer organization newsletters. Inclusion criteria for SCI consisted of: (i) aged between 18 and 80 years; (ii) proficient in English; (iii) sustained an acute SCI, (iv) at least 6 months post-injury from inpatient rehabilitation, and (v) no evidence of severe psychiatric disorder such as bipolar disorder or psychoses, as determined by a structured psychiatric interview. Two AB controls failed to complete the study, leaving 44. Inclusion criteria for the controls included (i) and (ii) above, as well as (iii) no history of neurological injury, and (iv) no evidence of a current severe psychiatric disorder, such as major depressive or bipolar disorder, or psychoses, as determined by a structured psychiatric interview. Controls were approached using flyers advertising the study and delivered to community contacts and were recruited so that there were similar numbers of males and females and similar ages to the SCI sample.

Table 1
Injury characteristics of SCI participants (N = 45).

	Frequency	Percentage
Cause of injury		
Motor vehicle	14	30.1
Sport	6	13.3
Falls	19	42.2
Non-traumatic	3	6.7
Other	3	6.7
Level of injury		
Cervical	21	46.7
Thoracic	20	44.4
Lumbar/Sacral	4	8.9
Completeness		
T3 and above		
Complete	11	42.3
Incomplete	15	57.7
T4 and below		
Complete	16	84.2
Incomplete	3	15.8
Compensation		
T3 and above	24	92.3s
T4 and below	19	100.0

At the time of assessment, around 25% of participants in both groups were taking anti-hypertensives. The most commonly prescribed medications in the SCI group were muscle relaxants (n = 24) and anti-convulsants (n = 19). SCI injury characteristics are shown in Table 1. There were no significant differences in level of education between the groups (p = 0.32).

2.2. Research ethics

Compliance with the World Medical Association Code of Ethics occurred and ethics approval was granted by the local institutional research ethics committee. All institutional regulations concerning the ethical use of human volunteers were followed during this research, and written informed consent was obtained before participation in the study.

2.3. Study design and procedure

A repeated measures factorial design was employed with two groups (SCI and able-bodied control) assessed at three time periods. Participants took part in a 40-min behavioral sleepiness test (OSLER) during which electrophysiology recording occurred (electrocardiography and electrooculography). Additionally, participants completed a battery of psychophysiological measures three times: first at baseline before the test, immediately after the test, and third, after a 5 min recovery period. Participants were asked to refrain from drinking caffeinated/alcoholic beverages on the assessment morning. To control circadian influences [11, 12], assessment occurred between 9 am-1 pm and was conducted in a quiet semi-darkened room in the participant's home, health clinic, or research institution. The participants with SCI were seated in their wheelchair and controls were seated in a chair with armrests, while electrophysiological assessment occurred.

2.4. Assessment

Completeness of the lesion was assessed by a trained medical specialist according to the International Standards for Neurological Classification of SCI (http://ais.emsci.org/). BMI was assessed from self-reported height and weight, and classified according to World