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Upper limb function is normal in patients with restless legs syndrome (Willis-Ekbom Disease)

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HIGHLIGHTS

- Restless legs syndrome, now called Willis-Ekbom Disease (RLS/WED), is a sensorimotor-related sleep disorder characterised by an abnormal urge to move.
- The aim of the current study was to investigate upper limb function in RLS/WED patients using objective methodology.
- RLS/WED patients manipulate objects in a normal manner and exhibit normal maximal pinch grip, tremor during movement, and movement speed and rhythmicity compared to age- and gender-matched healthy controls.

ABSTRACT

Objective: Restless legs syndrome, now called Willis-Ekbom Disease (RLS/WED), is a sensorimotor-related sleep disorder. Little is known of the effect of RLS/WED on motor function. The current study investigated upper limb function in RLS/WED patients. We hypothesised that RLS/WED patients exhibit subtle changes in tremor amplitude but normal dexterity and movement speed and rhythmicity compared to healthy controls.
Methods: RLS/WED patients (n = 17, 59 ± 7 years) with moderate disease and healthy controls (n = 17, 58 ± 6 years) completed screening tests and five tasks including object manipulation, maximal pinch grip, flexion and extension of the index finger (tremor assessment), maximal finger tapping (movement speed and rhythmicity assessment), and the grooved pegboard test. Force, acceleration, and/or first dorsal interosseus EMG were recorded during four of the tasks.
Results: Task performance did not differ between groups. Learning was evident on tasks with repeated trials and the magnitude of learning did not differ between groups.
Conclusions: Hand function, tremor, and task learning were unaffected in RLS/WED patients. Patients manipulated objects in a normal manner and exhibited normal movement speed, rhythmicity, and tremor.
Significance: Further research is needed to assess other types of movement in RLS/WED patients to gain insight into the motor circuitry affected and the underlying pathophysiology.

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1. Introduction

Restless legs syndrome (RLS), also called Willis-Ekbom Disease (WED), is a sensorimotor-related sleep disorder that affects 5–15% of the population (Yeh et al., 2012). RLS/WED is characterised by an abnormal urge to move, usually the legs, that begins or worsens during periods of rest (Allen et al., 2003; Walters, 1995). The urge to move is usually accompanied by uncomfortable or unpleasant sensations. Symptoms are typically worst in the evening and at night and can be partially or totally relieved by moving the affected limb (Allen et al., 2003; Walters, 1995). The symptoms commonly result in sleep disturbance and reduced quality of life (Allen et al., 2011).

There is no definitive diagnostic test for RLS/WED and the pathophysiology is not fully understood. Mechanisms that are thought to play a role include genetic variants (Winkelmann et al., 2007), iron dysregulation (Connor et al., 2011; Dusek et al., 2012), reduced D_2 receptors in the putamen (Connor et al., 2009), and dopamine dysregulation (Trenkwalder and Paulus, 2010). Sensory disturbance (Stiasny-Kolster et al., 2004), altered neurochemistry in the thalamus (Allen et al., 2013; Rizzo et al., 2012), and reduced intracortical inhibition in the hand (Nardone et al., 2006; Tergau et al., 1999) and leg (Tergau et al., 1999) area of motor cortex have also been observed.

Given that RLS/WED is characterised by an abnormal urge to move, it is surprising that relatively little is known about the effect of RLS/WED on movement. Only three studies have been published on lower limb movement in this population and kinematics of gait (Paci et al., 2009), foot tapping (Mrowka et al., 2005), and rising from a chair (Jimenez-Jimenez et al., 2009) appear normal. There has been much discussion about possible symptomology in the upper limb (Alisky, 2007; Freedom and Merchut, 2003; Horvath et al., 2008) but the three published studies on upper limb movement suggest normal resting tremor (subjectively rated) (Ondo and Lai, 2006) and performance on simple tasks (e.g. finger tapping and forearm pronation and supination (Jimenez-Jimenez et al., 2009)). However, subjective rating of tremor in the hands is deemed to be mildly abnormal in 30–40% of patients during a postural task and finger-to-nose movement (Ondo and Lai, 2006). Subjective rating of tremor does not provide information about the amplitude and frequency of tremor. Therefore, the current study sought to further investigate tremor and possible upper limb symptomology in RLS/WED patients using objective and comprehensive methodology. This included detailed assessment of motor planning, movement execution, kinematics of movement, and learning during various tasks. We hypothesised that RLS patients exhibit (a) subtle changes in tremor amplitude during movement, but not tremor frequency, and (b) normal dexterity and movement speed and rhythmicity when compared to healthy age- and gender-matched controls. Our hypothesis is based on previous preliminary arm movement findings (Jimenez-Jimenez et al., 2009; Ondo and Lai, 2006) and observations of altered circuitry of the hand area of the motor cortex (Nardone et al., 2006; Tergau et al., 1999), sensation, and thalamic neurochemistry (Allen et al., 2013; Rizzo et al., 2012; Stiasny-Kolster et al., 2004). This study provides the first detailed investigation of upper limb movement in RLS/WED patients and will further understanding of the functional sequelae.

2. Methods

Upper limb function was examined in 17 RLS/WED patients (aged 59 ± 7 years; 3M, 14F) and 17 age- and gender-matched healthy and neurologically normal controls (aged 58 ± 6 years; 3M, 14F). Inclusion criteria for the RLS/WED group were diagnosis according to International Restless Legs Syndrome Study Group guidelines (Allen et al., 2003) and no co-morbid neurological damage and/or illness. Experimental procedures were approved by the local ethics committee, performed during the day (2:11 pm ± 2.12 h), and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained. Each subject underwent screening tests and five movement tasks. Patients were tested OFF medication (>12 h).

2.1. Screening tests

Each subject completed a medical history questionnaire (Rossi et al., 2009) and neuropsychological assessment involving WMS-R Logical Memory I and II subtests (Wechsler, 1987), Verbal Trails (Grigsby and Kaye, 1995), Verbal Fluency (Benton and Hamsher, 1983), and Digit Span forwards and backwards (Wechsler, 1981). Performance on each test was compared to published normative data matched for age and years of education. Each subject also underwent a neurological examination, performed by a neurologist with expertise in movement disorders, for confirmation of RLS/WED diagnosis and completion of the Restless Legs Syndrome Symptom Checklist (Allen et al., 2003), International Restless Legs Syndrome Study Group Rating Scale (IRLS Rating Scale) (Walters et al., 2003), and the third (motor) part of the Unified Parkinson's Disease Rating Scale (UPDRS-III) (Fahn and Elton, 1987).

2.2. Experimental protocol

Subjects performed five movement tasks with the dominant hand while seated (94% of subjects were right handed). The first task involved gripping and lifting a light-weight object (342 g; Fig. 1A) (Westling and Johansson, 1984). It consisted of a dual axis accelerometer (model ADXL311J, RS Components, Smithfield, Australia) and two load cells (model MPL-100; Transducer Techniques, Temecula, CA, USA) mounted orthogonally for measurement of horizontal grip force and vertical lift force. Subjects contacted the object on polished brass disks positioned 35 mm apart. Subjects were instructed to: 'Lift the object off the table to the height indicated (~10 cm), hold the object there for 3 s and then replace it on the table'. The task was demonstrated to the subject prior to their first attempt and no practice was allowed. Three trials were performed with a pinch grip at ~10-s intervals.

The second task involved three brief (2–3 s) maximal voluntary contractions (MVCs) to enable normalisation of some parameters measured during the grip and lift task. MVCs were performed with a pinch grip and were separated by ~1 min rest intervals to avoid fatigue. Subjects were given verbal encouragement and visual force feedback.

The third task involved estimation of tremor amplitude at the index finger. A small accelerometer (dimensions 5 × 5 × 2 mm; ±2 g dual axis, ADXL212, Analog Devices, Norwood, Massachusetts, USA) was attached to the fingernail (Fig. 2A) for detection of small perturbations in the vertical plane (flexion–extension) with respect to acceleration due to gravity. Tremor was measured at rest and during two flexion and extension movements of the index finger (Fig. 2D) whilst blindfolded. Resting tremor was measured with the subject's hand resting on a table (30-s duration). Subjects were then asked to raise their hand off the table for measurement of tremor during flexion and extension of the index finger (~2 s duty-cycle, 30 s duration, termed 'internally-paced movement'). Standardised verbal and visual instructions were given to each subject. Subjects then repeated the movement task with an auditory cue delivered to signal the turning point between flexion and extension (2 s duty-cycle; termed 'auditory-paced movement').

The fourth task involved tapping a linear strain gauge (MLP-100; Transducer Techniques, USA) as fast as possible with the