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Research Report

Postural sway in idiopathic rapid eye movement sleep behavior disorder: A potential marker of prodromal Parkinson's disease

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ABSTRACT

There is compelling evidence that postural instability occurs at very early clinical stages of Parkinson's disease (PD), making it tempting to speculate that changes in postural sway may even occur at a prodromal phase. Studies estimate that approximately half of patients with idiopathic rapid eye movement (REM) sleep behavior disorder (RBD) will eventually develop PD, so RBD may be an indicator of prodromal PD. This study was undertaken to investigate postural sway and its relation to stereopsis function in patients with RBD. We examined 24 patients with polysomnography-confirmed RBD and 23 healthy, sex-and age-matched control subjects. Postural sway was measured with an accelerometer at the center of mass at the lower spine. Subjects were asked to stand quietly for 30 s under two usual conditions (eyes open and eyes closed) and three challenging conditions (eyes open with dual task, eyes closed with dual task, and tandem standing). Stereopsis was assessed using the Titmus fly test. RBD patients showed an increased variability of trunk acceleration and a decrease of smoothness of sway, compared to control subjects. These differences reached significance in the challenging conditions. RBD patients demonstrated significant impairment in stereopsis. There were statistically significant correlations between log seconds of arc of the Titmus test and some sway parameters within the RBD group. RBD patients with abnormal stereopsis showed a significant increase of JERK values compared to patients with normal stereopsis in the challenging conditions. Our results indicate that idiopathic RBD patients, especially with abnormal stereopsis, have subtle signs of postural instability under challenging conditions. Postural sway performance may serve as a biological marker for prodromal PD.

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1. Introduction

Idiopathic rapid eye movement (REM) sleep behavior disorder (RBD) is characterized by loss of the normal atonia of REM sleep. Affected patients have excessive motor activity such as punching, kicking, or crying out in association with dream content. Longitudinal studies estimate that over 50% of patients with idiopathic REM sleep behavior disorder will develop neurodegenerative parkinsonism (almost exclusively Parkinson's disease, multiple system atrophy or dementia with Lewy bodies) with a mean latency from REM sleep behavior disorder onset to disease diagnosis of 13 years (Schenck et al., 1996; Iranzo et al., 2006; Postuma et al., 2009a, 2009b). This high conversion rate to neurodegenerative disease provides a unique opportunity to observe directly the development of clinical parkinsonism.

Postural instability plays a major role in the motor manifestation of Parkinson's disease (PD). Until recently, it has been considered to occur relatively late in the disease course. This is reflected by the Hoehn&Yahr scale where "postural instability" is represented only in the advanced stages 3 to 5 (Hoehn and Yahr, 1967). However, there is accumulating evidence that changes of postural stability occur even at early PD stages (Beuter et al., 2008; Mancini et al., 2011; Stylianou et al., 2011), and that postural instability increases with the progression of the disease (Mancini et al., 2012).

PD is thought to have a long prodromal phase (Postuma et al., 2010; Lang, 2011). Powerful compensatory mechanisms may mask these clinical symptoms and make them difficult to identify and evaluate in the earliest stages of the illness. Years before PD can be diagnosed clinically, motor signs such as slowing of fine hand movements, reduced arm swing, changes in walking patterns, stiffness, tremor, and imbalance may be detected (de Lau et al., 2006; Gaenslen et al., 2011). A recent study found altered gait parameters in LRRK2 G2019S mutation carriers without a clinical diagnosis of PD (Mirelman et al., 2011). This mutation leads to a Parkinsonian syndrome with relatively high probability. Also, trunk acceleration and smoothness of sway under challenging tasks, measured by accelerometers positioned at the lower back, are greater in people at high risk for Parkinson's disease, defined as the presence of prodromal non-motor markers (Maetzler et al., 2012). In a longitudinal study of idiopathic RBD patients, among the subjects developing clinically overt PD, abnormal Unified PD Rating Scale (UPDRS) motor scores were observed 4.5 years before the diagnosis could be made, whereas impaired motor performance was detected 6–9 years before diagnosis using the Purdue Pegboard, alternate-tap and timed up-and-go test (Postuma et al., 2012). Since many patients with idiopathic RBD are at risk of developing PD, we hypothesized that sway parameters may be changed in patients with idiopathic RBD, even in those who were free of parkinsonism.

Stereopsis, or binocular depth perception, depends on the disparity between the views perceived by each eye. The two images are fused in the cerebral cortex and experienced as a single three-dimensional representation under normal circumstances. A recent study found deficits of stereopsis are common in drug-naive Parkinson's disease patients and associated with nondominant extrastriate cortical atrophy (Koh et al., 2013). Since color vision abnormalities have been well-described in PD and idiopathic RBD (Postuma et al., 2009a, 2009b), we hypothesized that dysfunction of stereopsis was also in idiopathic RBD.

In the current cross-sectional study, we investigated postural sway in patients with idiopathic RBD, measured by wearable accelerometers, to test the hypothesis that the postural control system was affected already at a prodromal stage of PD. Moreover, we identified cases of dysfunction of stereopsis in RBD patients, and evaluated the relationship between stereopsis and sway parameters.

2. Results

2.1. Clinical characteristics

The clinical characteristics of the subjects are shown in Table 1. The RBD and control groups were similar with respect to age, gender, height, weight, Body Mass Index, scores on the GDS, UPDRS motor scores ,and cognitive

Table 1 – Subject characteristics and stereopsis.

	RBD ($n=24$)	Controls ($n=23$)	p-Value
Age (ys)	65.37±8.50	64.21±7.27	0.62
M/F*	17/7	16/7	0.59
Weight (kg)	68.23±8.12	71.61±10.19	0.21
Height (m)	1.66±0.08	1.67±0.07	0.59
BMI (kg/m^2)	24.64±1.60	25.45±2.24	0.16
RBD duration(ys)	9.13±7.70		
MMSE (0–30)	28.20±1.79	28.74±1.66	0.30
MoCA (0–30)	25.83±1.63	26.74±1.79	0.08
GDS (0–30)	5.38±3.02	4.70±2.75	0.43
UPDRS III (0–100)	3.13±2.35	1.91±2.02	0.07
Stereopsis, Normal/Abnormal*	11/13	18/5	0.02

BMI=Body Mass Index; RBD=rapid eye movement sleep behavior disorder; MMSE=Mini-Mental State Examination; MoCA=Montreal Cognitive Assessment; GDS=Geriatric Depression Scale; and UPDRS III=motor part of the Unified Parkinson's disease Rating Scale.
* Expressed as number of subjects and p-values based on the Pearson Chi Square test.