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Research article

Vestibulo-ocular reflex abnormality in Parkinson's disease detected by video head impulse test

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HIGHLIGHTS

- Evaluation of the vestibular function in the patients with Parkinson's disease.
- A potential modality for generation of an adequate set of biofeatures for screening and diagnosis in Parkinson patients.
- The Vestibular-ocular reflex gain was compared between the Parkinson patients and healthy volunteers.

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ABSTRACT

Background: Parkinson's disease (PD) is a common neurodegenerative disease characterized by dopaminergic neuronal loss. The underlying cause of PD is unknown.
Objective: To assess the clinical relevance of vestibular-ocular reflex (VOR) gain in patients with PD, especially those in the early stages.
Methods: Sixty-three PD patients and 56 control healthy individuals were enrolled in this study between Mar 2015 and Aug 2015. VOR gains were determined by video head impulse test (vHIT) device. Statistical analysis was performed to assess the difference in VOR gains between PD patients and normal people. The relationship of VOR gain with age, duration and severity of disease was also assessed.
Results: In the control group, average VOR gain was 0.98 ± 0.09 on the left side and 0.99 ± 0.16 on the right side. No statistically significant difference was observed between the two sides in the control group ($P > 0.05$). In the PD group, average VOR gain was 1.20 ± 0.22 on the left side and 1.23 ± 0.23 on the right side. No statistically significant difference was observed between the two sides in the PD group ($P > 0.05$). There was a significant difference in VOR gain between the PD (both in early and mid-late stages) and the control group ($P < 0.05$). A weak correlation was observed between VOR gain and the motor Unified Parkinson Disease Rating Scale score. No correlation of VOR gain with age, duration of disease or the Hoehn and Yahr Scale score was observed. VOR gains in PD patients were found to be higher than normal, especially in the early stages of the disease.
Conclusion: vHIT is a potential tool to determine the VOR gain in PD patients and may help detect PD at an early stage.

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1. Introduction

Pakinson's disease (PD) is a common neurodegenerative disease characterized by dopaminergic neuronal loss. The condition has no specific predilection for race, or geographical location. The incidence of PD rises with age; median age of onset is approximately 60 years. Mean duration of this disease from diagnosis to death is about 15 years [1]. There are four cardinal features of PD: bradykinesia, resting tremor, rigidity, and postural instability. It presents with subtle features such as loss of manual dexterity, which may remain unnoticed for a long time. The underlying cause of PD is unknown, however, deranged function of basal ganglia and dopaminergic signals lead to impairment of postural reflexes. Dopamine receptors (D2) are located in medial vestibular nuclei and lateral vestibular nuclei. There is a link between dopamine and the vestibular system. Unrecognized degeneration in vestibular-ocular reflex (VOR) circuits and impaired control of the nigrostriatal reflex by cerebral

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hemisphere have been previously documented [2]. In healthy subjects, the angular VOR stabilizes gaze in space by compensating the head rotation with equal eye rotation in the opposite direction. In case of deficient VOR, the eyes move with the head; this forces the patient to make a catch-up saccade. Age has been shown to influence VOR. Older individuals have decreased ability to enhance or suppress the VOR, as compared to that in young individuals. Moreover, impaired VOR suppression has been shown to be associated with age-related neurodegenerative diseases such as PD. However, no further studies have been conducted.

Previous studies have documented reduced or absent vestibular responses in patients with PD; the deficit was shown to be associated with postural instability and increased severity of other symptoms. Patients with PD showed reduced gain of saccades as compared to that in healthy controls [3,4]. Moreover, these patients manifested a lack of vestibulo-ocular reflex. Further, the phenomenon of absent vestibular evoked myogenic potential (VEMP) was significantly higher in patients with PD as compared to that in healthy controls [5–8]. The lack of vestibular neuronal activity in PD patients has been demonstrated by electrovestibulography (EVestG) [8–10]. However, the above-mentioned studies were conducted with small sample sizes and the findings have not been replicated on a larger scale in clinical settings. It is vital to seek another more sensitive method for detection of PD at an early-stage.

The bedside head impulse test (bHIT) has been shown to be effective in detecting VOR deficit in patients with unilateral vestibular loss [11]. In the presence of vestibular deficit, however, the sensitivity of bHIT is lower because the residual peripheral function results in a smaller gain. The video head impulse test (vHIT) is a new lightweight, minimal-slip, high-speed diagnostic modality which measures eye velocity during head rotation. The system is easy to use, and provides an objective quantitative measure of the VOR and detects both overt and covert saccades [12]. Theoretically, the normal value of VOR is 1. In clinical practice, we have found higher than normal VOR gains with increased catch-up saccades in most patients with PD. In the early stages of PD, some patients may walk steadily without any overt sign of postural instability; the VOR gains in such patients may even be up to 1.6–1.8. Whether this represents a vestibular compensatory mechanism in patients with PD is not known. If this vestibular compensation is common in early PD, it could help in early diagnosis of PD.

This was a prospective randomized study. The purpose of the study was to estimate the clinical relevance of the VOR gain in patients with PD, especially those in the early stages of the disease.

2. Patients and methods

2.1. Patients

This study was approved by the institutional review board at Sir Run Run Shaw Hospital and Ningbo No.2 Hospital while performed in accordance with the ethical principles of the Declaration of Helsinki (2013). Written informed consent was obtained from all participants prior to their enrolment in the study. This study was performed from Mar 2015 until Aug 2015 and involved 63 PD patients and 56 healthy individuals as controls. An experienced movement disorder neurologist completed the patient evaluation using the motor Unified Parkinson Disease Rating Scale (m-UPDRS) and the Hoehn and Yahr Scale (H&Y). PD patients with an H&Y score in the ranges of 1–2.5 and 3–5 were considered to be in early and mid-late stages, respectively.

The exclusion criteria were: severe vision damage with inability to focus on visual target or impaired eye movements, history of ear surgery, chronic otitis media, deafness and vertigo, limited neck movement because of neck injury. In order to avoid potential interference of eighth cranial nerve dysfunction on the test results, patients who had hearing threshold frequency above 40 dB were also excluded from this study.

2.2. Video head impulse test

The measurement of VOR gain by vHIT is detailed elsewhere [13]. Briefly, vHIT tests were carried out by prototype ICS Impulse video goggles system (GN Otometrics, Denmark). The subjects were tested in a well-lit room and wore a pair of goggles with an in-built video camera for recording the real time eye movements. There was a motion sensor for measuring head movement. Before each test, calibration was performed to ensure accurate measurement. Subjects were instructed to maintain ocular fixation by maintaining a steady gaze at a target at eye-level, such as a laser dot placed at a distance of 1 m. Fifty horizontal head impulses were applied with unpredictable direction. The impulse peak head velocity was gradually increased from 50° up to 250° per second (acceleration 750°–5000° per second^2 and amplitude 5°–20°). Tracings of head and eye velocity were displayed simultaneously on the screen. Corrective saccades were identified as delayed eye movement on the tracing. The software calculates the VOR gain as the ratio of peak slow phase eye velocity to peak head velocity. All recordings were performed over 15 times to ensure accuracy and consistency of data. The experimenters were unmasked as to whether they were testing a PD patient or a healthy subject. All experimenters have at least 10 years of experience in vestibular research. In order to minimize the potential impact on vestibular function, all PD patients were required to maintain the original drug, and the tests were completed between 9:00 AM and 11:00 AM or between 2:00 PM and 4:00 PM.

2.3. Statistical analysis

Quantitative data are expressed as mean ± Standard Deviation (SD) or as frequency (percentage). One-way Analysis of Variance (ANOVA) was performed to compare VOR gains in PD and control groups. Statistical significance was determined at $P < 0.05$. All data acquisition and analyses were performed blinded. All statistical analyses were performed using SPSS 20.0 software (SPSS, San Rafael, CA, USA).

3. Results

Mean age in the PD and healthy control group was 65.7 years and 65.9 years, respectively. According to H&Y and m-UPDRS scores, 43 patients were categorized as early and 20 as mid-late PD patients (Table 1). There were no statistically significant between-group differences with respect to gender and age ($P > 0.05$).

Average VOR gain was 0.98 ± 0.09 on the left side and 0.99 ± 0.16 on the right side in the control group; the mean asymmetry between the two sides was 4.37 ± 3.45% ($P > 0.05$). In the PD group, average VOR gain was 1.20 ± 0.22 in the left and 1.23 ± 0.23 in the right side; the mean asymmetry was 4.38 ± 4.03% ($P > 0.05$).

There was a statistically significant difference in VOR gain between the PD and control groups in the left and right side separately ($P < 0.05$) (Table 2). In the left side, there was a statistically significant difference in VOR gain in early and mid-late PD groups, when compared with that in the control group ($P < 0.05$). There was no statistically significant difference in VOR gain between the early PD and the mid-late PD groups ($P > 0.05$). Similar results of VOR gain were observed in the right side(Table 2). The covert saccades during head rotation and overt saccades after head rotation were recorded in the PD group and the control group. The positive rate of abnormal scanning in the PD group was 93.7% (Fig. 1).

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