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Subjective visual vertical perception and sense of smell in Parkinson disease

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Abstract—This article describes an open cross-sectional observational study involving 47 participants with Parkinson disease (PD) and 47 (age- and sex-matched) nondisabled controls without PD. The aim was to determine the profiles of subjective visual vertical (SVV) perception and sense of smell perception in both groups. There was a statistically significant difference ($p < 0.001$) between patients and controls on their smell test performance. Controls were more likely to correctly identify odors, with a median score of 10 out of 12 compared with 6.5 out of 12 for patients with PD. The median SVV error for the PD group when the frame was untilted was 0.75 degrees compared with 0.50 degrees for controls. This difference was statistically significant ($p = 0.02$). When the frame was tilted, the median SVV error for the PD group was 2.31 degrees compared with 2.00 degrees for controls (not statistically significant), with both groups showing similar distribution pattern of errors. There was no statistical correlation between number of correctly identified odors and an individual's SVV error. However, a statistically significant negative correlation ($r = –0.45$, $p = 0.01$) was found between Mini-Mental State Examination score and mean time taken to complete each rod and frame test in patients with PD, suggesting that SVV errors might be more correlated with cognitive function than with loss of sense of smell.

Key words: computerized rod and frame test, correlation, Mini-Mental State Examination, motor functions, Parkinson disease, rehabilitation, sensory functions, smell, subjective visual vertical, visual perception.

INTRODUCTION

The clinical diagnosis of Parkinson disease (PD) relies heavily on the presence of akinesia or bradykinesia, plus one or more of the other core features such as tremor, rigidity, and postural instability [1]. It is, however, widely recognized now that PD involves nonmotor, as well as the typical motor, features [2]. These nonmotor features may include visual, olfactory, autonomic, cognitive, and affective function. However, whether all of these nonmotor features are affected in all patients with PD and at what stage is not fully understood.

In addition to impaired sense of smell, which is usually affected at an early stage [3–4], subtle visual dysfunction is common in PD. Patients with PD were reported to have reduced visual acuity [5], color vision [6], and contrast sensitivity [7]. It has also been reported that there is an increased visual dependence perceptually in patients with

Abbreviations: CRAF = computerized rod and frame, MMSE = Mini-Mental State Examination, PD = Parkinson disease, RFT = rod and frame test, SVV = subjective visual vertical, UPDRS-III = Unified Parkinson Disease Rating Scale part III, UPSIT = University of Pennsylvania Smell Identification Test.

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PD [8]. Interest in visual dysfunction is enhanced by the possible relationships between gait disorders and visual perception [9]. Gait problems such as festination and freezing are thought to be strongly influenced by visual stimulation [10]. The increased visual dependence may also limit a patient's ability to compensate fully for gait disorders, particularly in situations involving sensory conflict caused by excessive visual motion [11]. Further studies suggest that visual dysfunction may also contribute to PD disability through influences on cognition and locomotion [12]. A better understanding of these events and their interrelationships will provide the underpinning for efforts to improve rehabilitation.

Existing computer software programs currently being used in rehabilitation are very limited, and those that do exist are either restricted to very specific tasks or are complex and not user friendly. The rod and frame test (RFT) is one of the key measures of the cognitive style construct of field-dependence-independence [13–14]. During the RFT, patients view a tilted square frame and an adjustable rod that tilts on the same center as the frame. They are asked to adjust the rod to the gravitational vertical, and these adjustments vary greatly. Over the years, the RFT has been used in many areas of psychology, education, interpersonal behavior, and musculoskeletal disorders [15–16]. Until recently, all published research has employed mechanical rod and frame systems that require specialized facilities and would not be easy to use in a field setting. This article describes a computerized rod and frame (CRAF) test that is portable and easy to use and will run on a standard office computer.

We investigated visual perception using the CRAF test and its relationship with sense of smell in patients with PD with a view to identifying a simple test that can be used as a marker when considering rehabilitation programs. The question was prompted by the observation that patients with balance disorders often report worsening of symptoms in complex visual environments [17–18]. No study has yet linked subjective visual vertical (SVV) perception with olfactory perception in patients with PD. Our aim, therefore, was to determine the profiles of SVV (as measured by the CRAF test) and sense of smell perception (as measured by the University of Pennsylvania Smell Identification Test [UPSIT]) in patients with PD and compare them with age- and sex-matched nondisabled controls.

METHODS

Participants

This was an open cross-sectional observational study involving 47 participants with PD and 47 age- and sex-matched nondisabled controls. We recruited participants with PD from patients attending a movement disorders clinic at a local hospital. All patients fulfilled the UK Brain Bank diagnosis criteria for idiopathic PD [19]. Those willing to take part were seen for an assessment visit to ensure that they fulfilled the study inclusion criteria. We tested those who fulfilled the criteria during the "on" state (i.e., the state in PD when symptoms "such as tremor and bradykinesia" have responded to anti-PD medications [1]).

We recruited participants without PD (controls) from among partners and caretakers of patients with PD and volunteers working at the same hospital. They were selected so that the distribution of sex and age (in 10-year bands, i.e., 50–59, 60–69, 70–80) was as close as possible to the PD group in order to make it easier to match the two groups. All participants had a Mini-Mental State Examination (MMSE) score greater than 26 (out of 30), and their vision was normal or corrected to normal.

We used the motor section of the Unified Parkinson Disease Rating Scale part III (UPDRS-III) to quantitatively evaluate motor function in the PD group. UPDRS-III scores range from 0 to 56, with higher scores indicating greater motor impairment.

Olfactory Perception

We investigated olfactory perception using the 12-item UPSIT, which is the abbreviated version of the 40-item UPSIT. During testing, an examiner scratched the impregnated card and asked the participant to identify the smell from the four choices provided. We scored participants based on the number of correctly identified odors.

Perception of Subjective Visual Vertical

We used the CRAF test to examine perception of SVV. The test consists of a series of 12 presentations of a white square frame surrounding a white line, which represents the rod, on a homogenous black background (**Figure 1**). There were three possible frame alignments: untilted (or neutral), tilted 18° clockwise, or tilted 18° counterclockwise. The starting position of the rod was 20° from gravitational vertical in either a clockwise or counterclockwise

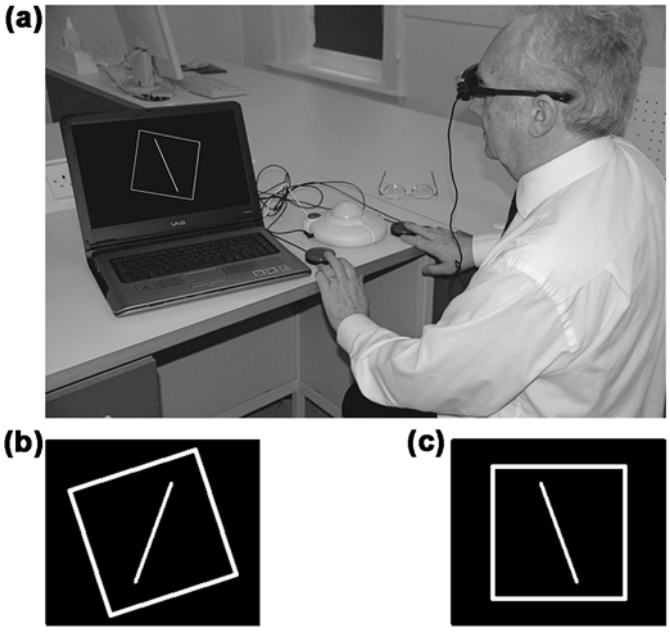

Figure 1.
Computerized rod and frame test in use. (**a**) Computer screen shows rod surrounded by frame tilted clockwise +18°. Subject viewed display through head-mounted video glasses and rotated rod using two large buttons. Other possible frame positions were either (**b**) tilted counterclockwise (–18° from vertical) or (**c**) untilted.

direction. We presented each frame orientation four times with an even distribution of the two rod positions. The computer randomly assigned the order of presentation during the test. Each test began with two practice presentations (one untilted and the other tilted) that we used as examples to explain the procedure. In some cases, participants misunderstood the task and began aligning the rod with the frame rather than gravitational vertical. In this situation, we reminded them once that the task was to move the rod to the vertical position.

We carried out all testing in a room with natural lighting. Participants viewed the images not directly from the computer screen but through a pair of video eyeglasses [15,20]. Participants used a switch adapted BIGtrack Trackball (Infogrip Inc; Ventura, California) instead of a regular computer mouse to move the rod during the test (**Figure 1**). The left button rotated the rod counterclockwise, and the right button rotated the rod clockwise about its center. When the participant was satisfied with the rod alignment, he or she pressed the space bar on the keyboard, prompting the computer to record any error from the vertical to 0.5° accuracy and display the next presentation.

Statistical Analysis

The UPSIT scores used for analysis were the number of correctly identified odors (from a possible 12). For the CRAF test, values used represent the unsigned mean of four presentations (in the case of the untilted frame condition) and eight presentations for frame tilted, where the results for clockwise and counterclockwise tilted frame have been combined. We tested data for normality using the Kolmogorov-Smirnov test and found it to be not normally distributed. Consequently, the data are represented by box plots (SPSS version 17.0, IBM Corporation; Armonk, New York) in which the median is identified by a line inside the box and the length of the box is the interquartile range. We used nonparametric statistics for the analysis. We used Mann-Whitney U tests to investigate differences between groups and Wilcoxon signed rank tests for testing within groups.

RESULTS

Demographics and Clinical Characteristics

A total of 94 subjects agreed to participate in the study: 47 patients with PD (27 male and 20 female) with a mean ± standard deviation age of 69.35 ± 7.70 years and 47 nondisabled controls (27 male and 20 female) aged 68.89 ± 8.40 years. However, one female patient with PD withdrew during testing. The MMSE score for the PD group was 28.59 ± 1.40, whereas the MMSE score for the controls was 29.40 ± 1.00. We found no statistically significant difference in age or in MMSE score between patients with PD and controls.

All patients were diagnosed as having idiopathic PD according to the UK Brain Bank diagnostic criteria [1]. The duration of the disease was 4.71 ± 3.30 years, with a UPDRS-III motor score of 15.72 ± 6.90. We tested all participants with PD during the on state.

Sense of Smell Test

Figure 2(a) shows a marked difference between patients with PD and controls in their performance on the abbreviated UPSIT test. Controls were more likely to correctly identify the odor with a median score of 10 out of 12 (range: 5–12) compared with 6.5 out of 12 (range: 0–12) for patients with PD. This difference was highly

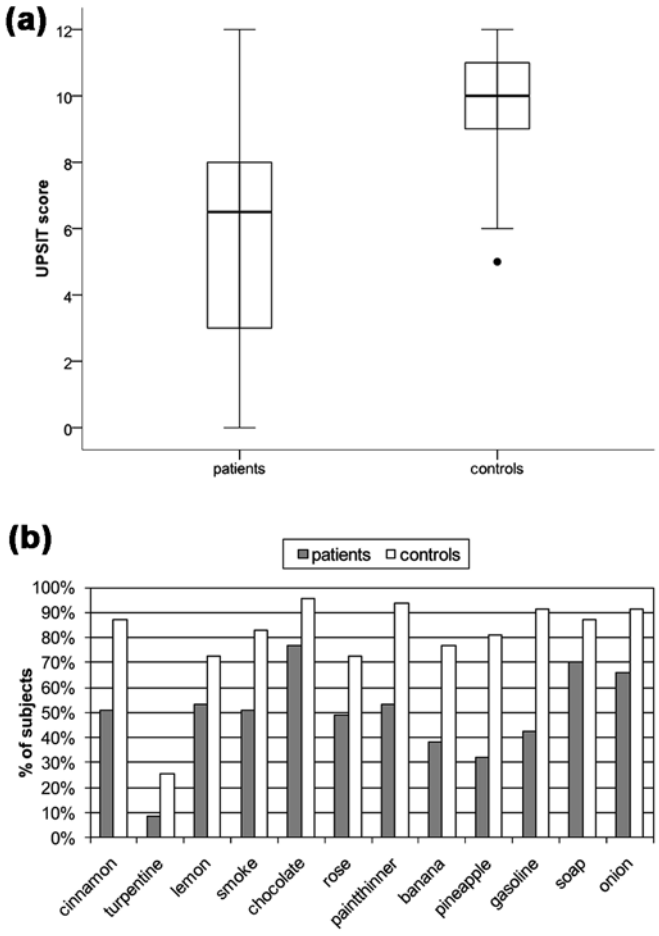

Figure 2.
Comparison between patients with Parkinson disease and controls with regards to (**a**) number of correct responses in University of Pennsylvania Smell Identification Test (UPSIT) and (**b**) correct identification of individual odors in UPSIT.

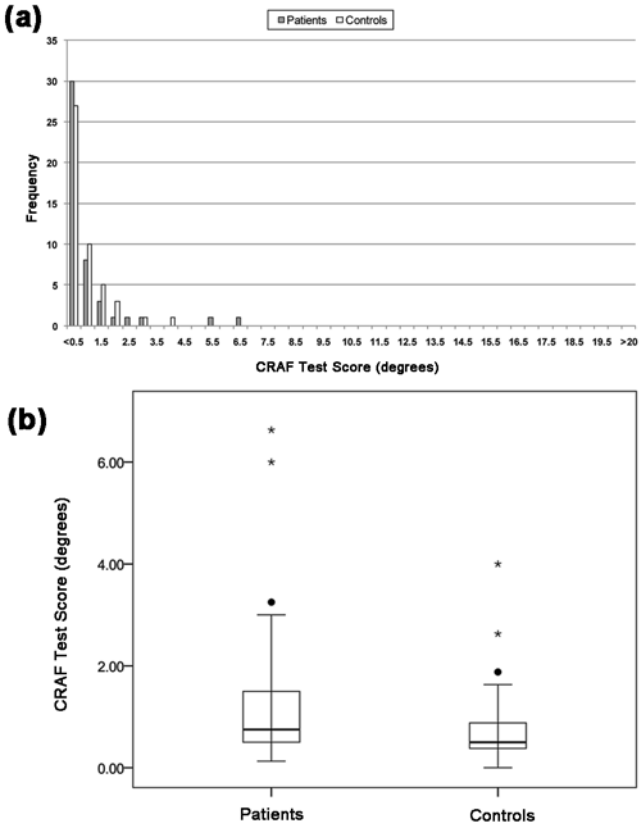

Figure 3.
(**a**) Distribution of errors (degrees from gravitational vertical) recorded during computerized rod and frame (CRAF) test for subjective visual vertical for patients with Parkinson disease (PD) and controls when frame was untilted. (**b**) Comparison of errors (degrees from gravitational vertical) recorded during CRAF test for patients with PD and controls when frame was untilted. Dots represent outliers, i.e., those values falling outside 1.5 times interquartile range. Stars represent extreme values, i.e., those values falling outside 3 times interquartile range.

significant (U = 388.50, $p < 0.001$). **Figure 2(b)** shows the pattern of distribution and the difference in the profile of loss of sense of smell between the two groups. Most people could identify chocolate. Pineapple had the greatest difference between the two groups.

Subjective Visual Vertical

Frame Untilted (Neutral)

Both groups showed a similar pattern of distribution of SVV errors when the CRAF test frame was untilted or neutral (**Figure 3(a)**). For the PD group, the median SVV error for the untilted frame condition was 0.75° (range: 0.13°–6.63°) compared with 0.50° (range: 0.00°–4.00°) for controls. This difference between patients with PD and controls was statistically significant (U = 786.00, p = 0.02; **Figure 3(b)**).

Frame Tilted

Both groups showed a similar (but wider than the untilted) pattern of distribution of unsigned SVV errors when the CRAF test frame was tilted (**Figure 4(a)**). For the PD group, the median unsigned SVV error for the tilted frame condition was 2.53° (range: 0.56°–16.81°) while the median for the control group was 2.06° (range: 0.50°–18.5°). However, we found no statistically significant

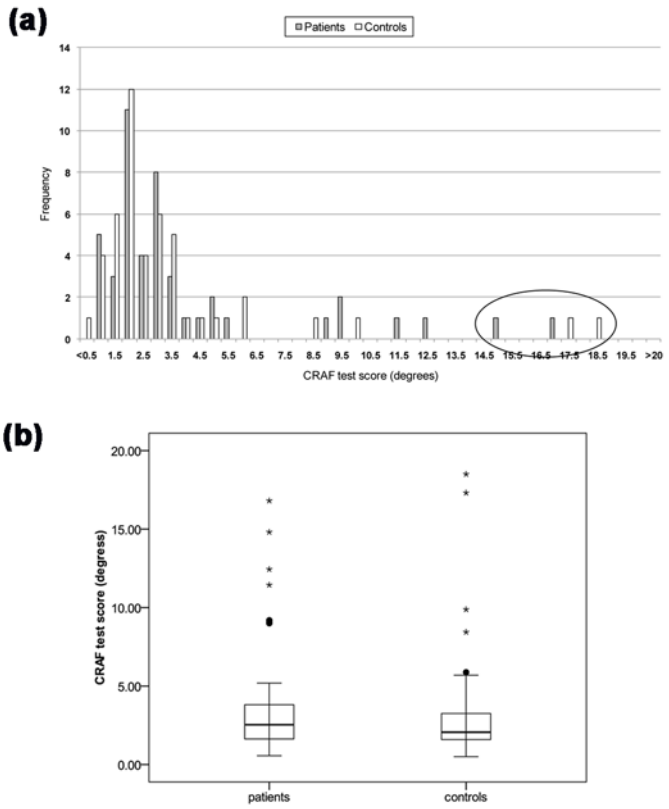

Figure 4.
(**a**) Distribution of unsigned errors (degrees from gravitational vertical) recorded during computerized rod and frame (CRAF) test for subjective visual vertical for patients with Parkinson disease (PD) and controls. Errors in circled area represent individuals aligning rod with frame angle (18°) rather than gravitational vertical. These individuals were excluded from analysis. (**b**) Comparison of unsigned errors (degrees from gravitational vertical) recorded during CRAF test for patients with PD and controls when frame was tilted. Dots represent outliers, i.e., those values falling outside 1.5 times interquartile range. Stars represent extreme values, i.e., those values falling outside 3 times interquartile range.

difference between these results (U = 987.00, p = 0.47; **Figure 4(b)**). **Figure 4(a)** also highlights the errors (around 18°) of those individuals who misunderstood the task and aligned the rod to the frame angle rather than to gravitational vertical.

Correlation Studies

We found no correlation between the number of correctly identified odors and an individual's mean unsigned SVV error in patients with PD (Spearman ρ = 0.13, p = 0.39, n = 46). Only two of the age bands contained sufficient participants to do a meaningful statistical analysis (n = 17 for 60–69 and n = 22 for 70–79, while n = 5 for 50–59 and n = 2 for >80). Within these, we found no significant correlation between SVV and UPSIT score.

We found no correlation between SVV errors and duration of disease in the PD group, nor did we find a correlation between SVV errors and UPDRS-III motor score. In addition, we found no correlation between the UPDRS-III motor score and the UPSIT score for the PD group (Spearman ρ = –0.185, p = 0.45, n = 46).

However, we found a medium but negative correlation that was statistically significant (Spearman ρ = –0.45, p = 0.01, n = 46) between the MMSE score and the mean time taken by each participant to complete each CRAF test in the PD group (**Figure 5**), although we found no similar correlation in the control group. Note that we found no correlation between the UPDRS-III motor score and the mean time taken to complete each CRAF test in the PD group (Spearman ρ = 0.18, p = 0.24, n = 46).

DISCUSSION

Sensory deficits have been documented in PD, particularly in the olfactory and visual domains [5–7,21–22]. Visual deficits in PD are subtle and not likely to be

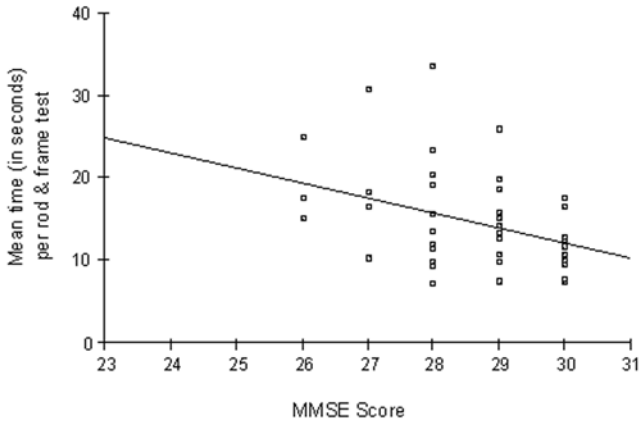

Figure 5.
Correlation of results for Mini-Mental State Examination (MMSE) score and mean time taken by each participant with Parkinson disease to complete each rod and frame test (Spearman ρ = –0.45, p = 0.01, n = 46).

discovered during routine neurological examination. They can only be detected with more specific psychophysical or electrophysiological tests. Nonetheless, these subtle visual deficits probably contribute to some of the disabilities that are commonly encountered in PD, such as gait freezing, falls, and visual hallucinations. The CRAF test might help identify patients who have visual perception problems and are at risk of falls and will allow us to tailor a rehabilitation program accordingly. The exact etiology of visual dysfunction in PD is not fully understood; it may be related to retinal dopamine deficiency or higher order visual cortical dysfunction [12,23].

The RFT provides a quantitative measure of errors in vertical perception. Although the test is simple, a number of different systems have been used, all of which require specialized facilities and would not be easy to use in a clinical setting [20]. This article describes a CRAF test that is portable and easy to use in an outpatient or rehabilitation setting and runs on a standard office computer.

Is There Any Difference in Subjective Visual Vertical Score Between PD and Control Groups?

One of the aims of this article is to document whether patients with PD have an objectively different response to visually disorienting stimuli (using the CRAF test) than a control group. The results show that when the frame was neutral (i.e., untilted), the PD group's ability to estimate visual vertical was slightly different from an age- and sex-matched control group. These findings agree with Proctor et al. [24], who suggested that there is a slight difference in SVV between PD and control groups. Our findings are also consistent with Metzel et al. [25], who concluded that there are marked differences between PD and controls for SVV and subjective visual horizontal. However, both studies were undertaken more than 40 years ago and the resolution of the equipment used in these studies cannot be established [24–25]. Most RFT equipment used at that time was manual and heavily reliant on the experience of the operator. Furthermore, although the difference we found was statistically significant (U = 703.00, p = 0.02; **Figure 3(b)**), it was very small (0.25°). It could therefore be argued that its value in a clinical setting as an early test for assessing people with PD is questionable.

The results also show that when the frame was tilted (either 18° clockwise or 18° counterclockwise), both groups showed a similar pattern of distribution of unsigned SVV errors (**Figure 4(a)**). This means that the PD group's ability to estimate visual vertical did not differ significantly from the control group (**Figure 4(b)**). This suggests that patients of mild to moderate PD severity (with normal cognitive function) do not have any increased impairment in perception of SVV. These findings are different from a similar study by Azulay et al. [8], who reported that patients with PD made significantly more errors on the RFT than nondisabled controls. These contrasting results between us and Azulay et al. might be caused by a number of factors, including:

- Different equipment to assess visual perception. We used a CRAF test software package, whereas other studies used a wide range of manual equipment with huge variation in precision.
- Intact cognitive function of PD group. All participants had an MMSE score greater than 26, and their vision was normal or corrected to normal. It was not clear whether the cognitive function of patients with PD in Azulay et al. was tested or not [8]. However, it could be argued that the MMSE score has limited value in detecting subtle cognitive impairment in patients with PD [26].
- Difference in sample size. Our sample size was double that used in Azulay et al., which might, in part, be responsible for these differences in results [8].
- High degree of SVV errors reported in most studies using manual RFT techniques. This might be caused by the fact that they did not exclude SVV results that were around 18°. The software program we used is capable of identifying people who misunderstood the task and ended up aligning the rod with one arm of the frame, thereby recording SVV errors between 15° and 18°. Note that a number of participants (2 in control group and 2 in PD group) performed the task incorrectly despite being reminded that they should align the rod to vertical and ignore the frame. **Figure 4(a)** highlights the errors (around 18°) of those individuals who aligned the rod to that frame angle rather than gravitational vertical.

Although we tested all participants with PD during the on state, it could be argued that the patient's medication profile could potentially affect the result. Barnett-Cowan et al. recently suggested that patients with PD have increased SVV dependence when taking dopaminergic medications [27]. However, they acknowledge that their study involved a very small number of participants and they proposed that future studies use large numbers of patients with PD in order to characterize the effect of

medication on the individual performance using SVV. In our PD group, 44 participants were on anti-PD medications and 2 were on no prescribed medications; our future work will explore the possible link between the medication profile of our participants with PD and their performance on the CRAF test.

In summary, the finding that patients with PD had slightly higher SVV errors than controls has no clinical significance despite the fact that this difference was statistically significant (when the frame was in neutral position). It could be argued that the two parts of the test (i.e., neutral and tilted) require different visual and cognitive skills and could therefore be relying on different neuronal pathways. For example, when the frame is tilted and participants are required to factor out this element, they rely more on maintaining attention and concentration. Because all patients with PD have a globally intact cognitive function, this meant that their attention and concentration power were intact as well. On the other hand, it could also be argued that since the perception of relative orientation of a stimulus in the environment requires integration of visual, vestibular, and internal representation of body orientation, objective assessments of vestibular problems within the study population need to be taken into account when comparing the PD group with nondisabled controls. Although we did ask questions (in the medical history of each participant) about balance problems and dizziness, we did not specifically assess participants for vestibular problems.

Is There Any Correlation Between Subjective Visual Vertical Score and Loss of Sense of Smell in Patients with PD?

Although our results confirmed that patients with PD exhibited an olfactory deficit significantly different from the control group (**Figure 2(a) and 2(b)**), we found no significant correlation between visual dysfunction (measured by SVV score) and loss sense of smell (number of odors correctly identified) in the PD group. This suggests that the loss of olfactory ability in these patients is not part of a generalized disturbance of perceptual ability. Note that loss of sense of smell in patients with PD usually occurs very early during the natural history of PD, whereas visual perception might be affected later on or even not at all. It could, therefore, be argued that as most of our PD patients' conditions were diagnosed less than 5 years ago and are of mild to moderate severity as evidenced by UPDRS-III score, we understandably did not find any correlation between visual dysfunction and loss of sense of smell in the PD group.

Furthermore, the CRAF test used in our study can provide not only static data (namely the degree of SVV errors), but also dynamic data (such as the time taken to finish each task). We found a statistically significant negative correlation between the MMSE score and the mean time taken by each participant to complete each CRAF test in the PD group (**Figure 5**). On the other hand, we found no similar correlation in the control group. This means patients with PD with a lower MMSE score took, on average, a longer time to complete each task (i.e., CRAF test) than those patients with PD with a higher MMSE score, suggesting that SVV errors correlate more with cognitive function than with loss of sense of smell.

Meanwhile, we found no correlation between the UPDRS-III score and the mean time taken to complete each CRAF test in the PD group. Note that UPDRS-III is a PD-specific instrument and that we tested all participants with PD in this study during the on state.

CONCLUSIONS

The concept of visual dependence derives from the fact that spatial orientation is based on both vestibule-proprioceptive and visual cues and that nondisabled people make variable and idiosyncratic use of such cues for spatial orientation [11,14,28] and postural control [29]. It has been suggested that such perceptual preferences observed in nondisabled people are also present, if not enhanced, in patients with a balance disorder [11] and in patients with PD. However, our findings did not confirm this assumption. It could therefore be argued that SVV score is more correlated with cognitive function than with loss of sense of smell. This was supported by Uc et al. [12], who suggested that patients with mild to moderate PD showed impaired visual perception and cognition compared with elderly control subjects [12]. Although patients with PD exhibited an olfactory deficit, there was no correlation between visual and olfactory dysfunction. Patients with PD (of mild to moderate severity who are cognitively intact) do not have any increased impairment in perception of SVV, and their ability to estimate SVV did not differ significantly from an age- and sex-matched control group. Therefore, further research is planned in which SVV scores for patients with PD and cognitive impairment will be compared with SVV scores for patients with PD without cognitive impairment. Furthermore, future studies should

include objective measures such as electrophysiological testing (e.g., visual evoked potential) to support subjective findings, since it is not clear whether vision problems are the result of the degeneration in the brain or whether some may be caused by lowered dopamine levels in certain cells of the retina. In the meantime, research exploring the use of the CRAF test in assessing patients with neurological conditions as an aid in planning their rehabilitation programs should continue.

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Analysis and interpretation of data: A. Khattab, S. Docherty, J. Bagust, P. Thomas, K. Amar.
Drafting of manuscript: A. Khattab, S. Docherty, J. Bagust, K. Amar.
Critical revision of manuscript for intellectual content: A. Khattab, S. Docherty, J. Bagust, R. Willington, P. Thomas, K. Amar.
Statistical analysis: A. Khattab, S. Docherty, J. Bagust, P. Thomas.
Study supervision: A. Khattab, J. Bagust, K. Amar.
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Participant Follow-Up: The authors will inform participants of the publication of this study in one of the PD support group meetings held each month.

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