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STUDY PROTOCOL

A protocol to examine vision and gait in Parkinson’s disease: impact of cognition and response to visual cues

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Abstract

Background
Cognitive and visual impairments are common in Parkinson’s disease (PD) and contribute to gait deficit and falls. To date, cognition and vision in gait in PD have been assessed separately. Impact of both functions (which we term ‘visuo-cognition’) on gait however is likely interactive and can be tested using visual sampling (specifically saccadic eye movements) to provide an online behavioural measure of performance. Although experiments using static paradigms show saccadic impairment in PD, few studies have quantified visual sampling during dynamic motor tasks such as gait.

This article describes a protocol developed for testing visuo-cognition during gait in order to examine the: 1) independent roles of cognition and vision in gait in PD, 2) interaction between both functions, and 3) role of visuo-cognition in gait in PD.

Methods
Two groups of older adults (≥50 years old) were recruited: non-demented people with PD (n=60) and age-matched controls (n=40). Participants attended one session and a sub-group (n=25) attended two further sessions in order to establish mobile eye-tracker reliability. Participants walked in a gait laboratory under different attentional (single and dual task), environmental (walk straight, through a door and turning), and cueing (no visual cues and visual cues) conditions. Visual sampling was recorded using synchronised mobile eye-tracker and electrooculography systems, and gait was measured using 3D motion analysis.

Discussion
This exploratory study examined visuo-cognitive processes and their impact on gait in PD. Improved understanding of the influence of cognitive and visual functions on visual sampling during gait and gait in PD will assist in development of interventions to improve gait and reduce falls risk. This study will also help establish robust mobile eye-tracking methods in older adults and people with PD.
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Introduction
Parkinson’s disease (PD) is a common neurodegenerative disease characterized by the death and dysfunction of dopaminergic neurons in the substantia nigra. PD causes progressive motor symptoms such as problems with gait and non-motor symptoms such as visual and cognitive impairment. Cognitive impairment is common in PD with reports of dementia ranging up to ~80%1, and may occur early in the disease process.2 Visual dysfunction is also common in people with PD, with up to 78% of people with PD reporting at least one visual problem.3 Gait impairment in PD is complex, involving multi-system dysfunction and has been widely related to cognitive, and to a lesser extent visual deficits. A more robust understanding of these complex processes and their interactions will inform underlying mechanisms of gait impairment in PD, which may provide insight for future therapeutic intervention. Interventions, such as visual cues (prompts; transverse tape lines to step over) are currently used to ameliorate features of gait disturbance in PD resistant to dopaminergic medication, such as festination, hesitation and freezing of gait.4 However, visual cue response is selective and the mechanisms that contribute to the response are unclear.

To date, associative (correlational) and online manipulation (via dual tasks and environmental changes) studies have investigated the independent contribution of cognition and vision in gait in PD. However, cognitive and visual functions likely interact and have a combined - impact on gait in PD. Recent technological progress has enabled the monitoring of online visuo-cognition through behavioural outcomes such as visual sampling which reflects both visual5–8 and cognitive9–12 processes. Visual sampling is the combination of saccadic fast eye-movements and fixations (pauses between saccades on areas of interest) made during real-world activities13. However, research is compromised by several technological limitations which need to be addressed to ensure robust data collection and analysis. For example, there is currently no ‘gold standard’ visual sampling measurement device or outcome measure and there is also a lack of device accuracy or reliability reporting in all previous studies14.

Visual sampling (specifically saccades) allow orientation to the visual environment bringing areas of interest into high visual acuity (foveation or focus)15,16. Saccades are impaired in PD and exhibit reduced speed, amplitudes and latencies17–22. Impaired saccadic eye movements, with reduced latencies and increased error rates have also been reported in PD dementia and dementia with Lewy Bodies, further implicating central neuro-degeneration as a determinant of ocular motor function23,24. However, the specific contribution of cognitive and/or visual functions to visual sampling during gait in PD and how this impacts gait deficit is currently poorly understood.

Much of the previous saccadic activity research is limited due to the almost exclusive use of static testing protocols (e.g. computerised tasks in sitting)24,25, which may not be applicable to real-world situations. A recent review of dynamic motor tasks (e.g. gait, obstacle crossing, turning etc.) in PD and older adults26, demonstrated that visual sampling is task dependent and relates to specific goals27. For example: during locomotion over even terrain, saccades may not be required. Over uneven (complex) terrain or during turning saccadic frequency, amplitude and fixations increase28–30. However many previous visual sampling protocols during dynamic task studies use small cohorts and often do not assess cognitive or visual functions31, which limits interpretation and conclusions regarding underlying mechanisms. Visual sampling during gait therefore has not been fully investigated and further research is required to understand this important feature of gait control. Improved understanding will assist with interventions to improve gait performance in PD.

Aims
The aims of this study are to better understand: 1) the independent roles of cognition and vision in gait in PD, 2) the interaction between both functions (termed visuo-cognition), and 3) the role of visuo-cognition in gait in PD.

Secondary aims were to:

1. Investigate accuracy and reliability of mobile eye-tracking during gait in people with PD and older adults

Methods/Design
Study design
We used a repeated-measures observational design of visual sampling during gait. We also embedded accuracy and reliability testing of a mobile eye-tracker within the study. It involved 100 older adult participants who were separated into two groups (people with PD and older adult controls).

Participants and setting
Two groups of participants were recruited: i) People with idiopathic PD (PD) (n=60); and ii) Age-matched older adults (controls) (n=40). Inclusion criteria and exclusion criteria are highlighted in Table 1. Vision-specific criteria (identified through medical notes) were included due to the impact of certain conditions on eye-tracking capabilities. The setting for the study was the gait laboratory at the Clinical Ageing Research Unit (CARU), Campus for Ageing and Vitality, Newcastle University, United Kingdom.

Recruitment
People with PD were identified through the Movement Disorders Clinic at the Clinics for Research and Service in Themed Assessments (CRESTA) in Newcastle upon-Tyne. Research personnel were available at clinics as required to invite participants to consider the study. If sufficiently interested, participants were given a Participant Information Sheet (PIS) and letter concerning the study. The invitation was followed up by a telephone call during the week to assess willingness to participate. If willing, a mutually convenient time for assessment was organised and the invitation to attend was extended to a carer or spouse.

The older adult control group was recruited via advertisement using posters placed within neurology and geriatric departments. The advertisement was sent via the university email system to staff and students at Newcastle University. Recipients were asked to pass on the poster to potential interested parties (i.e. family or friends). Participants received reimbursement of travel expenses for their own vehicle or for public transport, if this is preferred.
Table 1. Inclusion and Exclusion Criteria.

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
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<tr>
<td><strong>Common to all groups</strong></td>
<td><strong>Common to all groups</strong></td>
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<tr>
<td>• Aged ≥50 years</td>
<td>• Psychiatric co-morbidity (e.g., major depressive disorder as determined by geriatric depression scale (GDS-15); &gt;10/15&lt;sup&gt;36&lt;/sup&gt;)</td>
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<td>• Able to walk unaided</td>
<td>• Clinical diagnosis of dementia or other severe cognitive impairment (PD = MoCA &lt;21/30; Controls = MoCA &lt;26/30&lt;sup&gt;37&lt;/sup&gt;)</td>
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<td>• Adequate hearing (as evaluated by the whisper test; stand 2 m behind participant and whisper a 2 syllable word, participant repeats word) and vision capabilities (as measured using a Snellen chart – 6/18–6/12).</td>
<td>• History of stroke, traumatic brain injury or other neurological disorders (other than PD, for that group)</td>
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<td>• Stable medication for the past 1 month and anticipated over a period of 6 months</td>
<td>• Acute lower back or lower extremity pain, peripheral neuropathy, rheumatic and orthopaedic diseases</td>
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<td><strong>Group Specific Criteria</strong></td>
<td>• Unstable medical condition including cardio-vascular instability in the past 6 months</td>
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<td>Participants with PD:</td>
<td>• Unable to comply with the testing protocol or currently participating in another interfering research project</td>
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<td>• Diagnosis of idiopathic PD, as defined by the UK Brain Bank criteria&lt;sup&gt;31&lt;/sup&gt;</td>
<td>• Interfering therapy</td>
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<td>• Hoehn and Yahr stage I–III&lt;sup&gt;32&lt;/sup&gt;</td>
<td><strong>Vision Specific Criteria</strong></td>
</tr>
<tr>
<td>• Stable medication for past 1 month and anticipated over next 6 months or stable Deep Brain Stimulation for at least one month and expected following 6 months</td>
<td>• Any pupillary diameter disorder; such as significantly non-round pupils, Adies pupil (tonic or dilated pupil), Argyll-Robertson pupil (absence of light reaction), unilateral small pupil</td>
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<td>• Score ≥21/30 on Montreal cognitive assessment (MoCA) which is used to classify non-demented PD (PD dementia is &lt;21/30)&lt;sup&gt;37–39&lt;/sup&gt;</td>
<td>• Neuromotility disorders, such as Nystagmus or other ocular oscillations</td>
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<tr>
<td>• Free from any neurological disorders that may have caused cognitive impairment</td>
<td>• Significant left eye disorders (i.e. squint, twitching, Ptosis (drooping eyelids))</td>
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<tr>
<td>• No restriction was made for medication usage and participants on stable doses of medication or treatment were permitted.</td>
<td>• Known significant visual field deficits; such as hemianopia</td>
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<td><strong>Executive function.</strong> Clock drawing was used as a measure of executive function (i.e. planning). Clock drawing assessment is a measure of cognitive impairment, which is an internally consistent measure that is easy to administer and has good reliability. Participants were required to plan and draw a clock from memory with the numbers and arrows pointed at a particular time, which is then marked out of 15 for certain criteria (e.g. hour hand shorter than the minute hand = one point).</td>
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</table>

**Working Memory.** Working memory was assessed using the maximal Wechsler forward digit span<sup>41</sup>, performed while seated. The forward digit span is reported as a simple span test, which measures storage and manipulation of information by working memory<sup>43</sup>. The forward digit span consists initially of two numbers being played over loud speaker at a rate of 1 per second for the participant to recall, and continues to a maximum of nine numbers<sup>31</sup>. Three trials per span length were conducted and the test continued until a participant fails two out of three trials. The maximal length of the digit span was determined, defined as the most numbers a participant could remember two out of three times without error.
Visuo-spatial assessment
Clock copying (specifically Royall’s CLOX 2)\(^4\) measured visuo-spatial ability (i.e. ability to identify the spatial relationship of objects). Clock copying is considered a valid measure of visuo-spatial ability linked with right parietal pathology\(^5\). For CLOX 2 the researcher draws a clock and the participant must then copy the clock drawn, similar to the cube copying in the MoCA.

Benton’s Judgement of Line Orientation (JLO) test was also used as a measure of visuo-spatial ability. The JLO test has been shown to be a valid and reliable measure of visuo-spatial abilities\(^6\). The JLO test involves a participant viewing a set of numbered lines and then being shown two lines of the same orientation. They then have to name the numbers that the shown lines correspond to.

Specific sections of the visual object and space perception (VOSP) battery was used for more specific visuo-spatial assessment, such as; incomplete letters (visual object perception), dot counting and position discrimination (both spatial perception). The VOSP has been shown to be a valid measure of visuo-spatial abilities\(^7\) and consists of a screening test to establish requisite sensory acuity and specific clinical tests\(^8\). The VOSP test has been used before in older adults and neurological disorder studies\(^9\).

Visual Function Assessment
Visual function assessment included measurement of visual acuity (VA) and contrast sensitivity (CS) using basic eye-charts.

Visual acuity (VA). VA was measured binocularly using a standard LogMAR chart\(^10\). Participants were seated at a distance of 4m from the chart. Participants were instructed to read aloud down the chart starting from the top left. All correct answers are recorded on a pre-set score sheet. The test is terminated if the participant makes two consecutive errors\(^11\). Assessment was done for each eye and binocularly.

Contrast sensitivity (CS). CS was measured using the Mars CS sheets (Mars letter CS chart, Mars Percetrix™, New York, USA) placed on an adjustable holder\(^12\). The sheet consists of 48 Latin letters of uniform height; the contrast from the white background decreases with subsequent letters. Room illumination was adjusted so that average CS sheet luminance was between 80 and 120cd/m² (measured via a luminance meter). Assessment was done for each eye and binocularly with the average distance from the participants eyes being 50cm. Participants read aloud down the sheet starting at the top left. Errors were recorded on the pre-set score sheet and testing was terminated after two consecutive errors.

Parkinson’s disease-specific assessment
The Unified Parkinson's disease Rating Scale (UPDRS). The Unified Parkinson’s Disease Rating Scale\(^13\) (Movement Disorder Society revised version) was used to assess motor and non-motor features of PD and disease severity. The UPDRS was scored from a total of 195 points; higher scores reflect worsening disability.

Hoehn & Yahr (H & Y). The Hoehn and Yahr rating scale\(^14\) is a widely used clinical rating scale, which defines broad categories of motor function in PD. Only PD participants with mild to moderately severe motor function (HoY stages I–III) were included.

The FOG questionnaire (FOGQ). Freezing of gait (FOG) was evaluated using the FOG questionnaire\(^15\). This is a ten-item questionnaire intended to classify FOG. The questionnaire has three parts; distinction of freezers from non-freezers, freezing severity, frequency and duration and impact of freezing on daily life.

Assessments common to both groups
The Geriatric Depression Scale (GDS-15) short form. The geriatric depression scale (GDS-15) short form\(^16\) was used to evaluate participant depression. The GDS-15 was created in 1986 by Sheikh and Yesavage and involves 15 questions about the mood of participants\(^17\). The GDS-15 classifies depression via the following scores; 0 to 4 indicates a normal range, 5 to 9 indicates mild depression, and 10 to 15 indicates moderate to severe depression\(^18\).

Falls Efficacy Scale – International version (FES-I). Fear of falling was measured using the falls efficacy scale – international version (FES-I). This is a short validated measure of fear of falling in older adults, which assesses basic and demanding activities (both physical and social)\(^19\). It consists of 16 scenarios (e.g. cleaning the house) and participants must rate their fear of falling on a scale from 1 (Not at all concerned) to 4 (Very concerned).

Measurement of visual sampling during gait
Participants walked under different environmental (Figure 1) and attentional conditions in order to assess the impact of more complex (visual) environments and (cognitive) tasks.

Environmental conditions included; walking straight, walking straight through a doorway and turning while walking through a doorway (see Figure 1). The visual sampling during gait testing was also repeated with a visual cue in place for the straight walks. The visual cue consisted of transverse black tape lines on a white floor placed 50cm apart (approx. a ‘normal’ step length) as depicted in Figure 1, which participants were asked to step over as they complete the walk. A visual cue was used as they are known to help ameliorate gait impairments in PD\(^20\), which may be due to the increased task-related visual information\(^21\) or greater attention being allocated to gait\(^22\).

Attentional conditions included; single task (i.e. just walking) and dual task (i.e. repeating numbers while walking based on a maximal forward digit span obtained in sitting). A dual task was used as a representative of real-world walking, in which carrying out several tasks at once is common (i.e. walking and talking)\(^23\).

Both groups (PD and controls) performed the same walking conditions (Figure 1); with repeat measures (three trials for each condition) taken for an average to be created.

Equipment
Visual sampling (the combination of saccades and fixations) was assessed with a Dikablis (Ergoneers, Germany) head-mounted infra-red eye tracking system, synchronised with a 3D motion
capture system (Vicon, Oxford, UK) and an electrooculography (EOG) system (Zerowire, Aurion, Italy), to allow for simultaneous and comprehensive recording and analysis of gait and eye movement data. Dikablis calibration was performed while standing using the manufacturer 4-point procedure for each participant prior to data collection. Similar to our previous research\textsuperscript{29}, EOG was also calibrated prior to data collection via asking participants to blink for 30 secs and move their eyes horizontally between set-distance visual targets (5°, 10° and 15°) for 30 secs in time with an auditory cue (a metronome beat) while seated.

The Dikablis eye-tracker recorded eye movement using an infra-red camera\textsuperscript{63–65}, this data was combined with EOG data which involves two small electrodes being applied bi-temporally on the forehead of the participant. Importantly, the Dikablis has an adequate sampling frequency (50Hz) to detect saccades during gait\textsuperscript{66,67} and EOG has a high sampling frequency (1000Hz) which allows accurate acquisition of specific visual sampling characteristics such as velocity, acceleration, distance etc.\textsuperscript{15}. The Dikablis device includes two aspects; a head unit and a transmitter bag. Both the head unit (approx. the same size as a pair of glasses) and the bag (approx. 1kg) are lightweight. The head unit was taped, with a small amount of double sided tape, to the forehead of the participants to prevent error due to slippage. Eye movement data from the Dikablis was collected at 50Hz and from the EOG system at 1000Hz; this was saved onto a computer to be analysed using proprietary software\textsuperscript{66}.

Video recording and the Vicon 3D motion capture system recorded participants movement during walking using a camcorder and infra-red sensors attached to the skin of the participants at specific locations (Figure 2; 2× shoulders, 1× sternum, 2× anterior superior iliac spine (ASIS), 2× posterior superior iliac spine (PSIS), 2× big toe, 2× instep, 2× heel and 4× head) using a small amount of double sided tape. Participants were required to bring their own shorts and a vest to wear in order for the markers to be placed onto the appropriate body locations. Vicon 3D motion analysis is a valid and reliable method of assessing the spatiotemporal parameters of gait in older adults and in people with PD\textsuperscript{68}.

**Accuracy and reliability testing of visual sampling**

Mobile infra-red eye-tracking and EOG have been shown to be a valid and reliable method for assessing saccadic activity in younger adults\textsuperscript{69}, and both have previously been used in older adults and in people with PD\textsuperscript{29,70–73}. We were interested in the accuracy and test-retest reliability of mobile eye-tracking in people with PD and older adult controls to ensure the robustness of data interpretation. Therefore, a subgroup (PD and control; up to n=25) were asked to return approx. one week later for a second and third visit for accuracy and test re-test reliability testing (Table 2). The Dikablis eye-tracker recorded eye movement and was used in the same manner as the previous study\textsuperscript{63–65}, combined with video recording of individuals body movement and a tri-axial accelerometer (Axivity, AX3, York, UK) recording head movement.

In the second session the sub-group of participants were asked to repeat the walking tasks from session 1 (single task, without a visual cue) to provide visual sampling during gait reliability data. Accuracy of visual sampling measurement was determined by asking participants to sit (with chin rest in situ), stand (without moving their head) and walk (free head movement) on a treadmill, while performing several eye movements to visual targets (horizontal and vertical visual angles such as 5°, 10°, 15°) in time with an

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**Figure 1. Walking conditions.**

- Straight
- Left turn with door
- Straight with door
- Right turn with door
- Straight with cue
- Straight with cue and door

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*Note: Figure 1 shows various walking conditions with specific distances and angles marked.*
auditory cue (a metronome). The subgroup was asked to return for a third visit (within approx. 1 week of the second visit) to repeat the accuracy testing (as above) in order to derive test-retest reliability results.

**Primary outcome measure**

**Saccade frequency during gait**

The primary outcome measure was saccade frequency (number of fast eye movements per second when walking) during gait, which was recorded via the Dikablis mobile eye-tracker and EOG systems.

**Secondary outcome measures**

**Visual sampling.** Secondary visual sampling outcomes included: saccade number, velocity, acceleration, amplitude and duration, as well as fixation number and duration.

**Gait characteristics.** Gait characteristics were measured via video recording and a Vicon 3D motion capture system for all walking conditions in order to examine associations between cognitive and visual functions and gait, and saccadic frequency and gait (Figure 1). Spatiotemporal gait characteristics included step velocity, step length, step time, single support time and double support time,

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**Figure 2. Reflective marker body placement locations.**
which were chosen because they have been selectively associated with cognitive and visual functions in people with PD and older adults in previous research.

**Safety considerations.** All measurements were non-invasive and placed the participant at no risk other than those that normally may occur during walking. To prevent excessive fatigue, participants were encouraged to take breaks as needed throughout all study procedures. The hypoallergenic double-sided tape used to fix the infra-red markers and Dikablis head unit onto the skin of the participants did not cause any adverse effects. The amount of tape was small and it has been used on numerous occasions in other research projects at the CARU and no issues have been reported. The bi-temporal EOG electrodes also did not cause any adverse effects. The treadmill used within the accuracy and reliability testing was equipped with a safety harness to avoid any falls-related injuries, as the harness could support the participant and trigger the treadmill to automatically stop in the event of a fall.

**Ethical approval.** Ethical approval for this project was obtained from the NRES Committee North East -Newcastle and North Tyneside 1 Research Ethics Committee (approved 6th June 2013, Reference 13/NE/0128). Written informed consent was obtained for every participant prior to testing. The study began 1st July 2013.

**Dissemination.** Data collection for the study finished in July 2015 and results will be published within peer reviewed scientific journals, open-access publication will be preferred. A public engagement event will also be used to disseminate findings to participants and public. All participants were assigned participant numbers, allowing data to be anonymised and reported confidentially. All results from the study will be uploaded to Clinicaltrials.gov (ID: NCT02610634) once analysed. No contractual agreement limits access to data.

**Statistical analysis**

### Sample size

This was an exploratory study and therefore few specific previous examples were available to guide estimates for sample size. We have based the estimate (≥40 participants in each group) on our previous work (PD; n=21) and other previous similar studies. Similar studies in this research area have used small sample sizes (n=2–26) and reported between-group differences, demonstrating that we will be able to see differences between our sizable PD and control population.

### Table 2. Study protocol overview.

<table>
<thead>
<tr>
<th>Participants (n = 100)</th>
<th>Session 1 (up to 150min)</th>
<th>Session 2 (up to 60min)</th>
<th>Session 3 (up to 60min)</th>
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</thead>
<tbody>
<tr>
<td>1. Older adult controls (n = 40)</td>
<td>Applicable to all participants (n=100)</td>
<td>Applicable; for a subgroup of PD and control participants (n=25)</td>
<td>Applicable; for a subgroup of PD and control participants (n=25)</td>
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<tr>
<td>2. Parkinson’s disease (n = 60)</td>
<td>Initial screening, cognitive and visual function assessments (45–60min)</td>
<td>Approx. 1 week after session 1</td>
<td>Approx. 1 week after session 2</td>
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<td></td>
<td>Informed consent</td>
<td>1st Reliability testing (45–60min)</td>
<td>2nd Reliability testing (45–60min)</td>
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<td></td>
<td>Demographic and diagnostic evaluation</td>
<td>• Repeat visual sampling during gait testing in gait laboratory (single task, without a visual cue)</td>
<td>• Sit, stand and walk on a treadmill while making eye-movements to set distance targets (5°, 10° and 15°)</td>
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<tr>
<td></td>
<td>Global cognitive assessments:</td>
<td>• Sit, stand and walk on a treadmill while making eye-movements to set distance targets (5°, 10° and 15°)</td>
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<td>• MoCA</td>
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<td>Specific cognitive domain assessment:</td>
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<td>• CLOX 1 and 2</td>
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<td>• VOSP battery</td>
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<td>Visual function assessments:</td>
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<td>• Visual acuity</td>
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<td>• Contrast sensitivity</td>
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<td>PD-Specific assessments:</td>
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<td>• FOG-questionnaire</td>
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<td>Common assessments:</td>
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<td>• GDS-15</td>
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<td>• FES-I</td>
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<td>Visual sampling during gait testing in gait laboratory (60–90min)</td>
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groups. It is a general recommendation to include 30 cases per group to be able to carry out basic statistical tests (e.g. between group comparisons)\(^1\). This study will inform future power calculations.

Data analysis will follow a predetermined plan:

**Analysis common to all studies**

Statistical analysis will be undertaken using SPSS version 20 (SPSS, Inc. an IBM company). Demographic characteristics and baseline data will be summarized using descriptive statistics, including means, standard deviations, median, minimum, maximum and inter-quartile ranges for continuous or ordinal data and percentages for categorical data. The descriptive statistics will be tabulated and presented graphically for clarity. One-sample Kolmogorov-Smirnov tests will be used to check for normally distributed data. Non-normally distributed continuous distributions will be transformed where appropriate to meet the requirements of parametric tests; otherwise equivalent non-parametric tests will be adopted. Data will also be assessed graphically (such as histograms or scatter plots) for clarity of information. As this is an exploratory study a threshold of \(p < .05\) (two-sided) will guide statistical interpretation.

**Further analysis**

To analyse visual sampling during gait, a series of mixed analysis of variance (ANOVA) will be used with effect of PD (PD and control) as between participant factor and attention (single task, dual task) and environment (Straight walk, Door, Turn) as within group factors. Pearson’s correlations will be used to test the strength and direction of the relationships between clinical, gait and saccade frequency outcomes. Gait characteristics will also be assessed with the same mixed ANOVA method.

To test the effect of visual cueing on visual sampling and gait; a mixed ANOVA will be used with group (PD and control), visual cue (no cue and cue) and attention (single task, dual task). Comparison with and without a visual cue will also be made via the same mixed ANOVA for the various gait characteristics, while controlling for the influence height.

Associations between cognitive and visual functions will be made using Pearson correlations. Cognitive and visual function contribution to visual sampling will be assessed using multiple regression analysis, while controlling for demographic factors (age, motor severity, depression, global cognition).

To analyse reliability; repeated-measure \(t\)-tests, Bland and Altman plots, intra-class correlation coefficients (Model 2, 1) and Pearson’s correlations (or non-parametric equivalents) will be used to assess bias, absolute and relative agreement and consistency of saccadic outcomes measured with the Dikablis eye-tracker on two separate occasions a week apart. A similar statistical approach will be used to assess accuracy of the Dikablis system against targets of a known angle (5°, 10° and 15°).

**Discussion**

The aims of this study were to provide a greater understanding of the roles that cognition and vision play in gait in PD. Specifically this study provided data regarding the role that visuo-cognition plays in gait in PD, as well as relationships between cognitive and visual functions (termed visuo-cognition). What sets this project apart from other work in this field is that the study is taking into consideration the combined and interactive impact that cognitive and visual function impairments have on gait in PD.

The study protocol was developed in response to recently reviewed evidence and study recommendations for visual sampling during a dynamic motor task\(^1\). The protocol focussed not only on cognitive impairments but also visual dysfunction which is commonly reported in PD and until now has not been fully investigated. Little quantitative data has been previously reported regarding visual sampling during real-world tasks (e.g. gait, reaching etc.) in PD and the few previous studies available only involve small cohorts often performing simple static motor tasks (i.e. mouse clicks or button pressing or reaching\(^{2,23}\)).

This study investigated the online visuo-cognitive behavioural measure of visual sampling during a real-world task (i.e. gait), and data analysis will examine interaction between visual sampling, cognitive and visual functions and task performance. The study will determine the influence of cognitive and visual functions on visual sampling during gait and gait characteristics in PD. This will allow us to determine whether gait impairments in PD are influenced by basic visual function (CS and VA) impairment or cognitive impairment (particularly attention) or a combination of these aspects.

Finally, an important feature of this study is that it is expected to provide the first evidence on the accuracy and reliability of using mobile eye-tracking equipment during gait with older adults and people with PD, which will develop the standard of research being conducted in this area and allow for more definitive conclusions.

**Conclusion**

This exploratory observational study will assist with understanding the role that cognition and vision play in gait in PD and how combined visuo-cognitive processes influence gait outcomes. In addition, it will provide evidence on the interaction between cognitive and visual functions in PD, as well as how visual sampling during gait is affected by the use of clinical interventions such as visual cues.

**List of Abbreviations**

ACE-R: Addenbrookes cognitive examination (revised version)
ANOVA: analysis of variance
CARU: clinical ageing research unit
CDR: Cognitive drug battery
CRESTA: Clinics for Research and Service in Themed Assessments
CS: Contrast sensitivity
EOG: Electro-oculography
FES-I: Falls efficacy scale (international version)
FOG: Freezing of gait
FOGQ: Freezing of gait questionnaire
GDS-15: Geriatric depression scale (short form)
JLO: Judgement of line orientation
MMSE: Mini mental state examination
MoCA: Montreal cognitive assessment
PD: Parkinson’s disease
PIS: Participant information sheet
UPDRS: Unified Parkinson’s disease rating scale (Movement Disorder Society revised version)
VA: Visual acuity
VOSP: Visual object and space perception battery

Author contributions
LR is the Chief/Principle Investigator for the study. SS is carrying out this study as part of his PhD and is responsible for the day to day running of the study. He drafted this manuscript and also wrote the study protocol with BG, SL and LR from its inception. SS and BG designed the statistical analyses, along with Dr Shirley Coleman (Statistician, Industrial Statistics Research Unit, Newcastle University) and SL is involved with participant recruitment. All authors are involved in academic oversight of the study and were involved in the revising this manuscript, giving final approval for publication.

Competing interests
The author(s) declare that they have no competing interests.

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