EXIT 360°—EXecutive-Functions Innovative Tool 360°—A Simple and Effective Way to Study Executive Functions in Parkinson's Disease by Using 360° Videos

Francesca Borgnis [1,2], Francesca Baglio [1], Elisa Pedroli [3,4], Federica Rossetto [1], Mario Meloni [1], Giuseppe Riva [2,3] and Pietro Cipresso [3,5,*]

1 IRCCS Fondazione Don Carlo Gnocchi ONLUS, 20148 Milan, Italy; fborgnis@dongnocchi.it (F.B.); fbaglio@dongnocchi.it (F.B.); frossetto@dongnocchi.it (F.R.); mmeloni@dongnocchi.it (M.M.)
2 Department of Psychology, Università Cattolica del Sacro Cuore, 20123 Milan, Italy; giuseppe.riva@unicatt.it
3 Applied Technology for Neuro-Psychology Laboratory, Istituto Auxologico Italiano, Istituto di Ricovero e Cura a Carattere Scientifico, 20149 Milan, Italy; e.pedroli@auxologico.it
4 Faculty of Psychology, eCampus University, 22060 Novedrate, Italy
5 Department of Psychology, Università degli Studi di Torino, 10124 Turin, Italy
* Correspondence: p.cipresso@auxologico.it

Featured Application: The validation of EXIT 360° as an innovative tool for an ecologically valid assessment of executive functioning in Parkinson's disease will radically transform the assessment experience. The clinician will obtain faster (15 min), multicomponent, and multidomain evaluations of executive functioning. Moreover, the patients will be involved in a short task (vs. a long and complicated assessment) that can be experienced as a "game for health", increasing engagement and lowering the level of emotional charge typical of neuropsychological evaluation. Finally, EXIT 360° is easily transportable, so the assessment can also be performed in the patient's room or house, overcoming logistical challenges related to bringing a patient into the clinic.

Abstract: Executive dysfunction represents a common non-motor symptom in Parkinson's disease (PD), with a substantial negative impact on daily functioning and quality of life. Assessing executive functions (EFs) with ecological tools is therefore essential. The ecological limitations of traditional neuropsychological tests have led to increased use of virtual reality and 360° environment-based tools for the assessment of EFs in real life. The study aims to evaluate the efficacy and usability of the EXecutive-Functions Innovative Tool 360° (EXIT 360°), a 360°-based tool for the evaluation of EFs in PD. Twenty-five individuals with PD and 25 healthy controls (HC) will be assessed with a conventional neuropsychological battery and EXIT 360° delivered via a head-mounted display. EXIT 360° will show a domestic scenario and seven different subtasks of increasing complexity, and will collect verbal responses, reaction times, and physiological data. We expect that EXIT 360° will be judged usable, engaging, and challenging. Moreover, we expect to find a highly convergent (conventional test and EXIT 360°) and diagnostic validity (individuals with PD vs. HC). The validation of EXIT 360° will allow for the adoption of a fast, ecological, and useful instrument for PD screening, likely transforming the assessment for the clinic and the patient.

Keywords: executive functions; 360° environments; assessment; Parkinson's disease; virtual reality; EEG; eye tracker

1. Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disorder primarily considered as a movement disorder due to an extrapyramidal syndrome. However, in addition to the well-documented motor symptoms (e.g., bradykinesia, resting tremor, rigidity, and postural instability), people with PD frequently develop a wide range of non-motor symp-

toms (NMS) from the early stages of the disease course, even before the onset of motor symptoms in the prodromal state [1–3].

Cognitive dysfunction represents one of the major clinical NMS of PD. People with PD can exhibit a rapid decline in several cognitive domains, especially in executive, attentional, and visuospatial [1]. However, the profile and the severity of the neuropsychological deficits vary considerably, depending on factors including the timing of the onset and the rate of progression [1,3]. Executive dysfunction (ED) represents the best-defined cognitive impairment in early-stage non-demented PD [4]. ED is mainly characterized by deficits in attention, planning, set shifting, dual task performance, inhibitory control, working memory, and decision making, even compromising social-cognition skills [5]. As a result, patients experience difficulty in many essential goal-directed everyday activities, with critical adverse implications for daily functioning and quality of life [6–8]. Therefore, identifying early strategies for the evaluation and rehabilitation of executive functions (EFs) is crucial to achieving optimal multilayer PD management.

1.1. Executive Function Assessment

EFs are traditionally evaluated with standard paper-and-pencil neuropsychological tests, such as the Modified Wisconsin Card Sorting Test [9] or the Trail Making Test [10], which allow standardized procedures and goals that make them valid and reliable. However, these tests have been shown to be unable to predict the complexity of executive functioning in real-life settings reliably [11–16] and seem inadequate in terms of sensitivity and specificity [16,17]. Thus, a more ecological evaluation of EFs is essential to evaluate the specific cognitive profile of individuals [12,14,18] and how executive deficits affect daily functioning [14]. In an attempt to refine EF assessment, Burgess and colleagues proposed the development of neuropsychological assessments based on models derived from directly observable everyday behaviours. This "function-led" approach diverges from the emphasis on abstract cognitive "constructs" without regard for their ability to predict the complexity of "functional" behaviours found in real-life situations. Hence, there has been a need for new neuropsychological instruments that measure different components of executive functioning within real-life scenarios [18] such as the Multiple Errands Test (MET) [11] and the Executive Function Performance Test. For example, the MET evaluated patients while carrying out different daily tasks (e.g., shopping tasks) in a real supermarket, following specific rules within a specified time frame. The assessment in real-life settings provided a more accurate estimate of the patient's deficits than laboratory conditions [19]. However, it revealed further limitations, such as long times, high economic costs, difficulty of organization, lack of safety, poor controllability of experimental condition, or applicability to individuals with motor deficits [20]. For example, MET is conducted in real time in a real-life setting, limiting the use for patients who are not independent, and requiring high physician costs and time demands. Therefore, the ecological limitations of traditional neuropsychological tests and many difficulties in administering tests in real-life scenarios have led to the increasing use of technological tools and virtual reality (VR) for the assessment of EFs in real life.

1.2. New Challenges in the Evaluation of Executive Functions

The use of interactive technologies (e.g., virtual reality, mobile devices and sensors, serious games, and 360° video) is quickly becoming a promising instrument in simulating a real environment, with high use in the healthcare sector, including neuropsychological assessment, rehabilitation [21], educational training [22,23], and surgery [24].

1.2.1. Virtual Reality

VR allows for the development of realistic spatial and temporal scenarios, situations, objects, and stimuli that reproduce conditions of everyday life, allowing an ecologically valid evaluation of EFs [25–28], as well as reliability and psychometric validity [29–31]. In other words, VR appears to be an appropriate tool for the assessment of EFs because

it provides the chance to perform many everyday tasks in ecologically valid, secure, and controlled environments [26]. Thus, clinicians can directly observe their patients in an everyday setting (e.g., supermarkets, kitchens, or work office), while performing several executive tasks [32,33]. Moreover, the use of virtual environments in neuropsychological assessments guarantees better control of the perceptual environment, a more precise presentation of the stimulus, greater applicability, user-friendly interfaces, and the acquisition of data and analysis of performance in real time [27,28,31,34–37]. Several authors studied ED in PD through VR-based instruments that required performance of real-life tasks (e.g., a shopping task) in virtual environments that reproduced a real supermarket [13,38–41]. Among the EFs, planning represents an essential component of cognitive PD alteration. From the early stages of PD, planning deficits have been found and probably reflect frontostriatal circuit degeneration [42]. Klinger and colleagues developed a virtual supermarket to evaluate visuospatial and temporal aspects of planning using a 3D environment [13,38]. In this VR-based tool, clinicians evaluated the strategic choices and planning abilities of individuals with PD in buying a specific number of products. Data showed the absence of a significant difference between the PD group and the control group for the number of correct actions. On the contrary, the increased distance and duration and the inefficient trajectory observed in the PD group suggested a gradual decrease in planning processes in PD (slowness of information processing) and inefficient use of contextual elements. In other words, these results underlined the spatial and temporal aspects of planning deficits in PD. Moreover, the inefficient trajectory could also suggest a dysfunction in the switching mechanism necessary to process, in parallel, large amounts of information. Interestingly, VR allowed for the description of alterations in planning by testing "pure" mental sequences without the interference of possible motor disability.

In later years, several authors used the virtual version of the Multiple Errand Test (VMET) to evaluate executive disorders in PD patients ecologically. The VMET allows for the assessment of patients' abilities in formulating and checking a list of goals to effectively respond to environmental requests to achieve a series of tasks (e.g., buy a specific product, or ask the examiner information about a product to be purchased). In a preliminary study, Raspelli and colleagues showed the presence of many deficits in planning, which is the strategy that allows the correct execution of the task in problem-solving and set-shifting [43]. Specifically, individuals with PD use few strategies, and show more perseveration and difficulties in set-shifting and sustained attention. The following study conducted by Albani and colleagues also showed impairments in decision making in individuals with PD [44]. Patients showed strategies full of errors, suggesting impulsive decision making. These data can support the hypothesis that behavioural disturbance (in some individuals with PD) might precede cognitive dysfunctions in PD. Similar findings were found by Cipresso and colleagues that compared PD with normal cognition (PD-NC) and a control group [40]. Patients made more errors in the tasks of the VMET and demonstrated reduced use of effective strategies to complete the tasks, like careful planning before starting a subtask or using the map for navigating the virtual supermarket. These executive deficits may reflect impairments in cognitive flexibility, in which a person's conceptualization selectively changes to respond to external/internal stimulation. In the same study, it was shown that assessment in real-life contexts provides a more accurate estimate of the patient's impairment, revealing difficulties hidden by traditional measures. In fact, VMET appears more sensitive in the early detection of executive deficits, because these two groups did not differ in the standard assessment of EFs (Mini-Mental State Examination, Clock Drawing Test, and Tower of London). So, a more ecologically valid evaluation of EFs leads to better detection of subtle executive deficits, above all in the early stage of PD. An increasing number of longitudinal studies suggest early executive dysfunction is predictive of subsequent development of PD dementia [45,46]. Thus, the early identification of executive impairments could help identify those individuals with PD at risk of developing dementia and provide the opportunity for early neurorehabilitation interventions [40,41].

In recent years, some authors used a new technology for presenting neuropsychological stimuli, exploiting the potential of 360° environments (photographs or immersive videos) provided via smartphone [47]. The 360° technology can be included in the "virtuality continuum" of Milgram [48], in which stimuli are presented in a space between real and virtual, or "mixed reality", in which the extremes may coexist, producing new experiences. Advances in 360° technologies allow participants to be immersed in a real situation that they experience from a first-person perspective. Specifically, the enhanced realism offered by 360° video has great potential to lead to highly immersive, interactive, and engaging forms of experience [49]. Moreover, 360° environments allow for sequential focusing upon several elements and portions of the environment at different times, and sequential planning of a visual search. Today, 360° video appears to be a promising interactive virtual technology for creating virtual-reality-immersive applications at low cost [49]. The implementation of neuropsychological tests in 360° environments is an actual challenge; in this direction, Serino and collaborators have recently developed a 360° version of a validated paper-and-pencil test for the detection of executive deficits known as the Picture Interpretation Test (PIT) [50]. Serino and colleagues successfully tested the efficacy of PIT 360° as a highly sensitive ecological tool for detecting executive deficits from the early stages of PD [47]. First, results showed a correlation between indices of PIT 360° and two executive tests: the Trail Making Test and the phonemic fluency task. However, unlike traditional neuropsychological tests, PIT 360° can distinguish the pathological group from controls both in terms of the time taken to arrive at the correct answer and in the number of elements of the scene named. Compared with healthy controls, individuals with PD gave significantly more detailed descriptions of the scene, had delayed time to provide a correct interpretation of the scene proposed, and appeared more prone to distractor interference. Thus, PD showed more difficulties in focusing on the most crucial components for a correct interpretation of the scene. These results were in line with Luria's view, suggesting that this test can capture deficits in active visual perception [51]. Interestingly, Luria found that disturbances in active visual perception were reflected by a corresponding disorganized movement of the scanning gaze. From this point of view, it would be interesting to investigate patients' eye movements during the interpretation of the proposed scene, integrating this technology with other portable devices, such as an eye tracker.

1.2.2. Nonverbal Physiological Indices

Over the years, executive functioning has been further explored by the identification new nonverbal physiological indices obtained with different devices, such as the eye tracker (ET) and electroencephalogram (EEG).

ETs allow for online tracking and recording of subjects' eye movements (e.g., saccadic and antisaccadic movements, and fixations). Physiological indices obtained with ETs (e.g., pupil dilation, eye movements, fixation, and gaze direction) are generally considered reliable indicators of executive dysfunction (e.g., inhibitory control) [37]. For example, Mirsky and colleagues demonstrated that antisaccadic movements are a sensitive marker of ED and frontal-lobe structure in cognitively and functionally healthy older adults [52]. Recently, Ouerfelli-Ethier and co-workers demonstrated the suitability of the antisaccades test (AST) as a cognitive marker of EFs in aging and PD populations [53]. AST performance was a good predictor of decision-making and visual-memory abilities for both older adults and PD patients, while it predicted visual search performance to a larger extent in PD patients. The advantages of ET and VR/360° environments (e.g., natural stimuli, natural movement, controlled environment, and controlled data collection) make it possible to answer many research questions in a radically innovative way. It allows for calculating the subject's gaze in the 3D virtual environment and observing where the subject is looking during the session. Moreover, ET allows for the definition of regions of interest in 3D space and fixation time of each area [54].

EEG, on the other hand, can be used to analyse, monitor, and record electrical activity and any functional anomalies in the prefrontal cortex and associated cortico-subcortical

circuits, responsible for EFs [55,56]. "Dysexecutive syndrome" is common in neurological patients due to damage to the frontal lobe, such as following head trauma or related to specific conditions such as PD [57]. Slower oscillations within the theta frequency band in the frontal cortex, generally observed between 4 and 8 Hz, are associated with the involvement of the neural resources involved in executive tasks. EEG can be used to estimate the complexity of executive dysfunction in several clinical populations (e.g., [58,59]). For example, a study conducted by Teramoto and colleagues showed that decreased resting-state functional connectivity between the frontal and parietal cortex, especially in the left side, was related to executive dysfunction in PD [59]. Interestingly, recent technological advances allowed for the development of portable, wearable, and wireless EEG headsets [60–62]. These inexpensive and easy-to-use EEG devices, with few channels and/or dry-electrodes, could be interesting for the evaluation of EFs outside of the laboratory in real-world environments. However, additional studies need to be performed to validate their use to evaluate EFs.

In light of all these advantages and innovations, the integration of immersive, virtual, or 360° environments has the potential to simultaneously evaluate different components of executive functioning in a real-life setting via the use of ETs and EEGs. To date, only a few studies have integrated these methods, focusing mainly on executive dysfunctions in developmental age [63,64].

Our work evaluates the convergent validity, usability, and efficacy of the EXecutive-Functions Innovative Tool 360° (EXIT 360°) to assess EFs in Parkinson's disease. This 360° instrument will consist of a new 360° task for EFs delivered via a technological device: a head-mounted display (HDM) that integrates an ET and an EEG.

The EXIT 360° assessment tool will go beyond the effectiveness of standard tests, VR-based tools, or ET and EEG studies by combining different components and data for a multidimensional and multicomponent assessment of executive functioning with high clinical usability and ecological validity.

2. Materials and Methods

2.1. Participants

Following the sample-size calculation reported in the Statistical Analysis section, the sample will consist of 46 participants to guarantee optimal statistical power. Specifically, the study will include 25 individuals with Parkinson's disease (PD group), and 25 healthy controls (HC group) matched for age and education. Individuals with PD will be consecutively recruited from the Neurorehabilitation Unit of IRCCS, Fondazione Don Carlo Gnocchi ONLUS. All participants will have to show the following inclusion criteria: (a) age between 18 and 90 years; (b) education ≥5 (primary school); (c) absence of overt dementia as determined by the Montreal Cognitive Assessment [65] (MoCA score ≥17.54, cut-off of normality), corrected for age and years of education according to Italian normative data [66]; and (d) ability to provide written, signed informed consent. In addition, patients will have also to meet the following inclusion criteria: (a) Parkinson's disease according to MDS criteria [67]; (b) mild to moderate disease staging, with scores <3 on the Hoehn and Yahr scale; and (c) deficits in EFs confirmed by documented neurological and neuropsychological evaluation. Exclusion criteria will include: (a) severe hearing or visual impairment that could compromise the assessment with the new tool; and (b) major systemic, psychiatric, or other neurological illnesses. Particular attention will be used to exclude patients who experience visual hallucinations or suffer from vertigo.

The study was approved by the "Fondazione Don Carlo Gnocchi-Milan" Ethics Committee on 7 April 2021, project identification code 09_07/04/2021. The examiner will provide to all participants a complete explanation of the purpose and risk of the study before they sign a written informed consent based on the revised Declaration of Helsinki (2013).

2.2. Procedure of Study

The study will involve four steps: (a) introduction phase; (b) pretask evaluation; (c) EXIT 360° session; and(d) post-task evaluation. All studies will be conducted in a one-session evaluation at IRCCS Fondazione Don Carlo Gnocchi ONLUS in Milan.

A. Introduction Phase

Before study initiation, participants will receive a complete explanation of the study and sign the written informed consent. After that, the examiners will collect participants' socio-demographic data (e.g., age, sex, education level, and occupation) and technological expertise. Specifically, the participants will be asked to evaluate their perceived level of familiarity and competence with technologies (e.g., tablet, smartphone, computer, internet, social network, and videogames). To test their level of familiarity with technologies, we will administer an ad hoc questionnaire using a 5-point scale (from "never" to "everyday") that evaluates "How often in the last year, have you happened to use ... ". Moreover, the competence scale will consist of a 5-point scale (from "not at all" to "very much") to investigate "How competent do you feel to use ... ".

B. Pretask Evaluation

Participants will undergo a conventional paper-and-pencil neuropsychological assessment to obtain their global cognitive profile, focusing mainly on executive functioning (pretask evaluation).

The global cognitive level will be evaluated with the MoCA [65], a sensitive screening tool for detecting mild cognitive impairment. As regards executive profile, participants will complete a battery of tests to determine EFs, including the Trail Making Test (in two specific subtests: TMT-A and TMT-B) [10], phonemic verbal fluency task (F.A.S.) [68], Stroop Test [69], Digit Span Backward [70], Frontal Assessment Battery (FAB) [71,72], Attentive Matrices [73], and Progressive Matrices of Raven [74–76]. Table 1 gives a detailed description of the different EFs evaluated by each neuropsychological test mentioned above.

Table 1. Pretask evaluation: list of traditional neuropsychological tests for the assessment of EFs.

Name	Executive Function
Trail Making Test	Visual attention
	Task switching
Verbal fluency	Access to vocabulary on phonemic key
Stroop Test	Inhibition
Digit Span Backward	Working memory
Frontal Assessment Battery	Abstraction Cognitive flexibility Motor programming/planning Interference sensitivity Inhibition control
Attentive Matrices	Visual search Selective Attention
Progressive Matrices of Raven	Sustained and selective attention Reasoning

C. EXIT 360° Session

Participants will undergo an evaluation of about 15–20 min with the EXecutive-function Innovative Tool 360° (EXIT 360°). The EXIT 360° is a new tool for the assessment of EFs delivered via an innovative technological device: an HDM that integrates an ET and an EEG. This technological device will allow participants to be immersed in 360° environments similar to real situations that they experience from a first-person perspective.

EXIT 360°: A Complete Description of This EXecutive-Functions Innovative Tool

EXIT 360° aims to provide a complete evaluation of executive functioning, engaging participants in a "game for health" delivered via smartphones, in which they must perform several subtasks in 360° environments. EXIT 360° was based on three fundamental concepts for complete and integrated assessment: (1) ecological validity; (2) multicomponent assessment; and (3) clinical usability [77].

In light of the importance of evaluating EFs in real life (ecological validity), EXIT 360° involves domestic environments such as the kitchen, bedroom, and living room. In these different environments, the subjects must perform seven subtasks representing everyday-life situations and assignments.

An evaluation of the challenges faced by the subjects in their environments can provide insight into ways to optimize rehabilitation. Moreover, EXIT 360° will allow the clinician to obtain information about executive functioning while the participants are performing everyday tasks in an environment that reproduces real-life context (clinical usability).

Unlike the previous VR-based assessment instruments (e.g., V-MET-supermarket), EXIT 360° offers the subjects five different scenarios, in which they are asked to perform different subtasks that represent daily life assignments, depending on the environment in which they are immersed.

The 360° environments of EXIT 360° were developed with the Ricoh Theta S Digital Camera, which permits 360° spherical imageries. The camera can capture a 360° scene by stitching two 180° scans via integrated software (resolution of 1792 × 3584 pixels). This allows for a presentation of an immersive 360° experience directly on an HDM via a smartphone connected to the technological device.

The use of 360° environments allows overcoming some technical limitations regarding the development of virtual environments. In fact, 360° environments do not require specific technological skills or high costs (e.g., expensive software), as they consist of 360° photos or videos that require a 360° camera and free online applications ([78]. Moreover, some studies showed that VR could cause some negative effects, such as nausea and dizziness [28]. On the contrary, a preliminary study on individuals with PD has shown the complete absence of adverse events in 360° environments [47].

The Seven Subtasks of EXIT 360°

In EXIT 360°, the participants' main goal is to exit the domestic path in the shortest possible time. To do this, participants must plan a strategy and overcome seven different steps (subtasks) of increasing complexity: (1) Let's Start; (2) Unlock the Door; (3) Choose the Person; (4) Turn On the Light; (5) Where Are the Objects?; (6) Solve the Rebus; and (7) Create the Sequence.

EXIT 360° is designed to tap into and evaluate different components of executive functioning (multicomponent assessment) simultaneously and quickly. Each subtask evaluates one or more EFs, such as planning, decision making, problem solving, attention, and working memory (Table 2). The subtasks reproduce common scenarios of everyday life that require the subject to solve specific assignments in according to the instructions and requests of each subtask. To respond to these requests, the subject will have to choose between three or more "alternatives", which will allow them to solve the assignment in the best possible way and continue their journey.

Table 2 summarizes the seven subtasks involved in EXIT 360° with the EFs evaluated by each subtask.

Description of Seven Subtasks and 360° Environments

Task 1—"Let's Start": The subjects will be immersed in a completely neutral room. The participants will explore the environment until they see a map of a path. They will have to observe the map and choose from four proposed path alternatives, the one that allows them to complete getting to the exit in the shortest possible time. If the subjects plan a correct strategy, they will choose the alternative "2". If the answer is correct, they will enter the house and start their journey.

Table 2. Subtasks and related EFs.

	Name	Place	Executive Function
Task 1	Let's Start	Neutral room	Planning
Task 2	Unlock the Door	Landing	Decision making
Task 3	Choose the Person	Living room	Problem solving Divided attention
Task 4	Turn On the Light	Corridor	Problem solving
			Decision making
Task 5	Where Are the Objects?	Bedroom	Visual searching
			Selective attention
			Reasoning
			Problem solving
Task 6	Solve the Rebus	Bedroom	Planning
			Reasoning
			Problem solving
Task 7	Create the Sequence	Kitchen	Working memory

Task 2—"Unlock the Door": the participants will be immersed in a 360° landing with a closed door. The neuropsychologist will tell the subjects that they must open the door to continue their journey and to enter the house. While exploring the environment, the subjects will see three 3D objects appear in the hall (i.e., key, drill, and telephone). They will have to choose between the three options to find the best one to open the door (decision making). If the participant makes the correct choice, they will continue their journey and enter a living room full of people.

Task 3—"Choose the Person": this task is set in a living room with five people inside who are doing different activities. Specifically, a man is reading a book sitting on a chair; two people (mother and child) are sitting on the sofa and chatting while watching television; and a woman is sitting at the table and writing in her diary, while a girl is sitting next to her and working with a computer. The neuropsychologist will ask the subjects to explore the room and give them the instruction, "One of these people has a clue that allows you to move forward on your path", followed by a description of the person to find. Only by focusing on the whole description (divided attention), will the subject be able to correctly select the person (the woman who is writing in her diary) to continue.

Task 4—"Turn On the Light": the subject will enter a long corridor full of objects (e.g., table, pictures, and ornaments). The subject will be asked to explore the environment, but at some point, the corridor will become completely dark. The subject will be told "It's all dark! The power went out. Here are four objects that could help you: you can only choose one". In front of the subjects, four objects will appear: a torch, an unlit candle, a ball, and a lamp. If the subjects give the correct answer (torch), the room will light up again: "The light is back! We can continue with our journey".

Task 5—"Where Are the Objects?": the subject will find himself immersed in a bedroom with many different pieces of furniture: a bed, two bedside tables, a wardrobe, a chair, and a dresser (Figure 1). Above each item, various objects will be scattered: candles, pillows, soft toys, clothing, lamps, blankets, glasses, and telephones. The subject will be asked to identify the piece of furniture on which all these four objects are placed together: lamp, soft toy, blanket, and telephone. Individual objects will be found on throughout, but only the dresser will have all of them.

Figure 1. Task 5: 360° environment that represents the bedroom.

Task 6—"Solve the Rebus": the subject will be immersed in another bedroom. To leave this room, the subject will be asked to complete a rebus that will appear on the wall. Firstly, the subject will see a rebus consisting of many tiles, with each tile containing both a number and a geometric shape of different colours. Next to these tiles, a blank tile will be inserted containing two question marks for the subject to fill in. Then, a series of response alternatives will appear near to rebus, and the subject will have to choose from them. If they choose the correct one, they can explore the last room in the house, the kitchen.

Task 7—"Create the Sequence": this task represents the last room of the house, the kitchen. In this room, the subjects will see an exit door that must be opened with a numerical combination. A series of five numbers will appear in the room, one after the other, on top of a black sofa (Figure 2). The examiner will say to the subject: "I ask you to read the numbers and try to memorize them. Our goal is to unlock the door to exit. The combination is formed by the series of numbers you will see but backwards, from last to first. If you see 2 3 5, you will have to say 5 3 2. What is the correct combination?" If the sequence shown is correct, the same initial map will appear with the words "GOOD, NOW YOU ARE HERE!" with all path and rooms coloured.
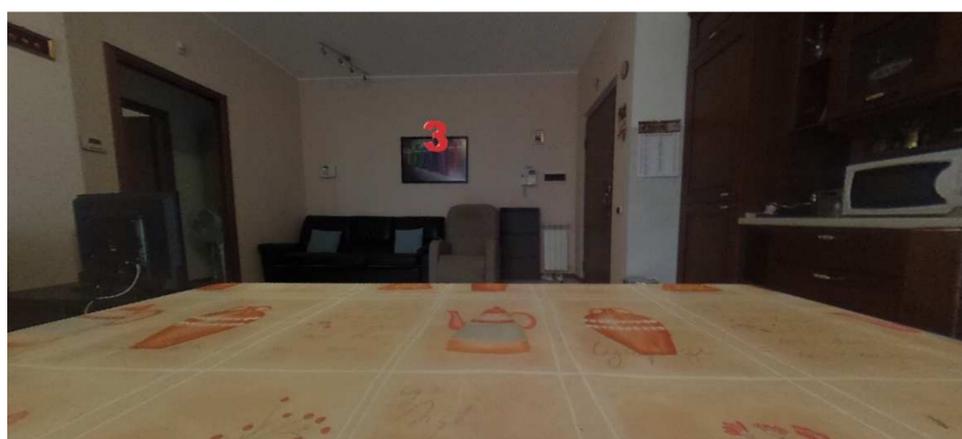
Figure 2. The representation of Task 7: the 360° kitchen showing one of the series numbers.

Evaluation Procedure

The neuropsychologist will begin the administration by inviting the participant to sit on a swivel chair and wear the HDM. Before wearing the HDM, the examiner will ask participants to keep their eyes closed. In the case of presbyopia, participants will wear their glasses.

Before starting the evaluation task, the participant will undergo a phase (3 min) aimed at familiarizing them with the technology and observing potential side effects (e.g., dizziness, nausea). If side effects occur, the examiner will immediately stop the test. After wearing the HDM, the examiner will instruct the participant to open their eyes, and simultaneously the examiner will start a timer and begin audio recording. Participants will be completely immersed in a neutral 360° environment that represents a living room, including a table with a plant, a sofa, various chairs, and objects spread throughout the room (Figure 3). First, the examiner will ask participants to explore the environments freely.

Figure 3. Example of neutral 360° environment that represents a living room.

Then, they will ask the participant to find three specific objects in the scene: a plant, red blanket, or pictures (e.g., "Let's search for the plant. Where is the plant?"). Upon completion of the familiarization phase, participants will be asked to close their eyes again.

The experimental session will begin with time registration (in seconds) and audio recording coinciding with the examiner's instruction "Open your eyes". At the beginning of the task, the subjects will be immersed in a 360° environment that represents a neutral room. They will receive the following instruction: "You are about to enter a house. Your goal is to get out of this house in the shortest time possible. To exit you will have to complete a path and a series of 'tasks' that you will encounter along your way. Are you ready to start?" After giving the initial instruction, the neuropsychologist will accompany and guide the participant along the entire path: they will provide subtask instructions, manage the passage from one room to another, and collect the subjects' answers. During the journey, the subject will have to freely explore the 360° environment, simply through the movement of the head, as in real situations [79]. As previously stated, the participant will have to perform seven subtasks. In each level, the subject will be asked to answer, choosing between three or more "alternatives", according to the task's request. The researcher will record all the subject's responses: if the subject chooses a wrong alternative, the test will be immediately stopped.

The following indices will be calculated:

(1). Correct answer for each subtask (and total score);
(2). Subtask reaction time: the time (in seconds) from the start of a subtask until the participant provides an answer. The maximum time allowed will be 180 s (as suggested by [47]);
(3). Total reaction time: The time in seconds registered from the examiner's instruction until the participant provides the last correct answer.

Moreover, the HDM will allow the detection of nonverbal indices related to EFs by collecting eye movements (saccadic and antisaccadic movements, and fixations) by ET and electrical activity of prefrontal cortex by EEG signals (six channels, 24 bit).

D. Post-Task Evaluation

At the end of EXIT 360° task evaluation, the subject will have to rate the quality of the experience associated with its use through an ad hoc questionnaire that assesses perceived levels of challenge and skill, appreciation, and sense of presence experienced (post-task evaluation). Specifically, the questionnaire will involve:

(a) Three items from the Flow Short Scale (5-point scale, from low to high) to assess level of skills in coping with the task, challenges, and the perceived challenge–skill balance, respectively [80].

(b) Five items (6-point scale) from the subscale "Enjoyment" of the Intrinsic Motivation Inventory (IMI) [81] to evaluate participants' appreciation of the proposed activity, including the item "This activity was fun to do".

(c) Three items of the Slater–Usoh–Steed Questionnaire [82] (7-point questionnaire) to evaluate the sense of presence, assessing the measure regarding whether: (1) to be in the 360° scene; (2) the 360° scene became the dominant reality; and (3) the 360° scene was remembered as a place.

Moreover, the participant will evaluate the level of usability of technological device on the System Usability Scale (SUS) [83] (5-point scale, from "disagree entirely" to "agree totally").

2.3. Statistical Analysis

The sample-size calculation was performed with G power software.
F test–ANOVA: Repeated measures, between factors
Analysis: A priori: Compute required sample size

Input:	Effect size f	=	0.369
	α err prob	=	0.05
	Power (1-β err prob)	=	0.80
	Number of groups	=	2
	Number of measurements	=	2
	Corr among rep measures	=	0.5
Output:	Noncentrality parameter λ	=	8.3512080
	Critical F	=	4.0617065
	Numerator df	=	1.0000000
	Denominator df	=	46.0000000
	Total sample size	=	46
	Actual power	=	0.8068335

The Effect size obtained from the validation study of the PIT 360° by Serino and colleagues was chosen as a benchmark, as the studies are similar in terms of methods and materials (e.g., experimental procedure, 360° environments, and clinical population involved).

Descriptive statistics of the sample will include frequencies, median and interquartile range (IQR) for categorical variables, and mean and standard deviation (SD) for continuous measures. The normality of data distribution will be assessed using the Kolmogorov–Smirnov test. An ANOVA between-group comparison will be run to assess significant differences between patients and healthy controls in traditional neuropsychological assessment and immersive experience evaluation indices. Specifically, the statistical analysis will have to highlight possible difference in verbal (correct answer and reaction time) and nonverbal indices (antisaccadic movements, fixations, and electrical activity of prefrontal cortex). A Pearson correlation will be applied to compare both the nonverbal with verbal indices and traditional neuropsychological tests with the verbal outcomes of the immersive experience. A Spearman's correlation will be applied to compare the usability tests and technological experience questionnaire scores with EXIT 360° outcomes. An ANOVA between-group comparison will be run to check significant differences between patients

and healthy controls in evaluating the usability of the mobile-powered headset. Finally, descriptive statistics will be conducted to evaluate the user experience, perceived levels of challenge and skill, appreciation, and sense of presence experienced while performing the EXIT 360°. All statistical analyses will be performed using Jamovi 1.6.7. ROC curves will evaluate the specificity and sensitivity of all the tests administered. These statistical analyses will be performed using the Statistical Package for the Social Sciences for Windows (IBM Corp, Armonk, NY, USA), version 23. Nonlinear stochastic approximation (i.e., machine-learning) methods will be used to compare the classification accuracy of traditional neuropsychological assessments versus the EXIT 360° indices for classifying participants into either the "Individuals with PD" or "Healthy Controls" groups. Different machine-learning algorithms will be employed: a logistic regression classification algorithm and a random forest classification. All these analyses will be computed using Python 3.4 with the Orange 3.3.5 data-mining suite, which is freely available as open-source code (https://github.com/biolab/orange3, accessed on 23 July 2021).

3. Conclusions

Executive dysfunction is one of the major clinical nonmotor symptoms in early-stage nondemented PD [4], and is particularly disabling due to its high negative impact on daily functioning and quality of life [6–8]. Since EFs play a key role in everyday life and independent functioning [84,85], identifying early strategies functional to the ecological evaluation of EFs is crucial to achieve optimal PD management. The ecological limitations of traditional neuropsychological batteries and numerous difficulties in administering tests in real-life scenarios have led to the increasing use of technological instruments, including virtual reality and 360° enviroment-based tools for the assessment of EFs in real-life. Advances in 360° technologies have allowed participants to be evaluated in virtual scenarios that they experience from a first-person perspective, overcoming some limitations (technical and clinical) regarding VR. A preliminary study that used a 360°-based tool (PIT 360°) for assessment of executing functioning (only visual-searching component) showed that PIT 360° could distinguish individuals with PD from controls.

EXIT 360° was designed to obtain information about executive-functioning components while the participants perform everyday tasks in 360° environments that reproduce different real-life contexts. Our study aims to evaluate the efficacy and usability of EXIT 360° as an innovative and ecologically valid tool for the evaluation of the EFs in PD. First, it is expected that all participants will evaluate EXIT 360° as usable, engaging, and challenging, and they will show a high sense of presence while immersed in EXIT 360°. Secondly, we suppose that EXIT 360° will reveal different performances in individuals with PD compared to HC. Specifically, in line with previous evidence, we expect patients to have more difficulty in responding correctly to subtasks, have delayed exit times from the house, take longer to provide a correct interpretation of the proposed scene, and be more prone to distractor interference. Moreover, patients should show greater difficulty in focusing on the most critical components for a correct interpretation of the scene. In addition, we expect to find a correlation between conventional neuropsychological tests of executive functions and performance on PIT 360°. In other words, we expect to see a convergent validity between the standard tests and EXIT 360°. In this way, EXIT 360° could be considered a quick, ecological, and useful screening tool capable of evaluating different aspects of dysexecutive disability in individuals with PD. Further, through the analyses, we expect the results obtained by the classifiers to indicate the potential of the EXIT 360° evaluation in distinguishing between individuals with PD and HC. It will be interesting to see if EXIT 360° will have a greater capacity in predicting patients in the PD group compared to a traditional neuropsychological assessment. Furthermore, thanks to an innovative technological device that integrates an ET and EEG, we expect to find, in line with the literature, differences between PD and HC in activating the frontal cortex, and in the antisaccadic eye movements and the number of fixations.

The validation of EXIT 360° as an innovative assessment tool for EFs in PD will allow a quick, ecological, and useful 360°-based instrument that is easily accessible and that will radically transform the assessment experience for both the clinic and the patient. The clinician will obtain faster, multicomponent, and multidomain evaluations. EXIT 360° will allow clinicians to simultaneously and quickly (15–20 min) collect data on several components of executive functioning through verbal responses (choosing between three or more "options") and reaction time. Moreover, the use of the easy-to-use technological device for delivering of the 360° environments and subtasks of EXIT 360° will allow collecting nonverbal data by ET (e.g., saccadic and antisaccadic movements, and fixations) and EEG (i.e., the electrical activity of prefrontal cortex). Interestingly, EXIT 360° will ensure that clinicians can obtain information about executive functioning while participants are performing everyday tasks in environments that reproduce real-life contexts, testing complex functions of daily life enjoyably. On the other hand, the patient will be involved in a short task (vs. a long and complicated evaluation) that can be experienced as a "game for health", increasing engagement and lowering the level of emotional charge that a neuropsychological assessment can entail. Moreover, this tool will allow participants to receive immediate feedback on their performance. Finally, unlike most VR-based tools, EXIT 360° delivered via the innovative technological device will be a portable device suitable for clinical settings and for individuals with motor difficulties who cannot walk. Compared to other technological devices, this device is easily transportable, so the evaluation can also be performed in the patient's room or house, overcoming logistical challenges related to bringing a patient into the clinic.

In conclusion, EXIT 360° will go beyond the effectiveness of standard tests, VR-based tools, or ET and EEG studies by combining different components and data for a multidimensional and multicomponent assessment of executive functioning with high clinical usability and ecological validity.

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