Cognitive inhibition difficulties in individuals with hemiparesis: Evidence from an immersive virtual reality target-distractor salience contrast visual search serious game

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Abstract

**Introduction:** Stroke can result in various impairments that require multidisciplinary rehabilitation. For example, preserved cognitive executive functions predict motor recovery success. Despite knowing these links, the evaluation of executive function in hemiparesis patients remains underexplored. Here, we examined whether post-stroke individuals with upper limb hemiparesis (SI:HP) had cognitive inhibition deficits using a new immersive virtual reality (IVR) serious game.

**Methods:** Twenty SI:HP with no known history of cognitive impairment and who were not undergoing any neuropsychological rehabilitation and twenty age-matched healthy control individuals (CI) were recruited. They performed the 6-level serious game requiring responses to spatial target presented amongst 11, 17 and 23 distractors with high versus low target-distractors saliency contrasts. Responses were made with less-effected hand for SI:HP group and dominant hand for CI. Response time (RT), and kinematic variables were measured.

**Results:** The SI:HP group was slower and more variable than the CI group. All participants were slower and more variable when responding to the low compared to high target-distractors saliency conditions, and when responding to targets with increased numbers of distractors. A significant interaction between task saliency and distractor number showed slower and more variable responses with increased numbers of distractors in the low saliency condition, but not in the high saliency condition. Interactions involving group and saliency for RT and CV showed that SI:HP compared to CI group showed a greater differences in responses to low versus high saliency conditions.

**Conclusion:** These results suggested that relative to the CI group, the SI:HP group showed cognitive inhibition impairments in the IVR serious game. As cognition plays a fundamental role in motor recovery, these results suggest a need for systematic cognitive screening of post-stroke patients.

*Trial registration* [http://www.clinicaltrials.gov](http://www.clinicaltrials.gov); *Unique identifier:* NCT04694833, *Date of registration:* 11/24/2020

**Introduction**

Stroke is a global health issue and the leading cause of disability worldwide (Avan & Hachinski, 2021; Duncan, 1994; Sacco et al., 2013). While spontaneous recovery of function typically occurs during the first weeks post-incident (Hatem et al., 2016; Kwakkel et al., 2006), performance deficits typically remain following the spontaneous recovery period, often leaving survivors with a combination of long-term cognitive and motor deficits (Jokinen et al., 2015; Mackay et al., 2004). These impairments typically result in social life participation difficulties, as well as limitations in daily-life activities such as preparing food or driving, thereby affecting overall quality of life for both the patient and their caregivers (Jaracz & Kozubski, 2003; Sreedharan et al., 2013). In order to address this issue, there is a pressing need to develop new rehabilitation strategies, as well as improve early detection of motor and/or cognitive impairments to further optimize intensive treatment programmes that enhance the chances of recovery (Cumming et al., 2013; Kwakkel et al., 2010; Poulin et al., 2012; Zucchella et al., 2014).

The prevalence rate of motor impairments following stroke is estimated to range from 83–90% (Bogousslavsky et al., 1988; Dutta et al., 2022; Herman et al., 1982; Lawrence et al., 2001), representing the most common post-stroke impairment. The impact on patient behaviour includes problems in gait, balance, and general physical ability, including arm and hand movements for object interactions (Bernhardt et al., 2015; Middleton et al., 2017; Verma et al., 2012). Currently, these latter motor impairments are evaluated using valid and reliable standardized measures of activity capacity (Prange-Lasonder et al., 2021). The Box and Block Test is recommended for outcome measures of unilateral gross motor dexterity, the Fugl-Meyer Assessment is recommended for outcomes measures of upper limb impairment, and the Action Research Arm Test is recommended for outcome measures of upper limb activity capacity (all with strong validity, reliability, and clinical usefulness) (Duncan et al., 1983; Fugl-Meyer et al., 1975; Lyle, 1981; Mathiowetz et al., 1985; Prange-Lasonder et al., 2021; Uswatte et al., 2005). New innovations in clinical evaluation of motor function allows for the inclusion of kinematic measures using new technology such as rehabilitation robots and interactive virtual reality (Burton et al., 2022; Dehem et al.,
The prevalence of cognitive impairments following stroke is less well understood, ranging from 24–96% of stroke individuals showing cognitive impairment (Douri et al., 2013; Gutiérrez Pérez et al., 2011). This large variance is caused by different types of cognitive deficits such as attention, executive functions, and speed processing (Jokinen et al., 2015; Laakso et al., 2019; Lešniak et al., 2008). Although the extent of these cognitive impairments varies across individuals with stroke, it is nevertheless clear that cognitive impairments are a major determinant of poor long-term recovery, including recovery from motor impairments (Shimada et al., 2018; VanGilder et al., 2020). In current clinical practice, paper-and-pencil tests are frequently used to screen the range of potential cognitive impairments, as well as provide more detailed evaluations of specific cognitive impairments, thereby determining specific cognitive impairments and their severity (Cullen et al., 2007; Woodford & George, 2007). Over the last 10–20 years, computerized tests have been developed to address weaknesses in paper-and-pencil test sensitivity, for example, using methods such as trial randomization and more precise response time measurements (Montedoro et al., 2018; Tynrshkin et al., 2014; Zimmermann & Fimm, 2004). Sensitive cognitive tests are particularly important for understanding the influence of cognition on motor function, particularly when the cognitive impairments are not obvious when interacting with the patient.

Traditionally, motor and cognitive post-stroke impairments have been studied, assessed and managed as two distinct issues (Chen et al., 2013; Langhome et al., 2011). In research, patients with cognitive impairments are often excluded from studies investigating motor impairments or the efficacy of motor rehabilitation strategies (Everard et al., 2020). Further, in clinical practice, motor dysfunction seems to be routinely evaluated for all patients with stroke, whereas cognitive evaluations appear to be conducted on only a subset of patients based on clinician intuition (Einstad et al., 2021; Montero-Odasso et al., 2018). This latter issue may be explained by the fact that motor impairments are more visible with clear impairments to daily life function, whereas cognitive impairments are hidden and less obvious (e.g., deficits in inhibition). This separatist approach obscures the understanding of underlying cognitive processes implied in motor recovery.

Various studies have demonstrated the importance of cognition in motor performance. For example, a meta-analysis of studies investigating cognitive and upper limb functions reported an association between cognitive impairment (such as inhibition) and improvements in upper limb motor impairment (Mullick et al., 2015). Similarly, dual-task paradigms that increase cognitive load (reduce cognition) disrupts the efficiency of motor ability learning (Wulf et al., 2007). In individuals with stroke, research reports links between motor and cognitive impairments (Čengić et al., 2011; Lowrey et al., 2022; VanGilder et al., 2020; Verstraeten et al., 2016). For example, Mc Dowd et al. (2003) showed that stroke-related attentional impairments predicted daily-life functioning. Verstraeten et al. (2020) reported evidence of correlation between motor and cognitive performance impairments in more than one hundred chronic post-stroke survivors. Finally, Lin et al. (2021) reported differences in motor recovery during rehabilitation for tests of Grip Strength (low cognitive load) relative to the Box and Blocks test (higher cognitive load). Using Voxel Lesion Symptom Mapping (VLSM), they showed that motor impairment in the Box and Blocks test was associated with lesions that included the dorsal anterior insula; implicated in complex attentional (selection / inhibition) cognitive processes, whereas Grip Strength performance was associated to sensorimotor lesions, and not implicated in areas associated with cognition.

Together, these data underline the importance of understanding how cognitive impairments influence motor impairments and recovery processes. This literature shows the importance of a thorough assessment that includes both motor and cognitive tests as an essential first step to define post-stroke rehabilitation (Bourke et al., 2016; Kleim & Jones, 2008; McDonald et al., 2019; Schaefer & Schumacher, 2011). It seems fundamentally necessary to tailor interventions and rehabilitation programs to the patient's clinical status, that incorporate both cognitive and motor neurorehabilitation where necessary, to more efficiently drive recovery. For example, for the restoration of motor abilities, patients must relearn to perform complex motor skills (Hodges & Franks, 2000; Wulf & Weigelt, 1997). These relearning processes involve cognition (Singer et al., 1989; Tennant et al., 2004), particularly executive functions, such as selective attention and cognitive inhibition (Barrett & Muzaffar, 2014; Hochstenbach & Mulder, 1999; McEwen et al., 2009). Impairments of selective attention and cognitive inhibition are
common consequences of stroke, and known to have a direct association to poor motor performance, specifically on the paretic upper limb (D’Imperio et al., 2021; Kim et al., 2021; Nijboer et al., 2014). Yet, the impact of selective attention and inhibitory control dysfunction on upper limb hemiparesis remains under investigated in the literature.

To better understand links between selective attention and inhibitory control (non-spatial attention) and motor performance in patients with motor impairments, it is important to develop tests that can measure cognitive and motor responses within the same test. An immersive virtual reality serious game “REASmash” have recently been developed (Ajana et al. 2023) based on Feature Integration Theory (FIT) (Treisman & Gelade, 1980) and the research of Duncan and Humphreys (1989). The task involves the patient searching for a spatial target presented amongst distractors. When the target differs from the distractors by a single feature, the search is said to be conducted in parallel. Attention is divided between the target and the distractors, and the visual features of the distractors are automatically registered and inhibited at a pre-attentional level of processing (Treisman & Souther, 1985). In this situation, the target is said to ‘pop-out’ from the distractors due to their high salience contrast (e.g., a red target presented with blue distractors). However, if the target shares a conjunction of features with the distractors (e.g., a red target with blue distractors and red distractors of a different shape), the search is conducted in serial due to a low salience contrast. The visual features of the distractors are attentively inhibited during a successive serial search of the stimuli in order to find the target (Koshino, 2001; Treisman & Sato, 1990). During this serial search, response time to find the target increases with the increased number of distractors (causing increased distractors inhibition demands) (Poisson & Wilkinson, 1992; Wolfe et al., 1989). In contrast, increasing the numbers of distractors has no effect on parallel search (Huang & Pashler, 2005; Wolfe et al., 1989). In our serious game, we manipulated the saliency between the target and distractors (low vs high), as well as systematically manipulating the number of distractors displayed (11, 17 and 23).

Participants made motor responses to the target by reaching and interacting within immersive virtual reality using a hand controller. This makes the test unique as it measures distractor inhibition using a motor response (whereas most cognitive tests involve pushing a button on a peripheral keyboard or button box).

The principal objective of this paper was to examine whether post-stroke individuals with upper limb hemiparesis have distractor inhibition attention deficits. We tested a group of post-stroke individuals with hemiparesis (SI:HP) and a group of mean age matched healthy control individuals (CI). Responses were made with the less-affected limb for SI to exclude confound motor-cognitive impairments in the hemiparesis limb. Therefore, any differences in performance between SI:HP and CI (dominant hand performance), specifically regarding the FIT would indicate distractor inhibition impairments. We hypothesised that: (1) mean response time (RT) and mean velocity (MV) will be slower, and coefficient of variation of speed will be higher for the SI:HP than CI groups. We also hypothesised that (2) RT time and MV will be slower, and CV will be higher for finding the target in the low target-distractors saliency condition (serial search) than in the high target-distractors saliency condition (parallel search) due to increased attentional load. We additionally hypothesised interactions. Firstly (3) an interaction between saliency and distractor number showing that in the high target-distractors saliency condition (parallel search), RT, MV and CV will show no differences between the number of distractors, whereas in the low target-distractors saliency condition (serial search), RT, MV and CV will show significant differences with increased numbers of distractors, with more distractors increasing attentional load and reducing performance (taking more time to respond to the target / more variance in responses). Secondly, we hypothesised (4) an interaction between search saliency and group showing that the SI:HP relative to CI groups will show a greater difference in RT to find the target between the low salience (serial) relative to high salience (parallel) search conditions, demonstrating a specific impairment of cognitive inhibition for individuals with hemiparesis relative to aged-matched healthy individuals. If this effect is found, it will indicate that patients with hemiparesis have underlying cognitive inhibition impairments that have not been identified during clinical diagnosis. We hypothesize similar effects for MV and CV, though we have no prior evidence to support this hypothesis.

Methods

Participants:
We tested 20 SI:HP (7 females; 8 left-handed (less affected)) and 20 CI (10 females, 1 left-handed) using convenience sampling. The SI:HP were aged between 47 and 80 years (M = 61, SD = 11), and were recruited from the physical medicine and rehabilitation department of the Cliniques universitaires Saint-Luc in Brussels. The participants were selected using the following inclusion criteria: (1) presence of an ischemic or haemorrhagic first stroke, diagnosed by CT or magnetic resonance imaging; (2) presence of upper-limb hemiparesis clinically diagnosed and documented through a physical medicine evaluation report, and; (3) a good understanding of the task instructions. The exclusion criteria were: (1) uncorrected vision deficiencies and (2) the presence of other neurological conditions such as dementia or orthopaedic dysfunction that could influence upper extremity function. None of these individuals had a known history of cognitive impairment, and they were not following any neuropsychological assessment. According to their medical record, 5 of the SI:HP had a left hemisphere lesion causing a right hemiparesis, and at the time of testing, they were between 1.3- and 142.2-months post-onset (see Table 1). The CI were aged between 60 and 69 years (M = 63., SD = 2.5). They were included if they had (1) corrected-to-normal vision, and (2) a good understanding of the task instructions, and they were excluded if they had (1) another orthopaedic or neurological condition that may influence their movement/motor function. The SaintLuc UCLouvain-Hospital Faculty Ethics Committee (reference number: 2015/10FEV/053) approved all the procedures prior to experimentation. All the participants volunteered to participate in the study, providing written informed consent before participation.
## Table 1
The demographic characteristics of the post-stroke individuals with hemiparesis (SI: HP)

<table>
<thead>
<tr>
<th>Gender</th>
<th>Age</th>
<th>Handedness pre-stroke</th>
<th>Handedness post-stroke (less-effected limb)</th>
<th>Stroke site</th>
<th>Stroke type</th>
<th>Months post-onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>SI:HP01</td>
<td>M</td>
<td>47</td>
<td>Right</td>
<td>Left</td>
<td>Left lenticulostriate intraparenchymal hematoma</td>
<td>Hemorrhagic</td>
</tr>
<tr>
<td>SI:HP02</td>
<td>F</td>
<td>62</td>
<td>Right</td>
<td>Right</td>
<td>Right sylvien fissure</td>
<td>Ischemic</td>
</tr>
<tr>
<td>SI:HP03</td>
<td>M</td>
<td>56</td>
<td>Right</td>
<td>Right</td>
<td>Right thalamus</td>
<td>Ischemic</td>
</tr>
<tr>
<td>SI:HP04</td>
<td>F</td>
<td>51</td>
<td>Right</td>
<td>Left</td>
<td>Left sylvien fissure</td>
<td>Ischemic</td>
</tr>
<tr>
<td>SI:HP05</td>
<td>M</td>
<td>62</td>
<td>Right</td>
<td>Right</td>
<td>Right internal capsule lacunar</td>
<td>Ischemic</td>
</tr>
<tr>
<td>SI:HP06</td>
<td>M</td>
<td>69</td>
<td>Right</td>
<td>Left</td>
<td>Left paramedian pontine</td>
<td>Ischemic</td>
</tr>
<tr>
<td>SI:HP07</td>
<td>M</td>
<td>46</td>
<td>Right</td>
<td>Left</td>
<td>Left sylvien fissure</td>
<td>Ischemic</td>
</tr>
<tr>
<td>SI:HP08</td>
<td>F</td>
<td>79</td>
<td>Right</td>
<td>Left</td>
<td>Left sylvien fissure</td>
<td>Ischemic</td>
</tr>
<tr>
<td>SI:HP09</td>
<td>M</td>
<td>73</td>
<td>Right</td>
<td>Right</td>
<td>Right sylvien fissure</td>
<td>Ischemic</td>
</tr>
<tr>
<td>SI:HP10</td>
<td>M</td>
<td>74</td>
<td>Right</td>
<td>Right</td>
<td>Right sylvien fissure</td>
<td>Ischemic</td>
</tr>
<tr>
<td>SI:HP11</td>
<td>M</td>
<td>61</td>
<td>Right</td>
<td>Right</td>
<td>Right superficial and deep sylvien fissure</td>
<td>Ischemic</td>
</tr>
<tr>
<td>SI:HP12</td>
<td>M</td>
<td>47</td>
<td>Right</td>
<td>Left</td>
<td>Left temporal</td>
<td>Ischemic</td>
</tr>
<tr>
<td>SI:HP13</td>
<td>F</td>
<td>56</td>
<td>Left</td>
<td>Right</td>
<td>Right internal capsule</td>
<td>Ischemic</td>
</tr>
<tr>
<td>SI:HP14</td>
<td>M</td>
<td>65</td>
<td>Right</td>
<td>Right</td>
<td>Right capsulo-lenticular territory</td>
<td>Ischemic</td>
</tr>
<tr>
<td>SI:HP15</td>
<td>F</td>
<td>72</td>
<td>Right</td>
<td>Right</td>
<td>Right sylvien fissure</td>
<td>Ischemic</td>
</tr>
<tr>
<td>SI:HP16</td>
<td>F</td>
<td>50</td>
<td>Right</td>
<td>Right</td>
<td>Right deep temporal</td>
<td>Hemorrhagic</td>
</tr>
<tr>
<td>SI:HP17</td>
<td>M</td>
<td>50</td>
<td>Right</td>
<td>Left</td>
<td>Left pontine</td>
<td>Hemorrhagic</td>
</tr>
<tr>
<td>SI:HP18</td>
<td>F</td>
<td>55</td>
<td>Left</td>
<td>Right</td>
<td>Right sylvien fissure</td>
<td>Ischemic</td>
</tr>
<tr>
<td>SI:HP19</td>
<td>M</td>
<td>69</td>
<td>Right</td>
<td>Right</td>
<td>Right frontoparietal intraparenchymal</td>
<td>Hemorrhagic</td>
</tr>
<tr>
<td>SI:HP20</td>
<td>M</td>
<td>80</td>
<td>Right</td>
<td>Left</td>
<td>Left corona radiata</td>
<td>Ischemic</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td></td>
<td>61 (11)</td>
<td></td>
<td></td>
<td></td>
<td>18 (33)</td>
</tr>
</tbody>
</table>

F = Female, M = Male, SD = Standard Deviation.

**Materials, Stimuli and Experimental Design:**

As described in the Introduction, we used an immersive virtual reality visual search serious game manipulating target-distractors saliency for measuring spatial and distractors inhibition attention (Ajana et al. 2023). The ‘REASmash’ was created using Unity 2019.3 software (in C# language). The hardware consisted of an IVR headset (Oculus Quest 2) and one Oculus Quest motion controller. The experiment was monitored through a live stream from the Oculus App to a digital tablet.
Participants sat on a chair with their feet on the ground, wearing the IVR headset. The S1:HP held the controller with their less-effected (post-stroke dominant) hand, and the CI held the controller with their dominant hand. They were then immersed into the virtual environment that consisted of a simulated cartoon-like garden, with a raised-bed garden patch composed of twenty-four molehills (a grid of six columns and four rows). The stimuli were stylized cartoon-like moles that appeared from the molehills (with animation). In each trial, one target mole was presented with several distractor moles. The target mole wore a red miner's helmet, and the distractor moles wore a blue miner's helmets, or red or blue helmets with horns (see Fig. 1).

At the beginning of the serious game, written and oral instructions were presented, instructing the participants to respond to the target as fast as they could using a virtual hammer controlled with the Oculus motion controller. They were also instructed to not make responses to the distractor stimuli. The target and distractors stimuli appeared for 7000 milliseconds maximum. If the participant correctly responded to the target within the 7000 milliseconds, the trial was recorded as a success. If no response was made by the participant within the 7000 milliseconds, the REASmash automatically registered the trial as an omission (i.e., the participant failed to find the target-mole). If the participant responded to a distractor instead of the target, the REASmash automatically registered the trial as a failed response (i.e., the participant failed to find the correct mole). After each response type, the next trial was automatically initiated.

The REASmash serious game was composed of 6 levels, with each level consisting of 24 trials (i.e., the target mole appearing from each of the 24 molehills, randomly across the 24 trials). In the three first levels, the target appeared among 11, 17, and 23 distractor moles wearing blue miner’s helmets or blue helmets with horns. These trials represented low inhibition demands due to the high salience difference between the target (red) and distractors (blue). In the latter three levels, the target again appeared among 11, 17, and 23 distractor moles, but this time wearing either red helmets with horns or blue helmets with horns, representing high inhibition demands due to the low salience difference between the target and distractors. The distractors (blue miner’s helmets and blue helmets with horns versus red helmets with horns and blue helmets with horns) were close to equally distributed (i.e., 5 + 6 for 11 distractors; 11 + 12 for 23 distractors etc.) across the 6 levels. The distractors were pseudo-randomly placed within the columns of the grid so that for 1 target and 11 distractors, 2 stimuli were presented in each column, for 1 target and 17 distractors, 3 stimuli were presented in each column and for 1 target and 23 distractors, 4 stimuli were presented in each column. Within each column, the distractor position was randomised for each trial. The levels were blocked as the original intention for the serious game was to allow selection of levels with patients based on their likely ability to perform the task (i.e., for some patients, levels 1 and 4 with 11 distractors may be too easy, while for other patients, levels 3 and 6 with 23 distractors may be too difficult). In the present study, we used all 6 levels. All trials were randomised for each participant.

Before every trial, the participant had to fixate a central stimulus (measured with the Oculus head position) and place their virtual mallet response hand on a central starting position (both positioned along the sagittal axis of the participant). This consisted of simultaneously fixating a floating red cube with an eye illustration and placing the virtual hammer on a second red cube with a hammer illustration. The eye-cube was positioned at the level of the participant's eyes, and the hammer-cube was at the level of the participant's arm. Once the participant successfully placed their gaze and hand on the cubes, they turned green, and the trial was initiated. This procedure was carried out to ensure that the participants-initiated responses from a consistent starting position across all trials.

Fig. 1 here

Procedure:

The experiments were run in the Cliniques universitaires Saint-Luc hospital in Brussels and in a laboratory in the Psychological Sciences Research Institute of the University of Louvain. Each experiment lasted approximately 40 minutes, and always started with an information session where the participant received oral explanations and instructions regarding the experimental design, followed by their signing of a consent form to agree to participate to the study. Once consent was
provided, the participant was seated comfortably on a chair, and the IVR headset and motion controller were placed on the participant. They were then immersed in the virtual environment of the REASmash. Instructions were displayed within the serious game, and a training session was initiated consisting of 10 trials, to confirm that the participants understood the instructions, and enhance the feeling of immersion. After the training session, the participants pushed a start button within the virtual environment to initiate the experiment (consisting of 6 levels of 24 randomized trials; 144 trials in total). After the participant completed each of the 6 levels, a break of 60 seconds was provided to reduce fatigue. The CI participants received a payment of 10 euros for their participation. All the participants completed the experiment.

**Methods of data analysis:**

The data analyses were performed using mixed measures (repeated and between) ANOVA, run using SPSS 27.0 (IBM). All post-hoc analyses used Bonferroni correction. The independent variables were search task saliency (low vs high), number of distractors (11, 17 or 23 distractors) and group (SI:HP vs CI). The dependent variables were mean response time (RT; time between stimuli presentation and response with the virtual hammer to the target stimulus; measure in milliseconds), mean velocity (MV, distance covered by the virtual hammer divided by the response time; measures in meters per second), and coefficient of variation of speed (CV, standard deviation of the virtual hammer velocity divided by mean velocity, expressed in percentage).

From the total data set of the SI:HP group (i.e., 144 trials x 20 SI:HP; 2880 trials), 93 omissions trials and 94 error trials (distractor response) were removed (see Table 2). From the total data set of the CI group (2880 total trials), 16 omission trials and 31 error trials were removed. For both groups, no participants made abnormal response times (<250ms). The analysis was performed on the remaining data of SI:HP and CI groups.

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**Table 2 here**
Table 2
The frequency of omissions and errors (/144 trials) made by SI:HP group. There were no abnormal responses for any participant. The omissions data showed no signs of lateral bias typically associated with hemineglect, strengthening the clinical decision that these patients were not evaluated by the neuropsychology clinic of the hospital. The targets presented within the garden grid (6 columns and 4 rows) were re-coded relative to hand so that targets presented in contralateral space corresponded to columns 1–3 and targets presented in ipsilateral space corresponded to columns 4–6 for SI:HP and CI using their right-hand (with the right-lesion SI:HP using their right non-hemiparetic limb). For left hand responses, contralateral space corresponded to columns 4–6 and targets presented in ipsilateral space corresponded to columns 1–3 (with left-lesion SI:HP using their left non-hemiparetic limb).

<table>
<thead>
<tr>
<th></th>
<th>Total Omissions (only in contralateral space)</th>
<th>Errors (responded to a distractor)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SI:HP01</td>
<td>0(0)</td>
<td>4</td>
</tr>
<tr>
<td>SI:HP02</td>
<td>9(4)</td>
<td>1</td>
</tr>
<tr>
<td>SI:HP03</td>
<td>1(1)</td>
<td>0</td>
</tr>
<tr>
<td>SI:HP04</td>
<td>2(1)</td>
<td>0</td>
</tr>
<tr>
<td>SI:HP05</td>
<td>6(2)</td>
<td>4</td>
</tr>
<tr>
<td>SI:HP06</td>
<td>1(1)</td>
<td>3</td>
</tr>
<tr>
<td>SI:HP07</td>
<td>0(0)</td>
<td>1</td>
</tr>
<tr>
<td>SI:HP08</td>
<td>18(10)</td>
<td>2</td>
</tr>
<tr>
<td>SI:HP09</td>
<td>1(0)</td>
<td>1</td>
</tr>
<tr>
<td>SI:HP10</td>
<td>10(3)</td>
<td>3</td>
</tr>
<tr>
<td>SI:HP11</td>
<td>1(0)</td>
<td>4</td>
</tr>
<tr>
<td>SI:HP12</td>
<td>6(3)</td>
<td>22</td>
</tr>
<tr>
<td>SI:HP13</td>
<td>4(1)</td>
<td>7</td>
</tr>
<tr>
<td>SI:HP14</td>
<td>2(1)</td>
<td>1</td>
</tr>
<tr>
<td>SI:HP15</td>
<td>0(0)</td>
<td>4</td>
</tr>
<tr>
<td>SI:HP16</td>
<td>0(0)</td>
<td>2</td>
</tr>
<tr>
<td>SI:HP17</td>
<td>1(0)</td>
<td>3</td>
</tr>
<tr>
<td>SI:HP18</td>
<td>17(13)</td>
<td>13</td>
</tr>
<tr>
<td>SI:HP19</td>
<td>1(0)</td>
<td>1</td>
</tr>
<tr>
<td>SI:HP20</td>
<td>13(7)</td>
<td>18</td>
</tr>
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</table>

Results
The analysis of RT showed that there was a main effect of group, $F(1,38) = 16.57, p < 0.001, \eta^2 = 0.30$, with SI:HP being slower than CI (SI:HP: $M = 2712.11, SD = 93.93$; CI: $M = 2171.41, SD = 93.93$). The analysis also showed main effects of search task saliency and distractors. For search task, $F(1,38) = 347.34, p < 0.001, \eta^2 = 0.90$, RT was significantly slower in the low compared to high target-distractors saliency condition (Low: $M = 3011.93, SD = 85.90$; High: $1871.59, SD = 57.58$). For distractors, $F(2,76) = 74.38, p < 0.001, \eta^2 = 0.66$, RT was significantly slowed when the number of distractors increased, with significant differences between a target presented with 11 distractors, compared to 17 or 23 distractors, and between 17 and 23 distractors, ($M = 2272.82, SD = 64.18$; $M = 2445.80, SD = 70.35$; $M = 2606.65, SD = 70.10$, for 11, 17, and 23 distractors). As
hypothesized, there was a significant interaction between search task saliency and distractors, $F(2,76) = 71.97$, $p < 0.001$, $\eta^2 = 0.65$ (Fig. 2a). Separated ANOVAs were run for each search task. This showed that the effect of distractors was not significant for high target-distractors saliency stimuli (levels 1–3), $F(2,76) = 2.06$, $p = 0.13$, $\eta^2 = 0.05$, but that there was a significant distractor effect for low target-distractors saliency stimuli, $F(2,76) = 79.96$, $p < 0.001$, $\eta^2 = 0.68$. A Bonferroni post hoc analysis showed that mean RT significantly slowed as a function of increased number of distractors for low target-distractor saliency contrasts (with significant differences between each distractor set) ($M = 2691.81$, $SD = 84.15$; $M = 3007.05$, $SD = 91.18$; $M = 3336.92$, $SD = 96.66$, for 11, 17 & 23 distractors respectively).

There was also a significant interaction between search task saliency and group, $F(1,38) = 7.50$, $p < 0.001$, $\eta^2 = 0.16$ (Fig. 3). Separate ANOVAs were run for each search task. This showed that the effect of group was significant for both sets of stimuli (high target-distractor salience contrasts: levels 1–3, $F(1,38) = 10.50$, $p < 0.001$, $\eta^2 = 0.22$, and low target-distractor salience contrasts: levels 4–6, $F(1,38) = 17.00$, $p < 0.001$, $\eta^2 = 0.31$). The alternative post-hoc analysis of the interaction was made by separating the ANOVA by group. This showed significant differences for search task saliency in both the SI:HP, $F(1,19) = 219.97$, $p < 0.001$, $\eta^2 = 0.92$, and CI groups, $F(1,19) = 131.45$, $p < 0.001$, $\eta^2 = 0.87$, with mean RT significantly slower for responses made to targets in the low compared to high target-distractor salience condition for both groups (SI: HP: Low: $M = 3366.09$, $SD = 121.48$; High: $M = 2058.12$, $SD = 81.42$ – CI: Low: $M = 2657.77$, $SD = 121.48$; High: $M = 1685.05$, $SD = 81.43$). To understand the interaction effect more clearly, we ran a third post hoc analysis that re-analysed the data by subtracting mean RT for target search to the high from low target-distractors saliency contrasts (i.e., low-high = inhibition cost; with the positive time illustrating the relative cost of inhibition and eliminating the speed differences observed between participant groups). This analysis showed a main effect of group, $F(1, 38) = 7.50$, $p < 0.001$, $\eta^2 = 0.16$ (SI:HP: $M = 1307.96$, $SD = 86.53$; CI: $M = 972.71$, $SD = 86.53$), demonstrating that the SI:HP compared to CI groups showed a bigger difference between high and low target-distractor salience contrasts. The interaction between distractors and group was not significant, $F(2,76) = 0.10$, $p = 0.91$, $\eta^2 = 0.00$, and the triple interaction between search task, distractors and groups was not significant, $F(2, 76) = 0.73$, $p = 0.48$, $\eta^2 = 0.02$.

The analysis of MV showed that there was a main effect of group, $F(1,38) = 7.43$, $p < 0.001$, $\eta^2 = 0.16$, with SI:HP making slower actions than CI (SI:HP: $M = 0.36$, $SD = 0.02$; CI: $M = 0.43$, $SD = 0.02$). The analysis also showed main effects of search task saliency and distractors. For search task, $F(1,38) = 181.64$, $p < 0.001$, $\eta^2 = 0.83$, MV was significantly higher to targets presented in high target-distractors salience contrasts ($M = 0.45$, $SD = 0.01$) than in low target-distractors salience conditions ($M = 0.33$, $SD = 0.01$). For distractors, $F(2,76) = 20.66$, $p < 0.001$, $\eta^2 = 0.35$, MV significantly decreased when the number of distractors increased (i.e., responses slowed), with significant differences between a target presented with 11 distractors, compared to 17 or 23 distractors, and between 17 and 23 distractors, ($M = 0.41$, $SD = 0.01$; $M = 0.39$, $SD = 0.01$; $M = 0.38$, $SD = 0.01$, for 11, 17, and 23 distractors). As hypothesized, there was a significant interaction between search task saliency and distractors, $F(2,76) = 15.68$, $p < 0.001$, $\eta^2 = 0.29$ (Fig. 2b). Separated ANOVAs were run for each search task. This showed that the effect of distractors was not significant for high target-distractors saliency, $F(2,76) = 1.69$, $p = 0.19$, $\eta^2 = 0.04$, but it was significant for low target-distractors saliency conditions, $F(2,76) = 25.35$, $p < 0.001$, $\eta^2 = 0.4$. A Bonferroni post hoc analysis showed that mean MV significantly decreased when the number of distractors increased (i.e., responses slowed), ($M = 0.36$, $SD = 0.01$; $M = 0.33$, $SD = 0.01$; $M = 0.31$, $SD = 0.01$, for 11, 17, and 23 distractors). There were no interactions between search task saliency and group, $F(1,38) = 0.02$, $p = 0.89$, $\eta^2 = 0.00$, distractors and group, $F(2,76) = 0.66$, $p = 0.52$, $\eta^2 = 0.02$, and search task saliency, distractors and group, $F(2,76) = 0.13$, $p = 0.87$, $\eta^2 = 0.00$.

The analysis of CV showed that there was also main effects of search task and distractors. For search task, $F(1,38) = 49.26$, $p < 0.001$, $\eta^2 = 0.56$, CV was significantly higher in the low target-distractors saliency ($M = 1.71$, $SD = 0.07$) than high target-distractors saliency conditions ($M = 1.43$, $SD = 0.05$). For distractors, $F(2,76) = 14.86$, $p < 0.001$, $\eta^2 = 0.28$, CV significantly increased with the number of distractors increasing ($M = 1.51$, $SD = 0.06$; $M = 1.56$, $SD = 0.06$; $M = 1.62$, $SD = 0.06$, for 11, 17, and 23 distractors). However, there was no main effect of group, $F(1,38) = 3.9$, $p = 0.056$, $\eta^2 = 0.09$. As for RT and MV, the analysis showed a significant interaction between search task saliency and distractors, $F(2,76) = 22.61$, $p < 0.001$, $\eta^2 = 0.37$.
(Fig. 2c). Separated ANOVAs were run for each search task. This showed that the effect of distractors was not significant for high target-distractors saliency, F (2,76) = 0.25, p = 0.78, η² = 0.00, but was significant for low target-distractors saliency conditions, F (2,76) = 25.84, p < 0.001, η² = 0.40. A Bonferroni post hoc analysis showed that mean CV significantly increased when the number of distractors increased (M = 1.59, SD = 0.07; M = 1.70, SD = 0.08; M = 1.83, SD = 0.08, for 11, 17, and 23 distractors).

The analyses of CV also showed a significant three-way interaction between search task saliency, distractors and group, F (2,76) = 3.65, p < 0.001, η² = 0.09. Separated ANOVA were run for each search task saliency. This showed that the interaction between search task and distractors was significant for SI: HP, F (2,38) = 18.49, p < 0.001, η² = 0.49, and for CI, F (2,38) = 5.24, p < 0.001, η² = 0.2. An alternative post hoc analysis, was performed for each group and search task. This showed that in high target distractors saliency, there was no effect of distractors for CI, F (2,38) = 0.007, p = 0.99, η² = 0.00 and SI:HN, F (2,38) = 0.38, p = 0.69, η² = 0.02. However, in low target distractors saliency, there was a significant effect of distractors in CI, F (2,38) = 6.09, p < 0.001, η² = 0.24, and SI:HN, F (2,38) = 21.25, p < 0.001, η² = 0.53. As in RT analysis, we run a third post hoc analysis that re-analysed the data by subtracting mean CV for target search to the high from low target-distractors saliency contrasts. This showed that there was no group effect, F (1,38) = 0.20, p = 0.66, η² = 0.00.

Discussion

The main objective of this paper was to investigate the cognitive inhibition difficulties of post-stroke individuals with hemiparesis. We tested a group of post-stroke individuals with hemiparesis and a group of age-matched controls using an immersive virtual reality serious game based on Feature Integration Theory (FIT) (Treisman & Gelade, 1980). Our findings supported our hypotheses and the state-of-the-art, firstly showing that individuals with hemiparesis made slower responses than age matched controls (RT and MV), and they were more variable (CV) (hypothesis 1). Secondly our results demonstrated that both participant groups showed the predicted effects associated with FIT. Specifically, both groups of participants were slower (RT and MV) and made more variable responses (CV) to find the target, when presented with low target-distractors saliency stimuli (levels 4–6; high inhibition demands) in comparison to high target-distractors saliency stimuli (levels 1–3; low inhibition demands), and participants response time to find the target was significantly slowed / move variable with increasing numbers of distractors, specifically in the low target-distractors saliency condition (levels 4–6), but not in the high target-distractors saliency condition (levels 1–3) (hypotheses 2 and 3). Contrasts between the patient groups and the FIT allowed us to demonstrate new findings showing that HPI compared to CI were particularly slowed with low target-distractors saliency stimuli (levels 4–6; high inhibition demands) in comparison to high target-distractors saliency stimuli (levels 1–3; low inhibition demands), suggesting that the SI:HP had cognitive inhibition impairments.

In addition to replicating the effects reported in the literature, our research showed an interaction effect between search task and group for RT and search task, distractors and group for CV, providing new evidence that the SI:HP group were particularly slowed / more variable relative to the CI group for the low compared to high target-distractors saliency conditions (hypothesis 4). This was demonstrated by calculating the difference between responses to the low compared to high target-distractors saliency conditions (allowing to control between group speed / variance differences), showing that RT / CV differences were greater for the SI:HP group relative to the CI group. This finding is interesting for two reasons. Firstly, the selected HPI group were believed to have no cognitive impairment, and therefore did not benefit from an early neuropsychological assessment and received no cognitive neurorehabilitation. Secondly, based on existing literature, we can predict that patients with hemiparesis may show impairment of inhibitory executive function cognition in addition to motor hemiparesis that may interfere with hemiparesis rehabilitation.

The finding that inhibition executive function mediates the efficacy of recovery is perhaps not surprising when one considers the role of cognition in motor learning (Chan et al., 2006; Kitago & Krakauer, 2013; Patten et al., 2006). Several studies have
highlighted the role of cognition in improving motor function (Aprile et al., 2021; Fregni & Pascual-Leone, 2006; Lincoln et al., 1989; Matthews et al., 2016; Mercier et al., 2001; Paolucci et al., 1996; Tatemichi et al., 1994). For example, Hummel et al. (2002) used electroencephalography (EEG) in a motor learning task where participants had to respond to cues with specific finger movements that they learned during a training session. While performing the task, EEG analyses clearly showed increased alpha oscillations in the sensorimotor areas typically engaged in primary motor inhibition of volitional learned motor movements. This finding was reinforced by the absence of these oscillations in patients with dystonia of the hand (Hummel et al., 2002). Similarly, Mooney et al. (2020) used transcranial magnetic stimulation (TMS) with a post-stroke upper limb paresis individuals compared to a healthy group. Participants were trained on a sequential visuomotor isometric wrist extension task. Their results showed that ipsilesional corticomotor excitability did not increase after skill acquisition in clinical population who successfully exhibited acquisition and retention skills, but their general performance was lower than the healthy group. This indicates an inhibition network within the primary motor cortex that is important to motor learning (Mooney et al., 2020). These studies are examples of the many studies that underlines the implication of inhibition in motor recovery (Coxon et al., 2007; Dora et al., 2021; Ridding et al., 1995; Schlaghecken & Eimer, 2002; Shadmehr & Holcomb, 1999; Toro et al., 2000).

From the present study, it is clear that we can repeat the call by Nys et al. (2005) that all individuals with stroke should undergo routine cognitive assessment. There are two solutions to facilitate this objective. Firstly, it could be that all individuals with stroke receive a rapid cognitive screening test, such as the recent test developed by Demeyere et al. (2015). The Oxford Cognitive screen is a valid and usable short cognitive screening tool that has been specifically developed for the post-stroke population. It is an inclusive tool that covers the different cognitive domains usually impaired after a stroke (e.g., attention, language, memory), can be completed in 15–20 min, and is available in different languages (Demeyere et al., 2021; Demeyere et al., 2015; Demeyere et al., 2019). Individuals showing cognitive impairments demonstrated by these screening tools should receive additional cognitive assessment, and furthermore, the rehabilitation programme should include cognitive neurorehabilitation. A second approach would be to develop motor assessments / rehabilitation that co-evaluate / co-rehabilitate cognition. The REASmash serious game, presented in this paper is a cognitive test involving direct motor responses to the target stimuli, and could be adapted to measure upper limb motor function as well as cognitive inhibition as demonstrated in the present paper. Alternatively, tests such as the box and block test could be adapted to contain non-response distractors that compete for attention with target stimuli, requiring inhibition. These combined tests could be presented to patients to offer multiple motor and cognitive assessments within the same test. Furthermore, serious game assessments could be modified to create rehabilitation serious games that exercise motor and cognitive responses (Dehem et al., 2019; Kaiser et al., 2022; Montedoro et al., 2018).

In conclusion, in the present paper we show that post-stroke individuals with hemiparesis show cognitive inhibition impairment in an IVR serious game. These data add to the existing literature showing an association between cognitive and motor functions, as well as highlighting the importance of cognitive assessment in stroke individuals with hemiparesis. Currently, cognitive impairments are not routinely assessed, and these unevaluated cognitive impairments may have severe consequences on overall recovery success. Therefore, we call for healthcare professionals and decision-makers to implement interventions embedding cognitive screening and neuropsychological evaluations for all stroke patients, and we also call for the researchers to be mindful of the integrative relation between cognitive and motor systems when developing new assessment tools for post-stroke individuals.

**Declarations**

**Ethics approval and consent to participate:**

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The Saint-Luc-UCLouvain-Hospital-Faculty Ethics Committee approved the study (reference number: 2015/10FEV/053). All participants provided written informed consent before enrolment.
Consent for publication:
Not applicable

Availability of data and materials:
The data that support the findings of this study are openly available in the open data archive of University of Louvain. (URL and Reference Number will be provided after article acceptance).

Competing interests:
The authors declare no potential conflicts of interest linked to the research, authorship and/or publication of this article.

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Authors’ contributions:
The authors confirm their contribution to the paper as follows: study conception and design: K.A. and M.G.E., data collection: K.A.; analysis and interpretation of results: K.A. and M.G.E.; drafted the article: K.A.; manuscript edition and writing participation: M.G.E., T.L., G.E., G.S.. All authors provided critical feedback and helped shape the research, analysis and manuscript.

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References


Figures
Figure 1

(a) The grid of 24 molehills, with 6 columns and 4 rows; (b) The target was a mole wearing a red miner’s helmet. In the high target-distractors saliency condition, the distractor moles wore blue miner’s helmets and blue helmets with horns. In the low target-distractors saliency condition, the distractor moles wore red helmets with horns and blue helmets with horns. In the two examples, the target is shown with 17 distractors: 3 distractors in each column.
Figure 2

Violin plots with boxplots illustrating high and low target-distractors saliency conditions with 11, 17, and 23 distractors and SI:HP and CI groups for (a) mean response time (milliseconds), (b) mean velocity (m/s), and (c) coefficient of variation of speed (%).
Figure 3

Violin plots with boxplots illustrating mean response time (milliseconds) to high target-distractors saliency (low inhibition demands) and low target-distractors saliency conditions (high inhibition demands) in SI:HP and CI groups. The figure shows that the difference between high and low target-distractor saliency was greater for the SI:HP than CI.