Robot diagnosis test for egocentric and allocentric hemineglect

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Abstract

Objective: Patients with hemineglect fail to respond to egocentric stimuli or allocentric parts of stimuli contralateral to the brain lesion. The clinical diagnosis of hemineglect mainly involves evaluation of the egocentric form, while less sensitive standardized tests exist for other forms. Our global aim is to develop an innovative integrative robot measure, the MonAmour test, combining the assessment of egocentric, allocentric and motor hemineglect. Here, we present the egocentric and allocentric evaluations. **Methods**: Thirty-five first stroke patients (25 hemineglect) and 56 age-matched healthy controls were assessed on the index test (MonAmour) and on three reference standard tests (Bells test, Apples test and Neglect subtest of the Test for Attentional Performance). Based on controls' performance, normative data were created. Validity was evaluated between the MonAmour and the reference standard tests through correlations and test sensitivity/specificity. Reliability of the MonAmour was measured with test-retest and minimal detectable change. **Results**: Results demonstrated moderate to strong correlations between the MonAmour and the reference standard tests (r = .40 - .88, p< .001 – p= .016). The sensitivity was high (50% - 96%), with accurate diagnosis of patients with hemineglect, and reliability was excellent (Intraclass Correlation Coefficient = .79 - .95, p< .001). **Conclusions**: The MonAmour robot test is a valid, sensitive and reliable tool that can diagnose egocentric and allocentric hemineglect. Future studies will deepen the assessment and understanding of the different forms of hemineglect by testing the motor component of the test in order to use this accurate and integrative measure in daily clinical routine. **Registration**: ClinicalTrials.gov(NCT02543424).

Introduction

Each year, 15 million people worldwide are affected by stroke, frequently leading to severe impairments in cognitive and/or motor function (Mackay, Mensah, Mendis, & Kurt, 2004).

Cognitive disorders after stroke typically affect memory, language, orientation and attention (Jaillard, Naegele, Trabucco-Miguel, LeBas, & Hommel, 2009; Tatemichi et al., 1994). Among the attention impairments, hemineglect is described as a failure to report or respond to stimuli contralateral to a brain lesion, and occurs in approximately twenty-three percent of stroke cases (Appelros, Karlsson, Seiger, & Nydevik, 2002; Heilman, Watson, & Valenstein, 1993; Kamtchum Tatuene et al., 2016). Large stroke cohort research has demonstrated that hemineglect is more common following right than left brain damage (Ringman, Saver, Woolson, Clarke, & Adams, 2004).

Hemineglect is a heterogeneous syndrome that affects different modalities, frames of reference and portions of the space (Rode & Pisella, 2011). Hemineglect can affect the sensory, motor or representational modalities. Sensory hemineglect is defined as an inability to perceive contralesional visual, auditory or tactile stimuli (Plummer, Morris, & Dunai, 2003), whereas motor hemineglect is described as an underuse of the contralesional limb in bimanual tasks (e.g., opening a bottle) despite normal strength, reflexes and sensitivity (Laplane & Degos, 1983; Sampanis & Riddoch, 2013; Siekierka-Kleiser, Kleiser, Wohlschläger, Freund, & Seitz, 2006). Motor hemineglect can also refer to a failure to execute a movement (e.g., showing delayed reaction time, slowness in the movement speed) towards the contralesional hemifield (using the ipsilesional limb) (Heilman, Bowers, Coslett, Whelan, & Watson, 1985; Mattingley, Bradshaw, & Phillips, 1992). Representational hemineglect is the failure to report contralesional internally generated spatial scenes (Bisiach & Luzzatti, 1978; Kerkhoff, 2001). Hemineglect can also depend on reference frames. Patients that experience egocentric hemineglect fail to respond to contralesional stimuli from a body-centered viewpoint, whereas patients that manifest allocentric hemineglect fail to respond to the contralesional side of stimuli irrespective to their viewpoint (Rorden et al., 2012). Patients who fail to explore the contralesional part of their body when grooming or dressing are said to be affected by personal hemineglect. Spatial peripersonal hemineglect refers to a failure to respond to contralesional stimuli within reach. This form differs from spatial extrapersonal hemineglect (i.e., the space beyond arm's reach, explored through oculomotor movements; Plummer et al., 2003). Dissociations between the different forms of hemineglect have been reported in the literature, suggesting that the different forms may be independent deficits (Marsh & Hillis, 2008; Rorden et al., 2012).

Different models have been provided to explain hemineglect. These can be distinguished according to the nature of the hemineglect. For attentional hemineglect, Heilman and colleagues (1993) suggests a dominance of the right hemisphere that orients attention to both sides of space, whereas the left hemisphere orients attention primarily to the right side of space. After a left hemispheric lesion, attention can still be orientated to the right hemispace thanks to the right hemisphere. However, a right hemispheric lesion causes reduced attention to the left hemispace, explaining the high prevalence of patients exhibiting left hemineglect. Kinsbourne (1993) hypothesizes a mutual inhibition of hemispheres, with a dominance of the left one. Lesions to the right hemisphere explain the prevalence of left hemineglect due to the hyper-attention towards the right hemispace. For representational hemineglect, Bisiach and Luzzatti (1978) suggest that the mental representation of space is disrupted by a lesion, causing an enlargement of space representation ipsilateral to the lesion. The model of Rizzolatti, Fadiga, Fogassi, and Gallese (1997) combines attentional and representational models, claiming that action planning defines space representation, which will in turn influence attention. Lesions to premotor structures lead to hemineglect in different portions of space. Nowadays, these and other interpretative hypotheses remain debated in the literature, and no single model explains the complexity of hemineglect, perhaps supporting the assumption that hemineglect may not be a unitary condition (Ting et al., 2011).

The heterogeneity of the syndrome makes diagnosis challenging (Grattan & Woodbury, 2017). One-third of hemineglect patients still show symptoms one year after stroke, creating difficulties in daily life activities (Karnath, Rennig, Johannsen, & Rorden, 2010). Therefore, there is a need to better assess the different forms of hemineglect in order to better define the conditions, and to increase the patient's quality of life using better targeted treatments. Hemineglect is typically assessed with several paper and pencil clinical measures. The most frequently used tests are the cancellation tests (e.g., letters, lines, stars and bells cancellation tests), principally because they are easy to administer and allow for a quantitative assessment of egocentric peripersonal hemineglect (Azouvi, Samuel, & Louis-Dreyfus, 2000; Bickerton, Samson, Williamson, & Humphreys, 2011; Bowen, McKenna, & Tallis, 1999; Halligan, Cockburn, & Wilson, 1991). Line bisection tests (Schenkenberg, Bradford, & Ajax, 1980) and figure copying tests such as the Clock, the Daisy or the Ogden scene drawings are also commonly integrated in the evaluation of hemineglect (Bailey, Riddoch, & Crome, 2000; Ogden, 1985). The Apples cancellation, line bisection and figure copying tests allow simultaneous assessment of egocentric and allocentric peripersonal hemineglect. However, the figure copying tests require some subjective interpretation for evaluation, whereas cancellation and line bisection tests are accurate and require no subjectivity (Azouvi et al., 2002; Bailey et al., 2000).

Several researchers have suggested that paper and pencil tasks used for the diagnosis of hemineglect are not sensitive enough to show slight impairments (Bonato, 2012; Bonato & Cutini, 2016; Buxbaum, Dawson, & Linsley, 2012). The development of computerized tests adds crucial value to paper and pencil tests, enhancing sensitivity through stimuli randomization and more precise measures (Erez, Katz, Ring, & Soroker, 2009; Zimmermann & Fimm, 2002). These developments increasingly involve new technologies such as Virtual Reality (VR). Fordell, Bodin, Bucht, and Malm (2011) developed VR-DiSTRO which transposes four paper and pencil tests in a virtual environment (lines bisection, stars cancellation, baking tray test and a visual extinction test). Their aim was to record more information such as start point, end point and scanning patterns. Similarly, another study demonstrated on two hemineglect single cases the usability of a head-mounted display for line cancellation tests (Tanaka, Ifukube, Sugihara, & Izumi, 2010). Ecological tests have also been developed. In Kim and colleagues (2010), patients cross a street and their head's deviation angle and reaction time are measured. In Buxbaum and colleagues (2012), patients walk along a track and report animal statues and the colour of trees, while avoiding collisions with dynamic distractor objects (i.e., Virtual Reality Lateralized Attention Test; VRLAT).

Unlike perceptual forms of hemineglect, diagnosis of motor hemineglect is rare. Although several experimental studies have presented tasks that assess different motor forms (Bartolomeo, D'Erme, Perri, & Gainotti, 1998; Chiba, Yamaguchi, & Eto, 2005), to our knowledge, these tasks are not yet used and standardized for routine clinical practice. Nevertheless, current developments in robotic devices provide new opportunities to measure action in the clinic. In the last years, the use of robots has raised an increasing interest in post-stroke neurological rehabilitation, especially in upper limb rehabilitation of hemiparesis and hemiplegia (Gilliaux et al., 2014; Mehrholz, Pohl, Platz, Kugler, & Elsner, 2015), but also in hemineglect rehabilitation (Choi et al., 2016; Heins et al., 2017; Varalta et al., 2014). For example, robot-assisted exercises of the wrist, elbow and shoulder while playing a game demonstrated a reorientation of attention towards the contralesional hemifield (Choi et al., 2016). In this context, the robot is defined as a programmable mechanical tool that allows the movement of a patient's limb across a given range of motion (Bien & Stefanov, 2004). The robot interacts with the patient's actions, either in a 'passive mode' where the user is passive and the robot completes the upper limb movement, in an 'active mode' where the user is active and the robot does not provide any assistance (but measures performance), and in an 'activo-passive mode' where the robot moderates the provided assistance based on the user's needs. The use of a robot, in the active mode, for diagnosis of motor hemineglect could provide an accurate measure of motor responses. As far as we know, no study has investigated the use of robot interaction to diagnose motor hemineglect in clinical practice to this day.

Previous research has shown that the assessment of hemineglect through several tests gives a more sensitive diagnosis than any unique measure (Azouvi et al., 2002). Despite these recommendations, clinicians do not have the time to administer an entire quantitative battery and often make choices for the most appropriate tests (Petzold et al., 2014). Additionally, therapists spend time scoring the tests (Fordell et al., 2011). These demands can lead to a loss of diagnosis information to adequately guide the rehabilitation (Grattan & Woodbury, 2017).

Our global objective in this project was to develop and validate a unique clinical test for the combined quantitative evaluation of egocentric, allocentric and motor hemineglect using a robot. As in computerized and new technologies tests, the robot provides multiple sensitive measures (e.g., reaction time, movement kinematics), a reduced learning effect through the randomization of stimuli presentation, and a standard administration of the tests between therapists. Combined, these elements allow the therapist to save time by providing a sensitive simultaneous assessment of three forms of hemineglect, and an immediate scoring that is compared to norms.

In order to achieve this global objective, the present paper focused on the egocentric and allocentric parts of the test; the MonAmour. Firstly, we created norms for the MonAmour from healthy control participants. Secondly, we validated the test on stroke patients (with and without hemineglect) using correlations and sensitivity/specificity analyses against three reference standard tests, namely the Bells test (Gauthier, Dehaut, & Joanette, 1989), the Apples test (Bickerton et al., 2011) and the Neglect subtest from the Test for Attentional Performance (TAP) (Zimmermann & Fimm, 2002). Finally, we analyzed the reliability of the

MonAmour through the test-retest measure and Minimal Detectable Change (MDC). Future studies will integrate and investigate the motor component of the MonAmour test.

Methods

Participants

Brain-damaged patients were recruited using a consecutive sampling from the neuropsychological and physical medicine and rehabilitation departments of the Cliniques universitaires Saint-Luc and the Centre Hospitalier Neurologique William Lennox in Belgium from April 2015 to December 2017. Patients were selected according to the following criteria: (1) presence of an ischemic or hemorrhagic first stroke; (2) presence of hemineglect and/or hemiparesis clinical diagnosis documented through neurological evaluation reports and; (3) a good understanding of the task instructions. Exclusion criteria were the presence of other neurological conditions such as dementia or orthopedic illness that limits the function of the upper limb. We recruited patients without a hemineglect diagnosis (inclusion criteria n°2) in order to test whether our new measure detected patients with and without hemineglect.

In addition to the patients' group, neurologically healthy adult participants paired by mean patient age were recruited. Presence of any orthopaedic illness limiting the upper limb's function was an exclusion criterion. The Saint-Luc Biomedical Hospital-Faculty Ethics Committee approved the research protocol prior to any experimentation and all participants volunteered to participate to the study providing a written informed consent. The study was registered at ClinicalTrials.gov (NCT02543424).

Materials

Apparatus. The REAplan® robot (Axinesis) (Figure 1) was used for the development of the MonAmour hemineglect test. The REAplan ® is a planar end-effector robot with position and force sensors allowing for precise action measures in the horizontal plane. This horizontal plane had dimensions of 93 x 52 cm. The robot has a visual interface for the patient (1920 x 1080 pixels), and a separate monitor for the therapist. The robot has already been used for the assessment and treatment of upper limb motor impairments carrying it on the horizontal plane (Gilliaux et al., 2014). In the context of the present study, the end-effector of the robot remained in a fixed position, with only the force sensors triggered to record reaction times when pushing or pulling the end-effector.

Index test. The MonAmour test (Figure 2) (created by Montedoro., V and Alsamour., M) consisted of a target search task requiring participants to find a gray colored musical conductor (the target) randomly presented among black colored musical instruments of four different types (the distractors). The different colors of the target and distractors (70 x 70 pixels) were defined after a pilot study to optimize the difficulty of the task (all stimuli in the same color made the test too difficult even for control participants, therefore the grayness was moderated to make the test possible but still challenging). The targets could be complete (full musical conductor) or incomplete (musical conductor missing part of the left or right arm) measuring egocentric and allocentric forms of hemineglect. When participants perceived a complete target, they were instructed to make a push response using the end-effector of the REAplan® robot towards the conductor's baton, and when the target was incomplete, they were instructed to make a pull response, towards the conductor's musical stand. Catch trials, where no target was presented, were included in order to verify that the participants understood correctly the instructions and to measure impulsive responses. For the catch trials, participants were instructed to make no response on the end-effector.

As in the three standardized tests administered in the present study (see description below), we used a high attentional load display in order to detect hemineglect (Azouvi et al., 2002; Gauthier et al., 1989; Kaplan et al., 1991). For each trial, a single target and 119 distractors were organized using an invisible grid composed of five columns and six rows (30 cells), with a balance of stimuli across the left, right, upper and lower spaces (in accordance to standardized tests such as the Bells and Apples tests). The target was always presented in the center of one grid cell, with three randomly presented distractor stimuli. In the remaining 29 cells, four distractor stimuli were randomly placed. The test was composed of 100 trials, with 30 complete target trials, 30 incomplete left target trials, 30 trials incomplete right target trials and 10 catch trials (defined in accordance to the proportion of target-distractors in the Apples test). Participants had a maximum of 7000 ms to make a response. If the participants made no response, the trial ended and the next trial initiated. Each trial was separated by a central musical note acting as a fixation cross (presented for 1500 ms) in order to standardize the starting point of the space exploration across participants. Breaks were possible at any time during the test. Before beginning the MonAmour test, standardized instructions and ten practice trials were given to the participants. During the practice trials, the different types of target and catch trials were presented to the participants in the same proportion as in the main test, but the targets were placed near the centre of the screen facilitating detection and allowing patients with hemineglect to understand the test correctly.

The MonAmour test provided the possibility to assess overall performance through the percentage of total omissions (i.e., where the participant failed to respond within 7000 ms to targets, independent of their position in the space) and total mean reaction time (i.e., mean reaction time of correct responses, independent of target position in the space). To define egocentric hemineglect in the MonAmour test, two variables were calculated. Firstly, the percentage of omissions asymmetry corresponded to the difference between contralesional percentage of omissions (i.e., where the participant failed to respond within the time limit to targets presented in the two contralesional columns) and ipsilesional percentage of omissions (i.e., where the participant failed to respond within the time limit to targets presented in the two ipsilesional columns). Secondly, mean reaction time asymmetry referred to the difference between contralesional and ipsilesional mean reaction time for correct responses. For these two first measures, positive values indicated reduced performance in the contralesional compared to ipsilesional space, whereas negative values indicated reduced performance in the ipsilesional compared to contralesional space. Allocentric hemineglect was evaluated through false positive responses, where an incomplete target is responded to as if it was a complete target (i.e., where the participant made a push response to the musical conductor missing part of the contralesional or ipsilesional arm). To establish the presence of allocentric hemineglect, the percentage of false positive responses asymmetry was calculated (i.e., the difference between false positive responses on contralesional incomplete targets vs. ipsilesional incomplete targets). Positive values indicated that allocentric contralesional parts of stimuli were responded to as full targets, while negative values indicated allocentric ipsilesional parts of stimuli were responded to as full targets.

Reference standard tests. Three standardized hemineglect diagnosis tests were administered to the patients in order to validate the MonAmour test. The Bells test (Gauthier et al., 1989) was chosen because it has proven over the years to be highly sensitive to detect hemineglect (Basagni et al., 2017; Oliveira de CR, Luara de FC, Karina, & Rochele, 2016; Vanier et al., 1990). The Apples test was chosen due to its ability to diagnose allocentric hemineglect (Basagni et al., 2017; Bickerton et al., 2011). We included the computerized Neglect subtest of the TAP as it allows assessment of hemineglect through both omissions and mean reaction time measures (matching the MonAmour test) (Zimmermann & Fimm, 2002).

The Bells cancellation test is an egocentric visual hemineglect test that requires patients to circle 35 bell target stimuli amongst 280 distractor stimuli evenly distributed on a sheet of paper (within an invisible grid of seven columns) placed in front of the patient. The percentage of total omissions (independently of the space) and the percentage of omissions asymmetry between contralesional and ipsilesional hemispace (i.e., difference of omissions between the three contralesional and three ipsilesional columns depending on the patient's lesion side) were calculated.

The Apples cancellation measures both egocentric and allocentric hemineglect. Patients were asked to cross out complete apples (50) and ignore incomplete apples (50 having a right opening and 50 having a left opening). Full and incomplete apples were equally distributed across an invisible grid of five columns and two rows. The recorded variables were the percentage of total omissions (independently of the space), the percentage of omissions asymmetry between contralesional and ipsilesional hemispace (i.e., difference of omissions between the two contralesional and two ipsilesional columns depending on the patient's lesion side) and the percentage of false positives asymmetry (i.e., the difference between response selected apples with a contralesional and ipsilesional opening).

The Neglect subtest is a computerized task where patients detect a blinking increasing number (target) as soon as possible among static numbers (distractors). Over the full task, 44 single targets are presented equally and randomly across an invisible 4 square grid (2 columns and 2 rows), with the targets appearing at variable time intervals. To control for hemianopia, patients could move their eyes during the task. The percentage of total omissions, the total mean reaction time for correct responses, the percentage of omissions asymmetry between the contralesional and ipsilesional hemifield, and the mean reaction time asymmetry for correct responses were analyzed.

Procedure

For the patients, the testing was divided into two sessions (30-45 minutes) separated by an interval of 2-5 days. During the first session, participants performed the MonAmour test and the three standardized tests. The aim of this first session was to validate the MonAmour test against the standardized tests and, establish sensitivity and specificity. The second session involved doing the MonAmour test a second time in order to measure reliability and calculate the minimal detectable change. The ipsilesional hand was used for all the tests. For the healthy controls, the testing consisted of a single session (30 min) where they were asked to do the MonAmour tests once with their dominant hand in order to create norms.

For the MonAmour test, participants were sat comfortably in a chair without wheels, centered in front of the participant's monitor of the REAplan® robot. Participants were sat at the edge of the robot's horizontal plane, approximately 52 cm from the monitor. The handle of the robot was centered at the edge of the horizontal plane. The height of the horizontal plane of the robot was adjusted to correspond to the navel position of the participant (using an automatized height-adjusted table). The feet of the participants touched the ground. For security reasons, patients on wheelchair were not moved from their chair. For the standardized tests, participants remained at the same location, and the end-effector of the robot was removed so that the horizontal plane of the robot became a table. The tests were either administrated in a laboratory at the Faculty of psychology at the Université catholique de Louvain or in one of the two hospitals were the patients were recruited.

Data Analyses

Statistical analyses were performed using SPSS software (IBM, SPSS statistics 25). The main objectives of the analyses were to provide norms, criterion validity and reliability.

Norms (95% confidence intervals) for the MonAmour test were created from the performances of the healthy control participants to detect patient's impairments (> $\bar{X}$+ 1.96*standard deviation; *SD*). For overall performance diagnosis, patients had to show a deficit either on percentage of total omissions or on total mean reaction time. To be diagnosed as having egocentric hemineglect, patients had to be impaired either on percentage of omissions asymmetry or on mean reaction time asymmetry. To be diagnosed with allocentric hemineglect, patients had to be impaired on false positive asymmetry.

Criterion validity consisted in verifying if the results of the MonAmour test were associated to the results of the standardized tests (Mokkink et al., 2012). This was investigated in the patient group using correlation coefficient analyses between the MonAmour test and each of the standardized tests. Following Cohen (1988), correlations can be rated as weak ($0.1 \leq r < 0.3$), moderate ($0.3 \leq r < 0.5$) or strong ($r \geq 0.5$). The validity of the MonAmour was also assessed calculating sensitivity (ability of the test to detect people with hemineglect; $\frac{True\ positive}{True\ positive + False\ negative}$) and specificity (ability of the test to detect people without hemineglect; $\frac{True\ negative}{False\ positive + True\ negative}$) using respective norms of the tests (Greenhalgh, 1997). Regarding overall performance, patients were classified according to whether they showed an impairment on the MonAmour test and on at least one of the three standardized tests (comparison to their respective norms for the percentage of total omissions and the total mean reaction time). Regarding egocentric hemineglect, patients were characterized according to whether they showed hemineglect on the medical clinical diagnosis and on the MonAmour test (comparison to our norms for percentage of omissions asymmetry and mean reaction time asymmetry). For egocentric hemineglect, patients were also categorized according to whether they were impaired on the MonAmour and on at least one of the three standardized tests of hemineglect (comparison to their respective norms for percentage of omissions asymmetry and mean reaction time asymmetry). Concerning allocentric hemineglect, patients were diagnosed according to whether they presented allocentric hemineglect on the MonAmour and on the Apples test (comparison to their respective norms for the percentage of false positives asymmetry).

Reliability analyses were run on a subgroup of 23 patients who were available to perform the task twice. An Intraclass Correlation Coefficient (ICC) between the two repeated measures of the MonAmour from the same person were performed (Koo & Li, 2016; Shrout & Fleiss, 1979). The ICC based on mean rating and absolute agreement parameters were calculated using a two-way mixed model. Reliability was rated as poor (ICC $\leq$ 0.40), moderate (0.40 $<$ ICC $<$ 0.75), or excellent (ICC $\geq$ 0.75) (Andresen, 2000). For future use of the MonAmour in the context of assessing patients' performance improvement (e.g. pre- and post-treatment measures or spontaneous recovery), the MDC was calculated. The MDC refers to the minimal change needed over two repeated measures to show an actual significant improvement in the patient's performance that cannot be attributed to a measurement error. For example, if the MDC of the percentage of omissions asymmetry was 9%, the patient had to have at least a difference of 9.1% between the first and second MonAmour test administration to demonstrate an improvement of the patient's performance. The MDC was calculated using a two-sided 95% confidence level ($MDC_{95} = \text{Standard Error of Measurement } (SEM) * 1.96 * \sqrt{2}$; the SEM = $SD * \sqrt{1 - ICC}$ where *SD* corresponded to the standard deviation of all observations in the test-retest) (Chuang et al., 2015; Kovacs et al., 2008; Wagner, Rhodes, & Patten, 2008).

Results

Thirty-five brain-damaged patients (11 females) were included in the study. According to the clinical medical report, 23 patients had a right hemisphere lesion and 25 were diagnosed with egocentric hemineglect. All patients except one were right handed. All patients were between 41 and 85 years old [mean age (*SD*) = 62.63 (11.89)] and between 1 and 54 months post-onset [mean post-onset (*SD*) = 11.17 (12.30)] (see Table 1 for precise details). Fifty-six healthy control participants were tested (38 females and seven left handed; aged between 50 and 79 years, mean age (*SD*) = 62.6 (8.4)). Healthy controls and patients were paired by mean age (t (53.46) = .46, p= .64).

Normative Data

The normative data were computed from the healthy participants' group (Figure 3). Note that healthy participants did not omit any targets, meaning that a single omission in patients was considered as an impairment. The norms created on the percentage of total omissions and on the total mean reaction time detected 22 out of 35 patients as having impaired overall performance (Figure 3a and b), though all 22 patients were also diagnosed as having egocentric hemineglect. Twenty-seven out of 35 patients were diagnosed as presenting egocentric hemineglect either on omission asymmetry or on mean reaction time asymmetry (Figure 3c and d). Note that one patient showed an inverse profile showing an important ipsilateral impairment on the mean reaction time asymmetry, and to a lesser extent on the percentage of omissions asymmetry. This behavior was also noted on the performance at the Apples and Neglect tests indicating an overcompensation of lateralized deficit. Norms on false positive asymmetry responses detected 10/35 patients with allocentric hemineglect (where 8/27 of patients showed egocentric hemineglect and only 2/35 patients showed exclusive allocentric hemineglect) (Figure 3e). The remaining 6/35 patients showed no evidence of hemineglect at the MonAmour.

Criterion Validity

Concerning the overall performance, percentage of total omissions on the MonAmour correlated strongly with the three standardized tests (Bells test: $r(33)= .88$, $p<.001$; Apples test: $r(33)= 0.78$, $p < .001$; Neglect subtest: $r(33)= .68$, $p < .001$). The total mean reaction time between the MonAmour and the Neglect subtest was also strongly correlated ($r(33) = .54$, $p < .001$). Compared to overall scores of the standardized tests, the MonAmour test was sensitive at 84% and specific at 54% (Table 2).

For egocentric hemineglect, moderate to strong correlations were found between the MonAmour and the standardized tests for the percentage of omissions asymmetry (Bells test: $r(33) = .70$, $p < .001$; Apples test: $r(33) = .69$, $p < .001$; Neglect Subtest: $r(33) = .40$; $p = .016$) and mean reaction time asymmetry (Neglect Subtest: $r(31) = .45$, $p = .008$; note that 2 patients made 100% omissions to contralesional targets meaning that there were no reaction time measures for these patients). Compared to the medical clinical diagnosis, results demonstrated that the egocentric component of the MonAmour test had a sensitivity of 96% and a specificity of 70%. With the standardized tests as reference, the MonAmour showed again a sensitivity of 96% and a slightly lower specificity of 58% (Table 2).

Regarding allocentric hemineglect, there was a strong correlation between the MonAmour test and the Apples test on the percentage of false positives asymmetry ($r(33) = .52$, $p < .001$). Comparing the patients diagnosed with allocentric hemineglect on the MonAmour and on the Apples test, results showed a sensitivity of 50% and specificity of 77% (Table 2).

Reliability

The test-retest ICC analyses of overall attention performance was excellent both for the percentage of total omissions (ICC = .95, p <.001) and total mean reaction time (ICC = .95, p<.001). The reliability of egocentric hemineglect showed excellent reliability for the percentage of omissions asymmetry (ICC = .94, p < .001), and the mean reaction time asymmetry (ICC = .79, p < .001). However, the reliability of allocentric hemineglect showed non-significant results for the percentage of false positives asymmetry (ICC = -0.13, p = .512).

The MDC showed that to demonstrate a pre- versus post- improvement of patients' performance with the MonAmour, a difference of at least 5% on percentage of total omissions, 370 ms on total mean reaction time, 13% on percentage of omissions asymmetry and 1202 ms on mean reaction time asymmetry is needed. The MDC of the percentage of false positives asymmetry could not be calculated as the ICC for this variable was not significant.

Discussion

In daily clinical routine, time constraints prevent clinicians from administering extensive and complete batteries of assessments, and instead, they are forced to select some tests, and miss the evaluation of some cognitive functions (Grattan & Woodbury, 2017; Petzold et al., 2014).

Moreover, literature has reported a lack of sensitivity of paper and pencil tests (Bonato, 2012; Buxbaum et al., 2012). These issues motivated the development of a new and innovative robot assessment, the MonAmour test developed on the REAplan® robot (though it should be noted that it could be implemented on other robots). As in recent VR assessments (e.g., Fordell et al., 2011; Tanaka et al., 2010), the MonAmour test was based on standardized tests (e.g. the Apples test). These innovations provide additional sensitive measures compared to paper and pencil tests (e.g., reaction time responses), allow for a standardized administration between clinicians (thereby reducing errors), and diminish learning effect (e.g., target position randomization). Specifically, the MonAmour measures movement kinematics, provides clinicians with immediate results compared to norms and allows for the combined evaluation of three different forms of hemineglect. In the present paper, the aim was to validate the egocentric and allocentric assessments of the MonAmour test.

Comparing our patients to the norms, we found evidence of patients having egocentric and allocentric forms of hemineglect, with patients showing egocentric and not allocentric hemineglect, and two patients showing allocentric and not egocentric hemineglect. This independence between forms of hemineglect replicates previous behavioral (Bickerton et al., 2011) and neuroimaging findings (Medina et al., 2009). The validation of the egocentric and allocentric components of the MonAmour was tested by comparing the results of the patients on the MonAmour test with three standardized assessments of hemineglect; the Bells test, the Apples test and the Neglect test from the TAP. Patients' performance for egocentric hemineglect at the MonAmour was highly correlated with patients' performance on the standardized tests for omissions asymmetry and mean reaction time asymmetry. The egocentric sensitivity of the MonAmour test was excellent, showing the capacity to include patient presenting hemineglect with greater sensitivity than some recently published tests such as the VRLAT (56% sensitivity; Buxbaum et al., 2012) and the VR-DiSTRO (33% sensitivity for the VR lines bisection test and 54% sensitivity for the VR stars cancellation test; Fordell et al., 2011). Specificity of the MonAmour was good at excluding patients without hemineglect when using the clinical diagnosis criteria as reference. However, specificity rate was lower (though still good) when using the standardized tests diagnosis. This may be explained by a practice effect on the standardized tests. For the MonAmour test, the diagnosis of hemineglect remained stable, possibly due to the use of randomized target and distractors positions, and because the MonAmour uses combined measures of omission and reaction measures making the test more precise. This is consistent with the finding that the MonAmour detected more patients with impairments than standardized tests (Table 2). Finally, test-retest reliability was excellent and minimal detectable change was established for future use of the test with the aim to assess patients' improvement (e.g. pre/post-treatment).

As well as showing validation of egocentric measures of hemineglect, the present results also demonstrated the validation of the allocentric part of the MonAmour with the allocentric measure of the Apples test (Bickerton et al., 2011). The correlations between both tests were strong. However, the reliability of the false positives asymmetry was non-significant. This null result can be partially explained by the low prevalence of allocentric relative to egocentric hemineglect (Bickerton et al., 2011). Further, we recruited patients based on the presence (or absence) of egocentric hemineglect, as allocentric hemineglect was not systematically tested in clinics where we recruited the patients. As a consequence, only a few of our patients showed allocentric hemineglect, often exhibiting mostly slight impairments (see Figure 3e for the severity of allocentric impairment in our sample). Results showed a weak sensitivity but a good specificity. Several arguments could explain this low sensitivity. Firstly, our sample contained only three patients showing severe allocentric hemineglect (with all three detected as impaired on both the MonAmour and Apples tests). Secondly, the low sensitivity might be explained by the definition of false positives that we used to calculate allocentric hemineglect in the MonAmour test. We defined false positive responses as an error on incomplete target trials where the participant pushed the end-effector as if the target was complete. However, false positive errors on complete target trials, where the participant pulled the end-effector as if the target was incomplete might also be considered as a measure of allocentric hemineglect. In this case, we could suggest that participants with allocentric hemineglect neglected the contralateral part of the complete target. This raises an interesting question about whether there may be different forms of allocentric hemineglect, or at least differences in the way in which allocentric hemineglect is evaluated and defined. Thirdly, there could be differences caused by the tasks. In the Apples test, participants have to detect the correct target (complete target). In the MonAmour, participants have to discriminate the targets (complete or incomplete) and make a choice-response (push or pull the handle). Since the discrimination takes more time than detection (Van der Lubbe, Vogel, & Postma, 2005), it could lead to a more conscious processing of the target, and to a different pattern of responses. Finally, we only compared the allocentric component of the MonAmour with the Apples test because it is the only clinically objective quantitative test for allocentric hemineglect. This raises two concerns. As recommended by Basagni and colleagues (2017) and Azouvi and colleagues (2002), one test is not enough to establish the true presence or absence of deficits. Moreover, the Apples test's allocentric sensitivity/specificity has never been established, therefore putting the present results into perspective.

In our evaluation, we considered asymmetric measures in order to reduce the chances that a clinician makes a false diagnosis of a patient who is equally impaired in both contralesional and ipsilesional space. However, this may cause us to fail to measure overall attentional impairment not related to hemineglect, especially as several studies have highlighted that non-lateralized deficits can occur in addition to hemineglect, and can even exacerbate it (Husain & Rorden, 2003). To solve this problem, we considered overall performance measures related to non-spatial impairments. Overall performance strongly correlated between the MonAmour and the standardized tests, with results showing high sensitivity and reliability. Overall performance demonstrated an impairment in 22 patients of our sample, in addition to their egocentric hemineglect deficit. Moreover, it showed that five patients had overall impairments without egocentric asymmetric deficit. This highlights the importance of combining asymmetric measures to overall performance measures for more depth in the assessment, and for a more adapted rehabilitation to the patients' deficits.

Within the scope of our study, our aim was to investigate asymmetric impairments in the contralesional hemispace independently of the patients' lesion side. For more specific results, detailed brain imaging could be used to refine the diagnosis of the patients especially since studies have shown that lesion side, site and size can impact the severity of hemineglect and the presence of additional non-lateralized deficits (Husain & Rorden, 2003). Similarly, as part of this study, hemianopia was not systematically assessed since participants were allowed to make eye and head movements in space exploration while performing the tests. In order to confirm any influence of hemianopia on patient's performance, the use of eye-tracker measures could be added to the testing (Tsirlin, Dupierrix, Chokron, Coquillart, & Ohlmann, 2009).

Future studies will include a larger sample of patients in order to confirm the validity of the egocentric and allocentric components of the MonAmour. Furthermore, we will deepen the assessment and understanding of the different forms of hemineglect. These investigations will consist of two related tracks. Firstly, in current clinical assessment of hemineglect, frequently, paper and pencil tests are completed with the ipsilesional hand. This is partially due to the definition that hemineglect should not be caused by motor deficits (Heilman, Valenstein, & Watson, 2000) such as hemiparesis that frequently co-exists with hemineglect (Jehkonen et al., 2000; Jehkonen, Laihosalo, & Kettunen, 2006). However, the definition of hemineglect would be better understood if both the non-hemiparetic and hemiparetic hands were included in the assessment. Future studies will therefore administer the MonAmour with both hands (if possible; i.e., in patients without hemiplegia), to investigate the common features of hemineglect across the two hands. Secondly, we will integrate the action component of the MonAmour test. Instead of pulling or pushing the end-effector of the robot to make a response, patients will be asked to reach to the target when it is complete, versus reach to the musical stand when it is incomplete. Importantly, the robot will measure different aspects of the action, including movement time, speed, smoothness, straightness and accuracy. As in the current version of the task, these measures will be analyzed online and the results will be compared to the norms giving instant results to the clinician. Administrating this action version of the MonAmour in addition to the original perception version of the MonAmour presented here will allow a thorough investigation of differences between perception and action in hemineglect, and allow the comparison of patients' performances in contrast to control hemiparesis patients (without hemineglect) and healthy participants. This will lead to a highly accurate assessment of different forms of hemineglect (acute to late post-stroke patients), improving the ability to plan a rehabilitation program tightly linked to the patients' performance and facilitating faster recovery.

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Tables

Table 1. Patients' demographic characteristics.

N°	Gender	Age	Hand-edness	Lesion	Months post-onset	Paresis	Egocentric hemineglect
1	M	65	R	Right ischemic occipital and thalamic stroke	13	Yes	No
2	F	51	R	Right ischemic superficial middle cerebral vein stroke	12	Yes	Yes
3	M	64	R	Left haemorrhagic deep thalamic stroke	17	Yes	No
4	M	71	R	Right ischemic superficial middle cerebral vein stroke	35	Yes	Yes
5	M	62	R	Left ischemic cortico-frontal stroke	3	Yes	No
6	M	66	R	Right haemorrhagic fronto-parieto-temporal stroke	2	Yes	Yes
7	M	80	R	Left haemorrhagic internal capsule and thalamic stroke	2	Yes	No
8	M	41	R	Right haemorrhagic intracerebral lentiform nucleus and corona radiata stroke	54	Yes	Yes
9	M	48	R	Left ischemic frontal stroke	2	Yes	Yes
10	M	50	R	Right ischemic middle cerebral vein parieto-temporo-occipital stroke	13	Yes	Yes
11	M	48	R	Left haemorrhagic thalamic stroke	12	Yes	Yes
12	F	70	R	Right haemorrhagic occipital and thalamic stroke	6	Yes	Yes
13	M	66	R	Left haemorrhagic parieto-occipital stroke	18	No	Yes
14	F	45	R	Right haemorrhagic intracerebral lentiform nucleus and internal capsule stroke	1	Yes	Yes
15	M	84	R	Right ischemic middle cerebral vein stroke	5	Yes	Yes
16	F	71	R	Left haemorrhagic thalamic and internal capsule stroke	22	Yes	No
17	M	60	R	Left haemorrhagic fronto-temporal and basal ganglia stroke	9	Yes	No
18	F	72	R	Right haemorrhagic intracerebral fronto-parietal stroke	2	Yes	Yes

19	M	72	R	Right ischemic middle cerebral vein stroke	48	Yes	Yes
20	M	58	R	Right haemorrhagic middle cerebral vein stroke	14	Yes	No
21	F	47	R	Right haemorrhagic lentiform nucleus stroke	11	Yes	Yes
22	F	51	R	Left haemorrhagic subarachnoid intracerebral stroke	8	Yes	Yes
23	M	62	R	Right ischemic middle cerebral vein stroke	18	No	Yes
24	F	56	R	Right haemorrhagic central fissure stroke	12	Yes	No
25	F	72	R	Right haemorrhagic intracerebral parietal stroke	3	Yes	Yes
26	M	62	R	Right haemorrhagic fronto-parietal stroke	5	Yes	Yes
27	M	82	R	Right ischemic middle cerebral vein stroke	3	Yes	Yes
28	M	85	L	Right ischemic middle cerebral vein stroke	4	No	Yes
29	M	58	R	Left haemorrhagic thalamic and internal capsule stroke	8	Yes	Yes
30	M	53	R	Right ischemic middle cerebral vein stroke	11	Yes	Yes
31	M	53	R	Left ischemic middle cerebral vein and internal capsule stroke	5	Yes	No
32	M	65	R	Left ischemic lacunar stroke	2	Yes	No
33	M	68	R	Right haemorrhagic thalamic stroke	4	Yes	Yes
34	F	52	R	Right ischemic middle cerebral vein stroke	6	Yes	Yes
35	F	82	R	Right ischemic middle cerebral vein stroke	1	Yes	Yes

Note: M= male; F= female; R= right; L= left; paresis and egocentric hemineglect was determined by clinical neurological evaluation.

Table 2. Patients diagnosed as impaired for the MonAmour and the standardized clinical diagnosis tests.

	MonAmour test	**Bells test**	**Apples test**	**Neglect test**
Egocentric hemineglect				
Percentage omissions asymmetry	21	10	11	15
Mean reaction time asymmetry	24	/	/	18
Allocentric hemineglect				
Percentage false positives asymmetry	10	/	8	/
Overall performance				
Percentage total omissions	22	9	13	13
Total mean reaction time	22	/	/	5

Note: / = not applicable.

Figure legends

Figure 1. The REAplan® end-effector robot (permission to use image allowed from Axinesis ; Copyright), with: (a) a handle for interaction that measures position and force, (b) a visual interface for the participant, and (c) a visual interface for the experimenter / clinician.

Figure 2. The MonAmour test, with: (1) the target search task with (a) the target musical conductor, (b) the four different type of distractor instruments, (c) the conductor's baton, (d) the conductor's musical stand; and (2) the three types of target (a) complete target, (b) left incomplete target, and (c) right incomplete target.

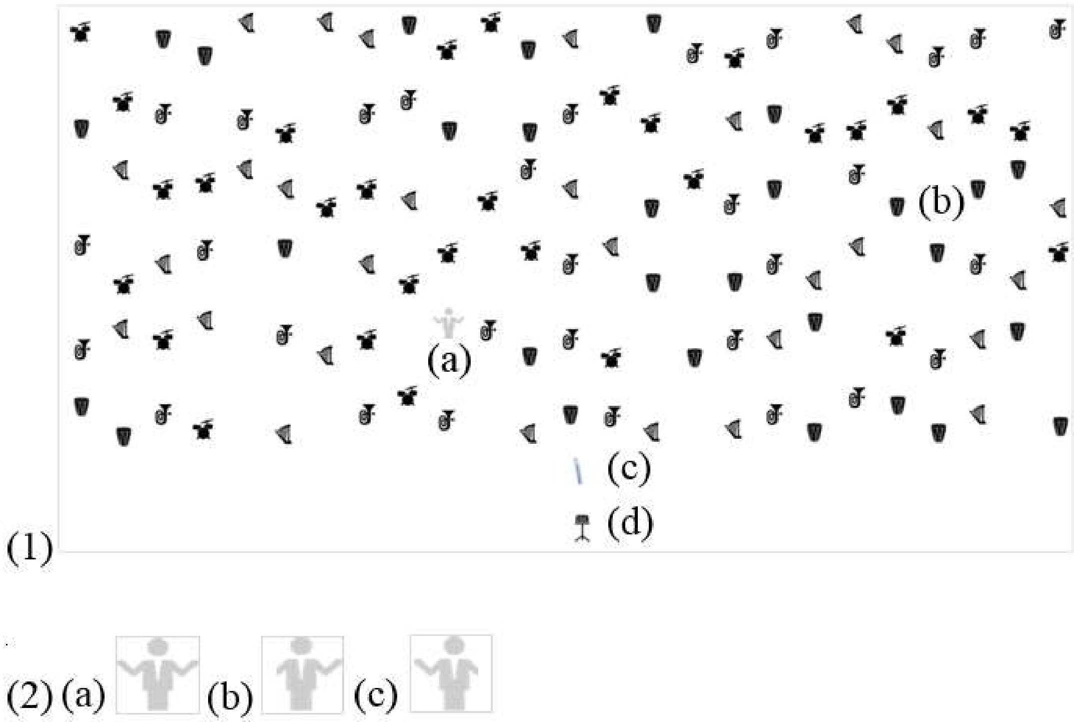

Figure 3. Individual egocentric hemineglect (determined by the clinical diagnosis; triangle) and hemiparesis without hemineglect (determined by the clinical diagnosis; square) patient responses to the MonAmour test relative to norms (mean full line, and 95% confidence interval dotted lines). The data points are organised by hemineglect severity respective to each measure at the MonAmour for: (a) percentage of total omissions, (b) total mean reaction time, (c) percentage of omissions asymmetry, (d) mean reaction time asymmetry, and (e) percentage of false positives asymmetry.