Assessment and monitoring of recovery of spatial neglect within a virtual environment

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ABSTRACT

Spatial neglect has proven to be a significant factor limiting the success of the rehabilitation process following stroke. Current tests for neglect however have several substantial drawbacks, which often lead to a misdiagnosis of less severe cases. Further, while asymmetries of performance have been reported in the past along independent spatial dimensions, current tests are mostly limited to the horizontal dimension and do not reflect the reality of a three-dimensional world. We have previously demonstrated the feasibility of virtual reality tools for detailed assessments of attentional deficits [1]. We now provide further evidence for the sensitivity of our Virtual Environment for Spatial Neglect Assessment (VESNA) application for assessment of neglect as well as for monitoring recovery of patients. Seven stroke patients with neglect, nine stroke patients without neglect and nine age-matched healthy controls were tested on a target-detection task. Subjects were exposed to a three-dimensional virtual scene and were instructed to press a response button when they detected a target appearing within the scene. Percent of correct detection and reaction time to initiate a button press were calculated. Our results indicated significant differences between neglect patients and control subjects. All neglect patients exhibited asymmetries of performance, where their mean reaction time and detection accuracy systematically varied across space. This asymmetry was not a harsh transition but instead showed a gradual reduction of attention across the space. Importantly, while these results indicated an obvious spatial neglect for all seven neglect patients, their performance on the standard paper-and-pencil tests, administered at the day of testing, was less conclusive. A follow-up study with two of the neglect patients (10 months following the initial testing) revealed an obvious recovery pattern, showing a reduction of the spatial bias over time. By contrast, the paper-and-pencil tests showed no obvious change. Thus, we demonstrated that our paradigm provided a quantitative and more sensitive assessment and monitoring of recovery of neglect. This might provide clinicians with a more precise description of a patient's deficit which will help direct training.

Keywords: Spatial neglect; spatial dimensions; virtual reality

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INTRODUCTION

Spatial neglect is a common and disabling deficit following unilateral brain damage, particularly following stroke. Neglect patients fail to respond, orient to, or report stimuli and events occurring on the contralesional side of space, even if primary sensory or motor areas remain intact [2]. Neglect has proven to be a significant factor limiting the success of the rehabilitation process following stroke [3]. It has been reported to have a negative impact on functional recovery, length of rehabilitation stay, and need for assistance after discharge [4].

Neglect is commonly assessed using batteries of paper-and-pencil tests, (e.g., the Behavioral Inattention Test (BIT), [5], a widely used battery of such tests). While these tests can be administered quickly and easily at the patient’s bedside, they have several substantial drawbacks. They hardly allow quantification of performance in different locations in space, they are mostly performed in peri-personal space and are limited to the horizontal (right-left) dimension, and they tend to lose sensitivity along the course of recovery due to their fixed and repetitive nature. Thus, they often lead to a misdiagnosis of less severe cases, e.g., [6].

Although neglect has been most commonly studied in the horizontal spatial dimension, recent studies have reported asymmetries of performance along independent spatial dimensions (horizontal, vertical and radial) [7]-[10]. The most common procedures used in the diagnosis of neglect in these studies however were line bisection and cancellation tests. In recent years, few studies have used virtual reality (VR) technology to study neglect [1], [11]-[13]. The use of VR enables easy relocation of objects in the three-dimensional space. Further, properties of objects can be changed in an instant with no setup and breakdown time.

The aim of the current study was to assess and quantify the visual deficits associated with neglect within a three-dimensional space. We hypothesized that the neglect population will show variations of reaction time and detection rate across space, and that our application would prove to be more sensitive for assessment as well as for tracking changes in the recovery of patients.

MATERIALS AND METHODS

Subjects

Three groups of subjects participated in this study - seven right-hemisphere stroke patients with spatial neglect, nine right-hemisphere stroke patients showing no signs for spatial neglect, and nine age-matched healthy adults. Patients from both groups showed no signs for left visual field deficits. Both the healthy subjects and stroke patients without neglect served as control subjects. Table 1 presents details for each group of subjects. All subjects were right-handed and had normal or corrected-to-normal vision. Subjects gave informed consent in accordance with the Institutional Review Board of Northwestern University.

Table 1 Personal and clinical details for the three groups of subjects

Group	Sex	Age (yr)	Lesion sites	Time since onset	Total BIT score
Neglect	3 males, 4 females	38-73	Parietal, temporal, frontal, basal	1 month - 5 yrs	60-142

			ganglia, thalamus		
Non-neglect	8 males, 1 female	48-73	Parietal, temporal, frontal, basal ganglia, thalamus	1-11 yrs	142-145
Healthy	5 males, 4 females	46-71	N/A	N/A	145-146

Apparatus and data collection

The VRROOM (Virtual Reality and Robotics Optical Operations Machine) system, developed in our laboratory, was used for this study. VRROOM utilizes a Personal Augmented Reality Immersive System (PARIS) display for rendering the virtual environment to subjects, and those images are superimposed over a large workspace [14], (Fig. 1a). The correct perspective and stereo projections for the view of the scene are computed using values for the current position and orientation of the head (6 DOF) supplied at 100 Hz by a tracking sensor (‘Flock of birds’, Ascension Technology) attached to the stereo shutter glasses worn by the subject (Crystal Eyes, StereoGraphics Inc.). The immersive virtual environment consisted of a 3D room-shape in which targets (generated as 3D virtual ball-shaped targets with a 1.5 cm radius) appeared at different locations and heights in space (Fig. 1b). Subjects sat in a dark room on a chair placed in front of the VRROOM system, holding a response button in their right (unimpaired) arm. A chin rest kept the head position constant.

(a) **(b)**

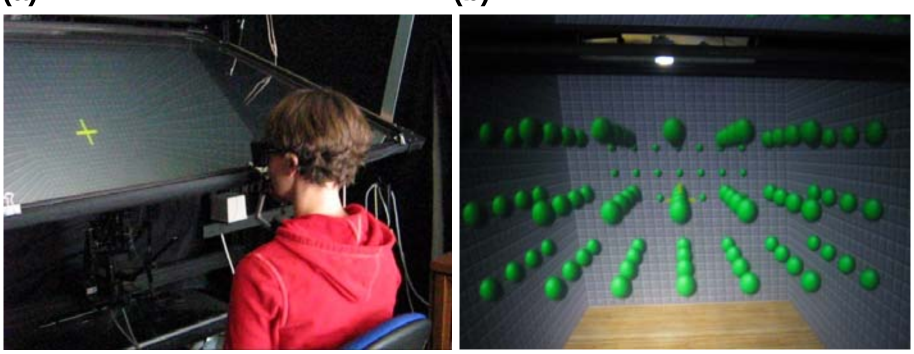

Fig. 1. (**a**) Screen shot of an individual performing in the VRROOM system. (**b**) Spatial arrangement of all possible virtual targets appearing within the 3D virtual environment.

Procedures

Prior to beginning of the testing, subjects completed six paper-and-pencil sub-tests of the conventional BIT. These sub-tests included line crossing, letter cancellation, star cancellation, figure copying, line bisection, and representational drawing. The total score of these six sub-tests is 146 with a cut-off of 129.

In the experiment there were 105 optional targets, distributed on a 7x5x3 grid (Fig. 1b). The targets were chosen such that they would appear on the right and left of the body midline. They also appeared above, below and at eye level, as well as in a close (peri-personal) and far (extra-personal) space relative to the subject’s body. On each trial only one target appeared randomly in space. Subjects were asked to indicate when they detected the target by pressing a response button as fast as they could. Each trial began with the appearance of a yellow fixation cross (positioned at the center of the 3D scene, aligned with the body midline) for a time interval ranging from 0.5 to 1 s. A visual target appeared simultaneously with the disappearance of the fixation cross, and remained visible until the button was pressed or 3 s elapsed. The next trial began after a 1.5 s interval, during which no virtual objects (fixation cross or target) appeared within the scene. To discourage anticipatory responses, occasional catch trials were included where no target appeared in the scene, and the subject was required to withhold button press. The experiment began with 10 practice trials and then was divided into blocks of trials, where 1-2 min rest period was given between blocks. In total, the experiment included 936 trials and took about 1 hour to complete.

Data analysis

Reaction time (RT) to initiate a button press and the success rate in detecting the visual virtual targets were calculated off-line. Fewer than 0.5% of trials were excluded from the analysis due to small RT (less than 180 ms) for both the patients and the healthy controls.

RESULTS

We found remarkable differences between neglect patients and control subjects (healthy and non-neglect stroke). While the performance of all neglect patients indicated an obvious visual neglect, their performance on the conventional BIT was less conclusive, indicating the presence of neglect in only three patients (based on total score and individual test cut-off).

Reaction time

The mean RT to initiate a button press for detecting targets, calculated for each of the 105 targets, is depicted in Fig. 2.

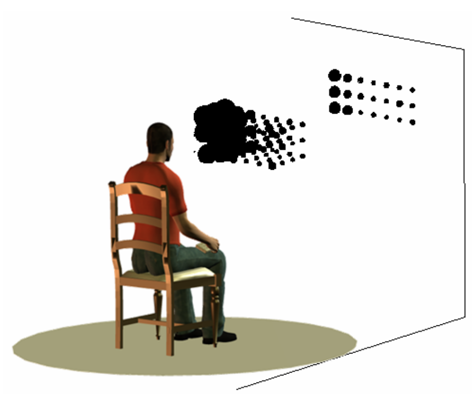

Fig. 2. Mean reaction times for a representative neglect patient. The sphere diameters are proportional to the mean RT value for each target location.

Figure 3a collapses results to single dimensions across the horizontal, radial and vertical spatial dimensions, (left, middle and right panels respectively). The mean RT value (± SD), across all target locations, was 541±65 ms for healthy controls and 627±96 ms for the control patients.

Whereas control patients exhibited significantly longer RT compared to healthy controls ($p<0.001$), both groups displayed no asymmetries in initiating a button press in all three spatial dimensions. By contrast, all neglect patients exhibited variations of RT across space. Moreover, their mean RT for all target positions was significantly higher compared to control subjects, (with average times exceeding 2SD of the control mean). One-way ANOVA revealed significantly longer RT for left than for right targets for all neglect patients ($F_{(6,98)}>7$, $p<0.0001$). A post hoc Bonferroni test confirmed that RT for each target on the left side was significantly different from that of all the other targets, indicating a gradual right-to-left increase in RT. In addition, significantly longer RT for near than for far targets was found for two patients ($F_{(4,100)}=3$, $p=0.02$; and $F_{(4,100)}=2.9$, $p=0.025$), where RT for the far target (on the extra-personal space) was significantly different from that of the nearest targets. Differences across the vertical spatial dimension, however, were significant for only one patient ($F_{(2,102)}=11$, $p<0.0001$). The total BIT scores for all neglect patient are shown in Fig. 3a, (colors of symbols and numbers are matched).

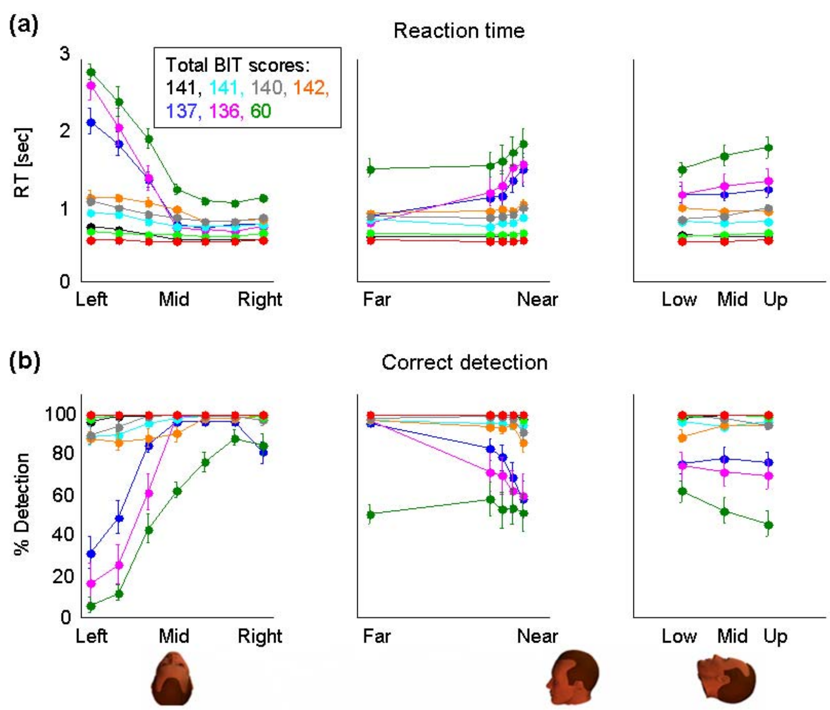

Fig. 3. (**a**) Mean reaction times in sec (±SE) and (**b**) percent of correct detection (±SE), collapsed across horizontal, radial and vertical spatial dimensions. Data presented for the seven neglect patients (black, cyan, gray, orange, blue, magenta and dark green), and mean values for nine control stroke patients (light green), and nine healthy controls (red).

Correct detection

While all subjects form both control groups were very good at detecting targets irrespective of target location, in all three spatial dimensions, neglect patients exhibited variations of percent of correct detection across space (Fig. 3b). As with the RT, their ability to detect targets correctly was significantly different from that of the control subjects. They displayed lower percent of correct detection, which exceeded 2SD of the control mean. In addition, one-way ANOVA revealed significantly smaller detection rate for left than for right targets ($F_{(6,98)}>3$, $p<0.01$; for 6 of the 7 neglect patients), showing the expected right-to-left gradient change with the two extreme left targets being significantly different from all other targets. Significantly smaller detection rate for near than for far targets was found for two patients as for the RT ($F_{(4,100)}= 5$, $p<0.001$; and $F_{(4,100)}= 3$, $p=0.02$), with the nearest targets being different from the rest of the targets. The difference in detection rate for the vertical spatial dimension approached significance level for only one patient ($F_{(2,102)}=2.7$, $p=0.07$).

Follow-up study

A follow-up study, conducted 10 months following the initial testing, with two patients from the neglect group (patients JC and PT) revealed a recovery pattern showing a reduction of the spatial bias over time. Both patients exhibited a horizontal (for RT: $F_{(6,98)}>29$, $p<0.0001$; for detection: $F_{(6,98)}>12$, $p<0.0001$) and radial (for RT: $F_{(4,100)}=2.4$, $p=0.05$; for detection: $F_{(4,100)}>2.8$, $p<0.03$) asymmetries, as in the initial testing. However, a two-tailed paired t-test revealed that these asymmetries of performance were significantly reduced in the follow-up test, (JC: $t_{104}=5.7$, $p<0.0001$ for RT, $t_{104}=7.9$, $p<0.0001$ for detection; PT: $t_{104}=2$, $p=0.05$ for RT, $t_{104}=4.6$, $p<0.0001$ for detection). By contrast, the total BIT score indicated no obvious change for both patients, (JC: 137, 138 and PT: 136, 138 for the initial and follow-up test respectively).

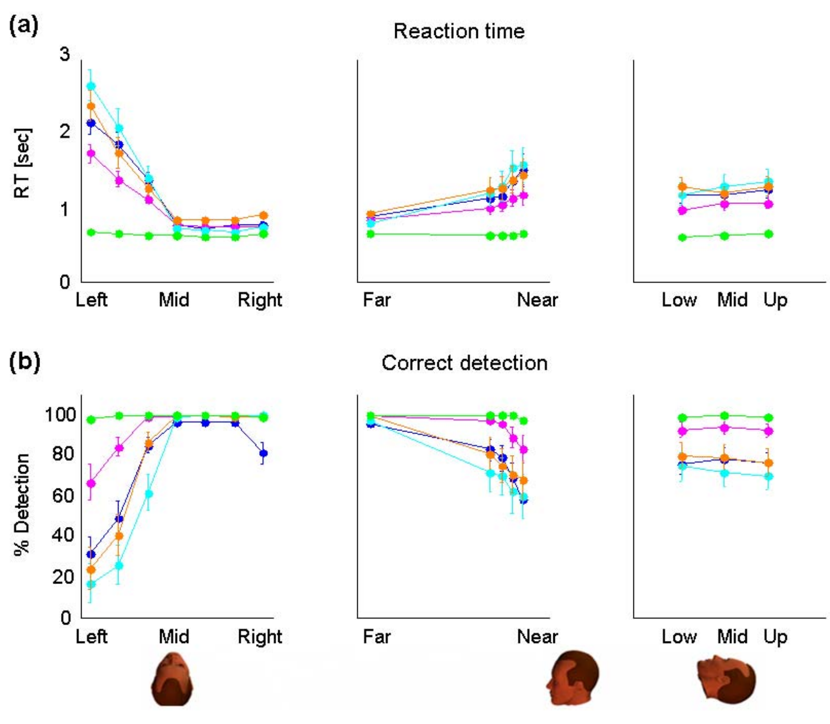

Fig. 4. (**a**) Mean reaction times in sec (±SE) and (**b**) percent of correct detection (±SE), collapsed across horizontal, radial and vertical spatial dimensions. Data presented for neglect patients JC (initial test: blue, follow-up: magenta) and PT (initial test: cyan, follow-up: orange), and mean values for nine control stroke patients (light green).

DISCUSSION

We have previously described our Virtual Environment for Spatial Neglect Assessment (VESNA) application and demonstrated its feasibility for detailed assessments of attentional deficits [1]. In the current study we provided further evidence for the sensitivity of the VESNA application for both assessment of neglect within a three-dimensional space and monitoring the recovery of patients.

Our results demonstrated an obvious difference in the performance of the neglect group compared to that of the two control groups. Furthermore, all seven patients in the neglect group exhibited asymmetries of performance in RT and percent of correct detection, indicating the presence of neglect. It has been shown that multiple paper-and-pencil tests are more sensitive than a single test [15]. Therefore, most clinicians and researchers use a combination of tests for assessment of neglect. As mentioned earlier, our subjects completed the six sub-tests that are included in the conventional BIT. Yet, in contrast with our findings, performance on the BIT indicated the presence of neglect in only three of the seven patients. Furthermore, it has been found that test sensitivity is improved by increasing the number of distracting stimuli [15]. Our approach however has proven to be sensitive even during a simple task with minimal distractions, (with only a target appearing with a simple background texture).

Findings from the follow-up test with two of our neglect patients (JC and PT) provided further evidence for the sensitivity of our application compared to the widely used BIT. It is interesting to mention that while both patients demonstrated a significant reduction of the spatial bias over time, exhibiting both decrease in RT and increase in detection rate, the observed reduction was more obvious for JC. This however might be due to the fact that JC was initially tested six months post stroke while PT was initially tested three years post stroke.

Despite the large number of intervention and training techniques that have been shown to ameliorate neglect, only a small number have been documented long-term beneficial effects (e.g., prism adaptation training) [15]. It has been suggested that many of the current shortcomings are due in part to limitations in assessment of neglect. Our paradigm overcomes serious shortcomings of paper-and-pencil tests by presenting targets throughout the three-dimensional volume.

Taken together, our approach provided a comprehensive quantitative assessment in three-dimensional space, but beyond that, it proved to be more precise and sensitive for diagnosis as well as for monitoring the recovery of patients. Results from this study would provide therapists and physicians with a more precise description of a patient's deficit in three-dimensional space which might help direct training, (for example, results would allow determining a specific sub-space within the three-dimensional space where a patient has the highest probability of missing a target).

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