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Coping with spatial attention in real space: A low-cost portable testing system for the investigation of visuo-spatial processing in the human brain

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ABSTRACT

While two-dimensional stimuli may be easily presented with any computer, an apparatus which allows a range of stimuli to be presented in three dimensions is not easily or cheaply available to researchers or clinicians. To fill this gap, we have developed the Realspace Testing System (RTS) which addresses the need for a flexible and multimodal stimulus presentation system capable of displaying stimuli in a three-dimensional space with a high degree of temporal accuracy. The RTS is able to control 26 channels of visual or audio stimuli, to send trigger pulses during each trial to external devices, such as a transcranial magnetic stimulator, and to record subject responses during the testing sessions. The RTS is flexible, portable and can be used in laboratory or clinical settings as required while being built at a low cost using off the shelf components. We have tested the RTS by performing an exploratory experiment on the role of right posterior parietal cortex in visuo-spatial processing in conjunction with online transcranial magnetic stimulation (TMS) and verified that the system can accurately present stimuli as needed while triggering a TMS pulse during each trial at the required time. The RTS could be appealing and useful to a range of researchers or clinicians who may choose to use it much as we have designed it, or use it in its current state as a starting point to customize their stimulus control systems in real space.

1. Introduction

Spatial processing has been a focus of a considerable amount of research using a variety of experimental paradigms in a range of animal species, in intact human participants and patient populations. One of the most popular ways to perform experiments on visual cognition has been through the use of computer-controlled displays and commercially available or custom-made stimulus presentation software such as Psychophysics Toolbox (Brainard, 1997; Pelli, 1997) which allows a researcher to easily control the display of visual stimuli in two dimensions on a flat computer screen. In response to a growing interest in studying visuo-spatial processing in a more naturalistic manner, we developed the Realspace Testing System (RTS). The RTS is designed to present visual or audio stimuli within a three-dimensional, egocentric frame of reference with high temporal accuracy. Given the range of cortical areas involved in spatial processing (Shaw and Shaw, 1977; Hughes and Zimba, 1985; Shulman et al., 1985 among others) and our own interest in transcranial magnetic stimulation (TMS), we designed the RTS to be able to interact with TMS devices, so that we could perform studies identifying causal relations between visually guided spatial processing as well as specific cortical sites and networks and examining the chronometry of such brain events.

Visual processing in general and visuo-spatial processing in particular have also been extensively studied in animal models and in patients who have developed hemispatial neglect or other spatial processing deficits (e.g., He et al., 2007) derived from focal brain lesions after parietal or occipital strokes. Therefore, an additional goal of ours in designing the RTS was to provide an alternative assessment technique for use with patients with such impairments. Assessing such patients with the RTS would allow for their spatial processing abilities to be evaluated while permitting a detailed analysis of their performance in spatial processing tasks as well as providing reaction times for their responses to individual targets, differences in which may indicate changes in their condition or incipient or incomplete signs of recovery. In parallel, we have performed research on animal models of hemispatial neglect using the predecessor to the RTS, which is a manually controlled real

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space stimulus presentation system designed for use with feline subjects (Valero-Cabre et al., 2005, 2006; Schweid et al., 2008). The design of the RTS took its initial inspiration from this manual system, although we have made many changes and improvements in the course of designing the RTS. Central among these was the use of computer hardware and software to control stimulus presentation, which also allowed us to make the RTS capable of accurately triggering external devices; a feature which we used in an experiment of the chronometry of visuo-spatial processing using online transcranial magnetic stimulation within each trial.

The Realspace Testing System we have developed represents a useful and accessible addition to the range of devices and procedures currently in use to evaluate spatial processing. It allows an experimenter to present a large number of stimuli anywhere in the visual field, rather than within the comparatively limited field of view afforded by a desktop display, while maintaining outstanding temporal control over stimulus presentation. We designed the RTS to use low-cost, off the shelf components; all of the parts required to build the system can be obtained from any well-stocked electronics supplier for two or three hundred dollars and the system can be built in a day or two by a researcher with modest soldering skills. As the barrier to entry is extremely low for such a research device, we believe that the RTS represents an affordable, easy to build and easy to use addition to the toolkit of any researcher. While we created the RTS in response to our own research needs, it was our goal to develop a system with broad utility and appeal to a range of researchers. With this in mind, in this paper, we provide the research community with a description of the RTS, the results of our tests of its capabilities and the results of a preliminary experiment we performed using the RTS which demonstrate its usefulness and reliability. We encourage other researchers to use our open designs for the RTS (provided in the Supplemental Materials) and to modify them as needed to suit their own experimental requirements.

2. Materials and methods

2.1. Overview

The design of the Realspace Testing System (RTS) grew out of a need for a flexible system to present multiple visual and auditory stimuli at different locations, including sites in the far periphery of the visual field. We required the presentation of these stimuli to be extremely accurate, and also needed the device to have the ability to record user input via a three-button response box and to trigger external devices. Finally, as the system was to be used in studies involving both neurologically intact subjects and neurologically compromised patients, it needed to be designed so that it could be brought to the patient. Such a requirement necessitated a design that was sufficiently durable to withstand the journey, physically compact yet easy and fast to set up, while remaining sufficiently flexible to accommodate a wide range of changes in the testing environment. The resulting design for the Realspace Testing System (RTS) is inexpensive and easy to build, versatile, flexible, portable and solidly constructed. The entire RTS can be packed inside a medium sized suitcase for transit and is durable enough to be quickly deployed and taken down. Using the RTS, stimuli can be presented at any desired elevation, azimuth or depth, constrained by the available cable length between the stimulus boxes and the RTS router.

A laptop computer controls the RTS, and through the RTS software (source code and executable provided in the Supplemental Materials) on the computer, the user is able to set all stimulus characteristics, including stimulus timing, sequencing and triggering. The computer is connected to the RTS router, which uses inexpensive integrated circuits to route signals from the computer to command up to 13 individual stimulus boxes. The system is built to accommodate 2 sets of 13 channels per stimulus modality, which in our design translate to 13 discrete visual stimuli, and 13 auditory stimuli. The ease of construction allows for the designer to control and build 26 discrete stimulus channels of virtually any modality (e.g., tactile stimulators, thermogenic stimulators, buzzers, etc.), limited only by the requirement that the stimulus of choice needs to run on a 3.5 V input. The router also provides two output trigger channels to integrate external devices (e.g., a transcranial magnetic stimulator) within the experimental design; in addition, the RTS router receives and logs input from a handheld subject-controlled response box.

2.2. Building the Realspace Testing System

The RTS is composed of four major components; the router, which is connected to a computer running the control software, the stimulus boxes and the response box (see Fig. 1A for an overall view of the RTS). The connections between the RTS router, the stimulus boxes and the response box are made using 50 Ω Bayonet Neill-Concelman connectors (BNC connectors) for ease of construction and long-term durability, and the router is connected to the computer via a parallel cable. While other connections are now more commonly used for peripheral devices, the DB-25 parallel port was chosen due to its low cost, minimal programming overhead and its presence on the great bulk of Windows-compatible computers. Other interfaces, such as the Universal Serial Bus (USB), require considerably more in the way of dedicated hardware and would complicate the design of the RTS router. While the parallel port is being phased out, it is likely that older systems with onboard parallel ports will be available for some time to come at minimal cost. All of the components used in the system can be easily soldered by hand. All components of the RTS are readily available from any large electronic parts vendor with the exception of the main circuit board for the router. The latter is a custom-designed printed circuit board (a fabrication-ready design is provided in the Supplemental Materials) that may be cheaply and quickly fabricated by a board production company at a low cost. Having a custom board fabricated for the router, rather than building a point-to-point board by hand allows us to have a minimum of wiring within the router while ensuring good connections between the router's integrated circuit components.

The router circuitry begins with the parallel connection from the computer; this provides us with eight addressable lines on the connector, which are used by the software to control the router's two independent stimulus circuits. The visual circuitry consists of a 4:16 demultiplexer; which receives a binary control signal from four pins in the parallel connector. Based on the control signal it receives, it will push one of its sixteen output lines to a ground (0 V) state. As this will not illuminate a visual stimulus, each of these outputs are then passed through a secondary multiplexer which is wired to pass voltage (3.5 V) out to one of the visual output lines. The audio circuitry is considerably less complicated; we used a dedicated 4:16 audio demultiplexer which receives the same four-channel control signal as the visual circuitry, as well as an audio input and a control line (which is used to keep the visual and audio circuits from being used simultaneously) and using these inputs, it routes an audio signal along one of its sixteen outputs to one of the audio output lines on the router.

2.3. Building the RTS router

The router was constructed using a medium sized metal project enclosure. Thirty-one holes were drilled in the enclosure for BNC connectors and a space was cut for a parallel port connector (see Fig. 1B). Twenty-six of the BNC holes are allocated for the stimulus

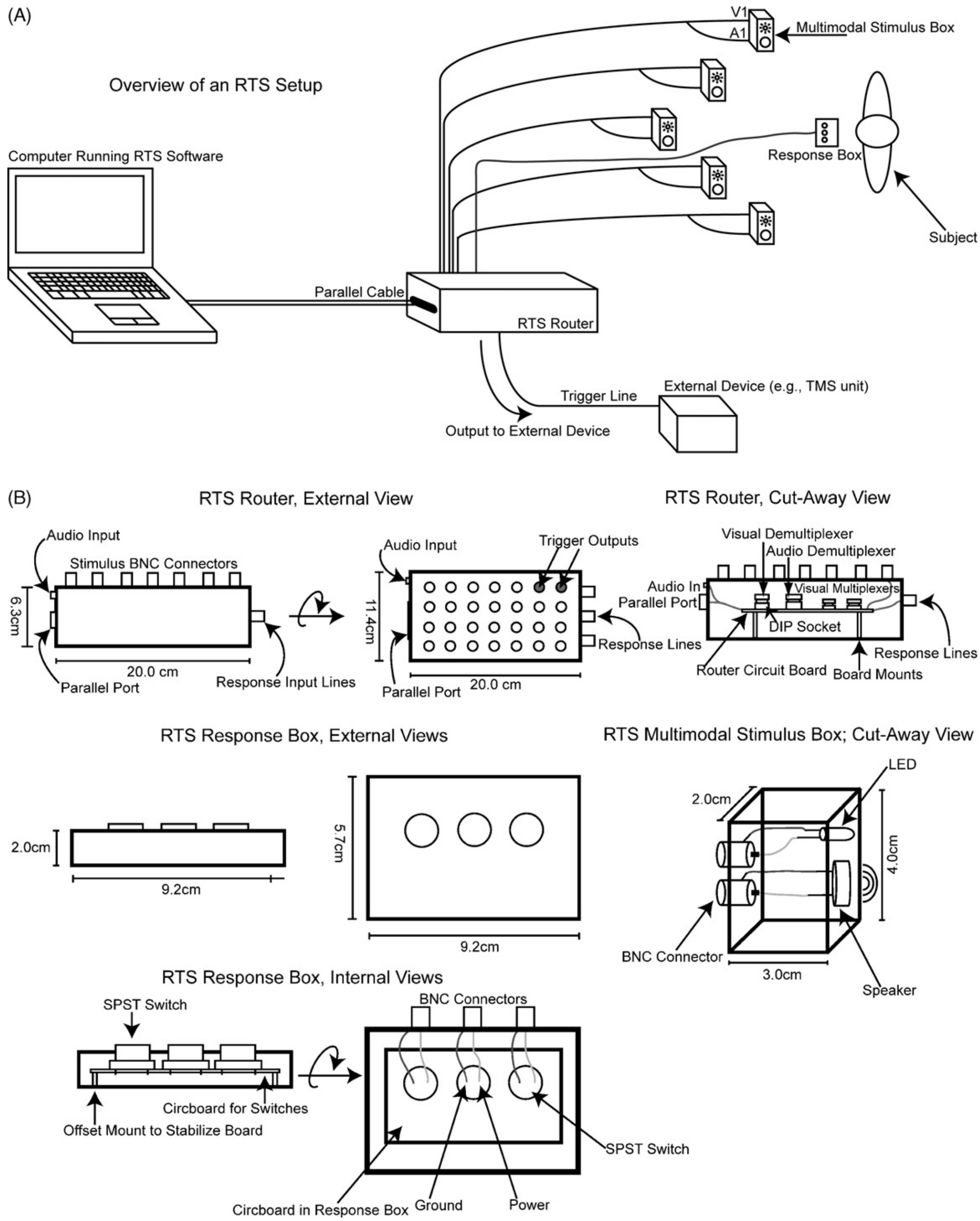

Fig. 1. (A) An illustration of a complete RTS setup, as configured for experimental use. The details of the RTS router, the multimodal stimulus boxes and the response box are shown in (B). Note that there are only five of a possible thirteen stimulus boxes shown in the figure for clarity reasons; the RTS can be run with one to thirteen stimulus boxes connected to the router. As the stimulus boxes in the illustration are multimodal, they have a single light emitting diode, for visual tasks, and a small speaker for audio tasks. The cabling for these two stimulus modalities is entirely independent, shown by the branching of the cable prior to its connection to the stimulus box. With the exception of the parallel cable, all connections shown in the illustration are made with BNC cables (e.g., between the router and the stimulus boxes, the response box and any external devices), but other types of connectors and cables could be used if necessary to reduce weight and cable rigidity. A complete RTS setup, as used to perform the online TMS experiment described in this manuscript, requires a $3\,m^2$ ($1.5\,m \times 2\,m$) space with sufficient power for the computer and the TMS unit. The stimulus boxes can be placed on stands or attached to any suitable surface due to their low weight and robust construction. However, the RTS may be deployed as dictated by the needs of the experiment; the overall view shown in the figure merely represents one of many possible configurations. Note that the figure is not to scale; detailed measurements are provided in (B) for all RTS components. (B) Illustrations of the major components of the Realspace Testing System. The RTS Router is shown in three different views; two external and one cut-away. The external views provide the size of the enclosure, the location of the parallel port, the audio input, the stimulus output lines, the trigger output lines and the response input lines. The circuit board, the DIP sockets, the integrated circuits (the visual demultiplexer and multiplexer chain as well as the audio demultiplexer) are labeled for clarity in the cut-away view of the router. In addition, the circuit board is shown hard-mounted to board mounts, which prevent the board from being damaged when the router is moved. The RTS multimodal stimulus box is shown in a cut-away view with the two BNC connectors on the left, wired to the LED and the speaker, respectively. The BNC connectors and the LED and speaker are passed through holes in the sides of the stimulus box enclosure and are secured as needed. The RTS response box is shown in four different views; two external, showing a side view and a top view, respectively and two cut-away views, showing the components from the side and from the top. In the internal views of the response box, the switches, the circboard on which they are mounted and the offset mounts, which secure the circboard are labeled; the second internal view also provides a basic wiring diagram for the SPST switches used.

output lines (in our case, visual and audio modalities; thirteen per modality), while two more provide the external trigger connections for interfacing the RTS router with other devices and the remaining three holes are used for the three response lines. Finally, a small hole was drilled for an audio input jack.

Dual, in-line package (DIP) integrated circuits were used and connected to the circuit board by appropriately sized DIP sockets which were soldered to the circuit board, which allowed the integrated circuit components to be easily installed without risking damage to the circuits during assembly. The parallel port and the BNC connectors were wired, and all the BNC connectors were properly grounded to the parallel port's ground pins. The trigger outputs were connected to the correct parallel port connectors and the audio input was connected to the audio multiplexer. The connectors were secured in place using epoxy and the router enclosure sealed.

2.4. Building the multimodal stimulus boxes

Small plastic project enclosures were used to construct the stimulus boxes. Those were designed to accommodate a light emitting diode (LED) and a speaker, but virtually any stimulus could be used, provided it can be activated by 3.5 V DC. We were interested in having auditory and visual stimuli in a single unit for maximum flexibility in deploying the RTS, which meant that we connected one BNC connector to each of the two stimulus generators (the LED and the speaker, respectively), which were exposed via appropriately sized holes in the box (see Fig. 1B). After being built, each stimulus box was assessed for its ability to generate consistent and reliable stimuli using a 3.5 V power source for the visual stimulus, and an audio input for the auditory stimulus.

2.5. Building the RTS response box

The response box was custom built to have quiet switches that provided physical feedback when they were engaged. We used 150 g, board-mounted single-push, single-throw (SPST) switches to fulfill this requirement. Any SPST switch can be used to actuate the response logging code in the RTS software, provided the switch is wired with power to one terminal and ground to the other. Building the response box required a project enclosure the size of a deck of cards (e.g., a Serpac 113), in which we drilled three holes in the front side of the box for the BNC connectors and three holes in the top of the box for the switches (Fig. 1B). The switches were lined up on a piece of plated circuit board with identical spacing to the holes in the top of the enclosure such that they could pass through the holes in the top of the box without being activated by static pressure from the side of the hole. With the placement verified, we then soldered the switches to the board and connected them to the BNC connectors mounted on the side of the enclosure (see Fig. 1B). We then secured the BNC connectors by epoxing the threads on the interior of the enclosure. Note that the RTS is not limited to using our design for a response box; any three-button response box or any other human controlled device, such as microphone headset to collect verbal responses or an eye tracking system configured to track voluntary saccades can be used with the RTS with the proper interface. Any such response system merely requires an output line connected to the RTS router and a circuit which can pull one of the router's response lines to a ground state to simulate the normal action of the response box and thereby trigger the next trial.

2.6. Using the RTS

Once the components are built, the RTS router is connected to a Windows-based PC laptop using its parallel port, the RTS stimulus boxes are connected to the desired outputs on the router and the RTS response box is connected to the router. The stimuli can be placed at any elevation, eccentricity or depth from the subject, constrained by the length of the BNC cables used and the dimensions of the testing space. The computer should be a PC running Microsoft Windows XP with a built-in parallel port. The authors recommend, at a minimum, a Pentium 4 or similar processor and 512 MB of RAM installed in the RTS host computer, as the system was developed with such a configuration. Prior to running the RTS software for the first time, the experimenter must install the freely available inpout32 library (logix4u.net; provided with the RTS software in the Supplemental Materials) on the computer; the RTS software depends on this library for direct access to the parallel port under Windows XP. Eventually, the current software could be modified to accommodate the control of the parallel port for other operating systems.

If external devices (e.g. TMS apparatus) are being used, they should be connected via BNC cable to the RTS router prior to the beginning of the experiment. The placement of the stimulus boxes is only constrained by cable length and the size of the testing space in which the RTS is deployed. Once the system is connected, running the RTS software (a compiled C++ executable) is simply a matter of double clicking on the software's icon and following the command line instructions which the software provides (complete instructions are provided in the Supplemental Materials, along with the source code). The order of stimuli for an experiment is set by the targets.txt file which is found in the same directory as the RTS software; each trial is denoted by one of thirteen stimulus locations, corresponding to one of the thirteen outputs for each stimulus modality. Within this file, the trial sequence is set by the user. When an experiment is being performed with the addition of external devices (e.g., online transcranial magnetic stimulation), the trigger output timings are set for each trial using the trigger.txt file in the same directory as the software. Once the experiment has ended, the data from the response box is saved to a text file in the application directory; one row corresponds to a single trial in the experiment. The file records the presented target, the subject's response time, the subject's response, whether that response was correct or incorrect and the external trigger delay, if applicable for each trial. This file can be read into Microsoft Excel, Mathworks Matlab or any other data analysis software.

2.7. Temporal accuracy with the RTS

One of the major design considerations with the RTS was achieving and maintaining the temporal accuracy of the system for stimulus presentation, response recording and external device triggering. Given that many of the experiments for which the RTS is most suited require a high degree of temporal accuracy, verifying the temporal characteristics of the RTS is critical if our design and results are to be credited. Furthermore, the ability to accurately and flexibly manipulate stimulus presentation time and duration is critical to titrate the difficulty of the tasks. To keep costs down, we opted to use direct software mediated control of the parallel port with a minimum of intermediating code between the RTS controlling code and the parallel port itself. This ensures minimum interference from other computer processes.

To validate this approach and to test the RTS overall, we performed a series of tests on the RTS router's stimulus output lines, response input lines and external trigger lines to verify the accuracy of stimulus presentation timing, subject response logging and external triggering capabilities, respectively. All of our temporal testing was performed using a full RTS setup (RTS router, and PC running the RTS Software) connected to a high temporal precision stimulus synchronizer (Master 8vp, A.M.P.I., Israel). We ran these tests using a Dell Inspiron 8500 laptop running the RTS software and produced blocks of 100 trials per output channel using an identical trial duration and structure as were used in sessions with human subjects. In order to evaluate the temporal accuracy of the stimulus presentation code, we funneled the visual output signals into a calibrated stimulus synchronizer (Master 8vp, A.M.P.I., Israel), induced a fixed delay of 350 ms, emulating an average human response time for our task, then passed the signal through the input ports on the RTS router (Fig. 2). To test the router's trigger outputs, we ran a series of tests with a custom "trigger.txt" file programmed for blocks of 100 trials at 20 different delays (0, 10, 25, 50, 75, 100, 125, 150, 175, 200, 225, 250, 275, 300, 325, 350, 375, 400, 425, and 450 ms post-sensory target onset) (Fig. 3). For both sets of tests, we computed the temporal shift in milliseconds between the programmed delay and the response time recorded by the router, as determined by the configuration of the software and the delay programmed into the Master 8. In our tests of the RTS router's accuracy for stimulus output, our data revealed a mean timing deviation (data pooled across all 13 channels; 100 trials per target channel) with an average of 0.001994 ± 0.116365 ms and a median of: 0.000070 ms (Fig. 2). During our testing of the RTS router's two trigger lines (20 different temporal delays tested; 100 trials per delay) we also found latency shifts less than ± 1 ms with respect to the programmed interval; the average deviation from the programmed trigger delay was 0.005402 ± 0.155316 ms with a median of 0.00200 ms (Fig. 3).

We performed additional tests during which we manipulated the laptop computer during the timing tests, performing operations such as opening text files, saving text files or searching and replacing elements in a text file. According to our results, and as it is the case in most stimulus presentation software packages, we must strongly advise against using the computer at all during the testing, since such operations induce erratic and temporally unpredictable alterations in timing presentations (mainly with shifts above 1 ms, and up to 32.0 ms). The authors recommend using a stripped down system (e.g., a computer dedicated to running the RTS software without any unnecessary software or hardware) to control the RTS router without an active connection to the Internet or active antivirus software, as these can adversely impact the timing accuracy of the system.

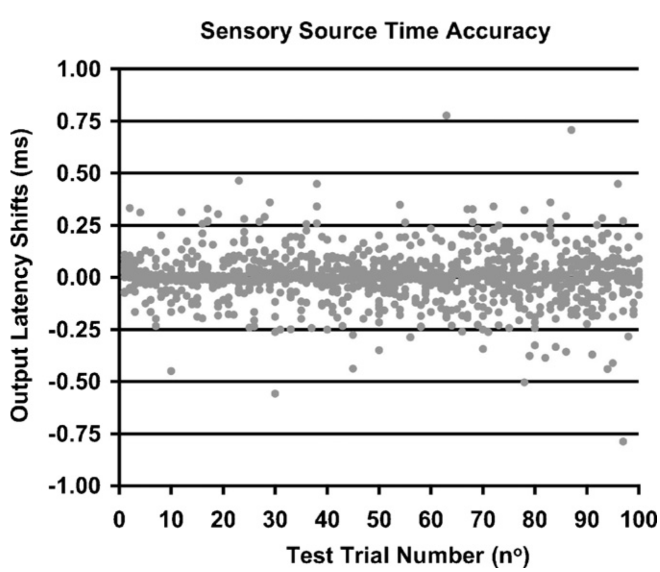

Fig. 2. Analysis of timing accuracy for all 13 (visual) output channels across 100 trials per output line. The plot shows one point for each trial (1300 total) showing the individual temporal shift for that trial versus the trial's location within its block. Positive or negative latency shifts indicate that the onset time of the signal sent to the multimodal stimulus boxes was acknowledged by the RTS software as having been earlier and later, respectively, than the fixed reference measure. Note that all measured values represent deviations of less than 1 ms, and a large majority of them (96.8%) were found to be less than ± 0.25 ms.

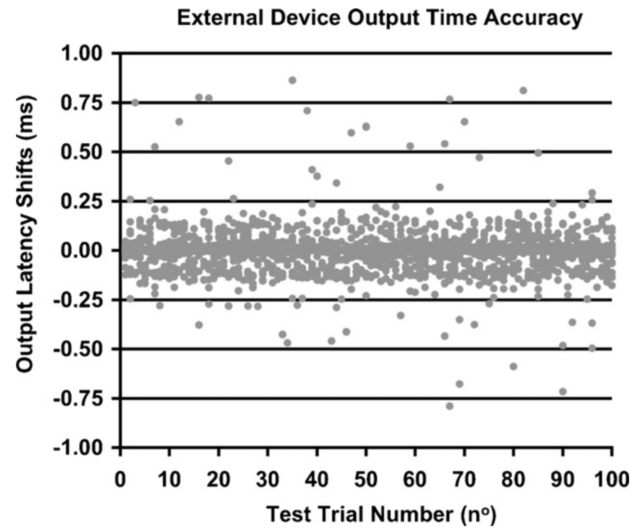

Fig. 3. Analysis of timing accuracy for one of the trigger outputs used for triggering a TMS machine in our experiment, on the RTS router. The graph displays the individual trial time shifts (in ms) with respect to the programmed temporal delay across 100 trial runs for each of the 20 delays tested (0, 10, 25, 50, 75, 100, 125, 150, 175, 200, 225, 250, 275, 300, 325, 350, 375, 400, 425, and 450 ms) for a total of 2000 trials. Positive or negative latency shifts indicate that the output trigger directed to an external device was noted by the RTS software as having been delivered earlier or later, respectively, than the programmed output delay. Notice that all measured values represent shifts of less than 1 ms, and that a large majority of them (97.5%) exhibit shifts of less than ± 0.25 ms.

2.8. *Stimulus sources and control in the RTS*

The RTS can be used to control up to thirteen independent sensory stimuli in visual or audio modalities, although any other stimuli may be used with the system provided they are electrically compatible. In other words, the current system can also handle any other type or combination of custom-made or commercially available stimulus source boxes for evaluating other sensory modalities (e.g., electro-mechanic actuators, electrical stimulators, or other visual or auditory stimulus presentation devices); such stimuli can be connected to the "visual" output channels, provided they can be activated by 3.5 V DC. Up to two visual stimuli can be presented simultaneously, whereas in the current design, the audio stimuli must be presented singly. This is a limitation of the integrated circuits used to drive the RTS router; if there is a need for three or more simultaneous visual stimuli or two or more simultaneous audio stimuli, a BNC splitter may be used on an output line, although this may require other alterations to the stimulus boxes due to a decrease in voltage which might affect the intensity of the visual or audio signal. In developing the RTS, no temporal differences were found when the signals were split, but intensity differences were noted, particularly in audio paradigms.

The router, in addition to its visual stimulus outputs, possesses the ability to present audio stimuli over the same number of lines. In auditory experiments, the source audio must be fed to the RTS router over the minijack connection built into the RTS router; any source can be used, although for reasons of temporal accuracy, we do not recommend using the controlling computer (running the RTS software) to provide audio for these experiments. The audio circuitry in the RTS router uses a dedicated audio demultiplexer, which allows for easy routing of the audio signal to any desired output line, but it has been our experience in developing the RTS that adding an in-line amplifier between the audio source and the RTS router allows for a greater degree of control in configuring the audio outputs and their volume. Finally it should be mentioned that through the use of several types of custom-made or commercially available stimulus generation devices, the RTS can be used to assess crossmodal sensory interactions or it may simply be used as a highly accurate stimulus control system in the manner we have described.

2.9. Basic experimental paradigms with the RTS

In the course of designing, building and using the RTS, we have programmed and tested visual, audio and crossmodal experimental paradigms. However, the RTS is not intrinsically limited to these paradigms; it is fully configurable in software and is flexible enough to be adapted to nearly any arrangement of stimuli within the physical limitations of the hardware and its communication interface with the computer. In the current version of the software, all stimulus durations and inter-stimulus intervals are set when the RTS software is initialized prior to an experiment and these can be changed as needed by restarting the application. We have described the basic procedure for modifying the trial order and the delays for external devices; new sequences can be generated easily in a range of software packages and exported as a formatted text file which the RTS software can read.

As a starting point, we have implemented a range of experimental paradigms in the current version of the RTS software (provided as part of the Supplemental Materials), which demonstrate the system's flexibility. The current version of the RTS software includes: uncued detection paradigms (for visual, auditory or tactile tasks), cued detection paradigms (with the same stimulus modality being used for the cue and the target stimulus) and crossmodally cued detection paradigms (in which the cue and the target stimuli are of different modalities; e.g., a visual cue and a auditory target). In the uncued detection paradigm, a single modality stimulus would be presented after fixation. In the cued detection paradigms, a single modality stimulus would precede or be presented simultaneously with the same modality stimulus after visual fixation; the cueing stimulus can be presented at an ipsilateral (validly cued) or contralateral (invalidly cued) spatial location with respect to the display location of the peripheral target, with different presentation probabilities. In the crossmodally cued detection paradigm, a sensory cue from a different sensory modality than the peripheral target would be used as a distracter presented between the fixation and the target stimuli. The use of cued paradigms provides more demanding versions of simple visual or audio detection/localization tasks, constitutes a specific evaluation of the subject's ability to orient or re-orient visuo-spatial attention and a more sensitive assessment of differences in stimulus eccentricities or differences in the attended spatial area. All of the aforementioned paradigms incorporate integrated catch trials as part of the general experimental procedure (the configuration and implementation of these catch trials is detailed in the Supplemental Materials).

To provide a sense of the control afforded the user by the RTS software, we will describe a simple uncued paradigm trial. Such a trial would begin with the activation of the fixation stimulus (by default, 1.5–3.0 s in duration), followed by a period of no active stimuli (default duration: 40 ms, set in 1 ms steps), followed by the presentation of the target stimulus (default duration: 40 ms; set in 1 ms steps). Following target presentation, subjects are asked to provide a response using the RTS response box during a fixed temporal window after the removal of the target stimulus (default response window duration: 2.0 s, set in steps of 1.0 s). All timings can be easily customized by the experimenter at the beginning of the experimental session or their default values used. During the response period, a trigger signal (by default, the trigger pulse is 1 ms in duration and provides a 5 V TTL signal; the duration of the trigger pulse can be changed as needed) can be sent to an external device (e.g., a TMS apparatus or other external device). The timing of this signal is set in the "trigger.txt" file, which is accessed by the application and must be present in the same directory as the system application.

2.10. Materials and methods summary

We designed the RTS to address the need for an accurate, human-scale, portable low-cost, real space testing system for visual and auditory stimuli, based on our previous work with a feline-scale version of a similar system. We chose to build the RTS from readily available and low-cost components to keep the design as simple as possible while affording the system a remarkable amount of flexibility with regard to its stimulus presentation capabilities.

3. Results

To provide a sense of the capabilities of the RTS, we performed an exploratory experiment using the RTS in conjunction with online single-pulse transcranial magnetic stimulation (TMS) triggered and synchronized by the system. Our goal was to use online TMS at a range of post-stimulus delays to corroborate the role of right posterior parietal cortex in visuo-spatial orienting and processing in the contralateral (left) visual hemifield. We expected that online stimulation at a certain temporal delay after stimulus onset would adversely impact subject performance in this task and that stimulation before or after this window would have little or no effect (as reported by Chambers et al., 2004). Our apparatus was designed and built at the Cerebral Dynamics Laboratory at the Boston University Medical Campus (BUMC). We performed this preliminary experiment with a group of neurologically sound subjects recruited from the BUMC community. Participants were screened for contraindications to TMS and the informed consent was obtained in accordance with the requirements of the BUMC IRB. TMS was administered using Magstim Rapid TMS equipment in single-pulse mode with a Magstim double 70 mm coil (Carmarthenshire, Wales, UK), which was handheld at the scalp region of interest, the posterior parietal cortex of the right hemisphere. The location of the region of interest was determined in both experiments by means of the 10/20 EEG coordinate system and stimulation was delivered to point P4 which according to a post hoc MRI analysis and the evidence collected in prior reports corresponded well with the right posterior parietal cortex (PPC) on the dorsal intraparietal sulcus (IPS). The experiment also included sham TMS runs within each experimental session, during which the coil was placed at P4 (right PPC/IPS location) with the lateral border tangential to the targeted location; the TMS coil was angled 90° from normal operating orientation in order to discharge the TMS pulse away from the scalp. The order of the real and sham TMS runs was counterbalanced across subjects. TMS was discharged in single pulses at a fixed intensity of 80% (∼140% of the motor threshold of the subject and ∼90% of their phosphene threshold in V1–V3). Visual stimuli were placed at three eccentricities (45°, 60° and 75°) left or right from fixation (0° relative to subject position) and the data for those locations was averaged to increase the statistical power for each of the selected time bins. Subjects were also presented with a number of catch trials in which fixation was not followed by any peripheral target to enforce central fixation and to estimate the subject's reliability. They were required to demonstrate an error rate on catch trials equal or below 5% per each of the testing blocks for the data to be analyzed further. In addition, potential eye movements were followed by the system operator using a video camera capturing a highly magnified image of the subject's eyes. The stimuli were placed at eye level at an approximate distance of 80 cm (arm's reach

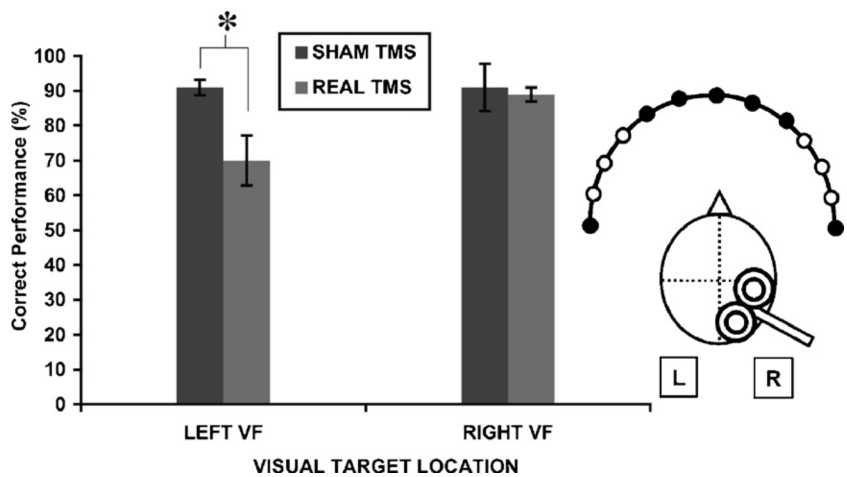

Fig. 4. Mean percent correct responses (±standard error) given the online administration of single pulses of sham TMS or real TMS. Accuracy is calculated as the number of correct detections divided by the total number of presented targets, multiplied by 100 and separated by visual field (VF) location (right and left). The task was performed at 77 cd/m^2 background illumination and baseline difficulty was set at a level of ~80–85% of presented stimuli having been detected correctly in a preliminary titration and familiarization session. Subjects performed at the expected accuracy levels under the sham TMS condition. Significant decreases in task performance were observed for the detection of targets presented in the contralateral visual field in the real TMS condition. Sham and real TMS runs were counterbalanced. Such disruptive effects of TMS demonstrate the well-known involvement of areas and sub-areas within the right posterior parietal cortex in visuo-spatial attention and localization processing (Hilgetag et al., 2001; Thut et al., 2005; Pascual-Leone et al., 1994). Statistical analysis by means of a one-sided *t*-test showed a significant difference between sham and TMS conditions for contralateral targets (*$p < 0.02$) but not for ipsilateral targets ($p > 0.05$). VF: visual field; L: left; R: right.

limit; real space presentation) from the subject. The task was performed at a level of 77 cd/m^2 background illumination and baseline task difficulty was set at 80–85% correct responses for peripheral targets after preliminary training and task titration sessions.

During the experiment, the fixation stimulus was randomly presented for 1.5–3.0 s, it was separated from the presentation of the target stimulus by a 40 ms delay and the target stimulus was then presented for 40 ms. During the experiment, the subject responded using our handheld three-button response box; the 'left' and 'right' buttons were used to signal the detection of a target to the left or right of fixation. The 'middle' button was used to signal the targets presented at the midline 0° position. Subjects were requested not to respond if they believed no target was presented after fixation (catch trials). Targets were displayed using several a pseudo-randomized sequences across 5 different blocks of 28 trials, each including 10 catch trials. Reaction times and response accuracy were recorded. For our analyses, data were averaged across all targets in each visual hemifield. During the TMS portion of the experiment, single pulses of TMS were delivered during each trial at post-stimulus-onset delays of 50, 100, 150, 200, 250, and 300 ms (Fig. 5). Reaction times and target responses were recorded with a mean accuracy of 0.005 ms. Data were analyzed using one-sided *t*-tests to determine significance.

Using this uncued testing paradigm, with the addition of online, synchronized single-pulse TMS, significant performance differences (*$p < 0.05$) were found between sham TMS and real TMS runs for targets presented in the contralateral visual field (for stimuli presented in the visual hemifield contralateral to the TMS stimulated hemisphere) but not in the ipsilateral visual field (i.e., stimuli presented in the visual hemifield ipsilateral to the TMS stimulated hemisphere) (Fig. 4). This result is consistent with the known contralateral effects of high frequency or low-frequency online and

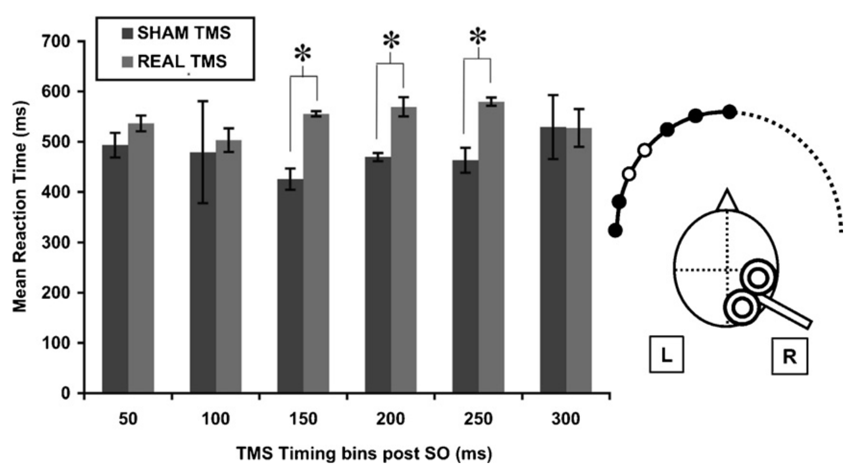

Fig. 5. Mean (±standard error) reaction time (in ms) averaged across significant target locations in the left contralateral visual field with respect to the TMS right hemisphere targeted site across the different time bins during which a single pulse of real TMS or sham TMS was delivered to the right PPC, at one of six post-stimulus onset (SO) time bins (50, 100, 150, 200, 250 and 300 ms). Significant increases in reaction times were found at specific temporal bins (150, 200 and 250 ms) and neither earlier (50 and 100 post-SO) nor later (at 300 ms post-SO). The data provides evidence that processing at this cortical location is critical for the performance of this task during a period of 100 ms, spanning from 150 to 250 ms post-stimulus onset. Such an increase in reaction time in these specific time bins post-stimulus onset is coincident with the a late temporal windows areas within the right PPC reported during a redirection of attention Posner type paradigm (Chambers et al., 2004) or a visual detection task similar to ours (Koch et al., 2005), as explored with TMS in single and double pulses in a similar chronometric design.

offline transcranial magnetic stimulation and the online disruptive impact of repetitive transcranial magnetic stimulation on right parietal regions obtained for close pericentral targets tested on standard computer screens (Hilgetag et al., 2001; Thut et al., 2005). A chronometric analysis of this data was carried out on the most significant left targets (i.e., those presented in the visual hemifield contralateral to the TMS stimulated hemisphere) and the average reaction time was computed for each of the post-stimulus-onset time bins in which real TMS or sham TMS were delivered. The chronometric analysis revealed a significant deviation from normal reaction time when real TMS was administered within a window of 150, 200 or 250 ms after the stimulus onset (Fig. 5). No significant effects were found from the use of real TMS prior to 150 ms post-stimulus onset (at 50 and 100 ms, respectively), nor after 250 ms (no significant effects at 300 ms post-stimulus onset).

4. Discussion

To the best of our knowledge, this is the first detailed report of a flexible and low-cost device and procedure to evaluate the orientation of spatial attention and stimulus detection performance in real space. In past studies, expensive, bulky and highly sophisticated perimetry systems have been used. We designed the RTS to address our needs, which were not fulfilled by preexisting systems (as used in Muller-Oehring et al., 2003; Poggel and Strasburger, 2004 among others). Their complexity, high purchase and maintenance costs, and a lack of flexibility with regard to stimulus modalities and locations made these systems unsuitable for the role for which we designed the RTS. In addition, the exploration of the deployment of visuo-spatial attention, visuo-spatial orienting and the impact of both on visual detection and discrimination in intact human participants and patients is being primarily performed using flat screens with a restricted array of stimulus sources and a limited range of eccentricities, mainly located at pericentral locations in the visual field. The RTS provides a valuable and efficient tool that can be expanded or modified at will by researchers and clinicians to explore the processing of visuo-spatial attention information in real space, by using the RTS alone or in conjunction with causal neurostimulation techniques such as but not restricted to transcranial magnetic stimulation (TMS).

The use of online TMS in our experiment reveals that real but not sham TMS of the posterior parietal cortex of the right hemisphere has a significant effect on performance of a visual detection task in real space and the area in question is therefore causally implicated in the processing of visual detection tasks driven by visual stimuli displayed on the contralateral visual field. Our findings are in agreement with prior observations reported in similar or analogous detection paradigms (Chambers et al., 2004; Koch et al., 2005). Furthermore, our analysis revealed a window of significant increases in reaction times when TMS was administered between 150 and 250 ms post-stimulus onset much as has been found using analogous paradigms (Fig. 5). Based on this data, we can posit that the right PPC around the higher portion of the intraparietal sulcus (according to 10–20 EEG system P4) is significantly implicated in the performance of the task for mid and far peripheral targets displayed contralateral to the stimulated right hemisphere at some point during this temporal window, but not earlier or later. Given our findings, a follow-up experiment could be performed with more closely spaced TMS delays within the window of effect (from 150 to 250 ms post-stimulus onset) to gain a better understanding of the precise chronometry of spatial processing and the exact time during which the right posterior parietal cortex is involved in processing visuo-spatial information. The potential effects of the sensory sensations which accompany TMS can be ruled out as the cause of our findings in this experiment since no effect was found in the sham TMS condition, which was identical to the real TMS condition with the exception of actual stimulation of cortex. In addition, any effect from these accompanying sensations would be observed in all time bins as the accompanying sensations do not vary with the TMS delivery delay. A comparison of pericentral targets versus a range of peripheral targets and use the of TMS to probe the role of left posterior parietal cortex are also experiments for which the RTS is well suited.

Overall, the current exploratory experiments demonstrates the utility and reliability of the RTS in studies aimed at exploring the chronometric contribution of cortical areas and associated brain networks to the spatial deployment of visual attention for stimuli in real space conditions. We did so by allowing testing to be performed with full array of pericentral and mid to far peripheral stimulus sources deployed in a customized and flexible manner throughout the subject's visual field. Furthermore, such mechanisms and the contribution of the targeted cortical site have been demonstrated causally using time locked control of a transcranial magnetic stimulation device via the RTS. The exploratory experiment wherein we used the RTS to probe the causal implication of the right posterior parietal cortex in attentional processing and its influence on a visual detection task executed in real space provides a sense of the overall flexibility and potential of our low-cost yet highly accurate system in this and other related research domains. This paradigm has been specifically chosen to demonstrate the capabilities of the RTS as it has produced robust and coherent results in prior rTMS and TMS experiments. Our preliminary results, gathered using targets presented at 45°, 60° and 75° from fixation, corroborate such prior observation and serves as a further demonstration of the reliability of the system and the procedure reported in this manuscript.

The Realspace Testing System (RTS) we have described in this paper has the potential to enable further research into the cerebral mechanisms of attentional deployment, visual detection and stimulus discrimination in real space conditions; in particular, it may be used to explore some relatively unchartered research territories such as the creation of detailed chronometric maps of cortical site contributions to attentional deployment in conjunction with a set of comparisons between target eccentricities; other uses of the RTS could include experimental assessment of the effects of near and far visual fixation and the effects thereof on attentional orientation, all of which are beyond the capabilities of a traditional two-dimensional computer display-based paradigm. As mentioned, the RTS system can also handle any other type or combination of custom-made or commercially available stimulus source boxes (such as electro-mechanic actuators, electrical stimulators or thermogenic devices) which may be used to evaluate other sensory modalities or crossmodal influences on visuo-spatial attention and visual perception. Furthermore, the RTS is not limited to using the response box which we have designed and used. With the correct intermediary circuit, any commercially made response device (e.g., a verbal response system or a high-speed eyetracker) can be made to interface with the RTS and to allow it to record subject responses in any way required by the experiment or the subject.

While we do not envision our device as a replacement for existing methodologies, we hold that its low cost, ease of use and portability will render it appealing to those engaged in laboratory and clinical research. Given its advantages, it has the potential to provide a useful supplemental tool for those engaged in such studies. The RTS constitutes a useful addition to the palette of experimental tools currently in use in the fields of sensory processing and its design addresses a range of deficiencies existent in other testing devices. We have designed the RTS for maximum flexibility and minimum restriction, while using readily available parts throughout the system. Specific instructions and parts lists for the RTS and the source code for the software is made available to researchers by the authors (Supplemental Materials) so that the system can serve to supplement other methodologies and the design of the RTS can be modified by those who choose to use it in order to better serve their own research needs and develop new applications of our original design. As described in this manuscript, the RTS is a foundation upon which other researchers can build to address specific research questions. By designing a simple and flexible system, we have reduced the barrier to entry, both in terms of cost and build time, such that interested researchers will endeavor to use our design rather than relegating it to the realm of interesting but impractical methods.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jneumeth.2010.01.007.

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