The Pivotal Role of the Right Parietal Lobe in Temporal Attention

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Abstract

■ The visual system is extremely efficient at detecting events across time even at very fast presentation rates; however, discriminating the identity of those events is much slower and requires attention over time, a mechanism with a much coarser resolution [Cavanagh, P., Battelli, L., & Holcombe, A. O. Dynamic attention. In A. C. Nobre & S. Kastner (Eds.), *The Oxford handbook of attention* (pp. 652–675). Oxford: Oxford University Press, 2013]. Patients affected by right parietal lesion, including the TPJ, are severely impaired in discriminating events across time in both visual fields [Battelli, L., Cavanagh, P., & Thornton, I. M. Perception of biological motion in parietal patients. *Neuropsychologia, 41,* 1808–1816, 2003]. One way to test this ability is to use a simultaneity judgment task, whereby participants are asked to indicate whether two events occurred simultaneously or not. We psychophysically varied the frequency rate of four flickering disks, and on most of the trials, one disk (either in the left or right visual field) was flickering out-of-phase relative to the others. We asked participants to report whether two left-or-right-presented disks were simultaneous or not. We tested a total of 23 right and left parietal lesion patients in Experiment 1, and only right parietal patients showed impairment in both visual fields while their low-level visual functions were normal. Importantly, to causally link the right TPJ to the relative timing processing, we ran a TMS experiment on healthy participants. Participants underwent three stimulation sessions and performed the same simultaneity judgment task before and after 20 min of low-frequency inhibitory TMS over right TPJ, left TPJ, or early visual area as a control. rTMS over the right TPJ caused a bilateral impairment in the simultaneity judgment task, whereas rTMS over left TPJ or over early visual area did not affect performance. Altogether, our results directly link the right TPJ to the processing of relative time. ■

INTRODUCTION

Time processing is a crucial dimension of our lives. It is at the basis of high-order cognitive functions such as verbal communication, comprehension, and motor coordination, and the ability to precisely process time in the visual domain is important for many daily activities such as driving a car or walking and avoiding obstacles. Analysis of time can be done over multiple timescales, from milliseconds to seconds and minutes (Buhusi & Meck, 2005). Here, we investigate "relative timing" defined as the ordinal relationship between events (i.e., the ability to perceive the sequential order of two events; Aghdaee, Battelli, & Assad, 2014), rather than the time interval between events.

We can behaviorally measure the temporal resolution of relative timing through the speed at which people can discriminate individual objects presented in a rapidly changing stream. The ability to discriminate events across time varies depending on the task; for instance, we are very good at noticing that something has changed, and we can detect visual flicker at a rate of up to 30 Hz (Lu & Sperling, 2001). However, our temporal resolution for determining which event came first is much lower. For example, human participants can discriminate when a stimulus is white or black when it is alternating between those two phases only at a maximum rate of around 8 Hz (Battelli, Pascual-Leone, & Cavanagh, 2007; Verstraten, Cavanagh, & Labianca, 2000). The resolution of relative timing is indicated by participants' ability to identify single objects within a stream of objects displaced with onset asynchrony in time between items (such as in an RSVP task; Shapiro, Raymond, & Arnell, 1994), or to identify which event occurred first between two (temporal order judgments), or to indicate whether two events occurred simultaneously or not (simultaneity judgment; Aghdaee et al., 2014).

The neural substrates of temporal judgments are still poorly understood. Critchley (1953) was the first to mention a possible role of parietal cortex in temporal processing (Aghdaee et al., 2014; Critchley, 1953). Subsequently, the right parietal cortex and, specifically, the right TPJ

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gained more attention as encoder of temporal information in the visual modality, demonstrated by psychophysical work on normal participants and on neurological patients. For instance, Husain and colleagues (Husain & Rorden, 2003; Husain, Shapiro, Martin, & Kennard, 1997) found a severe and protracted attentional blink (i.e., a failure to detect the second of two salient stimuli if presented between 150 and 450 msec after the first one) in patients with right parietal stroke. Duncan and colleagues demonstrated right-hemisphere patients' difficulties in encoding stimuli presented transiently in both sides of the visual space, a nonspatial deficit revealed only when patients were tested more systematically in both visual fields (Duncan et al., 1999). Right-parietal-damaged patients are also impaired in other tasks involving temporal attention such as rapid discrimination of changing visual features (i.e., temporal order judgments; Roberts, Lau, Chechlacz, & Humphreys, 2012; Berberovic, Pisella, Morris, & Mattingley, 2004; Robertson, Mattingley, Rorden, & Driver, 1998), subjective onset asynchrony tasks (Bartolomeo, Siéroff, Decaix, & Chokron, 2001), and in asynchronous flicker phase discriminations (Battelli, Cavanagh, & Thornton, 2003).

Relative timing differences are also linked to impairments across both visual hemifields. Battelli and colleagues (2003) demonstrated that right-parietal-lesioned patients have a bilateral deficit (involving both left and right visual field) in relative timing. Participants were asked to identify the "odd" (out-of-phase) target from among six flickering (alternating black and white) squares. The odd target is easy to identify when the squares alternate at a low frequency rate (e.g., 2 times per second, 2 Hz) and becomes more difficult to identify at higher frequency rate (e.g., 8 times per second, 8 Hz). Controls and patients with left parietal lesions performed the task with comparable rates of flicker (approximately 8 Hz), whereas right-lesioned patients had thresholds averaging around 3 Hz in both left and right hemifields. More recently, a study found that right parietal patients showed impaired performance on a continuous-monitoring test investigating temporal resolution of attention (Howard, Bashir, Chechlacz, & Humphreys, 2016). All in all, these studies demonstrate clear behavioral evidence of nonspatial deficits in right parietal patients; however, a clear causal link between brain and behavior in healthy individuals is still lacking.

Corbetta and Shulman (2011), in revisiting a series of functional studies, identified two networks of attention: a dorsal and a ventral attention stream, the latter likely involved in timing of visual events (Tyler, Dasgupta, Agosta, Battelli, & Grossman, 2015; Husain & Rorden, 2003). The dorsal stream is bilaterally distributed with each brain region organized by topographic maps of contralateral space and includes the intraparietal sulcus (IPS) and the FEF. The dorsal attention stream is specialized for the control of spatial attention directed toward salient events in the contralateral visual field. The nonspatial ventral stream is lateralized to right parietal cortex, and it includes the TPJ and the ventral frontal cortex. The right TPJ is involved in reorienting of attention and detection of behaviorally relevant stimuli outside the current focus of attention, general arousal, and vigilance. Other interesting fMRI studies, investigating the deployment of attention across time using competing stimuli, have pointed out that the ventral stream might have a central role in coordinating voluntary and stimulus-driven attentional control when stimuli compete for attention (Serences et al., 2005). The ventral stream of attention is also believed to be important for processing "when" an event occurs (Battelli, Walsh, Pascual-Leone, & Cavanagh, 2008; Battelli et al., 2007). A recent functional connectivity analysis study using a relative timing task has clearly shown different patterns of connectivity between visual sensory areas and TPJ that correlated with participants' ability to individuate rapidly changing events (Tyler et al., 2015).

Here, we investigated relative timing in the right and left parietal lesion patients on a synchrony judgment task (Experiment 1). We then studied the causal role of the right and left TPJ in relative timing by delivering 1 Hz inhibitory repetitive TMS over the right and left TPJ in healthy participants performing the same relative timing task (Experiment 2). Results showed that right (but not left) parietal patients were impaired in relative timing in both visual fields. Crucially, TMS over the right (but not left) TPJ in healthy participants mimicked patients' performance, therefore providing a clear demonstration of the direct role of right TPJ in visual relative timing (Hayashi et al., 2015).

EXPERIMENT 1A: PATIENTS, FLICKER TASK

Participants

Eighteen right-parietal-damaged patients were tested. They had a unilateral lesion due to cerebrovascular stroke, confirmed by radiological examination (CT or MR). None had any history or evidence of dementia or psychiatric disorder. All participants were Italian native speakers, were right-handed, and had normal or corrected-to-normal visual acuity. Table 1 reports their demographical data and lesion site. Figure 1 shows CT and MRI scans of a subgroup of patients. Patients were tested in the chronic stage, at least 6 months after the lesion. They gave informed consent before participating in the study according to the ethical standards of the Declaration of Helsinki. Research was approved by the ethical committees of the University of Trento and of the Carlo Poma Hospital in Mantua.

Patients were recruited and tested at the Center for Neurocognitive Rehabilitation (CeRiN) affiliated to the University of Trento and the Neuromotor Rehabilitation Department of the Carlo Poma Hospital, in Mantua.

Five left-parietal-damaged patients (5 men, average age = 61 years) and 18 age-matched neurologically unimpaired participants (8 men, average age = 63 years) served as controls. Independent samples t tests indicated

Table 1. Demographic and Lesion Data

Name	*Date of Birth*	*School*	*Clinical Symptoms*	*Lesion*	*Time of Onset (Month) prior Testing*	*Field Cut*
Right Lesions						
A.C.	10/01/1939	13 years	Mild neglect for the left visual field	Right middle cerebral artery stroke	12	No
B.D.	02/10/1939	8 years	Mild left neglect	Right frontal hemorrhagic stroke	12	No
B.G.	17/05/1941	5 years	Extrapersonal, peripersonal and personal left neglect	Right middle cerebral artery stroke	18	No
B.M.	29/11/1961	13 years	Left extinction	Right temporoparieto-occipital ischemic stroke	7	Partial field cut
C.S.	16/08/1938	11 years	Left extinction	Right temporoparietal ischemic stroke	24	No
F.A.	27/01/1943	5 years	Left extinction	Right temporoparietal ischemic stroke	16	No
F.C.	19/01/1948	18 years	Visuospatial deficits and left neglect	Right middle cerebral artery stroke	7	No
G.L.	13/05/1933	13 years	Left neglect	Right middle cerebral artery stroke	36	No
L.G.	05/01/1957	13 years	Left extinction	Right middle cerebral artery stroke	22	No
M.G	02/09/1947	22 years	Visuospatial deficits	Right temporoparieto-insular stroke	6	No
P.D.	16/06/1957	8 years	Left neglect	Right ischemic stroke due to internal carotid artery occlusion	38	Partial field cut
P.M.	20/04/1962	11 years	Visuospatial deficits	Right middle cerebral artery hemorrhagic stroke	7	No
P.C.	13/07/1945	11 years	Visuospatial deficits	Right middle cerebral artery stroke	9	No
R.F.	19/10/1947	8 years	Left neglect	Right middle cerebral artery stroke	108	No
R.R.	24/04/1944	10 years	Extrapersonal, peripersonal and personal left neglect	Ischemic stroke involving cortical and (mostly) subcortical parietal areas	8	No
S.B.	25/06/1946	8 years	Extrapersonal, peripersonal and personal left neglect	Right middle cerebral artery hemorrhagic stroke	6	No
S.B. (2)	06/02/1958	8 years	Visual and tactile extinction	Right middle cerebral artery stroke	8	No
T.E.	12/06/1946	5 years	Left visual and tactile extinction	Right middle cerebral artery ischemic stroke	13	No
Left Lesions						
L.L.	19/98/1970	13 years	Nonfluent aphasia	Left middle cerebral artery ischemic stroke	27	No

Table 1. (*continued*)

Name	Date of Birth	School	Clinical Symptoms	Lesion	Time of Onset (Month) prior Testing	Field Cut
C.O.	28/03/1951	8 years	Mild dysarthria	Left capsular-lenticular-thalamic ischemic stroke	13	No
Z.R.	04/04/1956	13 years	Aphasia with anomias, phonemic and semantic paraphasias and conduites d'approche.	Left temporoparietal stroke, involving lenticular nucleus, internal/external capsule and corona radiata.	144	No
Z.D.	12/07/1946	8 years	Right hemiparesis	Ischemic stroke in left posterior internal capsule and caudate nucleus	9	No
C.A.	16/02/1966	10 years	Executive slowing down and mild oral naming difficulty for nouns	Left centrum semiovale stroke	9	No
C.V.	08/07/1946	8 years	Right hemiparesis	Hemorrhagic stroke involving the temporoparietal cortex	26	No

All right parietal patients had a unilateral stroke due to cerebrovascular lesion. Symptoms described in the table refer to the neuropsychological evaluation carried out at the hospitals after the lesion. The sixth column indicates the time from lesion onset at which we tested them. The last column reports the presence of visual field cuts.

no difference between right parietal patients' mean age and left-damaged patients' mean age ($p = .86$) and between right damaged patients' mean age and controls' mean age ($p = .92$).

Methods

The experiment was conducted on an Apple MacBook Pro laptop. The computer ran on a Mac OS X version 10.6.8 operating system, Matlab (The MathWorks, Inc., Natick, MA) and Psychtoolbox (Brainard, 1997; Pelli, 1997).

We used a modified version of a task from Tyler et al. (2015). All trials in the experiments consisted of a quartet of disks (1° of visual angle) positioned in each of the four corners of a 4° radius virtual square. The disks counter-phase flickered between high-contrast uniform black and white for 3000 msec. At the beginning and at the end of each trial, the black (0.44 cd/m^2) and white (155 cd/m^2) flickering disks were masked by static texture patterns in the same positions for 350 msec (Figure 1). The texture patterns masked polarity phase cues at the onset of the discs and afterimage effects at the offset. The disks were visible against a uniformly gray background (59.6 cd/m^2) with a fixation cross positioned in the center of the screen for the entire duration of the experiment. Participants were positioned 57 cm from the monitor and were instructed to maintain fixation. We did not systematically monitor eye movements with an eye tracker due to technical constraints; however, one of the experimenters constantly observed participants' eyes during the entire duration of the trial to make sure they were fixating.

Patients and controls were asked to judge whether two of the four disks (on the right or on the left visual field, randomly across trials) were in-phase or out-of-phase. Before stimulus presentation, a cue (an arrow pointing to the left or to the right of the visual field) appeared for 3 sec in the center of the monitor indicating which side they were asked to judge (Figure 2). A series of practice trials was given to patients until they felt comfortable with the experiment (between 5 and 10). An experimenter recorded patients' answers by pressing one of two keys on the keyboard.

On some trials (about 50%), one disk (randomly assigned) flickered out-of-phase relative to the others (i.e., black while the other disks were white and vice versa). The experiment also included trials with no oddballs (about 25%, all flickering disks were in-phase) to ensure that participants directed their attention according to spatially directed cues to complete the task. In the other 25% of the trials, the stimuli in both the left and right visual field were out of phase. These additional manipulations were included to ensure that participants could not complete the task accurately on the basis of the position of the "oddball" feature only and forced participants to respond based on the features of the disks in the cued hemifield.

Participants completed a 3–1 double interleaved staircase (e.g., Levitt, 1970) to assess their individual flicker rate thresholds both for the right and left visual field. Flicker rates were adjusted to be slower (i.e., decreased

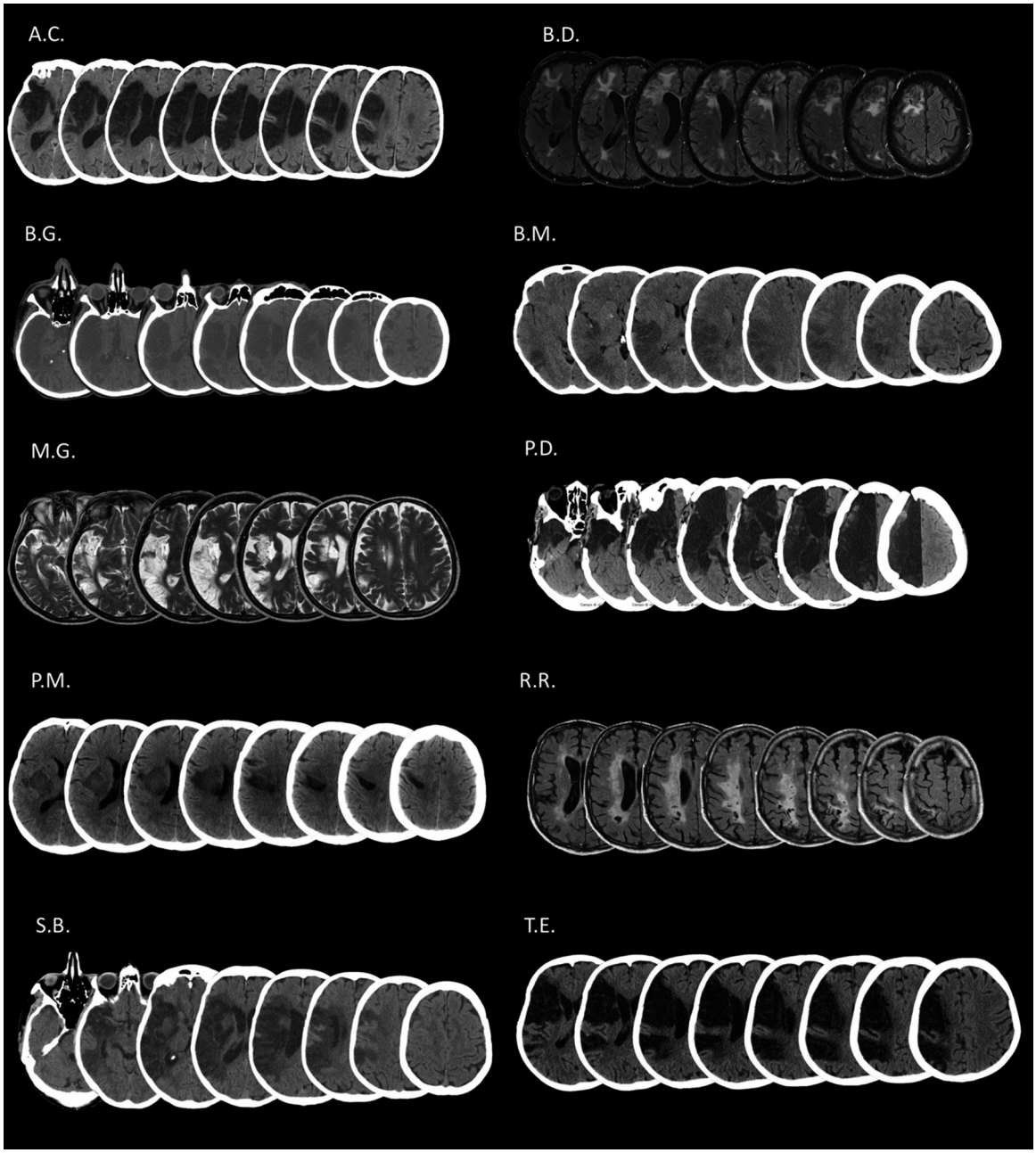

Figure 1. Neuroradiological (CT or MR) lesion documentation for 10 right-brain-damaged participants. Damage involves the territory of the right middle cerebral artery in all cases. Lesions are typically large (with the partial exception of patient PM) and involve both cortical and subcortical structures (with the partial exception of PM and RR, whose lesions are mostly subcortical).

difficulty) following a single incorrect judgment and adjusted to be faster (i.e., increased difficulty) following three correct and consecutive responses (step size: 0.5 Hz). The staircases terminated after a combined 30 reversals, with threshold parameters estimated from the last 15 reversals (average number of trials was 154 and 189 for patients and controls, respectively). Flicker frequency was adjusted to yield 80% accuracy in the same/different judgments. Patients and controls took, on average, 25 min to complete the task. They were given the opportunity to take a break if they were tired.

Data Analysis and Results

The dependent measure was flicker threshold (measured in Hz), defined as the temporal frequency required for 80% accuracy in each hemifield. All statistical analyses were performed using SPSS software (version 20.0, SPSS Inc., Chicago, IL). A mixed-model ANOVA was run with Visual field (right vs. left) as the within-subject factor and Group (right-parietal-damaged patients vs. left-parietal-damaged patients vs. age-matched controls) as the between-subject factor. *t* Tests were Bonferroni-corrected.

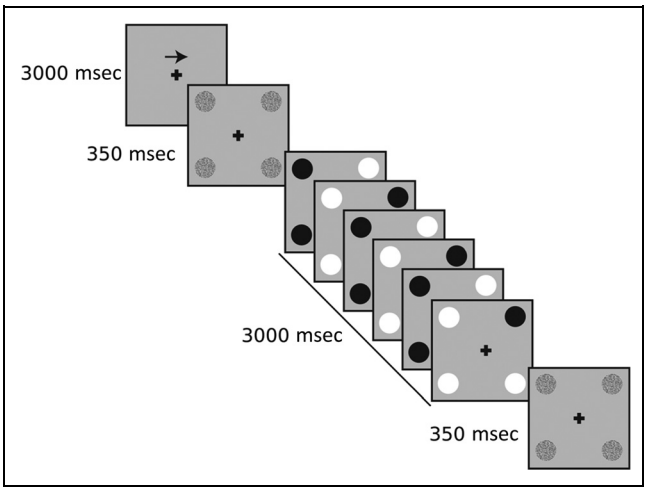

Figure 2. Simultaneity judgment task. (1) An arrow indicates whether to pay attention on the left or the right of a central fixation point. (2) At the beginning and at the end of the trial, a static texture pattern appears in the same position of the flickering stimuli. (3) Four disks, two displayed to the right and two to the left of a central fixation point, counterphase between black and white for 3000 msec. (4) Patients and controls are asked to judge whether two of the four disks (on the right or on the left visual field, randomly across trials) are in-phase or out-of-phase.

The ANOVA showed a main effect of Group ($F(1, 39) = 31.95$, $p \leq .001$, $\eta^2 = 0.621$), with right parietal patients' thresholds significantly lower relative to the age-matched controls' ($p \leq .001$, Bonferroni-corrected) and left parietal patients' thresholds ($p \leq .001$, Bonferroni-corrected). No differences were found between the left parietal patients and the age-matched control group ($p = .94$). Figure 3 shows left and right flicker thresholds for each group.

The Visual field ($F(1, 39) = 10.91$, $p \leq .002$, $\eta^2 = 0.219$) and the interaction between Visual field and Group ($F(2, 39) = 8.36$, $p \leq .001$, $\eta^2 = 0.3$) were also significant. To verify for which group the left and right thresholds were significantly different, we ran three paired-sample t tests (one for each group) with Visual field as repeated measure. We found a significant difference between left and right visual field performance for the left-parietal patients only ($t(18) = 6.5$, $p \leq .001$), indicating a higher flicker threshold for the left (10.86 Hz) than for the right visual field (8.92). No interhemifields difference was found for the right parietal patients ($p = .37$) nor for the control group ($p = .37$).

EXPERIMENT 1B: PATIENTS, TEXTURE TASK

In Experiment 1A, we showed that right parietal patients are critically impaired in phase discrimination, replicating the results found by Battelli et al. (2003). However one might argue that they simply could not discriminate contrast properly, and therefore, the deficit would not be ascribed to a high-level attentional dysfunction (Battelli et al., 2001). We therefore analyzed their low-level visual functions by testing a subgroup of the 18 right parietal patients on a contrast texture discrimination task.

Participants

A subgroup of eight right-parietal-lesioned patients (mean age = 72.3) and eight age-matched controls (mean age = 68.8) took part in the experiment.

Method

Stimuli consisted of a quartet of disks (in the same position as for the flicker task) appearing as stationary random grayscale texture patterns for the entire duration of the trial, visible until the participant gave a response. An experimenter recorded patients' answers by pressing one of two keys on the keyboard.

In a two-alternative forced-choice procedure, participants were asked to judge whether two of the four disks (either on the right or on the left visual field) were the same or different texture contrast (difference in Michelson contrast). Before stimulus presentation, a cue (an arrow pointing to the left or to the right of the visual field) appeared for 3 sec in the center of the monitor. On each trial, a randomly chosen disk was the target oddball with contrast texture pattern reduced relative to the remaining disks. Catch trials (no oddballs) were also interspersed in which all textures were of identical contrast to ensure that participants completed the task accurately by directing their attention to the cued hemifields.

The staircase procedure was the same as described above for the flicker task (3–1 double interleaved staircase). The reduction in the texture contrast was individually calibrated to yield 80% accuracy (step size: 0.5, difference in Michelson contrast). An incorrect response decreased task difficulty (i.e., increased texture contrast), whereas three consecutive correct responses increased task difficulty (i.e., decreased texture contrast).

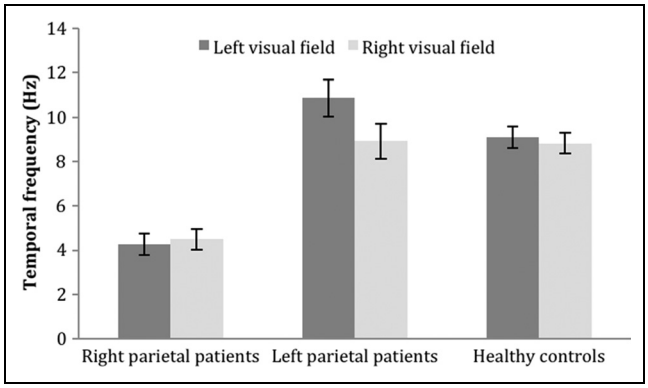

Figure 3. Flicker thresholds. Right parietal patients' thresholds ($n = 18$) are lower compared with healthy controls ($n = 18$) and left parietal patients ($n = 5$). Their thresholds are lower for both, left and right visual fields.

Data Analysis and Results

The dependent measure was texture contrast threshold (difference in Michelson contrast) for the left and right visual field. Patients required an average Michelson contrast difference of .59, whereas age-matched controls required an average Michelson contrast difference of .64, to accurately discriminate the same versus different texture contrast. A mixed ANOVA was run with Visual field (right vs. left) as within-subject factor and Group (right-parietal-damaged patients vs. age-matched controls) as between-subject factor. Neither the Visual field ($F(1, 14) = 1.65$, $p = .22$, $\eta^2 = 0.105$), nor the Group factor ($F(1, 14) = 1.74$, $p = .21$, $\eta^2 = 0.111$), nor their interaction ($F(1, 14) = 0.05$, $p = .82$, $\eta^2 = 0.004$) reached significance. No differences between right parietal patients and age-matched controls were found in low-level visual functions. Hence, the patients had intact low-level functions.

EXPERIMENT 2: TMS EXPERIMENT

In Experiment 1A, we showed that right parietal patients are impaired in discriminating whether two events are in-sync or out-of-sync in both visual fields compared with age-matched controls and left parietal patients. Moreover, we showed that this deficit does not depend on low-level visual impairment (Experiment 1B). It is important to note, however, that the lesions in the patients are quite heterogeneous within right parietal cortex, as is the time of testing relative to the onset of the lesion. As a result, drawing direct conclusions as exactly which cortical area is causally involved in computing relative timing in the healthy brain is difficult. There is clear functional and electrophysiological evidence in humans showing that the right inferior parietal lobule plays a critical role in nonspatial attention tasks (Park et al., 2016; Martinez-Trujillo, Cheyne, Gaetz, Simine, & Tsotsos, 2007; Claeys, Lindsey, De Schutter, & Orban, 2003; see Battelli et al., 2008, for a review). Therefore, in Experiment 2 we sought to extend our results by testing the causal role of the right parietal cortex in relative timing using inhibitory 1-Hz rTMS over the right TPJ in normal participants. We also compared performance before and after stimulation when stimulating over the left TPJ and left early visual area (EVA), which both served as control areas.

Participants

Ten healthy volunteers (six women, mean age 25, age range = 20–33) participated in the experiment. They were screened for TMS exclusion criteria, psychiatric and medical problems. All participants were right-handed and had normal or corrected-to-normal vision. They gave a written informed consent, approved by the ethics committee of University of Trento.

Materials and Procedure

This experiment was conducted on a 22-in. LCD Samsung 2233rz, connected to an Apple MacBook Pro laptop. The task in Experiment 2 was the same as the one described in Experiment 1A (Figure 2); with the exception that the presentation of the arrow cue was given at the end of the trial. We introduced this change to ensure participants kept attention engaged throughout the entire task, and they did not move their eyes from fixation, since the target side was unpredictable across trials. We also modified the entire duration of the flicker that was set to 750 msec instead of 3000 msec. Participants took on average 10–12 min to complete the task. Each participant completed four sessions, a pre-TMS baseline session and three subsequent post-TMS sessions.

TMS Protocol

Participants completed three 20-min sessions of 1-Hz rTMS over left TPJ, right TPJ, and left EVA. The sessions were completed at the same time of the day on three separate days. The order of stimulation conditions was randomly assigned for each participant. Stimulation was performed at an intensity of 65% of the stimulator output, with a commercially available figure-of-eight coil (7 cm in diameter) and a Magstim Rapid Magnetic Stimulator unit (Magstim Corporation, Whitland, UK).

To precisely target the stimulation site and keep the brain target constant throughout the stimulation session, we used a frameless stereotactic system (Brainsight, Rogue, Inc., Montreal, Canada) in conjunction with localization on each participant's individual anatomical brain MRI. Left and right TPJ was defined, as the intersection between the supramarginal, angular, and superior temporal gyri. MNI average coordinates of stimulation were −58, −53, 21 and 57, −54, 21 for the left and right TPJ, respectively.

Left EVA was localized functionally using phosphene induction (Fernandez et al., 2002). To select the stimulation location, we first marked on the head a location on the left hemisphere 2 cm rostral and 2 cm lateral to the inion. The experimenter then adjusted the coil location until a participant reported a phosphene. The resulting location was the target for TMS of EVA (average x, y, z coordinates: −15, −100, −12). The TMS coil was held in place tangentially to the scalp and oriented 45° to the central sulcus (for the right and left TPJ site) with the handle pointing posteriorly. For EVA stimulation, the handle was kept upward. All stimulation sessions were conducted with strict adherence to current safety guidelines and recommendations (Rossi, Hallett, Rossini, Pascual-Leone, & Safety of TMS Consensus Group, 2009; Wassermann, 1998).

Data Analysis and Results

The dependent measure was the flicker threshold (Hz). Flicker thresholds for the right and left visual field were

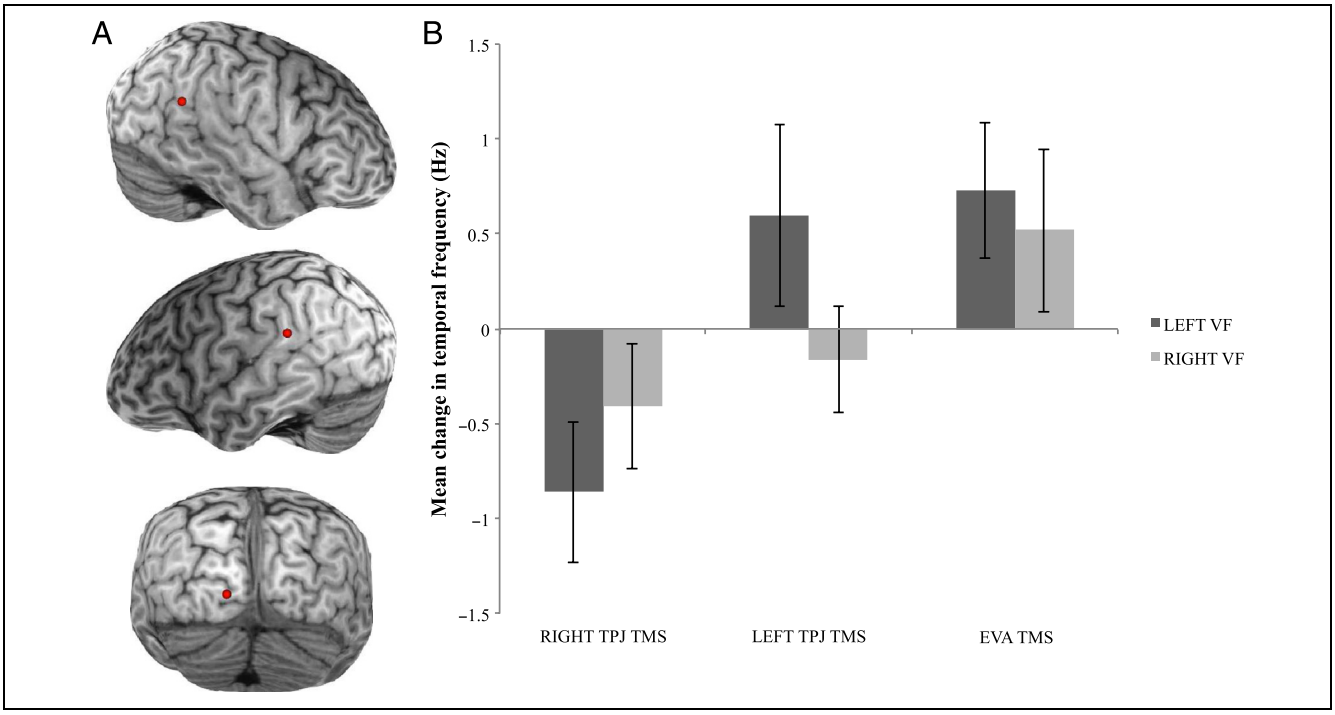

Figure 4. TMS experiment: change in the flicker threshold after stimulation. (A) 3-D brain reconstruction from a representative subject. The red dots indicate the location on the brain surface of the average MNI coordinates values (see text) for the 10 participants we tested, for the right TPJ (top), left TPJ (middle), and EVA (bottom). (B) Mean change in temporal frequency as a function of stimulation condition (right TPJ TMS, left TPJ TMS, and EVA TMS). Baseline thresholds were subtracted from the poststimulation thresholds so that positive numbers indicate improvement and negative numbers indicate impairment. After right TPJ stimulation, there was a significant bilateral impairment; no impairment was found after left TPJ nor for the EVA stimulation. Light gray bars indicate the right visual field, and dark gray bars indicate the left visual field.

measured before stimulation (pre-TMS) and after 20 min of rTMS (post-TMS).

For the baseline analysis, we tested prestimulation thresholds for effects of Session (pre-left TPJ vs. pre-right TPJ vs. pre-EVA) and Visual field (left VF vs. right VF) as within-subject factors. The ANOVA showed no main effects (Session: $F(2, 16) = 0.39$, $p = .68$; Visual field: $F(2, 16) = 0.651$, $p \leq .44$) nor interaction (Session × Visual field: $F(2, 16) = 1.88$, $p \leq .19$). Thus, no differences were found at baseline (pre-TMS) in the three prestimulation sessions. Average threshold for the left and right visual field were 11.17 and 10.96 Hz, respectively.

To study the effect of inhibitory 1-Hz TMS, we subtracted the baseline thresholds from the poststimulation thresholds, so that positive numbers indicated improvement and negative numbers indicated impairment. We then ran a repeated-measure ANOVA with Site of stimulation (right TPJ vs. left TPJ vs. EVA) and Visual field (right VF vs. left VF) as within-subject factors. The ANOVA showed a main effect of Stimulation site ($F(2, 18) = 6.353$, $p \leq .015$, $\eta^2 = 0.371$) and no effect of Visual field ($F(1, 9) = 0.529$, $p \leq .486$, $\eta^2 = 0.055$) nor their interaction ($F(2, 18) = 1.593$, $p \leq .231$, $\eta^2 = 0.15$). Planned pairwise comparisons showed that the threshold for right TPJ was significantly lower than for EVA ($t(9) = 4.1$, $p = .003$). A trend toward a significant difference in thresholds was found when comparing stimulations over right TPJ and left TPJ ($t(9) = -1.9$, $p = .096$). We found no difference in thresholds between the left TPJ and V1 stimulation ($t(9) = 1.0$, $p = .339$).

Moreover, to further investigate the improvement/impairment for stimulation over each brain area, we ran three one-sample t tests against zero, which indicates whether thresholds following stimulation are significantly changed relative to baseline. Thresholds following right TPJ indicated a significant impairment of the participants' performance after stimulation ($t(9) = 2.33$, $p = .045$), whereas stimulation over the left TPJ t test did not show any significant difference ($t(9) = -0.63$, $p = .543$). Finally, stimulation over the EVA trended toward significance ($t(9) = -2.04$, $p = .072$), indicating a tendency to an improvement after rTMS stimulation (Figure 4).

DISCUSSION

We used a simultaneity judgment paradigm to probe the discrimination of objects across time in parietal stroke patients. Our results clearly showed that patients with a right parietal lesion are severely impaired in visual relative timing, whereas patients with a left parietal lesion performed normally. Right parietal patients' performance was critically impaired in tasks requiring rapid discrimination of visual features across time across the entire visual field, in stark contrast to their spatial deficits lateralized to

the visual field contralateral to the lesion. The present results closely replicate the results previously found by Battelli and colleagues (Battelli et al., 2003, 2007, 2008) confirming a pivotal role of the right inferior parietal cortex in temporal attention. Critically, right parietal patients' performance is preserved for low-level visual features, as shown by the results in the contrast texture discrimination task. Interestingly, patients with a left parietal lesion overall performed like age-matched healthy controls, albeit left patients' performance was not equal across the two hemifields and paradoxically better than the controls in the left visual field. Altogether, this indicates that left parietal areas do not play a critical role in visual relative time processing (Battelli et al., 2003).

We subsequently hypothesized the potential involvement of the inferior parietal lobule in visual timing as suggested by previous neuroimaging and neuropsychological studies (Park et al., 2016; Tyler et al., 2015; Battelli et al., 2003), and we designed an inhibitory TMS experiment targeting the TPJ. TMS results confirmed the findings in the patients; specifically, in Experiment 2 we causally linked right (and not left) TPJ with visual temporal processing. Ten healthy volunteers underwent three sessions of 1-Hz inhibitory rTMS over right TPJ, left TPJ, and a control EVA. Results showed that TMS interfered with relative timing only when delivered over right TPJ, and the rTMS caused impairment in the flicker task in both visual fields, closely mimicking patients' results (Battelli et al., 2003).

Our present findings are in agreement with and extend the notion of the direct involvement of the right inferior parietal lobule in relative timing; however, few other studies found different results. For example, Davis, Christie, and Rorden (2009) found a bilateral (predominantly left) activation of TPJ in a temporal order judgment (TOJ) task, together with other parietal and frontal areas. Moreover, in a recent fMRI study, Binder (2015) found greater activation in left frontal and parietal areas when participants engaged in audiovisual TOJs as compared with simultaneity judgments. Finally, in a TMS study, Woo and colleagues (Woo, Kim, & Lee, 2009) stimulated participants' left and right posterior parietal cortex (P3 and P4, identified using the 10/20 EEG measurement system) while they were judging the temporal order of two consecutive visual stimuli presented on the left and right side of a central fixation. The authors found that TMS over right posterior parietal cortex (P4) delayed the detection of the left (contralateral) visual target *only*.

The difference between our findings and the results of Davis et al. (2009) and Woo et al. (2009) studies might be due to the differences in the tasks and methodological approaches. For example, the two previous studies that identified the left TPJ were both neuroimaging studies, which are tools that establish an association but not causal relation. In addition, in our task participants were asked to judge the simultaneity of two events always within the same visual field, eliminating the potential confounding factors of transmission delays between the two hemifields as a main cause of the deficit (Rorden, Mattingley, Karnath, & Driver, 1997). Interestingly, a recent study has shown that when two relative timing tasks, a TOJ and a simultaneity judgment task, are compared using the exact same stimuli (hence identical retinal stimulation), there are no hemifields' differences for the simultaneity judgment condition only (Matthews, Welch, Festa, & Clement, 2013), a result similar to what we found in this study.

Different tasks are likely to involve different cortical mechanisms, especially when both spatial and temporal components are manipulated. To reduce the spatial component of the task, we presented four disks on every trial, two in the right and two in the left visual field, and asked patients to judge only the disks in a single hemifield (either left or right). This is most similar to the work of Roberts et al. (2012), who studied the "point of subjective simultaneity" (i.e., point at which participants are equally likely to say that the left or right stimulus appeared first) to investigate the spatial component of the TOJ and the "just noticeable difference" (i.e., how long the interval between the stimulus onsets must be in order for the temporal order to be reported accurately) for the temporal deficits. They found that the spatial deficit was associated with damage to the contralateral temporoparietal cortex, whereas the temporal deficit was associated with lesions to the right hemisphere only, in particular the postcentral gyrus, the angular gyrus, and the superior temporal gyrus. These data are consistent with the results of the study presented here.

Interestingly, our study also indicates that TMS can help segregate the different functions of the superior and inferior parietal lobule for visuospatial and temporal tasks, respectively. For instance, stimulation of P4 and P3 (likely corresponding to the intraparietal sulci, IPS, in the right and left hemispheres, respectively) exerts a strong contralateral effect (Woo et al., 2009), demonstrating the well-known role of the IPS in spatial selective attention (Shulman et al., 2010; Corbetta & Shulman, 2002). However, TMS over more ventral regions within the TPJ, included in the inferior parietal lobule, more closely mimics the bilateral deficits in visual timing found in right-parietal-lesioned patients (Battelli et al., 2008; Husain & Rorden, 2003; Shapiro, Hillstrom, & Husain, 2002).

As a final remark, we should point out that in the present research we studied temporal attention in a less traditional way (Shapiro et al., 1994). Our experimental paradigm addresses relative timing between visual events and the ability to identify those events across time (Aghdaee et al., 2014; Battelli et al., 2007, 2008). This mainly entails bottom–up stimulus-driven perception in its ability to discriminate the order of events (and eventually act upon them). However, the visual environment has multiple dynamic stimuli that often must compete for attention; hence, a top–down mechanism might be necessary to select the relevant targets and inhibit irrelevant

stimuli (Serences et al., 2005). The change in frequency of the phase alternation sets the temporal limit to identify objects, and this limit never goes above 10 Hz for age-matched controls or slightly above 4 Hz for right parietal patients (Figure 3). This might indicate a capacity limit due to limited temporal resolution of attention. We believe that this task is particularly sensitive in identifying deficits in patients, while at the same time being easy to understand and thus suitable for the clinical population.

In conclusion, the present data strongly support a "when" pathway, with the right inferior parietal lobe playing a pivotal role in temporal attention computations for both visual fields (Aghdaee et al., 2014; Battelli et al., 2007, 2008). Specifically, the TPJ is identified as the core anatomical locus of the "when" pathway. Its disruption after stroke or TMS clearly demonstrates a direct involvement of the right TPJ in rapid individuation of objects across time. Our data also further demonstrate that patients with a right parietal lesion and affected by left visual neglect can also show severe visuoperceptual abnormalities in their "healthy" visual field, an aspect to keep in mind when planning cognitive rehabilitation (Vuilleumier & Rafal, 2000).

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