Interhemispheric coupling between the posterior sylvian regions impacts successful auditory temporal order judgment

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ABSTRACT

Accurate perception of the temporal order of sensory events is a prerequisite in numerous functions ranging from language comprehension to motor coordination. We investigated the spatio-temporal brain dynamics of auditory temporal order judgment (aTOJ) using electrical neuroimaging analyses of auditory evoked potentials (AEPs) recorded while participants completed a near-threshold task requiring spatial discrimination of left–right and right–left sound sequences. AEPs to sound pairs modulated topographically as a function of aTOJ accuracy over the 39–77 ms post-stimulus period, indicating the engagement of distinct configurations of brain networks during early auditory processing stages. Source estimations revealed that accurate and inaccurate performance were linked to bilateral posterior sylvian regions activity (PSR). However, activity within left, but not right, PSR predicted behavioral performance suggesting that left PSR activity during early encoding phases of pairs of auditory spatial stimuli appears critical for the perception of their order of occurrence. Correlation analyses of source estimations further revealed that activity between left and right PSR was significantly correlated in the inaccurate but not accurate condition, indicating that aTOJ accuracy depends on the functional decoupling between homotopic PSR areas. These results support a model of temporal order processing wherein behaviorally relevant temporal information – i.e. a temporal 'stamp' – is extracted within the early stages of cortical processes within left PSR but critically modulated by inputs from right PSR. We discuss our results with regard to current models of temporal of temporal order processing, namely gating and latency mechanisms.

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1. Introduction

Accurate processing of the order of sensory events on a sub-second time scale is crucial in both sensori-motor and cognitive functions (Mauk & Buonomano, 2004; Tallal, Merzenich, Miller, & Jenkins, 1998), and poor temporal processing has been implicated in a range of neurological and psychiatric conditions (e.g. Buhusi & Meck, 2005). Investigations of temporal discrimination have principally involved temporal order judgment (TOJ) tasks that require indicating which of two sequential stimuli was presented first. Irrespective of the sensory modality, a stimulus onset asynchrony (SOA) of ~30–60 ms is typically required for accurate TOJ performance (Hirsh & Sherrick, 1961; Pöppel, 1997; Swisher &

Hirsh, 1972), suggestive of a supramodal mechanism for temporal processing of sequences of distinct sensory events (Pöppel, 1997). Despite TOJ paradigms being extensively applied over the last decades, our understanding of the neural basis of TOJ specifically and temporal perception in general remains largely inferential.

From the extant neuroimaging and neuropsychological data, there is generally consensus that mechanisms supporting temporal discrimination are highly interactive with those mediating attention. However, it is controversial as to whether attention impacts the amplitude (McDonald, Teder-Sälejärvi, Di Russo, & Hillyard, 2005) and/or timing (Vibell, Klinge, Zampini, Spence, & Nobre, 2007) of brain activity during temporal processing. Still others focused specifically on the neural basis of accurate TOJ performance and found there to be increased AEP amplitudes ~200 ms post-stimulus (i.e. over the P2 component) during difficult versus easy TOJ conditions (Lewandowska, Bekisz, Szymaszek, Wrobel, & Szelaq, 2008). Additionally, these authors observed a significant positive correlation between the behavioral difference between conditions and the difference in P2 amplitude. Although these

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authors interpreted their findings as an index of TOJ processing, an alternative possibility is that their effect was driven by either varied attention and/or acoustics between the conditions. These results thus leave unresolved the brain dynamics of TOJ. More recently, Davis, Christie, and Rorden (2009) used functional magnetic resonance imaging (fMRI) to identify left temporo-parietal cortices as the mediator of visual TOJ, while also controlling for differences both with regard to participants' level of attention and also the physical properties of the stimuli (identical stimuli were used for both the TOJ and shape discrimination tasks). In agreement, patients with damage to the left temporo-parietal cortices exhibit impaired TOJ performance (e.g. Wittmann, Burtscher, Fries, & von Steinbüchel, 2004). Data nonetheless also suggest that right temporo-parietal structures might likewise play a role in TOJ performance. For example, Woo, Kim, and Lee (2009) reported that transcranial magnetic stimulation of the right, but not left, posterior parietal cortex impaired visual TOJ performance when applied 50 or 100 ms post-stimulus onset. Numerous other studies likewise implicate right-lateralized structures and their associated role in attention in influencing TOJ performance (Eagleman, 2008).

At least two aspects of the brain mechanisms of TOJ remain unknown and were the focus of the present study. First, it is unknown when during the course of stimulus processing a temporal 'stamp' is established to guide TOJ perception. Second, the extent of interplay between the cerebral hemispheres in engendering accurate TOJ performance is unresolved. To address these issues, we applied electrical neuroimaging analyses (Murray, Brunet, & Michel, 2008) to AEPs in response to accurate and inaccurate aTOJ performance.

2. Materials and methods

2.1. Participants

Twelve right-handed and one ambidextrous males, aged 21–28 years (mean ± SEM: 24.38 ± 0.7 years) participated in the study. Handedness was assessed with the Edinburgh questionnaire (Oldfield, 1971). No subject had a history of neurological or psychiatric illness, and all reported normal hearing. Each subject provided written, informed consent to procedures approved by the Ethics Committee of the Faculty of Biology and Medicine of the Centre Hospitalier Universitaire Vaudois and the University of Lausanne.

2.2. Stimuli and task

Stimuli were pairs of 10 ms duration white noise bursts (1 ms rise/fall time; 44,100 Hz digitization, generated using Adobe Audition 2.0) presented via insert earphones (model ER-4P; Etymotic Research) at 86 dB SPL either to the left and then to the right ear (left–right or LR) or alternatively to the right and then the left ear (right–left or RL). Within a pair, the sounds were separated by a constant stimulus onset asynchrony (SOA). For each subject, the SOA was individually adjusted before the experiment using an auto-adaptative one up–two down staircase procedure (starting at 60 ms SOA, with steps of 5 ms, over 60 trials) to reach a near-threshold difficulty level. The SOA ranged from 15 to 80 ms across participants (mean SOA ± SEM = 26.15 ± 5.04 ms). In the EEG experiment, participants completed 6 blocks of trials. Each block was composed of 200 pairs of sounds, resulting in a total of 600 pairs for each side condition (LR or RL), the order of which was randomly determined. After each pair of sounds, subjects were required to respond with their right hand within 2000 ms after trial offset by pressing the left response-box button when they perceived an LR pair and the right button when they perceived an RL pair, using two fingers of the same (right) hand for both responses. Visual feedback was given 1000 ms after responding, indicating whether the response was accurate (green square), inaccurate (red square), or no answer (yellow square). The next trial was presented 1000 ms after the presentation of the feedback. Subjects were instructed to respond accurately rather than quickly. The experiment was conducted in an acoustically attenuated and electrically shielded booth. Participants fixated a central cross while listening to the stimuli. Stimulus/feedback delivery and participant's responses were controlled by Eprime 2.0 software (Psychology Software Tools, http://www.pstnet.com/eprime).

2.3. EEG acquisition and preprocessing

Continuous EEG was recorded at 1024 Hz though a 128-channel Biosemi ActiveTwo system referenced to the CMS-DRL ground, which functions as a feedback loop driving the average potential across the montage as close as possible to ampli-

fier zero (Biosemi, Amsterdam, Netherlands). Peri-stimulus EEG epochs (100 ms pre-stimulus to 500 ms post-stimulus onset) were averaged according to response accuracy, yielding two experimental conditions (accurate and inaccurate). LR and RL pairs were averaged together, to ensure that any difference between accurate and inaccurate AEPs did not follow from differences in spatial perceptions, but rather from processes related to temporal order per se. Trials with blinks, eye movements, or transient noise were rejected using a semi-automated ±80 μV criterion and visual inspection. In order to maintain equivalent signal-to-noise ratios for AEPs leading to accurate and inaccurate performance, the same number of trials was included from each condition for a given subject. This was achieved in the following manner. First, performance was evaluated across all 6 blocks completed by a given subject in order to identify the lowest performance rate within a block (i.e. either the lowest percent of correct responses or incorrect responses). This value was then used to determine the number of EEG epochs included in the AEP for both trial types from each block. The average number of accepted EEG epochs per condition across the 6 blocks was: accurate: 307 ± 135 and inaccurate 301 ± 138. There were no significant differences between the number of accepted epochs ($t(12) = 1.43$; $p > 0.2$). Trials with no responses were not considered in the averaging. Prior to group-averaging, data at artifact-contaminated electrodes from each subject were interpolated using 3D splines (Perrin, Bertrand, & Pernier, 1987). Data were then recalculated against the average reference, band-pass-filtered (0.68–40 Hz), and baseline corrected using the pre-stimulus period.

In order to ensure that post-stimulus effects on the baseline corrected data set were not the consequence of DC offsets during the pre-stimulus period and/or anticipatory activity; analyses were also performed without the application of the pre-stimulus baseline correction. As the results without applying baseline correction were identical to those obtained with applying baseline correction, we present only the latter. All analyses were always conducted over the full AEP epoch (i.e. from 100 ms pre- to 500 ms post-stimulus onset) both when baseline correction was and was not applied.

Behavioral data were analyzed according to signal detection theory (Macmillan & Creelman, 1991). Sensitivity (d') was calculated according to the following formula: $d' = z(H) − z(FA)$; where $z(H)$ and $z(FA)$ represent the transformation of the hit (H) and false-alarm (FA) rates into z-scores (Green & Swets, 1966). Hits were the LR trials reported as LR and false-alarms were RL trials reported as LR (as the same number of LR and RL pairs were presented, the d' is symmetrical; hit + miss = false − alarms + correct rejection = 100%. Therefore, the d' would be identical if correctly perceived RL pairs were considered as Hits and LR trials reported RL as false-alarms). Consequently, the d' index takes into account the global behavioral performance. This calculation of d' reflects the sensitivity to both LR and RL pairs and provides an appropriate index of behavioral performance with regard to our electrophysiological analysis procedure in which LR and RL pairs were collapsed together.

2.4. EEG analyses and source estimation

Topographic analyses were performed to determine whether the configuration of intracranial generators changed with aTOJ accuracy. These methods have been detailed elsewhere, and have many analytical and interpretational benefits over canonical AEP waveform analyses (Murray et al., 2008). We provide only the essentials here. Major impetuses for the use of the present analyses were the ability to circumvent interpretational issues due to the reference-dependent nature of AEPs and to differentiate effects arising from topographic modulations from effects owing to changes in response strength. Moreover, the analyses used here require minimal a priori selection either of the electrodes or time periods of interest, which are two major sources of potential bias in AEP investigations.

Hierarchical clustering was performed to identify the pattern of predominating topographies (maps) in the cumulative group-averaged data. This is a hypothesis generation tool that is then statistically evaluated using single-subject data. Differences in the pattern of maps observed between conditions in the group-average data were tested by calculating the spatial correlation between these "template" maps from the group-average data and each time-point of single-subject data from each experimental condition (referred to as "fitting"). The resultant amount of time a given template map has the highest spatial correlation thus provides a measure of how well (in milliseconds) a given template map accounts for a given condition (i.e. map presence) over a specific time period. Because two template maps were identified (detailed below) and because map presence forcibly sums to a common value across template maps, a non-parametric Wilcoxon signed rank test was conducted.

Modulations in the strength of the electric field at the scalp were assessed using global field power (GFP; Lehmann & Skrandies, 1980) for each subject and stimulus condition. GFP is calculated as the square root of the mean of the squared value recorded at each electrode (versus the average reference) and represents the spatial standard deviation of the electric field at the scalp. It yields larger values for stronger electric fields. We analyzed GFP waveform data from all electrodes as a function of time post-stimulus onset in a series of pair-wise comparisons (t-tests). Correction was made for temporal auto-correlation at individual electrodes through the application of an 11 contiguous data-point temporal criterion for the persistence of differential effects (Guthrie & Buchwald, 1991).

We estimated the sources in the brain using a distributed linear inverse solution applying the local autoregressive average (LAURA) regularization approach

(Grave de Peralta Menendez, Andino, Lantz, Michel, & Landis, 2001; Grave de Peralta Menendez, Murray, Michel, Martuzzi, & Gonzalez Andino, 2004; also Michel et al., 2004 for a comparison of inverse solution methods). LAURA selects the source configuration that better mimics the biophysical behavior of electric fields (i.e. activity at one point depends on the activity at neighboring points according to electromagnetic laws). Homogenous regression coefficients in all directions and within the whole solution space were used. The solution space is based on a realistic head model and included 4024 nodes selected from a 6 mm × 6 mm × 6 mm grid equally distributed within the gray matter of the Montreal Neurological Institute's average brain (courtesy of R. Grave de Peralta Menendez and S. Gonzalez Andino; http://www.electrical-neuroimaging.ch/). The results of the above topographic pattern analysis defined time periods of stable topography for which intracranial sources were estimated and compared between conditions.

3. Results

Behaviorally, participants' mean percent correct (±SEM) was 68.1 ± 3% and did not differ between the LR and RL conditions (mean percent correct ± SEM = 68.8 ± 4% in the LR and 67.4 ± 3% in the RL condition; Wilcoxon signed rank: $t(12) = 0.80$; $p = 0.4$). Mean (±SEM) d' was 1.01 ± 0.2, which was indicative of near-threshold sensitivity.

The cluster analysis applied to the AEPs identified the same sequence of template maps both for trials resulting in accurate and inaccurate performance with the exception of the 39–77 ms post-stimulus interval (Fig. 2; see Fig. 1 for an exemplar AEP waveform (F4)). The global explained variance of the results of the cluster analysis was 98.31%. The spatial correlation of each of these two maps identified in the group-averaged AEPs was then calculated with the single-subject data from each condition to obtain a measure of map presence (Fig. 2). One map better correlated with and thus better accounted for responses to the accurate condition and another for the inaccurate condition (Wilcoxon signed rank: $t(9) = 2.6$; $p < 0.01$). This result indicates that topographic differences, and by extension distinct configurations of intracranial generators, account for accurate and inaccurate temporal order judgments. Analyses of global field power, by contrast, failed to reveal any significant sustained modulations in response strength.

The group-average AEP topography from each condition over the 39–77 ms is shown in Fig. 3. Both conditions exhibited frontal positivity that was right-lateralized. The mean difference topography is shown in Fig. 3 and exhibited at general dipolar configuration over the right PSR. Because the electric field topography at the scalp provides limited direct interpretability with regard to the likely intracranial sources, LAURA distributed source estimations were calculated. For these, AEPs for each subject and each experimental condition separately were first averaged across the 39–77 ms post-stimulus time period. Source estimations were then calculated and subsequently averaged across subjects (Fig. 3). The left and right posterior sylvian regions were activated for both accurate and inaccurate conditions (left maxima at [−53, −28, 3 mm] and right maxima at [53, −28, 8 mm], using the coordinate system of Talairach & Tournoux, 1988). While we highlight the maxima

here, it is important to note that the source estimations were distributed and likely encompassed several homologous functional regions within each hemisphere. The scalar values of left and right PSR maxima were extracted for each subject and condition and submitted to a non-parametric correlation analysis (Spearman's rho). The difference in activity between accurate and inaccurate conditions negatively correlated with sensitivity within the left PSR only (Spearman's rho left PSR $r(11) = -0.70$; $p < 0.02$; right PSR $r(11) = -0.25$; $p < 0.4$), indicating that the lower the left PSR was activated in the accurate as compared to the inaccurate condition, the higher was the participant's performance. Additional correlation analyses were conducted to examine the extent to which the magnitude of left and right PSR activity was coupled. There was a significant positive correlation between left and right PSR activity in the inaccurate ($r(11) = 0.66$; $p < 0.03$), but not accurate condition ($r(11) = 0.31$; $p < 0.28$). Functionally coupled responses were observed only when performance was inaccurate.

4. Discussion

We identified the spatio-temporal correlates of accurate near-threshold auditory spatial temporal order judgments. By contrasting AEPs to sound pairs as a function of aTOJ accuracy, we revealed that reduced activity within the left temporal cortex over the 39–77 ms post-stimulus period is associated with successful discrimination as compared to inaccurate aTOJ performance, which was associated with bilateral superior temporal activity. In addition, activity within the left, but not right, posterior sylvian regions predicted performance accuracy. Moreover, correlation analysis revealed variation of functional connectivity between left and right PSR according to performance accuracy. Specifically, the activity between these homotopic regions was correlated in the inaccurate but not in accurate condition, suggesting that the level of functional connectivity between PSR areas impacts temporal order perception accuracy. These results support a model of temporal order processing wherein behaviorally relevant temporal information – i.e. a temporal 'stamp' – is extracted within left PSR during the early stages of cortical processes, but critically modulated by inputs and/or activity of right PSR.

AEP modulations between accurate and inaccurate aTOJ manifested over the 39–77 ms post-stimulus period and were the result of changes in the topography of the electric field at the scalp (and by extension in the underlying configuration of intracranial sources). The latency of this effect supports (at least) two conclusions regarding aTOJ. First, behaviorally relevant brain processes contributing to accurate aTOJ occur during early stages of cortical processing. Converging evidence demonstrates initial cortical responses around 15–20 ms post-stimulus onset within core auditory cortices in humans (Cacace, Satya-Murti, & Wolpaw, 1990; Liégeois-Chauvel, Musolino, Badier, Marquis, & Chauvel, 1994; Pelizzone et al., 1987; Ponton, Eggermont, Khosla, Kwong, & Don, 2002; Yvert, Crouzeix,
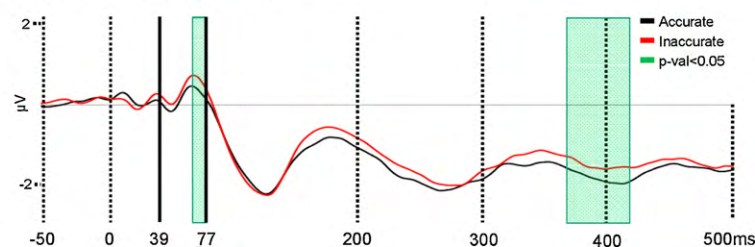
1. Exemplar AEP Waveform (F4)

Fig. 1. Exemplar AEP waveform (F4) from the accurate (black) and inaccurate (red) condition (only the first 300 ms are represented). The time period with a significant difference between accurate and inaccurate conditions is indicated in green ($p < 0.05$). (For interpretation of the references to color in this figure caption, the reader is referred to the web version of the article.)
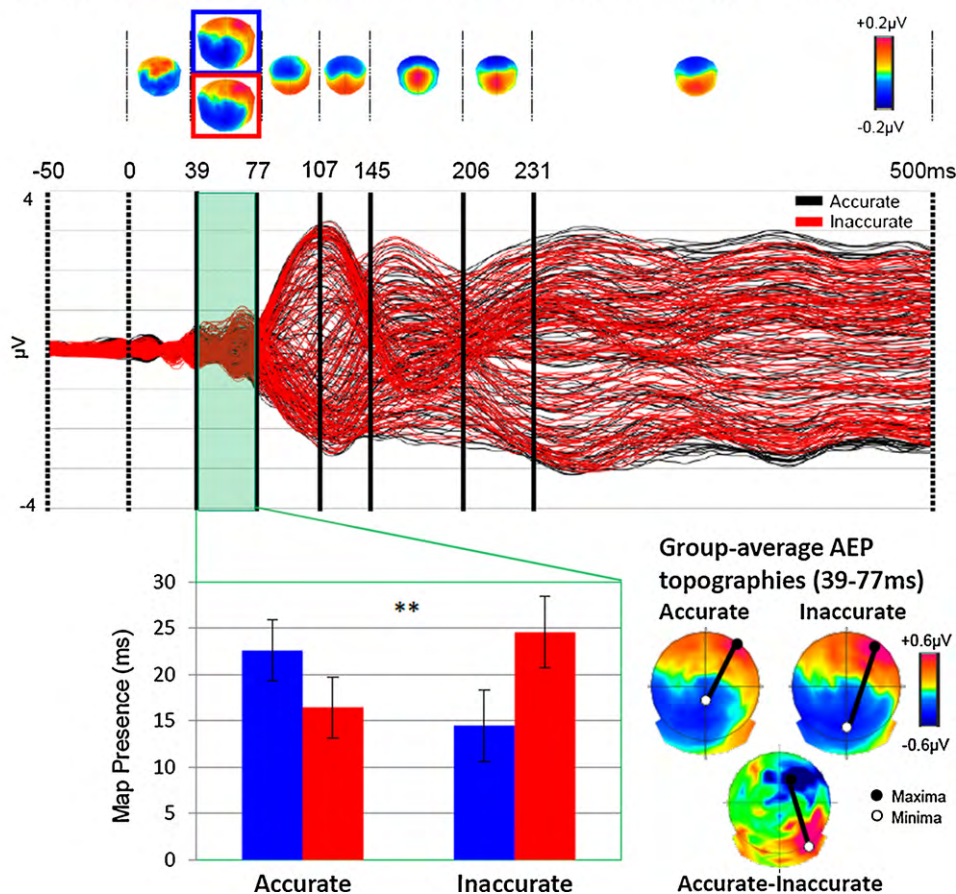
Fig. 2. Electrical neuroimaging results. (a) The topographic pattern analyses identified 7 time periods of stable topography across the collective 500 ms post-stimulus onset. All topographies (i.e. maps) are shown with the nasion upwards and left scalp leftwards. For one of these time periods (39–77 ms), two maps were identified in the group-average AEPs. These maps are framed. The reliability of this observation at the group-average level was then assessed at the single-subject level using a spatial correlation fitting procedure (see Section 2). Over the 39–77 ms period following stimulus onset, different maps (framed in blue and red; maxima and minima indicated) described AEPs in response to the accurate and inaccurate conditions. The blue map better accounted for the accurate condition and the red for the inaccurate condition. ** means $p < 0.01$. (For interpretation of the references to color in this figure caption, the reader is referred to the web version of the article.)

Bertrand, Seither-Preisler, & Pantev, 2001). Propagation to adjacent cortices has been documented to require an additional 2–3 ms, and responses within distant cortices have been reported within the ensuing 20–50 ms (e.g. Inui, Okamoto, Miki, Gunji, & Kakigi, 2006). These studies document on the one hand that the present effects at 39–77 ms post-stimulus onset are in many regards not 'early'. Such being said, however, studies that have examined response modulations with stimulus features tend to observe effects (e.g. due to spatial and pitch variation, De Santis, Clarke, & Murray, 2007) from post-stimulus latencies of roughly 100 ms onwards. Consequently, in light of the functional data we consider the present effects to be occurring during early processing stages, even if not forcibly early along a sensory responsiveness hierarchy.
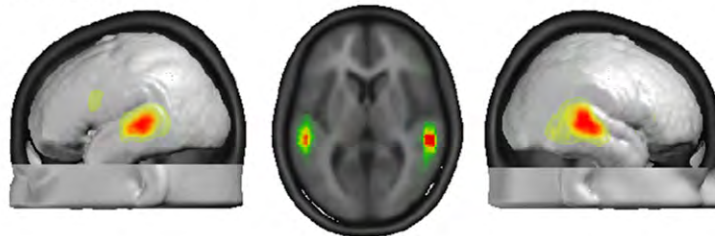
Second, the latency of our effect argues against previous reports suggesting that features by which stimuli differ might contribute to the judgment required by temporal ordering (e.g. luminance profile: Jaśkowski, 1993, stimulus dimension: McFarland, Cacace, & Setzen, 1998) as only few stimulus dimensions are integrated around 60 ms post onset (at least within the visual modality). For instance, it has been proposed that spatial information might be one feature used for temporal coding (Swisher & Hirsh, 1972; Jaśkowski, 1996). The latency of our effects would speak against a role for spatial encoding in temporal order perception (at least in the current paradigm), because our previous studies indicate that while spatial information is already partially processed during the first

15 ms post-stimulus onset along the ascending auditory pathways, spatial representations are built-up starting around 100 ms post-stimulus onset (e.g. Murray & Spierer, 2009; Spierer, Bourquin, Tardif, Murray, & Clarke, 2009; Spierer, Murray, Tardif, & Clarke, 2008; Spierer, Tardif, Sperdin, Murray, & Clarke, 2007). Moreover, a cancellation of the effects of space was obtained by collapsing across LR and RL pairs during the AEP averaging procedure. If specific stimulus features participated in TOJ, their effects on behavior would manifest at a later latencies, during processing stage involved in their encoding, suggesting that our effects related to the first sound at 39–77 ms likely reflect a spatial feature-independent process. It is also worth mentioning that the latency of the present effects is not the consequence of pre-stimulus baseline correction nor modulations in brain state over the 100 ms prior to stimulus presentation. That is, there is no evidence that subjects were attending to a particular feature and/or spatial location in a manner that systematically affected ongoing brain activity to in turn affect stimulus-locked processing.
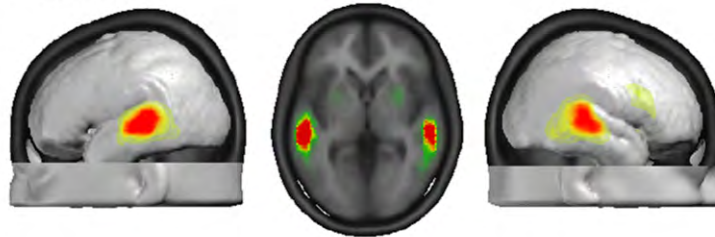
Our results suggest that a temporal "stamp" to the first-occurring stimulus is established during the initial 60 ms post-stimulus onset and determines TOJ accuracy. However, due to the individual adjustment of the SOAs, the second sound of each pair was presented at a constant delay at the single-subject level, but was presented at different delays across participants. Therefore, by averaging AEPs across subjects, a jitter was induced in AEPs
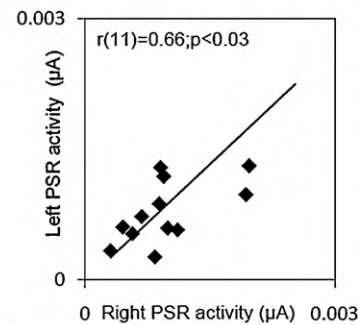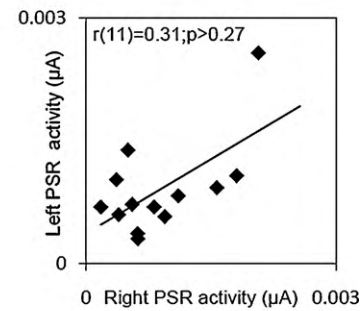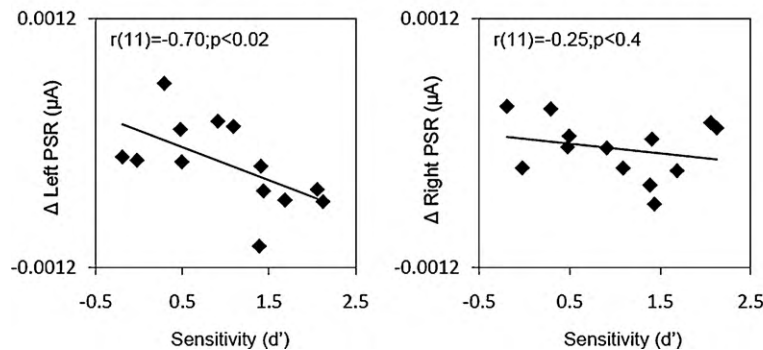
Fig. 3. LAURA source estimations. Over the 39–77 ms period following stimulus onset, accurate and inaccurate conditions exhibited activity within posterior sylvian regions (PSR). (a) A correlation between the accurate–inaccurate activity difference and performance sensitivity (d') showed that the more the left PSR was activated in the accurate versus inaccurate condition, the lower subjects' sensitivity in judging the order of stimuli occurrence. No significant correlations were evident for the right PSR. (b) The activity between left and right PSR was significantly correlated in the inaccurate but not accurate condition.

to the onset of the second sound, potentially masking differences between accurate and inaccurate conditions occurring during the processing of this latter stimulus. Among other TOJ related processes, masked differences in response to the second sound could have been related to feature dependent processes.

In addition to its latency, the present effect also provides information about putative mechanisms of aTOJ, including interhemispheric interactions. Our result of a significant correlation between activity within left but not right PSR and behavioral sensitivity is consistent with prior functional imaging, clinical and anatomical studies showing a prominent role for a left temporal network in TOJ. Using fMRI, Davis et al. (2009) found a selective activation pattern within the left TPJ during a visuo-spatial TOJ versus shape discrimination task performed on physically identical stimuli. Similarly, lesion data demonstrate TOJ performance impairments following left temporo-parietal damage (see also Ehrlé, Samson, & Baulac, 2001; Swisher & Hirsh, 1972; von Steinbüchel, 1998; Wittmann et al., 2004). Evidence for greater involvement of left than right supratemporal plane in the pro-

cessing of auditory temporal features (sequential processing, fast spectral variation, etc.; Samson, Ehrlé, & Baulac, 2001; Zaehle, Jancke, Herrmann, & Meyer, 2009; Zatorre, Belin, & Penhune, 2002), as well as greater temporal resolution for left auditory cortices (Belin et al., 1998), further supports left hemispheric functional specialization for temporal processing.[1] Converging evidence reveals that as compared to right temporal cortices, left supratemporal structures comprise neuroanatomical properties compatible with faster transmission and more efficient temporal processing including a larger number of cells, greater connectivity and more heavily myelinated neurons (e.g. Hyde, Peretz, & Zatorre, 2008; Zatorre & Belin, 2001). We interpret the present finding of the negative

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[1] We would note that the lack of correlation between right PSR activity and sensitivity could have resulted from factors including insensitive measures, inadequate sampling, or weak manipulations. However, that our analyses were sensitive enough to reveal a significant correlation between left PSR activity and behavioral sensitivity (i.e. other levels of the same factors) supports that the lack of correlation between d' and right PSR does not follow from the above-mentioned factors.

correlation between left PSR activity and sensitivity, as suggesting that precise temporal stamping of the sound occurrence could putatively rely on the engagement of a restricted population of temporally sharply tuned neurons (c.f. Ohl and Scheich, 2005 for review of plasticity mechanisms in audition).

Our results further revealed that over the 39–77 ms interval, the activity between left and right PSR was correlated in the inaccurate but not in the accurate condition. We interpret the degree of correlation between these two regions as reflecting the extent of functional connectivity, or coupling, between posterior temporal homotopic areas. According to this hypothesis, our results suggest that in a near-threshold context, TOJ is facilitated when temporal processing occurring within left PSR is released from an interfering influence of the right PSR. Due to the anatomo-functional disadvantage of the right PSR for processing rapid auditory temporal variations (e.g. Zatorre & Belin, 2001), activity within right PSR could have interfered with temporal integration mechanisms occurring in the contralateral (left) homotopic region. Such is not to discount the likely role of right-lateralized activity related to attentional processes and their contribution to temporal functions.

Alternatively, it could be hypothesized that the accurate condition regrouped easily perceived trials and the inaccurate condition difficult trials. Consequently, the contrast between these conditions putatively revealed differences in the difficulty to perceive the temporal order of the stimuli rather than accuracy per se. According to this hypothesis, the correlation between left and right PSR in the inaccurate but not accurate condition could have followed from an additional engagement of right-lateralized (attentional) processes under difficult conditions. A strong version of this hypothesis would predict that subjects with the worst performance would exhibit the strongest right-hemisphere PSR response. Based on the absence of correlations between right PSR in the incorrect and correct condition and sensitivity (p-values > 0.5), there was no evidence that this was the case.

These hypotheses could also account for previous reports that right-lateralized processes, including attention, influence left hemispheric temporal processing functions. Based on the evidence for the influence of attention on temporal order perception (e.g. Jaśkowski & Verleger, 2000; Stelmach & Herdman, 1991; Zackon, Casson, Zafar, Stelmach, & Racette, 1999), numerous investigations used selective attentional factors as independent variables to reveal the neurophysiological mechanisms mediating TOJ. Consequently, right-lateralized attentional functions were assumed to potentially influence relative timing tasks. These studies advanced that temporal order perception could depend on gating and/or latency mechanisms, respectively reflected by increases in ERP amplitude and/or decreases in the processing latency to attended versus unattended stimuli (see Vibell et al., 2007 for discussion).

Support for the involvement of gating mechanisms in TOJ comes from studies showing that the manipulation of exogenous attentional cues induces shifts in the point of subjective simultaneity accompanied by a gain in the amplitude of early visual evoked potentials (Anllo-Vento, Schoenfeld, & Hillyard, 2004; Eimer, 1998, 2004; Hillyard & Anllo-Vento, 1998; Luck, Woodman, & Vogel, 2000; Mangun, 1995). Gating would rely on an active inhibitory network, designed to reduce the flow of redundant sensory information associated with sensory overload (Adler et al., 1982; Kisley, Noecker, & Guinther, 2004). As accurate TOJs require unbiased perception of the first and/or second sound of the pair, they cannot be achieved if the processing of each of the two sounds interferes with each other. An adequate gating of the first sound would therefore facilitate TOJ by inhibiting the response to the second sound. While gating mechanisms typically manifest around 50 ms post-stimulus onset, a time period corresponding to the latency of the present effects (e.g. Huotilainen et al., 1998; Mäkelä, Hämäläinen, Hari, & McEvoy, 1994; Pelizzone et al., 1987; Reite, Teale, Zimmerman,

Davis, & Whalen, 1988; Yoshiura, Ueno, Iramina, & Masuda, 1995), it is unlikely that a gating mechanism explains our results as we found that accurate aTOJ was associated with a reduction of left PSR activity, rather than in a gain in response strength to the first sound as would be expected according to the gating hypothesis. Additionally, pure gating mechanisms would have likely manifested as a modulation in global field power in the absence of topographic modulations. Such being said, it is possible that gating-like mechanisms are indeed operating at a finer scale that what is currently resolved with high-density EEG. That is, super-imposed neuronal populations may be responding in opposite manners that would in turn appear as a null effect at the scalp surface. Additional data from other imaging methods and/or from invasive recordings would be needed to address this possibility.

More consistent with our results is the alternative prior entry hypothesis, which proposes that TOJ depends on the processing speed of sensory stimuli that in turn determines their order of arrival into consciousness (Titchener, 1908); though the precise neurophysiologic mechanism for such remains controversial. Accordingly, the general threshold model (Stelmach & Herdman, 1991; Ulrich, 1987), postulates that TOJ might depend on the arrival time of the sensory information at a hypothetical "temporal comparator"; Though our ERP measures cannot disentangle the neurophysiological mechanisms modulating the arrival time of auditory information, current hypotheses posit that the arrival time could depend on parameters including transduction time or transmission latencies of the information from the receptor to a comparator (Pöppel, 1988; Stelmach & Herdman, 1991). In an electrophysiological study using a cross-modal TOJ task while shifting attention between the visual and tactile modalities, Vibell et al. (2007) supported the prior entry hypothesis by showing that attention shifts the latency of visual evoked potentials, suggestive of a speeding-up of sensory processing. While indirectly, our pattern of results speaks in favor of prior entry as putative mechanism for temporal order perception as the topographic modulation could also result from a (rapid) latency shift across conditions. However, such latency shift was not evident from the visual inspection of AEP waveforms. Differences in stimuli processing prioritization might therefore account for our effect. In that sense, inputs from right PSR might have perturbed the processing latency, rather than or in addition to, the temporal stamping mechanisms occurring within left PSR. Greater interference from right to left superior temporal areas could have resulted from the higher level of functional coupling we found the inaccurate than accurate condition.

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