

Neural mechanisms of movement speed and *tau* as revealed by magnetoencephalography

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Abstract A fundamental aspect of goal-directed behavior concerns the closure of motion-gaps in a timely fashion. In this context, the critical variable is the time-to-closure, called *tau* (Lee in Perception 5:437–459, 1976), and is defined as the ratio of the current distance-to-goal gap over the current instantaneous speed towards the goal. In this study, we investigated the neural mechanisms of speed and *tau* in pointing hand movements by recording MEG

activity from the whole brain of 20 right-handed healthy human subjects operating a joystick with their right hand. The relations between neural signals and speed and *tau* were analyzed using an autoregressive multiple regression model, where the time-varying MEG signal was the dependent variable and the corresponding value of speed and *tau* were the independent variables. With respect to speed, we found that 81% of sensors showed significant relations over the left frontal-parietal, left parieto-temporal, and, less prominently, the right temporo-occipital sensor space. These results document the widespread involvement of brain areas with movement speed, especially in the left hemisphere (i.e., contralateral to the moving limb), in accord with previous studies. With respect to *tau*, 22% of sensors showed significant relations over the parietal (bilaterally), right parietal-temporal, and, less prominently, the left temporo-occipital sensor space. The *tau* effects often occurred concurrently with speed effects and spatially overlapped in the left fronto-parietal sensors. These findings document for the first time the time-varying, dynamic processing of information regarding *tau* in specific brain areas, including the right parietal cortex. This is of special interest, for that area has been found to be involved in processing information concerning the duration of time intervals in perceptual tasks (Harrington et al. in J Neurosci 18:1085–1095, 1998; Rao et al. in Nat Neurosci 4:317–323, 2001). Since *tau* is itself a time interval, we hypothesize that the right parietal focus of *tau* processing observed in this study reflects the ongoing processing of *tau* as an interval for a timely arrival of the hand to the target.

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Introduction

A fundamental aspect of goal-directed behavior concerns the closure of motion-gaps in a timely fashion. In this context, the critical variable is the time-to-closure, called *tau* (Lee 1976) and defined as the ratio of the current distance-to-goal gap over the current instantaneous speed toward the goal. Such timing information is available to the sensory system from the environment (Lee 1976, 1998; Lee et al. 1992). Numerous behavioral studies have implicated the role of such *tau* information in guiding behavior in both animals (Lee and Reddish 1981; Lee et al. 1992, 1995) and humans (Craig and Lee 1999; Craig et al. 1999, 2000a, b; Lee et al. 1999, 2001). There is accumulating evidence from neurophysiological studies (see review by Merchant and Georgopoulos 2006) that the nervous system can represent temporal information like *tau*. In a certain population of thalamic neurons (within nucleus rotundus) in pigeons, neural activities were found to signal the relative rate of expansion or ‘time-to-contact’ in response to looming visual stimuli (Sun and Frost 1998; Wang and Frost 1992). In addition, the neural activity in monkeys’ primary motor (M1) and posterior parietal (area 7a) cortices has been shown to vary significantly with *tau* as the animals intercepted a moving target (Merchant and Georgopoulos 2006; Merchant et al. 2004a, b). In particular, the neural activity, best related to the *tau* variable, increased as the time-to-contact between target and interception-zone decreased. Such *tau*-ramps as observed in parietal and (especially in) motor areas are useful signals for initiating interception because they provide neural correlates of ‘time-to-closure’ of motion gaps.

Interestingly, similar ramping activities found to be associated with the *tau*-variable have also been observed in the lateral-inferior parietal (LIP) neurons of the posterior parietal cortex (Leon and Shadlen 2003), which varied systematically with the monkey’s perception of elapsed time. A recent functional magnetic resonance imaging (fMRI) study offers complementary findings that showed the activation of sensorimotor areas and motion-sensitive area MT during perceptual judgments of ‘time-to-collision’, gap-closure, and size-expansion in humans (Field and Wann 2005). In addition to the activations within the sensorimotor regions observed during the gap-closure task, the authors also reported a unique involvement of the ventral portion of the premotor cortex, the bilateral superior parietal sulci, and the marginal ramus; areas implicated in cognitive processing to solve visuo-spatial tasks (Buneo and Andersen 2006; Graziano and Cooke 2006; Kakei et al. 2001). Therefore, in both the perception of gap-closures and in the participation of closing gaps during interception, the parietal and motor areas are actively involved.

Aptly, parietal and motor neural activities have also been well documented for their involvement in processing movement speed as well as other movement parameters like movement direction and position (Ashe and Georgopoulos 1994; Averbeck et al. 2005; Moran and Schwartz 1999). As a testimony to its prominence, neural correlates of movement speed have been used in brain-computer-interface applications for the control of prosthetic arms, particularly in the determination of the inverse kinematics required to bring the robotic arm to the desired location in space (Schwartz et al. 2006). Given that the variable *tau* is a term whose mathematical derivation involves instantaneous movement speed, it is appropriate to investigate the neural correlates of movement *tau* relative to movement speed, as previous neurophysiological studies have done so (e.g., Merchant et al. 2004a, b). The inclusion of movement speed does not necessarily imply that movement *tau* information may not be uniquely processed on its own. Similarly, it would seem appropriate to include movement amplitude (or ‘distance-to-goal’) as another variable to consider in conjunction with the investigation of movement *tau*. Although, neurophysiological studies (Boline and Ashe 2005; Fu et al. 1993, 1995; Messier and Kalaska 2000; Taira et al. 1996) have acknowledged significant neural correlates for non-time-varying movement amplitude, behavioral studies (e.g., Messier and Kalaska 1999) have also documented the existence of a large range of movement speeds with different peak acceleration, peak velocity, and movement duration that could yield movements with the same amplitude. It is therefore more fitting to focus the investigation of the present study on movement *tau* with reference to speed.

While the movements of human agents in various tasks have implicated the role of *tau* information in guiding behavior (e.g., Craig and Lee 1999; Craig et al. 1999, 2000a, b; Lee et al. 1999, 2001), a neural correlate of *tau* during self-regulated movement performance has not been demonstrated in humans. A few human neuroimaging studies have reported that neuromagnetic signals from sensors located over contralateral M1 (Kelso et al. 1998) or minimum-norm located area M1 (Jerbi et al. 2007) are critically involved in representing movement velocity, and simple movement directions (Waldert et al. 2008), but none has sought to investigate the relation between the time-varying neuroimaging signals and the *tau* variable.

In this research, the neural representations of the *tau* variable and movement speed were investigated. The neuromagnetic fluxes from the whole brain of human participants were recorded while they performed self-paced discrete hand movements aimed to stationary targets in space. The task involved self-regulated movements that can be described as closing motion gaps between targets. We performed a time-series analysis to assess the neural

correlate of speed and τ during the self-paced movements, as well as the distribution of these associations in MEG sensor-space. Given that frontal-parietal activities have been found to be critically involved in visuomotor tasks, we hypothesized that neural activity from these areas, as tapped by the first-order axial-gradiometer sensors, would be strongly associated with the movement speed and/or τ .

Methods

Subjects

Twenty healthy right-handed (Oldfield 1971) human subjects (10 women and 10 men; mean age \pm SEM = 32.05 ± 1.86 year) participated in the MEG-imaging study as paid volunteers. The study protocol was approved by the appropriate institutional review boards and informed consent was obtained from all subjects before the study, according to the Declaration of Helsinki.

Experimental setup

Subjects operated a non-magnetic 2-D joystick (model 541 FP, Measurement Systems, Norwalk, CT, remodeled with magnetic parts removed). An excursion of 5 cm of the joystick corresponded to a cursor displacement of 13.5 cm on the screen. The task stimuli (Fig. 1) were designed and implemented using Microsoft Visual Basic.NET 2003, which integrated the display with the joystick to provide visual feedback of its position through the cursor. The stimuli were presented using a LCD projector and via periscope mirror reflections onto a display screen ~ 65 cm

in front of the subject. The 2-dimensional movement task-space subtended approximately 16.8 degrees of visual angle (DVA) both horizontally and vertically, while the hexagonal target-space subtended 10.8 DVA horizontally and 9.2 DVA vertically of the visual field. All onsets and offsets of a target presentation were accompanied by a trigger and photo-detector detection (invisible to the subject). The joystick was placed in a suitably comfortable position to minimize various arm-elbow-wrist-joints torques.

Experimental task

Based on the previously demonstrated role of τ in self-regulated behavior (Craig and Lee 1999; Craig et al. 2000a; Lee et al. 1999) a self-paced target-to-target pointing task was used to investigate the neural correlates of movement speed and τ . In the present study, subjects moved a joystick-controlled cursor from one target to another using their wrist. Each movement target was presented at one of the six vertices of a hexagon, with sides measuring 6.2 cm as displayed. The actual extent of joystick movement was 0.4 times shorter; e.g., a 5-cm joystick excursion was manifested as a cursor displacement of 13.5 cm on the screen. All possible movements between the six vertices of the hexagon ($N = 30$) were performed in a random sequence. A sequence began at one of the vertices; all vertices were used as starting points (in a random sequence) yielding $30 \times 6 = 180$ movements. Finally, two sets of these 180 movements were repeated consecutively under different randomization. The design is illustrated in Fig. 1.

The task began with the presentation of a center target (red, diameter = 0.75 cm; 0.7 DVA) which instructed the subject to move the cursor into the center. After 200 ms, a movement target (white, diameter = 1.8 cm; 1.6 DVA)

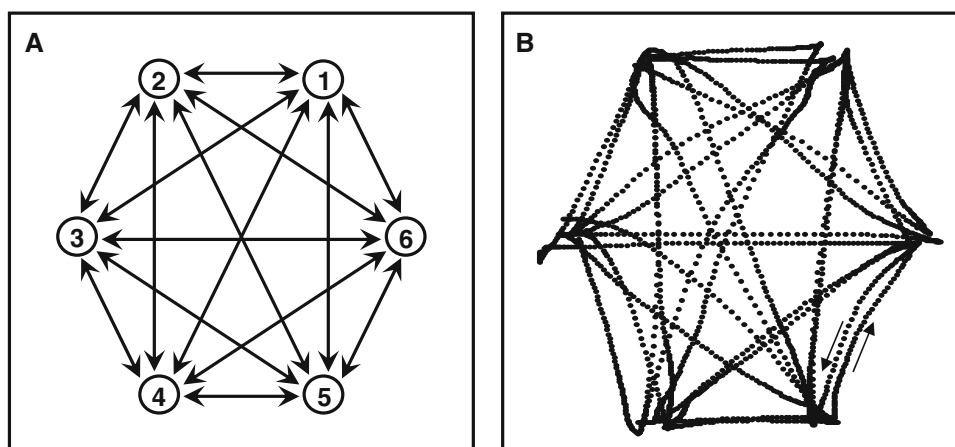


Fig. 1 Target-to-target movement task paradigm. **a** Each vertex of the invisible hexagon is a movement target, denoted as a circle, and numbered counter-clockwise. *Arrows* denote the possible trajectories between targets. Pseudo-random sequences of 30 target-to-target

movements were made by subjects for each set of movements, which began from a different starting vertex. **b** An example of the typical sequence of movement trajectories performed by subjects. Refer to text for further details

appeared while the center target disappeared. Subjects were instructed to move the cursor to the target in as straight a movement as possible. Once the cursor reached the movement target and was held within it for 200 ms, a new target appeared while the current target disappeared; only one target was present at any one time. After the cursor was brought to the last target in the sequence, the center target reappeared and the subject was instructed to bring the cursor back to it. A 5-s rest time was provided between movement sequences, during which subjects were required to bring the cursor back to the center, and they could blink and/or rest their eyes. This 5-s rest time was included to minimize the number of eye-blink artifacts during the actual movement tasks. As the endpoint requirements of each movement demanded sufficient precision that would benefit from fovea information, we did not include a fixation criterion in the task. Such a decision was also based on findings of previous studies that analyzed both fixated and non-fixated movement interception performances (Merchant et al. 2004a), or calculated movement speed predictions, which either included or omitted the eye-movement information (Averbeck et al. 2005), showing little difference between the results. Prior to experimental acquisition, the subjects performed the task for ~30 min to familiarize themselves with the task and the recording environment. Center → out movements were not included in data analysis.

Data acquisition

MEG data were acquired using a 248-channel axial gradiometer system (0–400 Hz, Magnes 3600WH, 4-D Neuroimaging, San Diego, CA) within an electromagnetically shielded chamber. Head movements were minimized to within 5 mm displacement using an individually made foam-helmet consisting of a 2-part foaming agent (Alpha Cradle[®], Smithers Medical Products Inc., OH, USA) that padded the space between the subject's head and the dewar helmet. (This material is commonly used for patient immobilization during radiotherapy.) Head stability was monitored using five electrodes placed on the left and right peri-auricular fiducial points, and spaced out on the forehead. The MEG data, the output of the joystick, the stimulus trigger and the photo-detector signals were sampled synchronously at 1017.25 Hz.

Data analysis

Movement data

The XY time series were low-pass filtered using a Parks-MacClellan Finite-Impulse-Response with equi-ripple. The filter had a frequency cut-off of approximately 6 Hz

(determined by the –3 dB threshold of the log-magnitude of the impulse response), which was within the 5–8 Hz range cited in movement research literature (e.g., Flanagan and Wing 1997).

We determined each movement onset as the point in time at which the speed (i.e., tangential velocity) exceeded 10% of its maximum value, and the end of each movement as the point in time at which the speed dipped below 10% of the maximum speed. The instantaneous speed of the movement was calculated as follows:

$$s_{(t)} = \frac{\sqrt{(x_{(t)} - x_{(t-1)})^2 + (y_{(t)} - y_{(t-1)})^2}}{1/F} \quad (1)$$

where sampling frequency (F) was 1017.25 Hz and thus sample time-interval ($1/F$) at each instantaneous time-point, t , was 0.000983 s. In addition, the index of linearity (Atkeson and Hollerbach 1985) assessed the general straightness of the movement trajectory. It was calculated as the ratio of the maximum perpendicular distance of the trajectory from the straight line connecting the start and end points of the movement, over the length of this line. Finally, the instantaneous $\tau_{(t)}$, was calculated as the ratio of the instantaneous distance-to-target over the instantaneous rate of change of distance-to-target (Lee 1998).

MEG data processing

Noise-reduction of data was performed post acquisition on all MEG sensor signals using 4D-Neuroimaging's algorithm, which accounted for the environmental signals detected by reference channels during acquisition. Fixed fractions of reference channels' signals (i.e., summed 'weighted' reference signals) were subtracted from the signals measured by MEG sensors in the noise-reduction procedure. (Data from sensor 182 were omitted from all analyses because it was faulty during the acquisition for subject 12).

Artifact removal

Cardiac-correction of the noise-reduced MEG signals was performed using synchronous event subtraction (Strobach et al. 1994; Leuthold 2003). To account for potential artifacts due to eye-blinks during the task performance, the cardiac-corrected MEG data were then subjected to an independent component analysis (ICA). The ICA is a process that detects and isolates independent sources of activity in signals consisting of mixed activity sources, e.g., MEG signals. The isolated components of the ICA were rank-ordered by magnitude (largest first). Signal artifacts such as eye-blinks are usually large in magnitude (e.g.,

vertical EOG can range around $\pm 100 \mu\text{V}$) and are typically reflected in the first or second ICA component. Six main ICA components from all 248 MEG-sensor signals were extracted using the *CuBICA34* algorithm (Blaschke and Wiskott 2004). Of those, the first component usually returned a waveform which closely resembled typical eye-blink artifacts. Movement segments and corresponding MEG data with ICA-detected eye-blink artifacts were omitted from further analyses.

Analysis of the relation between MEG signals and movement τ or speed

The association between the neural signals ($N_{(t)}^i$) and the corresponding movement τ ($\tau_{(t)}$) and speed ($s_{(t)}$) for all movement segments was assessed separately for each sensor ($i = 1\text{--}248$) using an autoregressive model of multiple regression where the time-varying MEG signal was the dependent variable and corresponding s and τ were the independent variables:

$$N_{(t)}^i = b_0^i + b_s^i s_{(t)} + b_\tau^i \tau_{(t)} + \varepsilon_{(t)}^i \quad (2)$$

$$\varepsilon_{(t)} = \rho \times \varepsilon_{(t-1)} + \xi_{(t)}$$

where the b 's are regression coefficients for the i th sensor, ε is the residual, ρ is the first-order autoregressive coefficient, and ξ is an uncorrelated, normally distributed random error term with zero mean and constant variance. The autoregressive component was included to take into account the expected serial correlation of the residuals, given that the data are time series (Box et al. 1978).

This analysis yielded the following three measures by which the relation of the MEG signal to speed and τ were quantified and summarized: (1) the regression coefficient itself, (2) its standard error, and (3) the probability value corresponding to that coefficient (based on a t test). The absolute value of the regression coefficient indicates the strength of the relation (i.e., MEG signal and speed or τ), whereas its associated probability value (derived from the ratio of the regression coefficient over its standard error) is a measure of the confidence by which the null hypothesis can be rejected that the regression coefficients $b = 0$. For quantitative analysis, the probability value P was log-transformed to normalize its distribution:

$$P' = -\ln P \quad (3)$$

The P value and its log-transform, P' , are similar to the commonly used functional magnetic resonance imaging (fMRI) statistical parametric maps (SPMs); image processes with voxel values distributed according to a known probability density function (typically the Student's t or F distributions) and according to the assumption of the null hypothesis. Although it is also possible to use the

correlation coefficient, its inference is most effective and intuitive when a single regressor is considered. In the case where many regressors are incorporated in the regression model, a more appropriate, general, and versatile means of assessing the significance of regional (and in this case, sensor-based) effects is given by the t statistic (which aptly takes account of the correlation relative to its standard error) or its P value.

Spatial distribution of speed and τ effects

The P' measure above was used to determine spatial gradients in sensor space of the speed and τ effects. For that purpose, the average (1) standardized partial coefficients, the corresponding (2) standard errors, and (3) P' (across subjects) were plotted for each sensor, with intermediate values interpolated using MATLAB® functions: *patch*, and *convhulln* (The Mathworks Inc. R2007b). This procedure renders images in a similar way to a fixed-effect analysis across a population of subjects in fMRI. However, instead of a SPM of t -statistics from averaged subjects' activation, an image of an average sensor map of probabilities is derived from individual P' ; the normalized P values for each sensor for each subject. It is also very similar to the suggested alternative approach for multi-subject analysis of fMRI data proposed by Bosch (2000), whereby individual standardized z maps were averaged across subjects.

Results

Behavior

Overall, 6,777 movements were retained for analysis with MEG data after discounting those contaminated by eye blinks. Subjects' movements manifested a single peak in the speed profile, which was not always symmetrically bell-shaped (Fig. 2). Maximum speed ranged from 3.71 to 36.35 cms^{-1} (mean \pm SEM, $14.01 \pm 0.05 \text{ ms}^{-1}$, $N = 6777$). Movements were generally straight, as evidenced by the low value of the index of linearity (0.09 ± 0.0008 , see "Methods"). Movement amplitude ranged from 0.94 to 4.54 cm ($2.86 \pm 0.01 \text{ cm}$) and movement time from 154 to 1131 ms ($408.15 \pm 1.62 \text{ ms}$).

Relations between MEG signals and movement speed or τ

Overall, the autoregressive multiple regression analysis revealed significant relations ($P < 0.05$) to speed in 81% of sensors (across all subjects), and to τ in 22% of sensors ($N = 20 \text{ subjects} \times 247 \text{ valid sensors} = 4,940$). The spatial distributions of these effects were assessed by

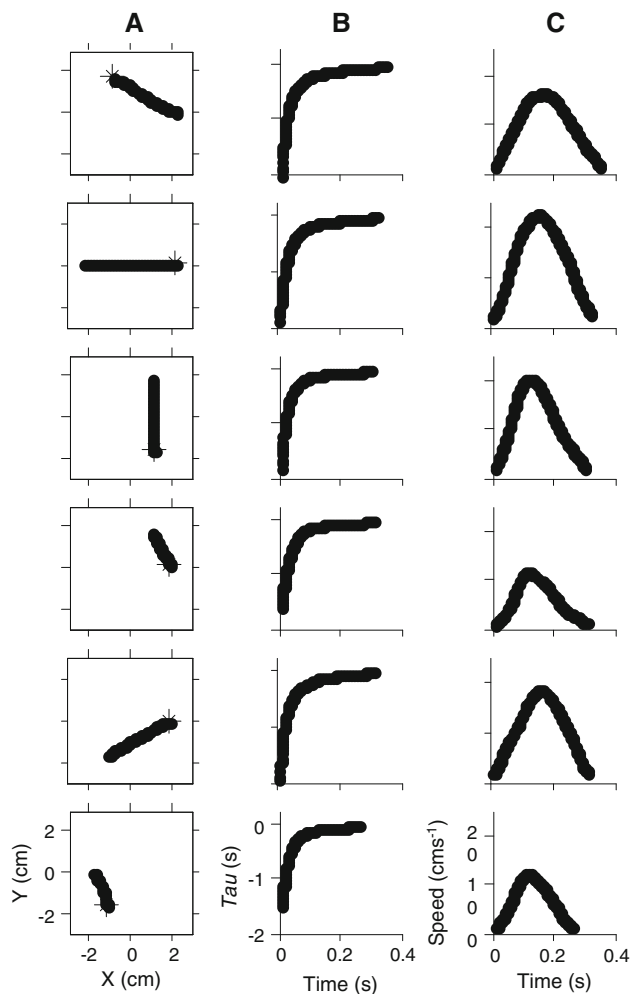


Fig. 2 Autoregression variables. Examples of the independent variables: movement *tau* (**b**), and corresponding movement speed (**c**) derived from their respective movement trajectories (**a**). Asterisks denote the end of movement segments

plotting the average (1) standardized partial coefficients, the corresponding (2) standard errors, and (3) P' (across subjects; see “Methods”) in sensor space, as shown in Fig. 3. With respect to the speed, there is a strong focus of regression coefficients in the left (contralateral to moving hand) dorso-lateral frontal motor area which extends with decreasing focus posterior-laterally as well as on the right hemisphere (Fig. 3a, left). Across subjects, the representation of these speed-related regression coefficients exists along a continuum of low variability in the same areas which manifested higher regression coefficients (Fig. 3b, left). The resulting confidence of the association between MEG sensor signals and speed processing (Fig. 3c, left) revealed that higher densities of reliability (i.e., lower probabilities) were localized in the left parietal region, with weaker foci in the left fronto-parietal regions and the occipital-temporal-rims. On the other hand, the spatial distribution of regression

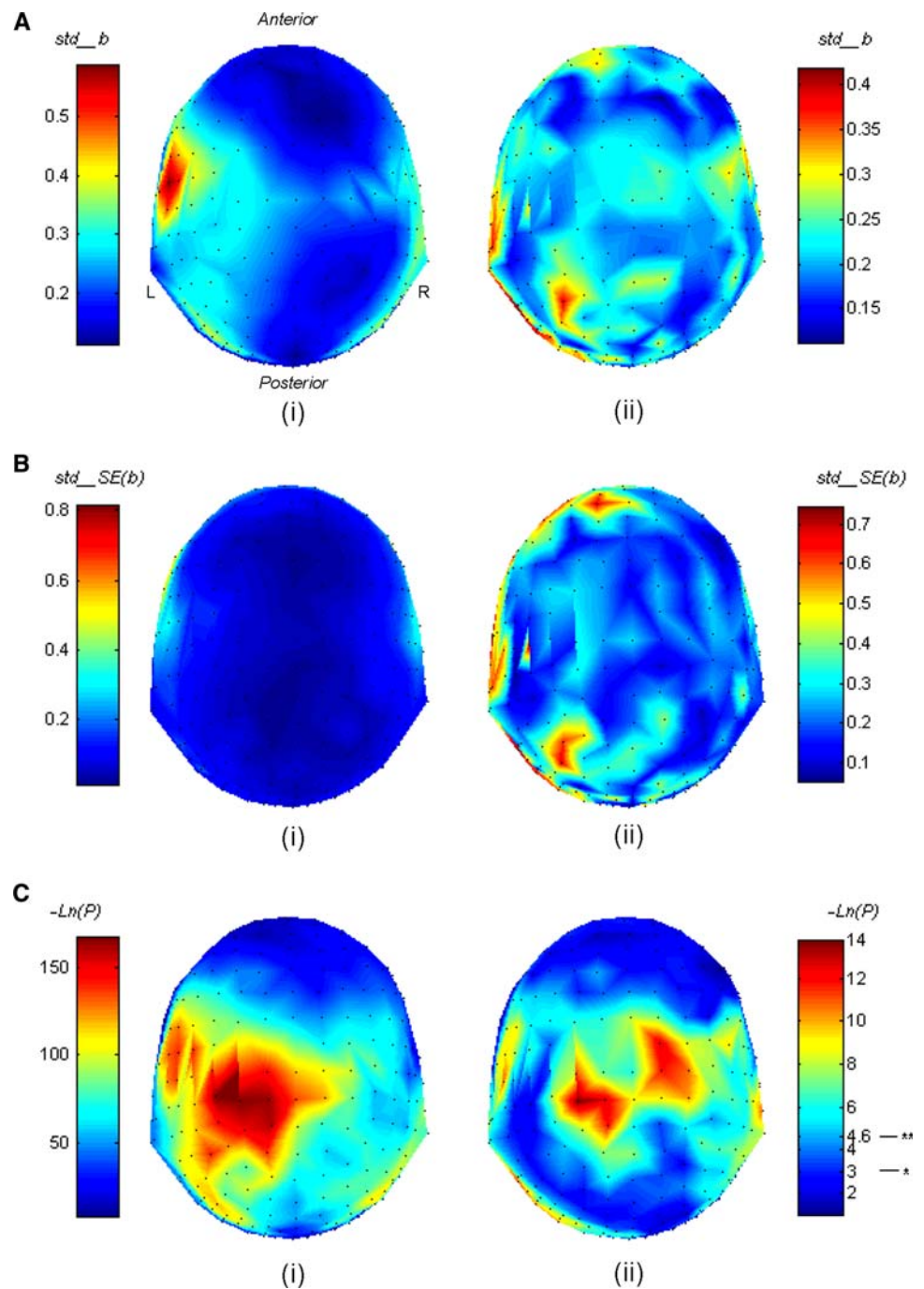
coefficients for *tau* effects revealed patches of high coefficients in left orbital-frontal, right dorso-lateral frontal, left lateral temporal-posterior and left occipital areas, with lower coefficients in bilateral dorso-lateral frontal and parietal sensor space (Fig. 3a, right). However, the representation of these *tau*-related regression coefficients manifested high variability in the same areas which showed higher regression coefficients (Fig. 3b, right). The resulting confidence of the association between MEG sensor signals and *tau* processing (Fig. 3c, right) revealed two prominent high densities over the left and right parietal regions, with weaker foci over the left fronto-parietal region, the left parieto-temporal-occipital, and right parieto-temporal rims. The left of the two main foci overlapped in similar location as the main speed focus.

Discussion

In this study we investigated the relations between brain signals and two movement parameters of special importance for arm movements, namely speed and time-to-closure (*tau*). We observed that while subjects made relatively straight trajectories, the speed was not always symmetrically bell-shaped. This finding is in accord with the findings of early studies demonstrating that simple pointing movements are not implemented in a purely feed-forward manner (Beggs and Howarth 1972). In addition, this observation provides a good indication that the timely and generally well-controlled closure of the motion gaps between targets is likely to be achieved by integrating saliently available information (e.g., like the sense of how fast one is moving and/or *tau*) during subjects’ movement performance.

The autoregressive multiple regression analyses performed in the present study indicated that speed and *tau* are represented by neuromagnetic signals. The strong associations between neuromagnetic signals and speed processing, as represented by the regression coefficients, are complemented with low variability of the distribution of these coefficients, revealing a focused representation of the reliability of speed-related sensors. The main locus of the speed-related sensors is localized in the left parietal region, with weaker foci in the left fronto-parietal regions and the occipital-temporal-rims. While strong associations between neuromagnetic signals and *tau* processing are manifested in the left orbito-frontal, temporal, and posterior-parietal sensor-space, these existed with high variability, and therefore low reliability. The resulting foci of *tau*-related processes are found in two prominent high densities over the left and right parietal sensor-space, with weaker densities over the left fronto-parietal region, the left parieto-temporal-occipital, and right parieto-temporal rims.

Fig. 3 Spatial distribution of the relations of MEG signals to movement speed (*left*) and τ (*right*). For the variables of interests, **a** standardized autoregressive multiple regression partial coefficients, **b** standardized autoregressive multiple regression standard errors of partial coefficients, and **c** the (log-transformed, i.e., $-\ln P$) probability value of the autoregressive multiple regression, were averaged across all subjects for each sensor and interpolated over the sensor-space coordinates. Higher log-transformed probability values indicated a more significant raw regression P value (e.g., $*P < 0.05 = -\ln(0.05) = 3$; $**P < 0.01 = -\ln(0.01) = 4.6$). The frame of reference indicating anterior, posterior, left (L , corresponding to hemisphere contralateral to moving arm) and right (R , corresponding to the hemisphere ipsilateral to the moving arm) MEG sensor space, applies to all spatial distribution images



Overlapping left fronto-parieto and right parieto-temporal processes are also present in the representation of movement speed and τ .

The choice to work in signal space was based on concerns of signal-to-noise ratio (SNR). At present, there is insufficient information in the literature to be confident that raw or derived MEG signal could be successfully related to movement τ and speed by the analysis method chosen for this work. Therefore, it seemed most appropriate to use raw sensor signals that will maximize the chances of detecting

any real effect for the initial investigation into the neural correlates of these important movement variables using the multiple regression analysis. We envision the extension of the present work to use derived data that allows for more accurate source localization. However, not all sources are appropriate for such methods. The cost will be the loss of some sources that are weaker, deeper, highly localized or more distributed, with no guarantee that any of the sources contributing to the results in this paper will survive the necessary pre-processing.

Source localization methods require that substantial signal be present in a number of detection coils to make the estimation of a source possible. However, single trial data is generally considered inappropriate for source analysis, and only the simplest of motor tasks allow averaging of trials. Moreover, the process of averaging relies on the heavy assumption that the brain is in a relatively steady state during the course of the experimental condition(s), with little habituation or adaptation to the stimuli or task. In reality, such steady-states do not generally exist; particularly when the number of trials is large (Baillet et al. 2001). Studies by Ioannides et al. (Ioannides 2001, 2006) have shown that the averaging of signals across trials, experimental sessions, and subjects usually reveals stereotypical responses that capture real-time activities of early responses in primary sensory cortical areas to strong sensory stimuli, but provides poor classification of late evolving and general underlying neural dynamics. The average signal can be viewed as a superimposition of subsets of histories, which does not necessarily reflect the temporal dynamics of neural processing (Liu and Ioannides 1996). The gradual appreciation that noise-elimination through averaging unwittingly undermines interpretation has motivated others (e.g., Jerbi et al. 2007; Karjalainen et al. 1999; Langheim et al. 2006) to analyze single-trial non-averaged data where possible.

An intermediate option would be to perform the regression analysis on the tangential derivative of the raw sensor data. This method has been used as preprocessing of data for spectral analysis (Bastiaansen and Knösche 2000; Van Der Werf et al. 2008), and does produce more focal results. Nonetheless, even the minimal processing involved in producing the tangential derivative is known to reduce SNR, especially for deeper sources (Bastiaansen and Knösche 2000). Moreover, an attempt at either source localization or calculation of tangential gradient assumes sources are strong and widespread enough to be seen substantially in multiple detection coils. Sources not meeting these requirements, especially if frequently recurring, may still be detectable in the raw sensor data by analysis methods operating over a period of time, such as in the current work.

As it is possible for first-order axial gradiometer coils in MEG systems, as used in the present research, when placed over a maximum field generated by a surface source to see a much stronger signal than neighboring sensors, the patterns of significance may be tight, and might even be limited to a single isolated detection coil (Williamson and Kaufman 1981). Therefore, the sparser distribution of *tau* was likely to have been from specific surface source(s). Multiple or deeper sources would be likely to spread this pattern, such that a broader cluster of sensors would be

involved; this was likely to be the case for signals significantly related to movement speed.

The prominent involvement of the left parieto-temporo-occipital processes is an interesting finding from two perspectives. First, the left inferior parietal cortex has been implicated in linking perception with the preparation of actions (Mountcastle et al. 1975), and second, apraxic patients with lesions to their posterior parietal cortex manifest impairments in visuomotor coordination, e.g., visually guiding their intended movements. Such visuomotor coordination is particularly affected when online correction of trajectories to intended goal is involved (Battaglia-Mayer and Caminiti 2002; Grea et al. 2002; Grefkes et al. 2004; Pisella et al. 2000; Rushworth and Taylor 2006). Specifically, unilateral left (c.f. right) lesion of the posterior parietal cortex (PPC; including the intra-parietal sulcus) induces a profound effect on the ability of these patients to adjust their hand movements or update their sensorimotor representations in response to a sudden change in target location (Rushworth et al. 2003). In addition, similar disruptive effects have also been observed in either left- or right-hand movements when transient transcranial magnetic stimulation (TMS) is applied to the left PPC of healthy subjects (Desmurget et al. 1999; Rushworth et al. 2001). Second, the fMRI study by Assmus et al. (2003) also reported the involvement of the left inferior parietal cortex (the supramarginal gyrus) in integrating spatial and temporal information during time-to-collision judgments.

Furthermore, the involvement of the right parietal and parietal-temporal processes, particularly distinct in the case of *tau*, is also in line with current appreciation of the right inferior parietal brain area in temporal processes. Recent neurophysiological studies have demonstrated that neurons within the lateral inferior area (LIP) of the posterior parietal cortex modulated their firing activities with the monkey's perception of elapsed time as well as the perceptual uncertainty of this temporal judgment (Leon and Shadlen 2003) in the animal's anticipation of impending behavioral consequence (Janssen and Shadlen 2005). Although these studies did not address the hemispheric lateralization of temporal processing, fMRI studies of temporal discrimination in humans have reported observations that the right inferior parietal cortex, along with the right caudate, left cerebellum (Harrington et al. 2004), and bilateral premotor cortices (Rao et al. 2001) are involved in the encoding processes of time intervals. In addition, lesion studies in patients with right but not left inferior parietal damage showed normal-range pitch perception but impairments in timing discriminations, which correlated with impaired attention switching (Harrington et al. 1998). Furthermore, accumulating evidence implicating non-spatial processing within the right inferior parietal cortex have come from

studying neglect patients whose deficits may not be adequately described as simply involving spatial-attention, but more appropriately, as a multifaceted impairment that also involves temporal processing (Basso et al. 1996; Battelli et al. 2007; Becchio and Bertone 2006; Husain et al. 1997).

Taken together, the role of the parietal cortex in online integration of sensorimotor information for the monitoring and control of movements in extrinsic-space, as well as the representation of a subjective appreciation of time intervals makes it aptly suited in processing movement variables such as *tau*, which affords prospective information in gearing actions in time to a goal. In addition, other neural areas that participate in the continuum of sensorimotor processes forming the dynamic parieto-frontal network are also likely to be intricately involved in processing timing-related information during visually guided movements (Battaglia-Mayer et al. 2003, 2006; Wenderoth et al. 2006). Indeed, the activity of dorsolateral prefrontal (DLPFC) cortical cells recorded in non-human primates during a delayed-response task that required an appropriate recall of the preceding trial's delay interval has been shown to reflect general aspects of elapsed time (Genovesio et al. 2006). Furthermore, average population firing intensity recorded in the medial (pre-supplementary; pre-SMA, and supplementary; SMA) motor areas have also been found to correlate well and modulate with the varying durations the non-human primates were required to “hold-still” prior to initiating their key-release response (Mita et al. 2009). Interestingly, the modulation of neuronal activity to the different “hold-still” durations observed in pre-SMA could be distinguished from those of SMA neurons in terms of an adjustable parameter fitting an exponential decay or build-up function. These findings are of particular relevance as similar build-up activities (or ‘*tau*-ramps’) have been observed in the motor and parietal cortices (Janssen and Shadlen 2005; Leon and Shadlen 2003; Merchant et al. 2004a; Merchant and Georgopoulos 2006). Furthermore, movement *tau* itself can be described as an inverse of an exponential function with an adjustable parameter that characterizes the slope of the ramp (Fig. 2). The apparent inverse relationship between *tau* and neural activities (e.g., in pre-SMA) may afford a neurophysiological signal for adaptive behavior.

Crucially, the observations of similar activities associated with temporal processing in these brain areas reflect the functional and anatomical interconnectivity of the parieto-frontal network (Chafee and Goldman-Rakic 1998, 2000; Johnson et al. 1996; Marconi et al. 2001). By integrating recent findings from the pre-SMA (Mita et al. 2009), to which DLPFC areas are connected (Luppino et al. 1993) and in which neural activities similar to those in DLPFC have been observed (Hoshi et al. 2000; Hoshi and Tanji 2004), one can speculate that perceptual (from ventral

DLPFC, which has connections to ventro-caudal posterior parietal regions) and action (from dorsal DLPFC, which has connections to the superior parietal areas) information could be integrated in pre-SMA before the relevant behavior is executed via the motor system (Hoshi 2006). Our observation that parieto-frontal sensor-space processes were involved and significantly related to speed and *tau* during the actual target-to-target movements may be inferred as simultaneously active parieto-frontal neural processes occurring during the unfolding of the movements.

Although the current autoregressive multiple regression analysis does not allow for precise anatomical localization, we speculate that the roughly defined frontal-parietal sensor-space processes, which are significantly related to *tau*, are likely to reflect similar brain activations involved in the judgment of time-to-contact in humans (Field and Wann 2005) and the previously reported associations between neuronal activity and *tau* in the both motor and posterior parietal cortices (Merchant et al. 2004a; Merchant and Georgopoulos 2006). Likewise, our findings of significant frontal-parietal sensor-space processes related to movement speed may also be interpreted as reflecting similar neural representation of speed in M1 and area 5 of the PPC (Ashe and Georgopoulos 1994; Averbeck et al. 2005; Moran and Schwartz 1999). MEG signals from sensors above the sensorimotor area have been shown to correlate highly with rhythmic metronome-regulated finger movement speed (Kelso et al. 1998). A recent study by Jerbi et al. (2007), who applied coherence analysis between (unaveraged time-series) MEG source-level current amplitude signals and track-ball motion speed, also demonstrated the significant involvement of M1 at the low 2–5 Hz range. In addition, these authors also demonstrated in their study (with non-threshold criteria), a network of areas related to their prominent M1-speed coherence, which included the contralateral dorsal premotor, primary somatosensory, inferior and superior parietal, and dorsolateral prefrontal cortical areas. While Jerbi et al. (2007) also reported the involvement of sub-cortical areas (e.g., the thalamus) and ipsilateral anterior cerebellum, it is generally assumed that deeper sources are weakly tapped by MEG sensors (Hillebrand and Barnes 2002), and therefore warrants caution in interpretation. Moreover, the functional significance of oscillatory interactions still awaits clarification.

The finding of a neural correlate of *tau* in humans in our MEG study suggests a neural process linked to the demonstrated role of *tau* in self-regulated behavior (Craig and Lee 1999; Craig et al. 2000a; Lee et al. 1999). We acknowledge that goals for movements do not always remain stationary, nor do moving targets necessarily maintain a steady course, and obstacles can also come in the movement path unexpectedly. Under uncertainty,

educated guesses (about environmental and physical attributes of the target or context), estimates of time to gap closures, and the instantaneous speed etc. are likely to occupy a larger confidence interval at any given moment in time (Georgopoulos 2007). Controlled variations on the estimation of τ are likely to account for the success of timely gap closures and the question of how this uncertainty is regulated warrants further exploration. Another important issue that is not resolved in the present study is how the τ information exerts influence in the forward planning, such as movement speed. The temporal interaction between speed and τ is currently being investigated and preliminary findings offer additional insights into how temporal information such as τ may be used to update the motor system in movement control.

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