

COGNITIVE NEUROSCIENCE

Object size modulates fronto-parietal activity during reaching movements

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Keywords: event-related potentials, human, kinematics, object size, reaching, visuo-motor integration

Abstract

In both monkeys and humans, reaching-related sensorimotor transformations involve the activation of a wide fronto-parietal network. Recent neurophysiological evidence suggests that some components of this network host not only neurons encoding the direction of arm reaching movements, but also neurons whose involvement is modulated by the intrinsic features of an object (e.g. size and shape). To date, it has yet to be investigated whether a similar modulation is evident in the human reaching-related areas. To fill this gap, we asked participants to reach towards either a small or a large object while kinematic and electroencephalographic signals were recorded. Behavioral results showed that the precision requirements were taken into account and the kinematics of reaching was modulated depending on the object size. Similarly, reaching-related neural activity at the level of the posterior parietal and premotor cortices was modulated by the level of accuracy determined by object size. We therefore conclude that object size is engaged in the neural computations for reach planning and execution, consistent with the results from physiological studies in non-human primates.

Introduction

In order to perform a successful reaching movement towards an object, signals about the limb starting position, eye position and target location have to be combined and integrated into common, distributed spatial representations (Buneo *et al.*, 2002; Battaglia-Mayer *et al.*, 2003; Mascaro *et al.*, 2003; Shadmehr & Wise, 2005). In both humans and monkeys, a central role for such integration is played by a neural circuit involving the frontal and parietal cortex, the so-called 'dorsal visual stream' (for review see Culham *et al.*, 2006).

By means of single-unit recording techniques, a number of studies have demonstrated the presence of visuo-motor-related neurons within the parieto-occipital (Galletti *et al.*, 1996, 1997; Battaglia-Mayer *et al.*, 2000; Fattori *et al.*, 2001, 2005) and intra-parietal (Grefkes & Fink, 2005) sulci, and premotor dorsal and premotor ventral cortices (Hoshi & Tanji, 2004a,b). Furthermore, a parietal reach region lying in the medial bank of the intra-parietal sulcus, a region probably corresponding to the medial intra-parietal area, has been defined (Andersen & Buneo, 2002; Buneo *et al.*, 2002; Connolly *et al.*, 2003; Gail & Andersen, 2006).

Results from human neuroimaging studies appear to fit nicely with the neurophysiological results reported above. Reaching-related activation has been revealed within motor and premotor areas (Decety *et al.*, 1992; Grafton *et al.*, 1996; Kawashima *et al.*, 1996; Kertzman *et al.*, 1997), and within specific sectors of the parietal cortex, namely the medial intra-parietal sulcus (Prado *et al.*, 2005; Cavina-Pratesi *et al.*, 2010; Konen *et al.*, 2013) and precuneus

(Connolly *et al.*, 2003; Astafiev *et al.*, 2004; Grefkes *et al.*, 2004; Grefkes & Fink, 2005; Filimon *et al.*, 2009).

Complementary to these approaches, evoked-related potentials (ERPs) measured by electroencephalography (EEG) have shown P300-like components related to reaching in premotor, motor and parietal areas (Berndt *et al.*, 2002; McDowell *et al.*, 2002; Naranjo *et al.*, 2007; Bozzacchi *et al.*, 2012).

A recent particularly noticeable finding has been that neural recording in the monkey shows that one of the areas of the dorso-medial pathway, the medial posterior parietal area V6A, hosts neurons that, in addition to being sensitive for the direction of arm reaching movements (Fattori *et al.*, 2001, 2005), are also sensitive to intrinsic features of target objects such as shape (Fattori *et al.*, 2012). A result that is in line with the evidence that, in humans, the kinematic organisation of reaching is affected by the precision requirements related to intrinsic features of objects, such as size, despite a change in the distal program (i.e. hand shaping) is not implied (MacKenzie *et al.*, 1987; Gentilucci *et al.*, 1991).

To date, it has yet to be investigated whether, in humans, the fronto-parietal network alerted during the planning and execution of reaching movements is modulated by the intrinsic features of objects. To fill this gap, our study investigated kinematic and EEG signals while participants performed a reaching action towards an object that could be of either small or large size.

Materials and methods

Participants

Twenty-two students, recruited from the Faculty of Psychology at the University of Padua, took part in the study. They had a mean

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Received 29 October 2013, revised 9 January 2014, accepted 13 January 2014

age of 23.68 years (SD 2.49; range 19–28 years; 11 females) and were all right-handed, as measured by the Edinburgh Handedness Inventory (Oldfield, 1971), with normal or corrected-to-normal vision, and without neurological or psychiatric pathologies. The experimental procedures were approved by the ethical committee of the University of Padua and were carried out in accordance with the principles of the revised Helsinki Declaration (World Medical Associations General Assembly, 2008). Written consent was obtained for each participant.

Apparatus and procedures

The participant was seated on a height-adjustable chair so that the thorax pressed gently against the front edge of the table and the feet were supported. The position of the head was controlled by means of a head–chin rest. A pressure-sensitive starting switch was positioned 15 cm anterior to the midline of the participant's thorax. With the hypothenar eminence of the right hand placed upon this switch, the starting position was slight shoulder flexion and 70–80° of internal rotation, 90° of elbow flexion, semipronation of the forearm, and 5–10° wrist extension. The experimental stimuli were either a small (3 cm diameter) or large (7 cm diameter) wooden spherical object (Fig. 1A). The object was placed upon the working surface 30 cm directly in front of a pressure-sensitive starting switch (Fig. 1A). The visual availability of the object was controlled via Plato liquid crystal shutter glasses (Translucent Technologies, Toronto, ON, Canada) worn by the participant throughout the test (Fig. 1A). Under computer control, the shutters changed from opaque to transparent within 10 ms and returned to opaque in 2 ms. Participants were requested to perform a reaching task in which they were asked to touch the object while maintaining the hand in a closed fist (the fist posture was the same for both small and large objects). The fist posture was chosen so as to minimise distal involvement (see Kinematic recording and data processing section below). Once the participants were comfortable with the task, they performed a total of 80 trials, 40 trials towards the large object and 40 trials towards the small object. The sequence of events was as follows. At the start, the shutter glasses were in a closed (opaque) state. At the time that the shutter glasses opened (i.e. became transparent), the object became visible. The participant was instructed to start the reaching movement at the opening of the shutter glasses. The shutter glasses remained open for the entire duration of the movement until the hand returned to the starting position. Trials were administered in two blocks presented in a pseudorandom order. The ERPs and kinematic recordings started at the time that the shutter glasses became transparent (Fig. 1B). Because the size of the sphere to be reached was unpredictable, participants could plan the specific movement only after the object was visually available. Therefore, a planning phase was involved in the task, taking place in the time window occurring between the opening of the shutter glasses and the start of the movement.

Kinematic recording and data processing

A reflective passive marker (0.25 cm diameter) was attached to the wrist (radial aspect of the distal styloid process of the radius) (Fig. 1A). Furthermore, a marker was attached to the thumb (ulnar side of the nail) (Fig. 1A) so as to be sure that the thumb was not behaving differently when reaching for the large, rather than the small object. The fist posture did not allow for differential movements of the remaining fingers (knuckles). We anticipated that

preliminary analyses for the thumb did not show significant differences depending on object size for all of the considered dependent measures (P -values > 0.05). Movements were recorded with the SMART system (BTS, Milan, Italy). This consisted of six infrared cameras (sampling rate 200 Hz) inclined at an angle of 45° to the vertical, and placed around the table (Fig. 1A). The calibrated working space was a parallelepiped (length 50 cm, breadth 50 cm, height 50 cm) from which the spatial error measured from stationary and moving objects was 0.4 mm. The coordinates of the marker were reconstructed with an accuracy of 1/3000 over the field of view and sent to a host computer. The SD of the reconstruction error was 1/3000 for the vertical (Y) axis and 1.4/3000 for the two horizontal (X and Z) axes. The SMART analyzer software package was used to assess the data. This gave a three-dimensional reconstruction of the marker positions. The data were then filtered using a finite impulse response linear filter-transition band of 1 Hz (sharpening variable, 2; cutoff frequency, 10 Hz). Reaching was assessed by analysing the trajectory and velocity profiles of the wrist marker. The reaction time was defined as the time interval between the opening of the liquid crystal lenses and the release of the start button upon which the hand was resting. The movement duration was calculated as the time between movement onset (defined as the time at which the button press was released) and the end of the action (defined as the time when the reaching hand touched the target). The dependent variables were: (i) reaction time, (ii) movement duration, (iii) time and amplitude of peak velocity of the wrist marker, (iv) time from peak velocity to the end of the movement (deceleration time), (v) time and amplitude of the maximum height of the wrist trajectory, and (vi) trajectory length.

Electrophysiological recording and data processing

The EEG was acquired by a portable amplifier system (SD-MRI; Micromed, Mogliano Veneto, Italy) from an array of 30 tin electrodes embedded in an elastic cap (ElectroCap International, Inc.) according to the 10–20 International System (AEEGS, 1991). The montage included the following scalp positions: Fp1, Fpz, Fp2, F7, F3, Fz, F4, F8, FT7, FC3, FCz, FC4, FT8, T3, C3, Cz, C4, T4, TP7, CP3, CPz, CP4, TP8, T5, P3, Pz, P4, T6, O1 and O2. All electrodes were referenced to linked mastoids. The ground electrode was placed in AFz. The impedance of all electrodes was kept below 5 k Ω . The signal were digitised at a sampling rate of 512 Hz (16 bit AD converter), and high-pass filtered at 0.15 Hz. Data processing was performed by Brain Vision Analyzer 2 software (Brain Products GmbH, Gilching, Germany). Continuous EEG was offline low-pass filtered at 30 Hz. Epochs were extracted time-locked to the time that the shutter glasses opening and lasted 2000 ms. The time window considered encompassed the time at which the shutter glasses opened and the time at which the object was contacted (see Fig. 1B). Artifacts were corrected by means of independent component analysis applied on all epochs together, regardless of object size. The independent component analysis correction was performed by using a toolbox in the EEGLAB software (Delorme & Makeig, 2004). This analysis allows for the identification of the independent components in the segmented EEG signal by simultaneously taking into account frequency, timing and location on the scalp. This procedure helps in isolating artifactual components, such as blinks and head muscle contraction (Jung *et al.*, 2000). In addition, epochs containing amplitude deflection greater than ± 75 μ V were rejected for all of the recorded channels prior to further analysis. The signal was then baseline-corrected against the mean voltage during the 200 ms prior to object appearance. Epochs containing erroneous movements

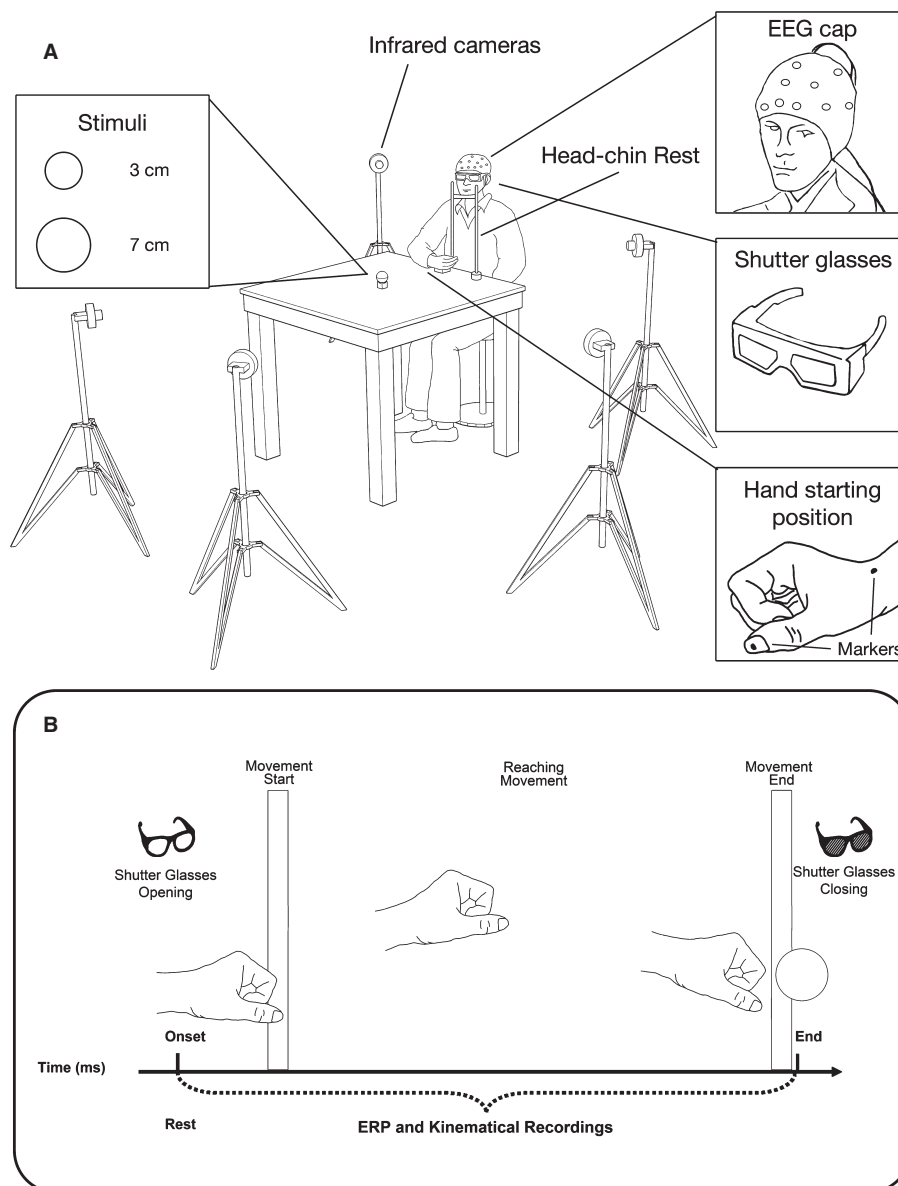


FIG. 1. (A) The experimental set-up. (B) The timeline of events, within which ERP and kinematic data were recorded.

were discarded. A mean of 38.88 epochs ($SD = 1.27$) were included within the statistical analyses. Based on visual inspection of grand average waveforms and amplitude scalp maps, the following ERP components were statistically analysed – amplitude and latency of P300, i.e. the positive peak evoked at 200–400 ms following object appearance at parietal sites (P3, Pz and P4); amplitude and latency of N400, i.e. the negative peak occurring at 300–500 ms after object appearance at frontal (F3, Fz and F4), fronto-central (FC4, FCz and FC3), and central (C3, Cz and C4) sites; and mean amplitude of the sustained negativity observed in the 400–800 ms time window at frontal (F3, Fz and F4), fronto-central (FC4, FCz and FC3), central (C3, Cz and C4), and parietal (P3, Pz and P4) sites.

Data analysis

The mean values for reaction time, movement duration and each kinematic measure were entered within ANOVAS with object size

(small, large) as a within-subjects factor. The ERP components were analysed by means of separate repeated-measure ANOVAS (see Results). The alpha level of significance was fixed at 0.05. Before running the analyses, we checked for all of the main assumptions behind this statistical parametric model (i.e. normality and sphericity). The Kolmogorov–Smirnov test revealed that the normality assumption was satisfied. In all ANOVAS, the Mauchly test showed that the sphericity assumption was not violated. The effect size of ANOVA results was quantified by means of partial eta-square values (η_p^2). *Post hoc* comparisons of ANOVA were corrected by the Bonferroni method. Correlation analyses by means of Pearson's r coefficient were performed between kinematic and ERP measures. Namely, the mean peak and latency values (the maximum ERP amplitude value measured in a specific time window and its corresponding point in time) of P300 and N400 components, and mean amplitude within the 400–800 ms time window, at relevant sites, were considered.

Results

Reaction time

The reaction time results suggested that participants reacted faster to execute a reaching movement towards a large (479 ± 86 ms) than a small (492 ± 97.25 ms) object. However, this difference only approached significance ($P = 0.053$).

Kinematics

The manipulation of object size determined significant effects on reaching kinematics (Fig. 2). Movement duration was longer for the small than for the large object (1183 ± 243 vs. 1099 ± 230 ms; $F_{1,21} = 233.60$, $P < 0.0001$; $\eta_p^2 = 0.75$) and the object size significantly modified the amplitude of peak velocity ($F_{1,21} = 9.76$, $P < 0.001$; $\eta_p^2 = 0.68$; Fig. 2A). The peak velocity was higher for the larger than the smaller object (1054 ± 114 vs. 1001 ± 116 mm/s; Fig. 2A) and the time of peak velocity occurred earlier for the small than for the large object (420 ± 31 vs. 431 ± 35 ms; $F_{1,21} = 11.12$, $P < 0.05$; $\eta_p^2 = 0.62$; Fig. 2A). The deceleration time was longer for the smaller than for the larger object (763 ± 43 vs. 668 ± 58 ms; $F_{1,21} = 51.12$, $P < 0.0001$; $\eta_p^2 = 0.80$; Fig. 2A). In terms of spatial trajectories, the point at which the wrist trajectory reached its maximum distance from the working surface was higher for the larger (115 ± 11 mm) than for the smaller (108 ± 10 mm) object ($F_{1,21} = 10.96$, $P < 0.003$; $\eta_p^2 = 0.76$; Fig. 2B). The total length of the trajectory was longer for the smaller than for the larger object (322 ± 19 vs. 303 ± 15 mm; $F_{1,21} = 11.75$, $P < 0.001$; $\eta_p^2 = 0.69$).

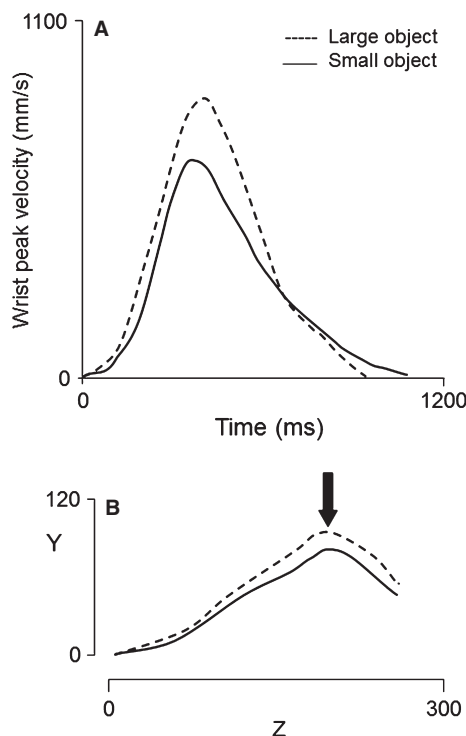


FIG. 2. (A) The velocity profile for a representative subject. (B) Representative examples of trajectories of the reaching component on the sagittal plane for the small and large object conditions. Values on the axis are in mm. Axis z, sagittal axis; axis y, vertical axis. The arrow indicates the point of maximum trajectory height.

Evoked-related potentials

Fig. 3 depicts grand-average waveforms locked to the time at which the shutter glasses opened (i.e. object appearance) in the two conditions. ERPs were characterised by an early negative peak at around 100 ms (N100), more marked at parietal and central electrode sites, which showed similar amplitude and latency for both the small and large object. The differences in amplitude between the two object conditions then became evident. Specifically, a positive peak at around 300 ms (P300), maximally expressed at parietal electrode sites, showed a higher amplitude for the large compared with the small object. Subsequently, a negative electrical activity, peaking at around 400 ms at central and frontal electrode sites, and sustained for a time window lasting from 400 to 800 ms, showed a higher amplitude for the small compared with the large object. The polarity, temporal trend and scalp distribution for such component suggested that this was linked to the motor component of action planning and to premotor areas; we therefore termed this component as motor-related N400 (m-N400) (De Sanctis *et al.*, 2013). From 800 to about 1200 ms after object visual availability, a slow ERP deflection from negative to positive values at all electrode sites was found. The following sustained positivity from 1200 to 1800 ms was similarly large for the two conditions and was distributed over central and frontal sites.

P300

The amplitude and latency of this component were analysed by means of a 2 (object size : small, large) \times 3 (electrode position: left, midline, right) repeated-measure ANOVA. The analysis revealed a main effect of object size ($F_{1,21} = 25.38$, $P < 0.001$; $\eta_p^2 = 0.55$), i.e. a higher P300 amplitude was found for the large than for the small object. No difference in peak latency between reaching conditions was present. Rather, the P300 latency was significantly affected by electrode position ($F_{2,20} = 4.53$, $P = 0.017$; $\eta_p^2 = 0.18$). *Post hoc* comparisons revealed that the P300 peak reached maximal amplitude earlier in the left site (P3) compared with the midline (Pz) and right (P4) sites ($P = 0.017$ and $P = 0.023$, respectively). No significant differences between Pz and P4 were detected. The scalp map in Fig. 4, showing the topography of the differential amplitude (Reaching Small – Reaching Large), confirms that, within the 300–350 ms time window, ERPs were larger for the large compared with the small object.

Motor-related N400

The amplitude and latency of the negative ERP deflection peaking at around 400 ms (m-N400) were analysed by means of a 2 (object size: small, large) \times 3 (anterior–posterior electrode position: frontal, fronto-central, and central) \times 3 (left–right electrode position – left, midline, right) repeated-measure ANOVA. This analysis yielded a main effect of object size ($F_{1,21} = 13.18$, $P = 0.002$; $\eta_p^2 = 0.41$), i.e. the m-N400 peak was found to reach higher (more negative) amplitude when participants were required to reach the small compared with the large object. A main effect of anterior–posterior electrode position was found ($F_{2,20} = 25.33$, $P < 0.001$; $\eta_p^2 = 0.57$). *Post hoc* comparisons revealed that, for both conditions, the m-N400 amplitude was higher at frontal compared with fronto-central ($P = 0.002$) and central ($P < 0.001$) sites, and at fronto-central compared with central sites ($P < 0.001$). Furthermore, a main effect of left–right electrode position ($F_{2,20} = 38.99$, $P < 0.001$; $\eta_p^2 = 0.67$) showed that, for both reaching conditions, the m-N400 amplitude was higher

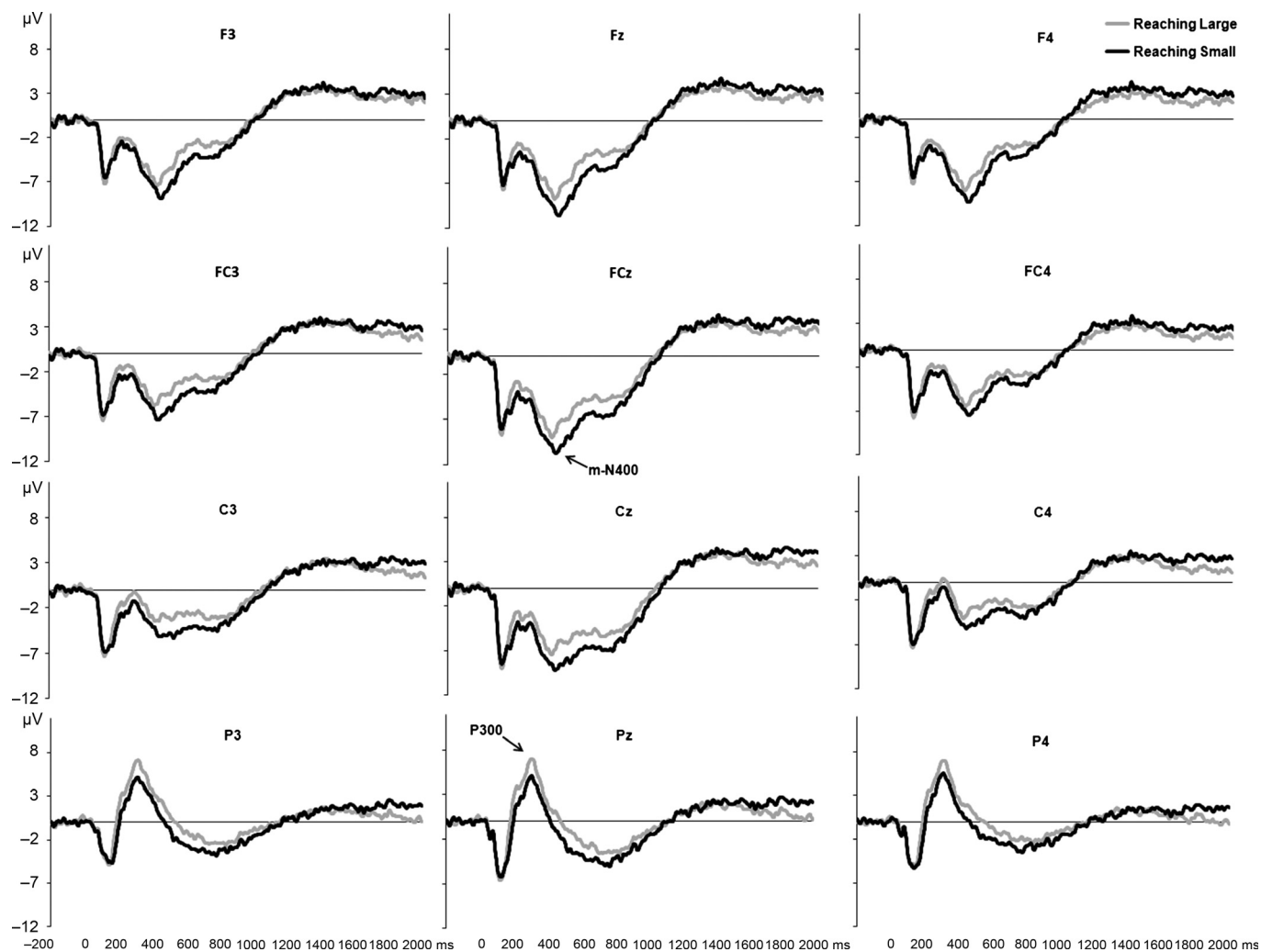


FIG. 3. The plot depicts grand-average ERP waveforms locked to the time at which the shutter glasses opened (i.e. object appearance) for Reaching Small and Reaching Large conditions.

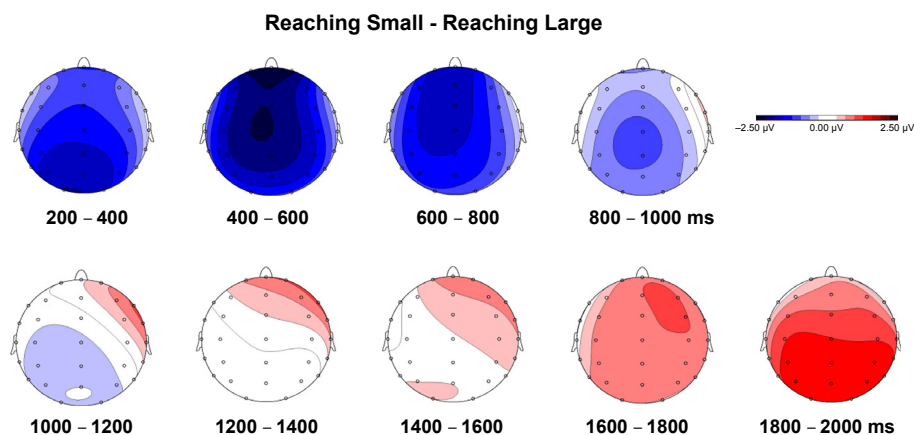


FIG. 4. The scalp maps show the topography of the differential ERP amplitude between Reaching Small and Reaching Large conditions, from 200 to 2000 ms.

at midline compared with left ($P < 0.001$) and right ($P < 0.001$) sites. The *post hoc* analysis of the anterior-posterior \times left-right electrode position interaction ($F_{4,18} = 27.67$, $P < 0.001$; $\eta_p^2 = 0.59$) revealed that, for both conditions, at left and right sites the m-N400

amplitude increased progressively from central to frontal areas ($P < 0.003$), whereas at midline sites it was more widely distributed along the anterior-posterior direction (only at FCz was the amplitude higher compared with Cz, $P = 0.004$).

Neither the object size nor electrode position effect was found on peak latency. In summary, the m-N400 showed a higher amplitude for the small than for the large object at all electrode sites considered. Specifically, the maximum peak value was reached at FCz (small object : Mean Amplitude = $-13.51 \pm 4.09 \mu\text{V}$, Mean Latency = $410.15 \pm 54.85 \text{ ms}$; large object : Mean Amplitude = $-11.29 \pm 3.73 \mu\text{V}$, Mean Latency = $409.96 \pm 53.83 \text{ ms}$). The differential scalp distribution for the m-N400 component, depicted in Fig. 4 clearly shows that in this time window the ERPs were higher and more negative for the small object condition at frontal and central areas.

400–800 ms

As shown in Fig. 4, a sustained potential was observed from 400 to 800 ms at frontal, fronto-central, central, and parietal electrode sites (F3, Fz, F4, FC3, FCz, FC4, C3, Cz, C4, P3, Pz and P4). The mean ERP amplitude in this time window was analysed. Similarly to m-N400 results, the 2 (object size) \times 4 (anterior–posterior electrode position) \times 3 (left–right electrode position) ANOVA revealed that the potential reached an overall higher (more negative) mean ERP amplitude for the small compared with the large object in all frontal, fronto-central and central electrode sites (main effect of object size – $F_{1,21} = 10.63$, $P = 0.004$; $\eta_p^2 = 0.35$). A significant main effect of anterior–posterior electrode position ($F_{2,20} = 42.68$, $P < 0.001$; $\eta_p^2 = 0.68$) revealed that, for both reaching conditions, the mean amplitudes were progressively larger from parietal to frontal areas (all P -values < 0.009), whereas they did not differ between frontal and fronto-central sites. As for the m-N400, a significant main effect of left–right electrode position ($F_{2,20} = 37.03$, $P < 0.001$; $\eta_p^2 = 0.65$) showed that the mean ERP amplitude within the 400–800 ms time window was maximal at midline compared with both

left and right sites (P -values < 0.001). The *post hoc* analysis of the anterior–posterior \times left–right electrode position interaction ($F_{4,18} = 27.67$, $P < 0.001$; $\eta_p^2 = 0.59$) revealed that, for both reaching conditions such sustained negativity at right sites was progressively larger from parietal to frontal sites, whereas at left sites no differences were found between frontal and fronto-central sites, and at midline electrodes no differences were found between frontal, fronto-central and central sites. This result reflects an equal distribution of such a component at Fz, FCz and Cz electrodes. The maximum mean values of this sustained activity were found at FCz (small object : Mean Amplitude = $-7.58 \pm 2.78 \mu\text{V}$; large object : Mean Amplitude = $-5.85 \pm 3.57 \mu\text{V}$).

Correlations between kinematic and evoked-related potential measures

The mean amplitude and latency of P300 were averaged across the P3, Pz and P4 electrodes; the mean amplitude and latency of m-N400 was considered where such a component was maximally expressed (i.e. at FCz). These values were correlated with the reaction time, movement time, and time of peak velocity (Fig. 5A). A positive correlation was found between movement time and m-N400 latency for both the small and the large objects (small object – $r = 0.59$, $P = 0.005$; large object – $r = 0.45$, $P = 0.039$). Figure 5B illustrates the individual mean individual latency values of the m-N400 component and individual movement times for the two conditions.

Discussion

The aim of the present study was to investigate the kinematics and ERP activity during reaching movements performed towards either a large or a small object. Differently from previous studies, we did

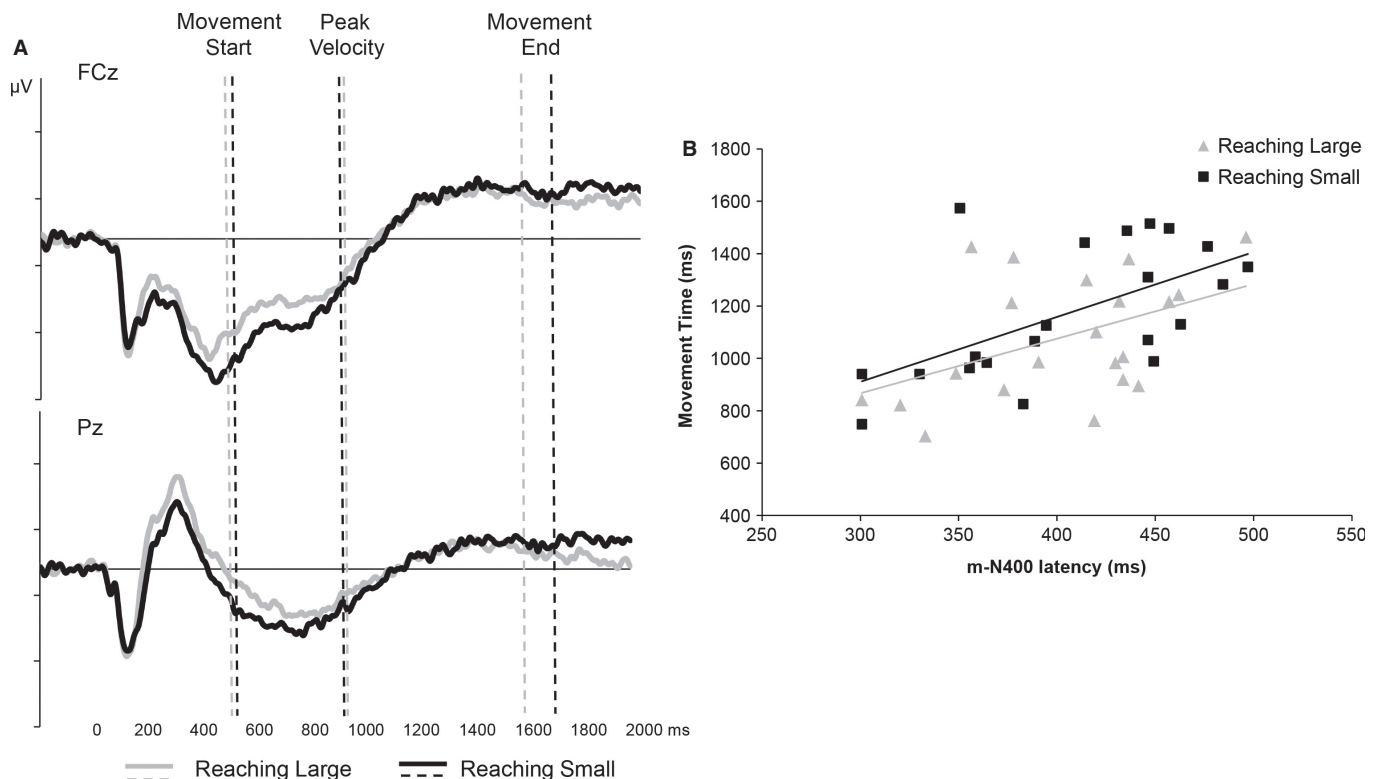


FIG. 5. (A) The timeline of events (Movement Start, Peak Velocity, and Movement End) together with the ERP grand-average waveforms at representative sites (FCz and Pz). (B) The correlation between individual movement time and individual m-N400 latency in Reaching Small and Reaching Large conditions.

not investigate ERPs evoked by a cue anticipating a specific object's intrinsic features, but by the target object itself. Such an approach may allow the examination of how information about an object's geometric properties is transformed into specific motor programs more directly. Overall, the results indicate that object size determines a modulation in the timing and amplitude of specific kinematic landmarks and ERP components during reaching movements. In particular, the novelty of the present study resides in the fact that (i) the modulation of parietal activity to object size precedes the beginning of the movement and (ii) fronto-parietal areas are modulated by object size although this property does not need to be integrated in the motor act.

Before we discuss how our results fit with previous studies, it is worth clarifying that previous experiments in humans have employed a variety of tasks to investigate the behavioral and neural correlates of reaching. These tasks include reach-to-touch (Pellijeff *et al.*, 2006; Levy *et al.*, 2007; Cavina-Pratesi *et al.*, 2010), pointing (Connolly *et al.*, 2000, 2003; DeSouza *et al.*, 2000; Astafiev *et al.*, 2003; Fernandez-Ruiz *et al.*, 2007; Hagler *et al.*, 2007), and joystick manipulation (Grefkes *et al.*, 2004). These tasks differ widely in the extent of arm movement, purpose and cortical recruitment (Culham & Valyear, 2006; Culham *et al.*, 2006; Filimon *et al.*, 2009). Furthermore, these tasks also differ in terms of initial hand posture, a factor that has the ability to influence the unfolding of reaching movements (Kritikos *et al.*, 1998). Therefore, we cannot exclude that adopting a different task might have brought different outcomes.

Consistent with previous reports, arm trajectories changed their shape when targets of different size were used, and this effect was chiefly due to modifications in the deceleration phase (MacKenzie *et al.*, 1987; Gentilucci *et al.*, 1991; Castiello, 2001). Fitt's law (1954) was found to apply, given that movement time increased as a function of task difficulty. The movement time was longer and maximum velocity was lower for smaller objects requiring a greater level of accuracy. Altogether these findings indicate that the size of the object had the ability to selectively influence the execution of a reaching movement. This is an important aspect of the present study because, in order to ascertain the effects that such differential processing might have on ERPs, it is necessary to demonstrate that the participants' movement showed differential kinematic signatures depending on reach conditions.

For an efficient reaching movement the brain must integrate information about the selected arm with information about the selected target. The general consensus is that this integrative action is accomplished through interactions between posterior parietal and premotor areas of the brain in both monkeys (Kalaska *et al.*, 1997; Wise *et al.*, 1997; Caminiti *et al.*, 1998) and humans (Grafton *et al.*, 1996; Thoenissen *et al.*, 2002; Astafiev *et al.*, 2003; Connolly *et al.*, 2003; Medendorp *et al.*, 2003, 2005; Culham *et al.*, 2006; Beurze *et al.*, 2007; Gallivan *et al.*, 2011; Bozzacchi *et al.*, 2012; Konen *et al.*, 2013). Our EEG recordings corroborate these findings, revealing that the planning and execution of reaching movements evolves across several cortical areas within the fronto-parietal network following a specific timing (Weinrich *et al.*, 1984; Kalaska & Crammond, 1992; Glover *et al.*, 2012).

Differences in amplitude between the small and the large object conditions become evident over parietal sites at around 300 ms (P300), during the planning phase of the movement. This activity reflects the involvement of parietal areas in the planning of reaching movements (Culham *et al.*, 2006; Beurze *et al.*, 2007, 2009; Gallivan *et al.*, 2011; Konen *et al.*, 2013). These areas include part of either the classic parietal reach region identified in the macaque

(Andersen & Buneo, 2002; Bhattacharyya *et al.*, 2009) and area V6A (e.g. Fattori *et al.*, 2005; Bosco *et al.*, 2010) or their putative human homologue, the superior parieto-occipital cortex region (Connolly *et al.*, 2003; Gallivan *et al.*, 2009; Cavina-Pratesi *et al.*, 2010).

The P300 peak amplitude was higher for the large than for the small object condition. This finding might indicate the greater amount of visuo-spatial information that is extracted from larger objects, reflecting parietal activity that, in both humans and macaques, appears to serve a variety of visuo-motor and attention-related functions. For instance, it might be concerned with the encoding of three-dimensional visual features of objects for action (Gallivan *et al.*, 2011; Fattori *et al.*, 2012) and the integration of both target and effector-specific information for movements (Beurze *et al.*, 2009). In this respect, attention research indicates that the focus of attention can be modulated depending on the size of the area over which focal attention is allocated (Castiello & Umiltà, 1990, 1992). Furthermore, this finding is also in line with recent functional magnetic resonance imaging research showing that parietal areas, such as the anterior intra-parietal sulcus, are involved in integrating information about real three-dimensional objects, such as the object size and the grasp-relevant dimension (Monaco *et al.*, 2013). In addition, it agrees with neurophysiological findings showing that neurons in area V6A are influenced by spatial attention. The general suggestion is that this area, primarily involved in visuo-motor transformation for reaching, may form a neural basis for coupling attention to the preparation of reaching movements (Galletti *et al.*, 2010). Overall, this particular finding might provide additional evidence for the integration of visuo-motor and attention-related processes during movement planning (Baldauf & Deubel, 2010; Gallivan *et al.*, 2011; Konen *et al.*, 2013).

Overall, the results concerned with parietal activity fit with neurophysiological findings suggesting that areas of the dorso-medial pathway are sensitive to intrinsic features of target objects such as shape (Fattori *et al.*, 2010, 2012).

In terms of frontal regions, we found a negative electrical activity, peaking at around 400 ms following object appearance (m-N400), that was evident over central and frontal electrode sites. The spatio-temporal characteristics of the m-N400 might be assimilated to an index of motor planning and it is strongly influenced by motor variables. The polarity, timing and scalp distribution suggest that such a component reflects motor planning and that it is linked to premotor activity (Shibasaki & Hallett, 2006).

In the frontal cortex of monkeys, premotor dorsal and premotor ventral neurons are shown to be involved in different aspects of reaching movements (Hoshi & Tanji, 2000, 2002, 2004a,b,c, 2006; Calton *et al.*, 2002; Hoshi *et al.*, 2005). Similarly, in humans, electrophysiological (Naranjo *et al.*, 2007), neuroimaging (Beurze *et al.*, 2007; Grol *et al.*, 2007; Glover *et al.*, 2012) and neuropsychological (Heilman & Gonzalez Rothi, 1993) evidence indicates that premotor cortices are central to the process of reach planning. Our findings are in agreement with these views, by showing that premotor cortices are activated during reaching preparation. Importantly, the m-N400 peak had a later onset and a wider fronto-central distribution for the small than for the large object. This result demonstrates that premotor activity during reach planning is concerned not only with reach direction or the integration of target location with information about the selected effector (Kertzman *et al.*, 1997; Hoshi & Tanji, 2000, 2002, 2004a,b,c, 2006; Batista & Andersen, 2001; Buneo *et al.*, 2002; Calton *et al.*, 2002; Medendorp *et al.*, 2005), but also with the intrinsic features of objects.

A point worth noting is that the difference in amplitude between the small and the large objects remained significant up to 800 ms. This suggests that the size-dependent modulation of premotor activity noticed during reach planning spreads into the execution phase of the action, implying that, before the action can begin, the motor programme has to be fully formulated and that kinematic planning might be fully fledged during the online control phase of the movement. In this respect, our behavioral results might support this view. Whereas there was a (non-significant) tendency for reaction time to be longer for the small than the large object, the time to peak velocity occurred significantly earlier for the small than for the large object. This indicates that planning continues to be influential and is optimised early in the movement. Such a gradual crossover between planning and control systems has the benefit of allowing for smooth rather than jerky corrections (Wolpert & Ghahramani, 2000; Glover, 2004). The differences between the small and the large object may reflect the need for additional sensorimotor control mechanisms for the more accurate condition (i.e. small object). In this respect, the present and previous psychophysical studies demonstrated that, as object size decreased, subjects had longer movement times, slower speeds, and more asymmetrical hand-speed profiles (Gentilucci *et al.*, 1991; Berthier *et al.*, 1996).

Altogether, the above-mentioned findings suggest that both preparatory and execution activity along the fronto-parietal circuit underlying reaching are modulated by object size. This result can be explained in terms of the intimate relationship between reaching and grasping components during prehension movements (Jeannerod, 1984). It is known that grasping in humans and macaques activates parietal and premotor areas that overlap with reach-related activations (Tanné-Gariépy *et al.*, 2002; Culham *et al.*, 2003; Raos *et al.*, 2004; Castiello, 2005; Davare *et al.*, 2006; Fattori *et al.*, 2009, 2010, 2012). Therefore, it might be conceivable that the neural network that controls proximal movements in reaching-to-grasp has information about object size, given that the two components should act in concert in order to determine the timing of hand preshaping during reaching. But why should the proximal neural channel be sensitive to object size during reaching alone, given that the distal program remains unmodified for small and large objects? In our opinion, it would be difficult to conceive how the reaching channel could act without extracting information regarding object size. From the mere fact that it occupies space, an object must have a size, and to locate it necessarily entails information about its dimension. In this respect, our findings might provide a novel demonstration that the reaching and grasping phases are represented by overlapping parieto-frontal circuits, suggesting a lack of strict functional segregation between parieto-frontal circuits for grasping and reaching in monkeys (e.g. Fattori *et al.*, 2010) and humans (Grol *et al.*, 2007; Filimon *et al.*, 2009; Filimon *et al.* 2010).

As a final issue, we found that, for both the large and the small objects, the individual mean latency for the premotor m-N400 component significantly correlated with the individual mean for movement time. According to behavioral evidence, reaching movements are characterised by a ballistic and a feedback-based phase. The ballistic phase is a product of a feedforward system that defines the initial state of the limb and the goal. The feedback phase is used at the end of this movement to achieve an accurate contact with the object. An alternative possibility is that the second phase is controlled, as is the first, by a feedforward system that takes into account the object size and accordingly sets its duration. This might indicate that an estimate of movement time, possibly performed at the level of premotor areas, might serve to plan the amount of online control required during the final part of the movement.

In summary, the present study demonstrates that the use of converging techniques with different characteristics might allow better understanding of how the human brain controls the reaching function. In particular, it presents the timing of activation of the cortical regions engaged for the planning and execution of a human reach, starting from the early coding of the intrinsic features of the object to the motor plan that leads to the actualisation of the movements. Although these findings confirm previous evidence concerned with reach planning and execution in general, they add to previous literature demonstrating that, in humans, the neural network underlying reaching movements is modulated by object size.

Abbreviations

EEG, electroencephalography; ERP, evoked-related potential; m-N400, motor-related N400

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