Competitive interactions in sensorimotor cortex: oscillations express separation between alternative movement targets

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ABSTRACT

Choice behavior is influenced by factors such as reward and number of alternatives, but also by physical context, for instance, the relative position of alternative movement targets. At small separation, speeded eye or hand movements are more likely to land between targets (spatial averaging) than at larger separation. Neurocomputational models explain such behavior in terms of cortical activity being preshaped by the movement environment. Here, we manipulate target separation, as a determinant of motor cortical activity in choice behavior, to address neural mechanisms of response selection. Specifically, we investigate whether context-induced changes in the balance of cooperative and competitive interactions between competing groups of neurons are expressed in the power spectrum of sensorimotor rhythms. We recorded MEG while participants were precued to two possible movement target locations at different angles of separation (30°, 60° or 90°). After a delay, one of the locations was cued as the target for a joystick pointing movement. We found that late delay-period movement-preparatory activity increased more strongly for alternative targets at 30° than at 60° or 90° of separation. This non-linear pattern was evident in slow event-related fields as well as in beta- and low-gamma band suppression. A comparable pattern was found within an earlier window for theta-band synchronization. We interpret the late delay effects in terms of increased movement-preparatory activity when there is greater overlap and hence less competition between groups of neurons encoding two response alternatives. Early delay period theta-band synchronization may reflect covert response activation relevant to behavioral spatial averaging effects.
INTRODUCTION

Seminal work by Georgopoulos and colleagues (1982) showed that individual neurons in the nonhuman primate motor cortex are only broadly tuned to a particular direction, and that the actual direction of a movement is coded by a population of neurons through a mechanism of vector averaging (Georgopoulos et al. 1986). Although current knowledge of directional tuning of motor cortex neurons and population coding of movement direction still largely derives from single-unit recordings in monkey, these phenomena are not intractable to noninvasive study in humans (e.g., Fabbri et al. 2010). Eisenberg et al. (2010) used fMRI to demonstrate that motor cortex neurons with similar directional preference tend to cluster in groups. Furthermore, spatial patterns of active voxels became less correlated with increasing separation of movement directions. These findings indicate a comparable structural organization of movement-direction encoding in humans compared to non-human primates, established by noninvasive means, but do not yet address how such an anatomical organization functionally shapes response selection and movement generation. Here, we address this functional question, using magnetoencephalography to investigate the competitive and cooperative interactions between cell groups coding for alternative movement directions.

Behavioral work on eye- and hand movement trajectories expressing a choice between alternative targets has distinguished between continuous and discrete modes of movement direction specification. At angular separations smaller than ~35 degrees, speeded hand and eye movements directed to one target frequently land between the targets (Ottos et al. 1984; Ghez et al. 1997; Van der Stigchel and Nijboer 2013). At wider separation, such responses to a central default value are rare. Computational models of (pre)motor cortex function (Cisek 2006; Erhagen and Schöner 2002) explain such behavior in terms of motor cortical activity being preshaped by the movement environment. Movement targets at close proximity will preactivate overlapping populations of neurons, thus explaining co-activation and an averaging tendency, resulting in a unimodal response distribution. At larger separation, the preactivated populations share fewer cooperative interactions while there are more mutually inhibitory connections, ensuring a bimodal response pattern. Data and models thus
suggest that target proximity is an important determinant of motor cortical activity in choice behavior, providing a window on neural mechanisms of response selection.

In the present study, we investigate whether varying spatial separation of two alternative movement targets is expressed in the power spectrum of MEG-recorded sensorimotor cortex rhythms, using angular distances of 30°, 60° and 90°, as originally used in related behavioral studies (Ottes et al. 1984; Ghez et al. 1997). Relevant previous neurophysiological work in humans was restricted to effects of target number or did not manipulate target proximity in isolation (Praamstra et al. 2009; Rawle et al. 2012; Tzagarakis et al. 2010). Based on the distinction between continuous and discrete modes of direction specification, we conjecture a non-linear attenuation of preparatory activity with increasing separation, most likely expressed in the motor cortex beta rhythms. In addition to this modulation in strength of preparatory activity (cf. Pastor-Bernier and Cisek 2011), we hypothesized that lateral interactions between competing cell groups, ‘producing’ this modulation, might be expressed in power and spectral properties of higher-frequency gamma rhythms, analogous to effects on visual cortex gamma oscillations dependent on the dispersion of horizontal connections (Pinotsis et al. 2012; Schwarzkopf et al. 2012). Although gamma oscillatory activity in the motor cortex is most pronounced during motor execution, there is a build up of gamma activity during preparation (Donner et al. 2009). The results confirm the predictions in part and provide new information on oscillatory signatures of motor cortical activity involved in the preparation for and decision between alternative movement options.
METHODS

Participants

Twenty healthy participants, all right handed (by self report), took part in the experiment. Data from eighteen of them (mean age 26.4 ± 9.8 years; 11 female) were included in the final analyses. Two participants were excluded because of technical problems or poor data quality. Participants were either paid (€ 8 / hour) or received student credit points for their participation. Written informed consent was provided after explanation of the task and experimental procedures, in accordance with local institutional guidelines (Committee on Research Involving Human Subjects, region Arnhem-Nijmegen, The Netherlands).

Experimental setup

The task was a cued center-out movement task with visually presented stimuli and pointing responses made with a Logitech ATK3 joystick (custom-modified to ensure MEG compatibility) to one of two precued target locations (Fig. 1A). A dark grey fixation dot (RGB 64-64-64, diameter 0.79° visual angle) was presented continuously, placed at the center of a slightly lighter grey screen (RGB 96-96-96) at 80 cm distance from the participants' eyes. Two dark grey target location dots (RGB 64-64-64, diameter 0.64° visual angle) were presented at precue onset and remained on screen during a delay period (1200 ms) and a subsequent response period (800 ms). The targets were displayed at locations above the central fixation dot on an imaginary circle extending 4.3° of visual angle (center-to-center distance). The two target locations were placed symmetrically around the vertical meridian, separated either by 30° (COND1), 60° (COND2) or 90° (COND3). These target separations were chosen on the basis of previous behavioral studies (Ottes et al. 1984; Ghez et al. 1997). The smallest separation is just in the range where spatial averaging is most frequent. The wider separations are both well into the range where it is rare. Intertrial interval varied randomly between 1500 and 2000 ms. The choice between alternative targets was cued by the response cue consisting of a small thin white line on top of the central fixation dot, with the line pointing in the direction of the designated target (see
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Fig. 1A, second column). Stimuli and joystick position feedback (presented as a small moving white cursor box across the screen; 0.43° x 0.43° visual angle) were presented with Presentation 16.2 software (Neurobehavioral Systems), using a liquid crystal display video projector, back projected onto a translucent screen with two front-silvered mirrors.

The experiment consisted of 10 blocks of 60 trials each (20 trials for each condition; 50% probability of left/right targets; duration ~4 minutes), preceded by two comparable practice blocks. The order of presentation of trials from the three conditions was randomized within each block of trials and for each participant. Participants were instructed to move as little as possible, to keep their eyes fixed at the fixation dot at all times, and to hold the joystick with their right hand in a relaxed grip. They were instructed to prepare for responding during the precue period and then respond as fast and accurately as possible with a ballistic joystick-guided pointing movement to the cued target after the onset of the response cue. They were also asked to make swift, ballistic responses instead of slow visually guided movements. Hence, they were allowed to overshoot the target location. Maximum hand displacement was 4-5 cm, corresponding to a displacement of the corresponding joystick cursor position on the screen of maximally around 10 cm (ca. 2 cm exceeding the target location). Participants were instructed to relax arm and hand as much as possible during the intertrial and delay periods, without releasing the joystick grip.

Recordings

MEG data were recorded continuously using a whole-head system with 275 axial gradiometers (VSM/CTF systems). Head position with respect to the sensor array was measured and monitored during the course of the experiment (Stolk et al. 2013), using localization coils attached to anatomical landmarks (the nasion and, using earplugs, the left and right ear canal). Furthermore, horizontal and vertical electro-oculogram (EOG) were recorded in a bipolar montage using electrodes placed below and above the left eye and at the outer canthi. Joystick position was sampled continuously on the stimulus presentation computer to enable updated joystick cursor positions at screen refresh rate (60 Hz) during task performance. In addition, the joystick XY-coordinates were continuously recorded.
together with the MEG data. All MEG, EOG, and joystick XY-streaming data were low-pass filtered at 300 Hz, sampled at 1200 Hz and saved to disk.

Structural T1 MRI scans were obtained for all subjects on a Siemens 1.5T Avanto (TR/TE 2250ms/2950ms) MRI scanner. During MR acquisition, identical earplugs (now with a vitamin E capsules in place of the MEG localization coils) were used to allow for off-line co-registration of the MRI and MEG data.

Behavioral analysis

Task performance was analyzed on the basis of the joystick position data. Reaction time (RT) was calculated from movement onset, defined as the time when the joystick displacement was first exceeding a threshold of 2.5 standard deviations above the mean amplitude during a 200 ms baseline before the response cue, determined separately for each condition. Error analyses were based on an off-line trial-by-trial visual inspection of movement trajectories. Errors were classified into three categories: 1) choice and timing errors, 2) corrections, and 3) inaccurately targeted responses. Choice and timing errors included: a) trials in which the movement trajectory ended or passed the incorrect target (wrong location), b) trials in which a response occurred during the delay period (premature response), and c) trials in which a response was too fast (< 200 ms) or too slow (> 800 ms) or missing altogether. Corrections were trials in which the joystick trajectories revealed online corrections from the incorrect to the correct location, estimated by comparing the cursor position at 50% and 75% of maximum velocity. In more detail, when the two positions were not on a single line through the center cue and one of the targets, the trial was classified as incorrect due to online correction. Finally, trials were classified as "inaccurately targeted" if the target location was missed by more than 10° (on either side) in the 30° separation condition or more than 15° in the other two conditions.

Differences in mean RTs and error rates (averaged across error types) between conditions were assessed using repeated-measures ANOVAs, including the within-subject factors CONDITION (30°, 60°, or 90°) and DIRECTION (left or right movements). Differences between conditions in terms of error types were tested separately, averaged across movement direction, using ANOVAs and the
within-subjects factors CONDITION (30°, 60°, or 90°) and ERRORTYPE (choice and timing error, correction, or inaccurately targeted response).

MEG sensor-data analysis

MEG data were analyzed with MATLAB (the MathWorks) using the open-source Fieldtrip toolbox (Oostenveld et al. 2011). Non-overlapping epochs of 3400 ms (800 ms baseline), centered around precue onset, were extracted separately per condition and for correct response trials only, combining the data from left and right target trials within each condition (as those were not behaviorally different between conditions). Preprocessing included the following steps. First, line noise contamination was removed by applying a digital 50 Hz discrete Fourier transform filter (including the first two harmonics: 100 and 150 Hz) on the continuous data. Second, artifact cleaning was performed, including semiautomatic removal of trials contaminated by muscle activity, slow drift, or SQUID jump artifacts, followed by ICA-based removal of eyeblink, eye movement, and ECG contamination, using down-sampled (300 Hz) data. This resulted in remaining datasets for further analyses consisting of on average 169 trials for COND1 (15.5 ± 6.8% rejected), 173 trials for COND2 (13.5 ± 8.9% rejected), and 172 trials for COND3 (14 ± 8.9% rejected).

Further analyses included time-frequency analysis, time-domain analysis, beamformer source estimation and statistical analysis. Time-frequency decompositions were performed for horizontal and vertical planar transformed MEG data that was subsequently combined to obtain the power at each virtual planar gradiometer location, regardless of the orientation of the gradient (Bastiaansen and Knösche 2000). This procedure simplifies the interpretation of the sensor-level data, as with planar gradients the maximal signal is located above the source (Hämäläinen et al. 1993). A comparable transformation was applied to time-domain event-related field (ERF) averages.

Time-frequency power representations (TFRs) were computed based on a sliding window Fourier approach, with a step size of 50 ms. Power of lower frequencies (range 1-60 Hz) were estimated based on 4 seconds of padded data (original length 3.4 sec), using an adaptive sliding window of 3 cycles per frequency bin (step-size 1 Hz), multiplying the data with a Hanning taper
before power estimation. From these data, beta (17-29 Hz) and theta (4-6 Hz) power estimates were extracted for further analysis. For the higher-frequency range, a multi-tapering approach was used with orthogonal slepian tapers (Mitra and Pesaran 1999), which allows better capture of the broadband oscillatory activity in the higher range, while reducing spectral leakage. For this frequency range (30-120 Hz; stepsize 5 Hz), power was estimated using sliding windows of 30 cycles per frequency bin and applying a spectral smoothing of 10 Hz by adapting the number of orthogonal Slepian tapers (2-9 tapers: higher number used for lower frequencies and v.v.). From these data, low-gamma (30-50 Hz) and high-gamma (60-80 Hz) band power estimates were extracted for further analysis.

**MEG source reconstruction**

Source estimation of oscillatory activity was performed using the Dynamic Imaging of Coherent Sources (DICS) beamforming approach (Gross et al. 2001; Liljeström et al. 2005). Participant-specific anatomical MRIs were used to linearly transform a 3D template grid (8 mm spacing) in Montreal Neurological Institute (MNI) coordinates to the co-registered MEG coordinates system specific to the participant's head. Subsequently, the inverse of this transformation was applied to obtain grid points at matched brain locations across participants. Spatial filters were constructed for each of the grid positions, passing the activity from the location of interest with unit gain, while maximally suppressing activity from all other possible sources of neural and non-neural activity. The beamformer spatial filter is constructed from the lead field and the cross-spectral-density matrix of the data. The lead field is the physical forward model of the field distribution calculated from an assumed source at a given location and the participant-specific volume-conduction model of the head. Here, we used a single-shell volume-conduction model of the brain, based on the brain boundaries determined by the segmented anatomical MRI to compute the lead field (Nolte 2003).

Source estimation procedures included DICS across conditions of 1) delay period event-related desynchronization in the beta and low-gamma range, using data from a window between 600-1100 ms following precue onset against a 500 ms precue baseline, and 2) response period event-related synchronization in the theta and high-gamma range, using data from a window between 1400-1900 ms.
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10 ms and 1450-1750 ms following precue onset against a 500 or 300 ms precue baseline, respectively.

In all cases, a common spatial filter was estimated first, based on the pooled data from both time intervals (active and baseline), using all single trials. Subsequently, this filter was used to obtain power estimates within each interval by projecting the single trial data of each time interval through the common spatial filter. Finally, source activity across conditions was estimated by computing the difference between active and baseline source activity as a relative power change from baseline (i.e., by dividing the difference between active and baseline source activity by the baseline source activity).

MEG statistical analysis

For sensor-level analyses, significance of left sensorimotor-cortex (LMtctx) related oscillatory activity and slow-wave ERF (event related field) changes among conditions were assessed with ANOVAs, using the within-subject factor CONDITION (COND1, COND2, COND3). Reported $p$-values were Greenhouse-Geisser corrected in order to deal with violations of sphericity. In case of a significant main effect of CONDITION, subsequent pairwise comparisons were used to further delineate significant differences between pairs of conditions. The reported $p$-values of these analyses were Bonferroni corrected in order to deal with the multiple comparison problem. For all these analyses, sensor-level LMtctx ROI data (for ROI location, see Fig. 2C) was used, averaged across ROI sensors, frequency bins and time points of interest. The LMtctx ROI contained a selection of 14 sensors covering the area of maximum grand-average pre-response (-200-0 ms; response-locked) beta-ERD activity, measured against a 500 ms baseline (1000 to 500 ms prior to response onset). Time windows of interest were a priori selected for beta, low-gamma and high-gamma band activity, covering the late delay period thus avoiding stimulus-related effects early in the delay period. The time window for analysis of early theta activity was defined on the basis of visual inspection of the grand average. For the delay period oscillatory activity the selected windows were 600-1100 ms for beta, low-gamma, and high-gamma band activity, and 150-450 ms for early theta band activity, all against a 500 ms precue baseline. For the ERF activity, however, delay period activity included the last 500 ms of the delay
period (700-1200 ms), as no backward shift of 100 ms was needed to avoid (frequency) bleeding of response-cue triggered activity into the delay period.

RESULTS

Behavioral performance

Figure 1 shows example trajectories of joystick responses from a single participant (panel A) and an overview of the behavioral response profiles across all participants and all conditions (panel B). Despite the emphasis on speed, movement endpoints and trajectories were generally highly accurate, even in the condition of smallest target separation (COND1 - 30°). Response onset times were not affected by the manipulation of target separation. The average left and right response times (and corresponding standard deviations of the mean) were 432 ± 44 ms and 428 ± 41 ms for the 30° separation condition (COND1), 430 ± 45 ms and 427 ± 39 ms for the 60° separation condition (COND2), and 430 ± 42 ms and 428 ± 40 ms for the 90° separation condition (COND3), respectively. Statistical analysis confirmed that participants responded equally fast in each condition and to each of the two targets. Error rates, however, although generally low, showed a significant main effect of CONDITION ($F(2,34) = 18.9, p < 0.0001$), independent of movement direction. Mean error rates were higher for COND1 (1.1 ± 1.1% left, 2.7 ± 3.0% right) than for COND2 (0.2 ± 0.2% left, 0.5 ± 0.6% right) and COND3 (0.4 ± 0.7% left, 0.6 ± 0.7% right), a pattern confirmed by pairwise comparisons between conditions (COND1 vs 2 contrast $p < 0.0001$, and COND1 vs 3 contrast $p = 0.004$, whereas COND2 vs 3 contrast was not significantly different).

The condition of smallest spatial separation between movement targets also induced a different pattern of error types, as apparent from the right histogram of Figure 1B. Although percentage of inaccurately targeted responses, averaged across movement directions (COND1: 0.5 ± 0.9%, COND2: 0.2 ± 0.3%, COND3: 0.03 ± 0.1%) and percentage of choice and timing errors (COND1: 0.9 ± 1.0%, COND2: 0.2 ± 0.4%, COND3: 0.5 ± 0.6%) were comparable across conditions, participants were more likely to correct their response during responding in COND1 (2.4 ± 2.4%) than in the other
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two conditions (COND2: 0.3 ± 0.5%, COND3: 0.5 ± 0.8%). This was statistically confirmed by significant main effects of CONDITION \((F(2, 34) = 18.9, p < 0.001)\) and ERRORTYPE \((F(1.2, 20.1) = 9.0, p = 0.005)\) and an additional CONDITION x ERRORTYPE interaction effect \((F(1.5, 25.0) = 5.1, p = 0.021)\).

To summarize, reaction times were identical across conditions and movement trajectories showed clear bimodal response distributions for all separation conditions. The absence of spatial averaging effects in movement trajectories, even in COND1 with 30° separation between targets, is attributed to the instructed delay before the response. The increased error rate for this condition (although still low in number and removed from the MEG analyses), may nonetheless be due to a residual averaging tendency. Since there were no effects of response direction, for further analyses, MEG data were pooled across movement directions.

*Delay period effects reflecting strength of motor preparation*

Neural field models of motor cortical activity involved in the representation and decision between alternative responses conceive this activity as sensitive to the layout of the movement environment. Specifically, the strength of competition between movement alternatives depends on the degree of overlap of the relevant neural representations. Empirically, at the cell level, monkey (pre)motor cortex neural activity during a delay period gets indeed weaker with increasing angular distance between two alternative movement targets (Pastor-Bernier and Cisek 2011). The present results comprise a similar effect of movement-related fields in humans, but also predicted oscillatory effects indicative of differential movement preparation dependent on target separation.

Time-frequency decomposition across conditions showed that, following the onset of the precue, preparatory sensorimotor-cortex activity (LMctx ROI - sensor locations see Fig. 2C) was evident at the sensor level as a general pattern of power suppression in the alpha, beta and lower gamma range during the later part of the delay period and during most of the response period (Fig. 2B). Furthermore, within the lower theta range (Fig. 2B; left panel ~3-7 Hz) a weak and more transient power increase was present early in the delay period (~200-500 ms) and during a later response.
selection and execution period (~1400-1900 ms). In addition, a clear transient power increase was
evident within the high gamma range (Fig. 2B; right panel ~60-80 Hz) around response onset (~1500-
1800 ms) and during movement. Source modeling localized the delay-period beta and low-gamma
activity and the response-related high-gamma and theta activity most clearly to the sensorimotor
cortex (Fig. 2A). In addition to event-related field activity, these frequency bands were analyzed further
for signs of differential preparatory activity between conditions.

Movement-related fields. The left-most panel of Figure 2C shows sensor-level event-related field
activity, for each of the three conditions separately, plotted across time and averaged across
LMtctx ROI sensors. The delay period shows the magnetic counterpart of the CNV (mCNV; Elbert et
al. 1994), typically of lower amplitude in MEG than in EEG. Visual inspection of the mCNV
nevertheless suggests that the condition of smallest spatial separation (COND1 - 30°), compared to
the other two conditions, induced increased negative slow-wave activity. The difference in amplitude
corresponded to a significant main effect of CONDITION ($F(1.7, 29.2) = 5.5, p < 0.02$). Subsequent
pairwise comparisons revealed that COND1 differed significantly from COND2 ($p = 0.01$), while the
difference between COND1 and COND3 reached a trend toward significance ($p = 0.08$).

Beta-band oscillatory power. The second panel of Figure 2C represents sensor-level time
courses of beta power for each of the three conditions, averaged across LMtctx ROI sensors. These
traces demonstrate the preparatory reduction in beta power typically seen in an instructed delay
before movement. Similar to the behavior of the mCNV, visual inspection suggests a difference
between the condition of smallest spatial separation on the one hand, and the two conditions with
wider separation on the other hand. Repeated-measures ANOVAs confirmed these observations
partially. A main effect of CONDITION was found for beta power ($F(2.0, 33.5) = 3.4, p < 0.05$).
Subsequent pairwise comparisons revealed that COND1 yield significantly more suppression of beta
power than COND2 ($p = 0.046$). The difference between COND1 and COND3 did not reach
significance.

Low gamma-band power. The third panel of Figure 2C shows the time course of low gamma
power. While the depth of the modulation is smaller than in the beta band, there is a similar pattern of
a gradual reduction in power during the delay period. This contrasts with the commonly observed movement-related augmentation of gamma power most consistently seen in the higher gamma range (Crone et al. 2011). The low gamma-ERD may, therefore, be functionally related more to beta-ERD. Importantly, the low gamma-ERD displays the same pattern of differences between conditions as beta-ERD and the mCNV. That is, there is a stronger ERD for COND1 compared to the other two conditions. The visual evaluation was confirmed by a main effect of CONDITION ($F(1.9, 31.5) = 5.9, p < 0.01$), while pairwise comparisons confirmed that COND1 differed significantly from COND2 as well as from COND3 ($p = 0.036$ and $p = 0.042$, respectively).

Together, the mCNV, beta-ERD and low gamma-ERD show a convergent non-linear pattern of stronger movement preparatory activity for alternative movement targets at 30°, compared to targets at 60° or 90°.

Gamma band signatures of lateral interactions

Based on previous work associating spectral characteristics of gamma activity with lateral interactions in the visual cortex (Pinotsis et al. 2012), gamma band activity is also a candidate rhythm to reveal interactions between cell groups in the motor cortex. Of particular relevance is the relation between peak frequency of MEG recorded gamma activity and the dispersion of horizontal connections (Pinotsis et al. 2012). As the width of interneuronal axon arbors is reflected in interneuron’s firing rate in frontal cortex (Krimer and Goldman-Rakic 2001), such a relation may exist in the motor cortex as well and provide a basis for spectral changes in gamma activity dependent on target separation.

Previous work in our group has also found gamma activity serving the maintenance of an action goal, providing further support to possible sensitivity of delay period gamma activity to target separation (van der Werf J. et al. 2008, 2010). As is evident from the top, most right, panel of Figure 2C, however, although there was a clear peak in high-gamma (60-80 Hz) band power around responding, this activity was not preceded by an increase (or decrease) of power in this frequency band during the delay period. Tested within the same window (600-1100 ms) as the beta-ERD and low gamma-ERD, high-gamma band activity was not different between conditions. So, unlike high gamma activity in the
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visual cortex, the current data on motor cortex gamma activity do not support an association of high gamma activity with lateral interactions.

Theta synchronization effects

Although we did not entertain an explicit hypothesis concerning the behavior of theta activity, we found a conspicuous modulation of theta power, with a brief phase of synchronization ~200-500 ms after precue onset and a second phase of theta-ERS concomitant with the motor response (Fig. 2C, lower right panel). As shown in Figure 2A (right top panel), this theta activity was clearly localized to the sensorimotor cortex, and displayed differences between conditions (Fig. 2C, lower right traces). Specifically, the early phase of theta-ERS was of higher amplitude for COND1 than for the conditions with wider target separations. Repeated-measures ANOVAs revealed a main effect of CONDITION for theta (4-6 Hz) power between 150-450 ms following precue onset ($F(1.8, 31.1) = 6.7$, $p < 0.01$). Subsequent pairwise comparisons revealed that COND1 differed significantly from COND2 in theta power ($p = 0.005$). The difference between COND1 and COND3 did not reach significance.

DISCUSSION

This study explored whether preparatory oscillatory activity in the motor cortex is influenced by the spatial separation between two alternative movement targets. The results show effects on slow event-related fields, beta-ERD, low gamma-ERD, and theta-ERS during the delay period. These neurophysiological effects tend to distinguish the small separation condition (30°) from the wider separation condition (60° and 90°), consistent with behavioral effects of target separation (i.e., spatial averaging). In the sections below, we discuss how the oscillatory changes may be associated with the interactions between competing cell groups encoding alternative movements.
Both for saccades and reaching movements, direction specification is such that, with small separation between alternative targets, responses tend to land at a central default or averaged value. Beyond a certain separation, the distribution of endpoints is bimodal (Ottes et al. 1984; Ghez et al. 1997; Chapman et al. 2010; Van der Stigchel and Nijboer 2013). Very strong averaging tendencies are found for separations up to 30° for reaching movements (Ghez et al. 1997) and 35° for saccades (Van der Stigchel and Nijboer 2013).

While these previous behavioral experiments strongly emphasized response speed, the present study used a delayed response task, and neural measures obtained during the delay, to investigate motor cortical correlates of target separation. Based on a theoretical framework assuming simultaneous encoding of alternative movement targets (Cisek and Kalaska 2010), such an approach may detect delay-period effects related to competitive interactions between the neural populations encoding the targets. However, the experimental approach cannot be expected to induce behavioral averaging effects, dependent as they are on speeded responses immediately upon a temporally and spatially unpredictable target display (Edelman and Keller 1998; Ghez et al. 1997; Meeter et al. 2010).

Accordingly, none were obtained, unless the slightly higher error rate for the smallest separation condition results from a residual averaging tendency.

As to reaction times, there is, likewise, no meaningful comparison with studies reporting averaging behavior. A few previous studies have also used a delay between target exposition and response signal. Similar to the present study, Pellizzer and Hedges (2003) found, for their two target condition, no effect of target separation. Praamstra et al. (2009) reported extremely small (< 10 ms) effects. The absence of RT effects in the present study is therefore in agreement with previous work, albeit surprising in the light of differential delay period motor preparation between conditions. We have previously suggested that this apparent contradiction is probably explained by the fact that close target proximity is a disadvantage for visual selection (Bahcall and Kowler 1999; Hilimire et al. 2009), canceling out any motoric advantage.
Oscillatory brain activity and competitive interactions between neural populations

Several reasons predict that the geometrical relations between groups of neurons encoding the cued directions will translate into delay-period effects on oscillatory activity. First, neural oscillations play a fundamental role in shaping cortical circuit activity, for example, by providing precise timing of action potentials of pyramidal cells and by controlling local network interactions (Buzsaki and Chrobak 1995; Bartos et al. 2007). Second, given the orderly structure of the motor cortex, with a clustering of cells that share directional preference (Eisenberg et al. 2010; Georgopoulos et al. 2007), interactions between groups of neurons coding for widely separated targets requires interneurons with wide horizontal arbor spans, whereas cell groups coding for more closely spaced targets interact through interneurons with a narrower span. In the prefrontal cortex, different horizontal arbor spans are associated with different interneuron firing rates, with rates going up with increasingly narrower arbor span (Krimer and Goldman-Rakic 2001). If the same applies for the motor cortex, oscillatory activity may be modulated by different spatial arrangements of alternative movement targets. Especially gamma oscillations have been suggested to play a role in cell tuning and associated mechanisms of lateral inhibition (Bartos et al. 2007; Merchant et al. 2012). In line with this reasoning, MEG-recorded visual cortex gamma activity was reported to reflect columnar size, and hence range of horizontal connections, in the gamma peak frequency (Pinotsis et al. 2012).

The present results do not contain similar effects for the most prevalent sensorimotor gamma activity in the higher frequency range > 50 Hz. While there was robust gamma synchronization concomitant with the response, gamma power in this range was low during the delay period, and unaffected by target proximity. In the lower gamma range of 30-50 Hz, by contrast, there was task-related desynchronization, the amplitude of which was modulated by target proximity. The desynchronization is similar to the well-known movement-preparatory desynchronization of beta activity, biasing the interpretation towards a movement preparatory function. To our knowledge, however, this behavior of lower range gamma activity is unusual. Hence, it is possible that these effects express changes in lateral interactions as a function of target proximity, the more so since relevant visual gamma effects occur in this frequency range (Pinotsis et al. 2012).
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Non-linear effects of target separation on movement preparatory activity

We tentatively distinguish between oscillatory changes expressing the regulatory action of horizontal connections (see previous section) and the resulting net effect on known indices of movement preparation, such as the mCNV and beta-ERD. Modulation of the strength of preparatory activity by target separation is suggested by single-unit recordings in monkey premotor cortex (Cisek and Kalaska 2005; Pastor-Bernier and Cisek 2011). A similar modulation occurs with variation of target number in various cortical and subcortical structures (Churchland and Ditterich 2012). The present results show a convergent pattern of stronger delay-period motor preparatory activity in the 30° separation condition compared to the 60° and 90° separation conditions, expressed in mCNV, beta-ERD, and low gamma-ERD. The mCNV modulation replicates CNV effects previously found in an EEG study (Praamstra et al. 2009).

This non-linear effect of target separation on neural indices associated with movement preparation is presumably related to microstructural properties of the motor cortex underlying the interaction between competing movement representations, resulting in spatial averaging for angular separations up to ~30-40° in direct instead of delayed response paradigms. As Pastor-Bernier and Cisek (2011) put it succinctly, the competition between potential actions is determined “…..by simple facts of geometry: when choosing between two nearby targets, the nervous system can mix their neural representations and start moving between the targets. However, choosing between two targets in opposite directions implies that the choice has to be all-or-none”.

An important remaining question is whether the modulation in strength of movement preparatory activity directly reflects the sensorimotor system’s representation of alternative movement targets at different separation, and the changed interaction between the involved cell groups, or whether it just signals that close proximity of movement targets elicits in subjects a stronger inclination to prepare for responding. The latter explanation has been put forward for the observation of stronger beta-ERD with a smaller number of response alternatives, expressed in the proposal that response (un)certainty is an important determinant of beta power (Tzagarakis et al. 2010). While there is no reason to favor such an explanation of the present effects as endogenously driven over an explanation as exogenously
induced, that is, shaped by the task space, the former cannot be ruled out without dissociating visual input and motor requirements. We are currently exploring this approach.

**Theta synchronization and spatial averaging**

Theta activity was characterized by an early synchronization phase following the precue and a later, higher amplitude synchronization concomitant with the response, well-localized to the sensorimotor cortex. Theta activity is observed in parieto-frontal regions in reaching and pointing tasks (Tombini et al. 2009; Perfetti et al. 2011; Rawle et al. 2012), as well as with simple finger movements (Yamanaka and Yamamoto 2010). Rawle et al. (2012) found a time course as in the present study, with the amplitude of the early phase modulated by the number of possible pointing targets. They proposed that the common factor in reported work on theta synchronization in motor tasks is that they require spatial attentional selection of a target in order to capture it with a movement. On this interpretation, the theta synchronization can be regarded as a precursor to movement (Cisek and Kalaska 2010).

Furthermore, the stronger the early theta-ERS is, the more easy attentional capture will evolve in an exogenously elicited response tendency.

The modulation of the early theta synchronization may be relevant to spatial averaging behavior. While the neural basis of spatial averaging in reaching is uncertain, it is more extensively investigated in eye movements (McPeek et al. 2003; Edelman and Keller 1998; van Opstal and Van Gisbergen 1990). Based on recordings in the superior colliculus, there is no evidence for loss of spatial segregation of targets for express saccades exhibiting spatial averaging. Instead, spatial averaging of saccade targets is seen as the result of a premature launch of the saccade before the process of saccade target selection, and computation of the saccade vector, is completed. A premature launch of saccades is facilitated by the greater salience of targets at close proximity, exerting a pull on the saccade system likened to the visual grasp reflex (Edelman and Keller 1998). The covert response activation represented by the early theta synchronization in our data, may thus represent a cortical correlate of a premature response tendency when alternative targets are close.
Conclusion

The results of this study show that motor cortical activity preceding a choice between two alternative pointing targets is not immune to the layout of the work space, here the spatial separation of targets. The well-characterized neural population coding of movement direction makes spatial separation of alternative movement targets a suitable testing ground for the question whether cooperative and competitive interactions between involved cell groups is expressed in modulations of ongoing oscillatory activity. The results do not show the modulation in the higher frequency range where we expected such effects. The effects that we found in lower frequency bands have a prima facie interpretation as a modulation of movement preparatory activity, suggesting the downstream effect of altered interactions between the relevant cell groups.

ACKNOWLEDGEMENTS

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Competition in sensorimotor cortex


FIGURE CAPTIONS

Figure 1. Behavioral data. A. At the top, the timeline of a single trial, independent of conditions. Below, an example of stimuli shown in each of the three conditions. The dashed white lines between the central cue and one of the two peripheral target locations in the response cue (respcue) display indicate joystick trajectories. Following the onset of the response cue, example joystick traces are shown of one participant's correct trials in each condition. B. Left histogram shows mean reaction times (RTs) for all conditions, separately for left and right targets. Right histogram shows corresponding error rates, broken down into the three main categories (cat 1: timing and choice errors, cat 2: online corrections, and cat 3: inaccurately targeted responses). Error bars represent standard deviations from the mean.

Figure 2. MEG activity. A. Left panel: beamformer source reconstructions of baseline-normalized, late delay (600-1100 ms) beta (17-29 Hz) and low-gamma (30-50 Hz) band activity, averaged across trials from all three conditions, projected onto the surface of an MNI template brain. Right panel shows the same for response period activity in the high-gamma (60-80 Hz; 1450-1750 ms) and theta range (3-7 Hz: 1400-1800 ms). All four frequency bands show left sensorimotor cortex activity of comparable location. B. Grand-average (n=18) time-frequency representations of lower-frequency range (1-60 Hz: left figure) and higher-frequency range (30-120 Hz: right figure) left sensorimotor cortex (LMtctx ROI) activity across conditions. The LMtctx ROI sensors, indicated with red dots on cartoon head, were selected on the basis of maximum grand-average beta-power suppression prior to responding. C. LMtctx ROI derived grand-average (precue-locked) traces of baseline-normalized relative changes in event-related field (ERF), beta, low gamma, high gamma and theta band activity, separately per condition (black lines representing COND1, red lines COND2 and green lines COND3). Grey boxes indicate statistical windows of significant differences between conditions.
A.  

**PRECUE**  
COND1: 30 degrees of separation  
COND2: 60 degrees of separation  
COND3: 90 degrees of separation  

**RESPCUE**  

**JOYSTICK TRACEDATA**  

**FIXATION**  

B.  

**mRTs (ms)**  
- COND1  
- COND2  
- COND3  

**errors per type (%)**  
- cat 1  
- cat 2  
- cat 3  
- total % errors  

COND1: 30 degrees of separation  
COND2: 60 degrees of separation  
COND3: 90 degrees of separation
ACROSS CONDITIONS

A. DELAY PERIOD

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RESPONSE PERIOD

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BETWEEN CONDITIONS

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LMtctx ROI