

Theta oscillations reflect a putative neural mechanism for human sensorimotor integration

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Cruikshank LC, Singhal A, Hueppelsheuser M, Caplan JB. Theta oscillations reflect a putative neural mechanism for human sensorimotor integration. *J Neurophysiol* 107: 65–77, 2012. First published October 5, 2011; doi:10.1152/jn.00893.2010.—Hippocampal theta oscillations (3–12 Hz) may reflect a mechanism for sensorimotor integration in rats (Bland BH. *Prog Neurobiol* 26: 1–54, 1986); however, it is unknown whether cortical theta activity underlies sensorimotor integration in humans. Rather, the mu rhythm (8–12 Hz) is typically found to desynchronize during movement. We measured oscillatory EEG activity for two conditions of an instructed delayed reaching paradigm. *Conditions 1* and *2* were designed to differentially manipulate the contribution of the ventral visuomotor stream during the response initiation phase. We tested the hypothesis that theta activity would reflect changes in the relevant sensorimotor network: *condition 2* engaged ventral stream mechanisms to a greater extent than *condition 1*. Theta oscillations were more prevalent during movement initiation and execution than during periods of stillness, consistent with a sensorimotor relevance for theta activity. Furthermore, theta activity was more prevalent at temporal sites in *condition 2* than *condition 1* during response initiation, suggesting that theta activity is present within the necessary sensorimotor network. Mu activity desynchronized more during *condition 2* than *condition 1*, suggesting mu desynchronization is also specific to the sensorimotor network. In summary, cortical theta synchronization and mu desynchronization may represent broadly applicable rhythmic mechanisms for sensorimotor integration in the human brain.

mu rhythm; reaching

ELECTROENCEPHALOGRAPHIC RECORDINGS from the hippocampus of many animals reliably display a robust, large amplitude oscillation with frequency 3–12 Hz. These theta oscillations have been implicated in various animal behaviors, including locomotion (Black and Young 1972; Buno and Velluti 1977; Komisaruk 1970; Vanderwolf 1969; Yoshii et al. 1966), exploratory behavior (Buzsaki 2005; Grastyan et al. 1966; Kahana et al. 2001; Macrides et al. 1982; Routtenberg and Kramis 1968), neural coding of place (Jensen and Lisman 2000; O’Keefe and Conway 1978; O’Keefe and Recce 1993; Sutherland and Rodriguez 1989; Yamaguchi et al. 2007), and memory (Berry et al. 1978; Berry and Thompson 1979; Griffin et al. 2004; Winson 1978). As well, theta oscillations have been implicated in modulating synaptic plasticity [long-term potentiation (LTP) and long-term depression (LTD)]; Holscher et al. 1997; Huerta and Lisman 1996; Larson et al. 1986; Orr et al. 2001; Pavlides et al. 1988]. However, Bland (1986) proposed an alternative (but compatible with the learning function) view of the general function of theta oscillations: to integrate sen-

sory and motor information during sensorimotor behavior (Bland 2009; Bland and Oddie 2001). Bland’s theta sensorimotor integration model posits that theta oscillations function like a carrier wave, which the sensory and motor systems use to inform and update one another and coordinate their activity (Bland et al. 2007). The model was developed to explain integration in rats, and it is not clear whether and how the model might apply to the human brain.

The theta rhythm is more difficult to study in human subjects, because it is not as robust as in the hippocampus of animals. Characteristics of theta activity in the adult EEG are even still debated (Mitchell et al. 2008; Niedermeyer and Lopes da Silva 2005). Nevertheless, many researchers have documented large-amplitude rhythmic activity occurring symmetrically over the frontal region of the scalp in the 4- to 8-Hz range, termed frontal midline theta. Researchers have been interested in determining its significance and whether or not it is related to the hippocampal theta rhythm, without clear resolution (Mitchell et al. 2008). Given this controversy, it is perhaps not surprising that the behavioral correlates of human cortical theta activity remain unclear. Cortical theta activity has been implicated in a variety of behaviors, many of which overlap with correlates of rat hippocampal theta, and others which do not. For example, cortical theta activity has been proposed to be involved in higher cognitive functions, attention, and concentrated effort (Aftanas and Golocheikine 2001; Banquet 1973; Brookings et al. 1996; Ishihara and Yoshii 1967; Mizuki et al. 1982; Mundy-Castle 1957; Nakashima and Sato 1993; Smith et al. 2001), memory processes (Gevins et al. 1997; Gruber et al. 2008; Jensen and Tesche 2002; Klimesch et al. 2001; Krause et al. 2000; Onton et al. 2005; Sederberg et al. 2003), and learning and spatial navigation (Caplan et al. 2001, 2003; de Araujo et al. 2002; Ekstrom et al. 2005; Kahana et al. 1999, 2001) and has been proposed to underlie sensorimotor integration in analogy with Bland’s model (Caplan et al. 2003). One reason for the lack of clarity about the behavioral relevance of human theta activity may be a lack of task specificity. Many of the paradigms that have been employed require such complex, multifaceted behavior on the part of the participant (e.g., mental arithmetic, meditation) that it is difficult to pinpoint a potential functional role for theta activity. Human cortical theta activity needs to be examined more systematically, and our aim was to directly test the hypothesis that this rhythm is involved in sensorimotor integrative processes, motivated by Bland’s model of theta activity in the rat. Furthermore, theta activity could be the expression of the neural phenomenon that itself guides state-dependent neural and information processing in a given area.

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Cortical theta activity has seldom been reported before in purely sensorimotor tasks (Perfetti et al. 2011; Pfurtscheller et al. 2006; Tombini et al. 2009). More commonly, the large-amplitude mu rhythm appears robustly during human sensorimotor function. This rhythm has a fundamental frequency around 10 Hz and is often thought to represent an idling state of the brain, present during periods of stillness and desynchronizing with movement (Niedermeyer and Lopes da Silva 2005). The mu and human cortical theta rhythms that have been documented are nearby in frequency (8–12 Hz and 4–8 Hz, respectively) as well as recording site on the head (central lateral and frontal bilateral sites, respectively). If Bland's proposal that theta activity reflects sensorimotor integration is applicable to humans, we would expect theta activity to synchronize most during movement initiation and execution times, precisely when we know the mu rhythm desynchronizes. Because of the concurrent fluctuation of two closely related rhythms, we speculated that theta activity during sensorimotor tasks may have been previously overlooked by researchers primarily interested in mu activity.

To test whether Bland's theta sensorimotor integration model extends to humans, we employed a sensorimotor reaching task in which subjects were auditorily cued to reach toward target dots appearing on a touchscreen. We directly compared the amount of theta activity that was present during the preparatory (PREP), movement initiation (INIT), and movement execution (MOVE) phases for two different kinds of reaching. The reaching conditions were designed to manipulate the contribution of the ventral visuomotor stream by controlling the visibility of the target at different stages of the reach. Previous research has demonstrated that when a target object is in full view for the duration of a movement, the real-time visual image is able to guide the action to completion. Such "visually guided" actions are known to depend on mechanisms residing in the parietal cortex of the dorsal stream. If, however, immediate visual information is unavailable at the time a response is initiated, a perceptual memory of the target's characteristics must be used to initiate the action instead. These types of actions still engage dorsal structures (Murata et al. 1996), but according to the influential perception-action model of Goodale and Milner (1992), they also critically depend on perceptual mechanisms residing in the ventral stream. Behavioral and neuroimaging evidence suggests that even when occlusion of a target coincides with a response cue, or occurs shortly beforehand, ventral stream mechanisms are necessarily recruited (Armstrong and Singhal 2011; Singhal et al. 2006, 2007; Westwood and Goodale 2003). In the current study, the target disappeared at either the end of the participants' reaction time (*condition 1*) or the beginning (*condition 2*), thereby altering the contribution of the ventral stream at the response initiation phase. Although the target did not endure throughout execution of the movements (neither condition was visually guided), the dorsal stream should still be engaged, because a persistent target is a sufficient but not necessary criterion for the stream's activation. On the other hand, ventral stream neural activity should differ between the two conditions, because recruitment of perceptual mechanisms should update and modify the motor plan at different stages of the response. We reasoned that if theta oscillations reflect the coordination of activity in sensory-processing and motor-production areas, theta activity should be adaptable and present within sensory

and motor regions that are required for a given task. Thus we hypothesized that the pattern of observed theta activity, reflecting these changing sensorimotor networks, should differ between conditions, particularly at electrodes overlying the ventral visual stream. Our chief hypothesis was that theta oscillations reflect sensorimotor integration in general, leading to the prediction that theta activity would be present during movement, coinciding with the mu rhythm desynchronizing. Our second hypothesis was that there should be greater theta activity over ventral stream areas when the visual target is occluded at the beginning (*condition 2*), rather than at the end (*condition 1*), of the behavioral reaction time, during movement initiation.

METHODS

Participants. Twenty-seven (20 female, 7 male) right-handed undergraduate students, ages 18–25 yr (mean 21 yr, SD 1.86 yr) received payment for participating in this study. One participant's data were excluded from analyses due to persistent EMG contamination. All participants had normal or corrected-to-normal vision and normal hearing. Written informed consent was obtained before the experiment, and the methods were approved by the University of Alberta's ethical review board.

Procedure. The study was conducted in a darkened, electrically shielded, and sound-attenuated chamber. At the start of the experiment, participants were seated in front of a 430.4 × 270.3-mm touchscreen. At the beginning of each session, the touchscreen was recalibrated by the participant being tested to ensure that accuracy measures remained reliable across subjects. Based on average distance from the screen, the vertical and horizontal visual angles of the touchscreen were 33.78° and 46.82°, respectively. The vertical and horizontal visual angles of the stimuli were 1.98° and 1.13°, respectively.

Our task required that participants reach toward and touch 9 × 14-mm black dots displayed on a touchscreen using E-Prime presentation software version 1.2 (Psychology Software Tools). The participant depressed a button to begin a trial. One second after the button was depressed, a target appeared on the screen in a random location. An 800-Hz, 64-dB (SPL) tone sounded 1–3 s after the target appeared. The participant was instructed to continue holding down the button until he/she heard the tone and then to touch the target as quickly and accurately as possible. In *condition 1*, the target disappeared as soon as the button was released (i.e., with movement onset). After 1 s, if the participant had not yet initiated a movement, the target disappeared. In *condition 2*, the target disappeared simultaneously with the tone (Fig. 1). Similar timing has been used previously (Armstrong and Singhal 2011; Singhal et al. 2007; Westwood and Goodale 2003), and in our task the target disappeared in both conditions so that trials were made as similar as possible. By manipulating whether the target was available on the retina during movement onset, we were able to manipulate the network required to perform the task in a way that was imperceptible to participants (Singhal et al. 2007; Westwood and Goodale 2003). After participants made contact with the screen, they were to return their finger to the response button, which advanced the next trial. Before testing, four practice trials were administered to ensure that participants understood the task. *Condition 1* and *condition 2* trials were presented in random order with the restriction that a particular condition did not occur more than five times consecutively. A total of 360 test trials (180 per condition) were included in a session, and participants were given a break period, for a self-determined length of time, every 120 trials.

Behavioral analyses. For each condition, reaction time (RT), movement time (MT), and touch position were recorded. RT was defined as the time it took to initiate a movement in response to the beep, by lifting one's finger and releasing the response button, whereas MT

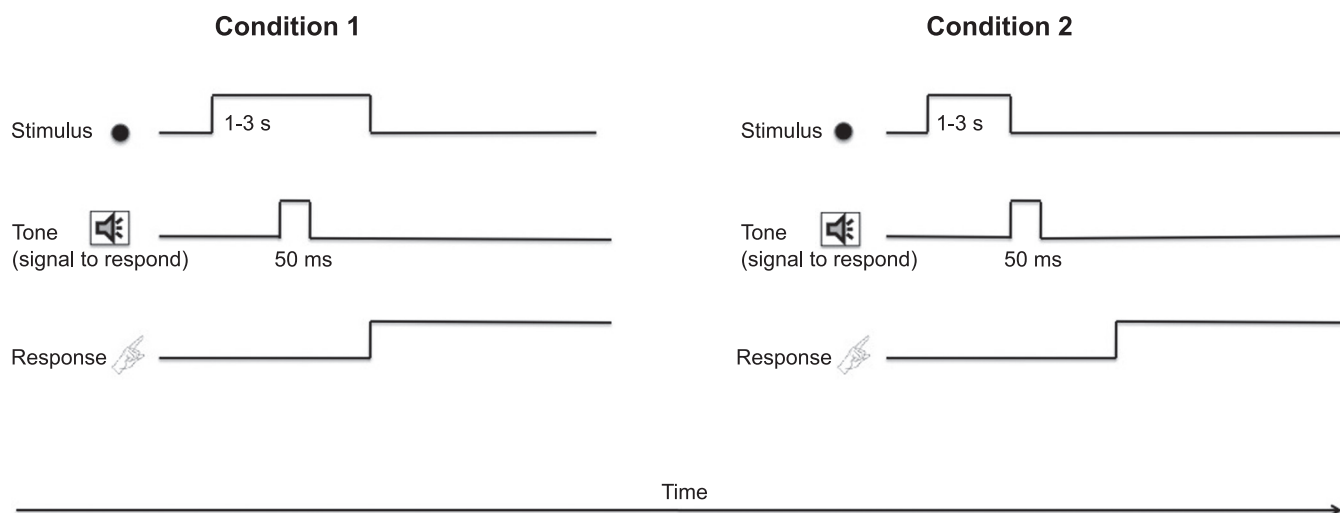


Fig. 1. Schematic of the behavioral procedure. One hundred eighty trials of each condition were presented to participants within a session. In *condition 1*, the tone sounds and the stimulus disappears when the participant lifts his/her finger from the response box. In *condition 2*, the tone sounds simultaneously with the disappearance of the target.

was defined as the time it took to fully execute a movement, from release of the response button to contact with the touchscreen. Trials were considered to be accurate if the participant responded within 8 mm of the center of the target. Trials were excluded from analyses if RTs were ≤ 150 or ≥ 800 ms or if MTs were ≤ 200 or $\geq 2,000$ ms. On average, 3% of trials were removed. Statistical analyses were carried out using Matlab 7.1 (The MathWorks) and SPSS version 18.0.

EEG recordings and preprocessing. EEG was recorded using a high-density 256-channel Geodesic Sensor Net (Electrical Geodesics, Eugene, OR), and impedances were typically kept below 50 k Ω . Voltage was sampled at 250 Hz and initially referenced to the vertex electrode (Cz). Signal was preprocessed using EEGLab 7.1.4 (Delorme and Makeig 2004), running under Matlab 7.1 (The MathWorks). Signal was bandpass filtered from 0.5 to 50 Hz and was re-referenced to a common average. The dimensionality of the data was first reduced using principal component analysis (PCA), keeping 150 components. Independent component analysis (ICA) was then performed to detect and remove artifacts from the data. Those components accounting for stereotyped artifacts, including eye blinks, eye movements, and muscle movements, were identified and removed from the data. Artifactual components were determined by visual inspection of the spectral characteristics, time courses, and spatial topographies of all components.

Oscillation detection: electrophysiological analysis. The EEG signal was analyzed for oscillations using the wavelet-based oscillation detection method, BOSCO (Better OSCillation detection; for further details, see Caplan et al. 2001; Whitten et al. 2011). One disadvantage of traditional spectral analysis is its sensitivity to nonrhythmic signals, possibly accounting for some of the lack of functional specificity of the neuronal dynamics underlying human theta oscillations (Mitchell et al. 2008). Transient artifacts may occasionally contribute to sharp increases in the power spectrum for a particular signal. To classify a signal segment as rhythmic, we wanted to ensure that sustained oscillations were occurring, and not simply increases in power (Caplan et al. 2001). In applying this method, signals were only classified as rhythmic if they exceeded a particular power threshold for a given frequency and a particular duration threshold. In calculating the power threshold for a given frequency, the BOSCO method allows us to exclude from oscillation detection 95% of the background, “colored noise” spectrum, which is characteristic of all EEG signals. This ensures that power normally occurring by chance for a given frequency is taken into consideration (Caplan et al. 2001). In addition, by setting a duration threshold of two cycles, we can be confident that the detected signal is rhythmically sustained. The proportion of BOSCO-

detected oscillations (P_{episode}) occurring at different frequencies was calculated to determine whether theta activity was present during this task. Analysis was confined to frontal, left motor, right motor, parietal, left temporal, and right temporal electrode clusters (Fig. 2), regions that we expected could take part in the sensorimotor network. Each cluster comprised seven adjacent electrodes, which centered around an electrode corresponding to the traditional 10-20 system. The frontal cluster was centered on Fz, a frontal midline site where frontal midline theta activity has been previously reported. The left motor cluster was centered on C3, a site where mu is commonly reported and which is contralateral to participants’ right-handed movements. The right motor cluster was centered on C4. The parietal (dorsal) cluster centered on Pz, and the left and right temporal (ventral) clusters centered on T5 and T6, respectively. We differentiated times of sensory processing, movement initiation, and movement execution by comparing oscillations during periods of 1 s before the auditory cue to move (PREP), between the auditory cue and when participants lifted their fingers from the response button (INIT), and between when participants lifted their finger from the response button and made contact with the touchscreen (MOVE). Frequency bands were defined as theta, 4–8 Hz, and mu, 8–16 Hz, and frequencies within a band were collapsed by averaging the proportion of oscillations present within that particular bandwidth. P_{episode} values were corrected for non-normality with a log (odds ratio) transform. P_{episode} values within each band were then averaged together, across individual electrodes within a cluster, and compared using repeated-measures ANOVAs. Greenhouse-Geisser correction was used to correct for nonsphericity where appropriate.

RESULTS

Behavioral measures. Average MT, accuracy, and RT were compared between the two conditions using two-tailed, paired-samples *t*-tests. One participant was excluded from the accuracy analysis due to a touchscreen calibration error. Average MT was significantly longer in *condition 2* compared with *condition 1* [534.7 vs. 528.6 ms; $t(25) = -3.16$, $P < 0.01$], and mean accuracy was also lower in *condition 2* [74 vs. 79%; $t(25) = 4.62$, $P < 0.01$]. These results replicate previous findings that actions requiring more perception-based information are slower and less accurate because they may rely on the recall of target features (Goodale et al. 1994), which is likely less precise than using directly visually available information.

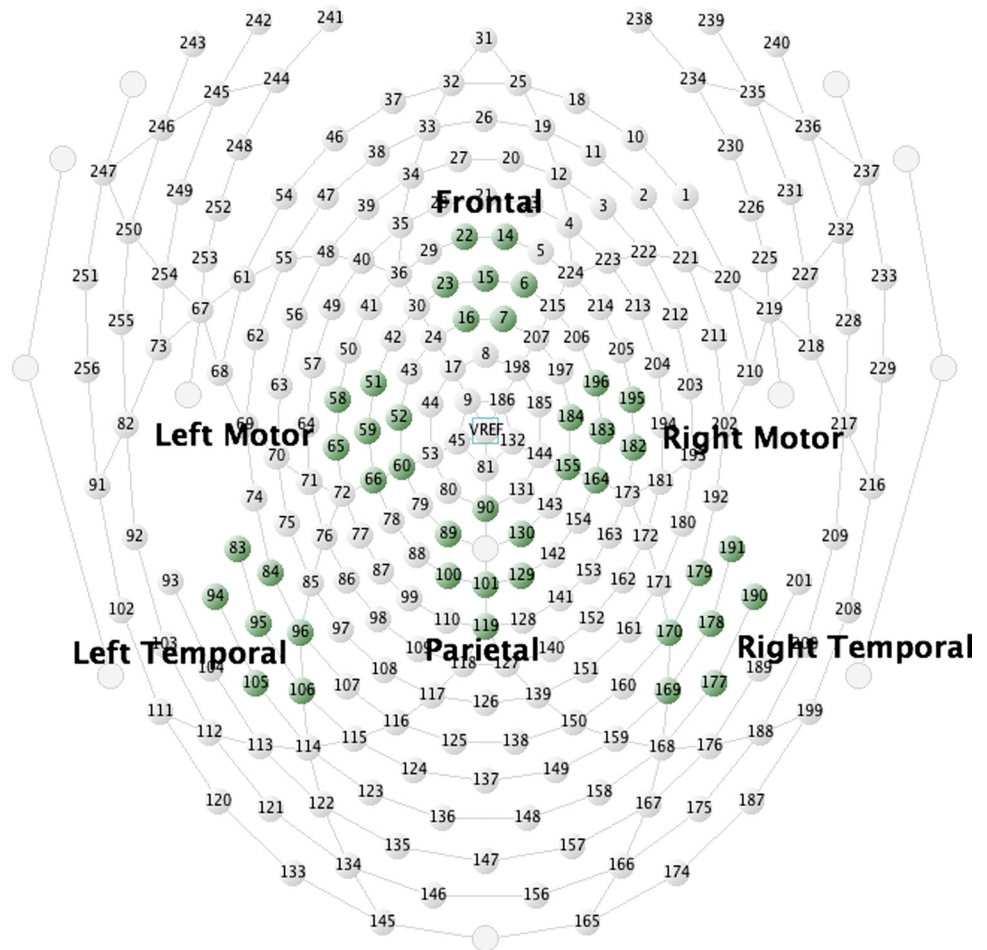


Fig. 2. Sensor layout and analysis clusters (shown in green). Oscillations within the mu and theta bands were analyzed at the frontal, motor, temporal (ventral), and parietal (dorsal) electrode clusters.

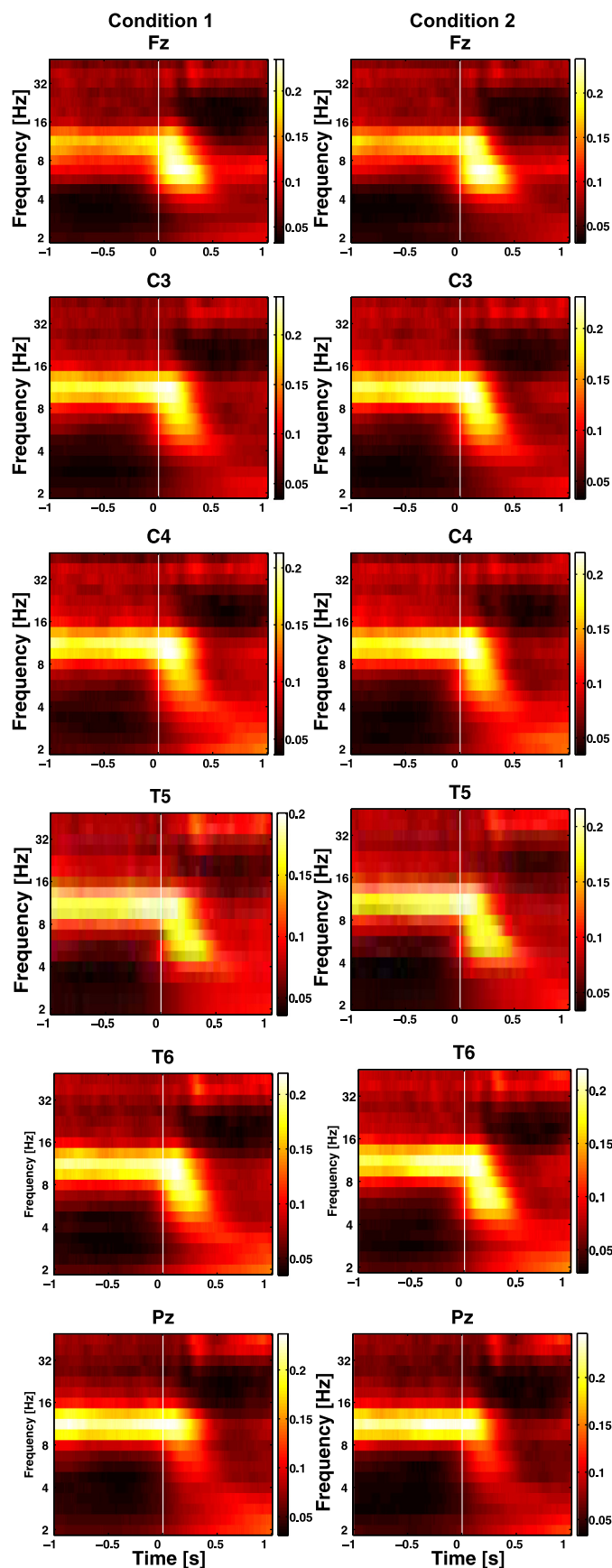
Finally, response initiation times were faster in *condition 2* than in *condition 1* [261.0 vs. 277.7 ms; $t(25) = 12.75$, $P < 0.01$].

Theta oscillations. The time-frequency plots averaged across subjects are shown in Fig. 3, and single-trial raw traces for a representative subject are shown in Fig. 4. The average P_{episode} (amount of time occupied by oscillations as a function of frequency) across subjects for each phase and condition is plotted in Fig. 5. We first analyzed average P_{episode} within the theta band. For each electrode cluster, we conducted 2×3 repeated-measures ANOVAs with factors reaching type (*condition 1*, *condition 2*) and phase (PREP, INIT, MOVE). A summary of results is presented in Table 1.

Frontal region. The first region examined was the frontal electrode cluster, because the majority of human theta activity has been reported over frontal-midline sites. We hypothesized that frontal-midline theta activity reflects executive or supervisory functions that could apply to a broad range of tasks, including many tasks that have not involved sensorimotor integration in the past. We asked whether frontal-midline theta activity was present during this basic goal-directed reaching task. If theta activity applies to sensorimotor behavior as well, there should be more theta activity at this region during INIT and MOVE than during PREP. There also should be no significant difference between the reaching types, because processes associated with the frontal lobe (executive functioning, attention, etc.) should be comparable between both types

of reach. Consistent with this prediction, there was a main effect of phase [$F(1.88, 47.10) = 40.20$, $P < 0.01$], which was explained by post hoc pairwise comparisons as INIT > MOVE > PREP (see Figs. 5 and 6A). All phases were significantly different from one another ($P < 0.01$). The main effect of reaching type and interaction did not reach significance.

Motor region. Because the task is sensorimotor in nature, integration of motor circuitry is necessary; thus we expected to see theta modulation at motor region clusters (centered around C3, which is contralateral to the right-handed movement behavior, and C4). These electrodes also may be sensitive to activity in neighboring somatosensory cortex due to proprioceptive feedback during the reach. Because this region should be sensitive to motor (or proprioceptive) nodes of the sensorimotor network, we hypothesized that there should be more theta activity in this region during INIT and MOVE than during PREP. Furthermore, because the movements being made in the two conditions are quite similar (basic pointing), we expected very similar levels of theta activity between conditions. Similar to the frontal region, there was a main effect of phase [$F(1.80, 45.10) = 28.16$, $P < 0.01$], which was explained by post hoc pairwise comparisons as INIT > MOVE > PREP (see Fig. 5). Again, all phases were significantly different from one another ($P < 0.01$; Fig. 6, C and D). The main effect of reaching type and interaction were not significant.



Ventral stream regions. The left and right temporal electrode clusters were chosen to be locations where we expected to see differences in reaching type, because these areas should be sensitive to ventral stream activity. On the basis of suggestions that the ventral stream is recruited to a greater extent in *condition 2* (see Introduction), we predicted that theta activity should be greater over ventral sites for this type of reaching. Both left and right temporal clusters were included, because although participants are making right-handed movements, stimuli are presented in both visual hemifields. We hypothesized that there should be more theta activity in these regions during INIT than during the other two phases, because the necessary perceptual information should be drawn on at this time. Motor planning will have begun before the INIT phase: the appearance of the target during PREP will initiate a series of sensory transformations and activate cortical sensorimotor networks (Gordon et al. 1994; Kettner et al. 1988; Messier and Kalaska 1997; Soechting and Flanders 1989a, 1989b). However, the motor plan will be further updated and modified at the time of INIT, and ventral stream mechanisms will likely be engaged earlier in *condition 2* than in *condition 1*. At both clusters, there was a main effect of phase [left temporal: $F(1.73, 43.29) = 30.65, P < 0.01$; right temporal: $F(1.77, 44.23) = 26.34, P < 0.01$]. Similar to the frontal and motor clusters, the main effect for each was explained by post hoc pairwise comparisons as INIT > MOVE > PREP (see Fig. 5). All phases were significantly different from one another ($P < 0.01$; Fig. 6, *E* and *F*). A main effect of reaching type was not significant. However, the two-way interaction between phase and reaching type was significant at the left temporal region only [$F(1.65, 41.36) = 4.49, P < 0.05$]. Post hoc paired-samples *t*-tests revealed that theta activity was significantly greater for *condition 2* reaching during the initiation phase at this site [$t(25) = -2.16, P < 0.05$; Fig. 6*E*]. To our knowledge, this is the first study to provide electrophysiological evidence that ventral stream areas are necessarily recruited during reaching tasks requiring perception-based information, corroborating previous behavioral and neuroimaging findings.

It is important to consider, however, an alternative explanation of the result. A sequence of evoked potentials induced by the tone stimulus, each of which is not “in principle” part of a rhythm, might happen to be evoked with approximately theta-period timing, and this type of pattern could be interpreted as reflecting either a rhythm or a rhythmic sequence of discrete, nonrepeating events. This difference is similar to a commonly made distinction between “evoked” (phase-locked to stimuli) vs. “induced” (not phase-locked to stimuli) oscillatory activity (Basar-Eroglu et al. 1996). Thus we sought to determine whether BOSC-detected oscillations in the event-related potential (ERP), which is reflective of evoked activity (whether rhythmic or not), could completely account for the BOSC-detected oscillations in the original raw trials (a combination of

Fig. 3. Time-frequency plots averaged across trials at sites Fz, C3, C4, T5, T6, and Pz, 1 s before and 1 s after movement initiation (when participants lift their finger from the response box). Increased brightness is indicative of increased oscillatory activity for a particular frequency oscillation. Movement initiation occurs at *time 0* and is indicated with a white bar, and touchscreen contact is made at *time 1*. At all electrodes, for both *condition 1* and *condition 2* reaching, 8- to 16-Hz mu oscillatory activity is present before the movement and desynchronizes with movement. Alternately, 4- to 8-Hz theta oscillatory activity synchronizes just before movement initiation and continues throughout movement execution.

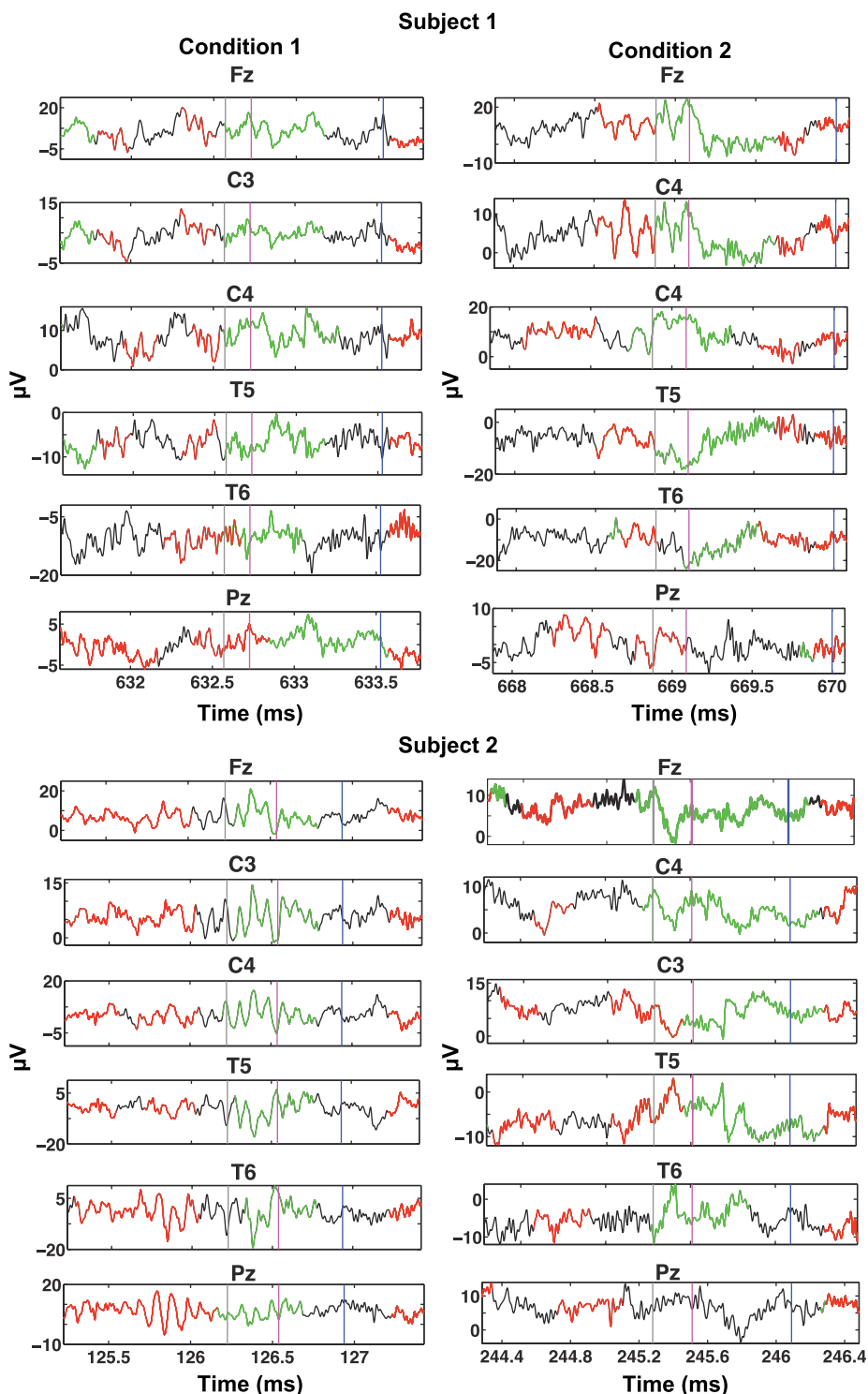


Fig. 4. Raw traces for single-trial data at each cluster's central electrode. *Conditions 1* and *2* are shown for 2 representative subjects. BOSC (Better OSCillation)-detected mu oscillations are plotted in red. This rhythm desynchronizes around the time of the auditory cue to move, which is indicated by a gray bar. BOSC-detected theta oscillations are shown in green. In contrast to the mu rhythm, this rhythm synchronizes around the time of the auditory cue to move. For every trial, the time at which the response button was released is shown in pink and the time at which touchscreen contact was made is shown in blue.

induced and evoked activity). If the reported rhythms could not be entirely explained by the portion of the signal observable in the ERP, then the activity could quite confidently be interpreted as truly rhythmic. In essence, it would be the brain producing the rhythmicity, not the timing of the task or an approximately rhythmic and coincidental sequence of evoked (nonrhythmic) potentials (but note, what follows conservatively eliminates any contribution from truly evoked oscillations, as well).

We first computed the ERP. EEG was segmented into 20-s epochs, time-locked to the auditory cue to move (epochs extended 10 s before the tone to 10 s after). The long window ensured that this cross-check analysis could accommodate the variable duration times of the INIT phase. Trials were averaged together and baseline-corrected relative to prestimulus activity (-100 to 0 ms). We then calculated the spectrogram of the ERP and divided each cell of this matrix by each cell of the initially computed trial-by-trial time-frequency matrix of

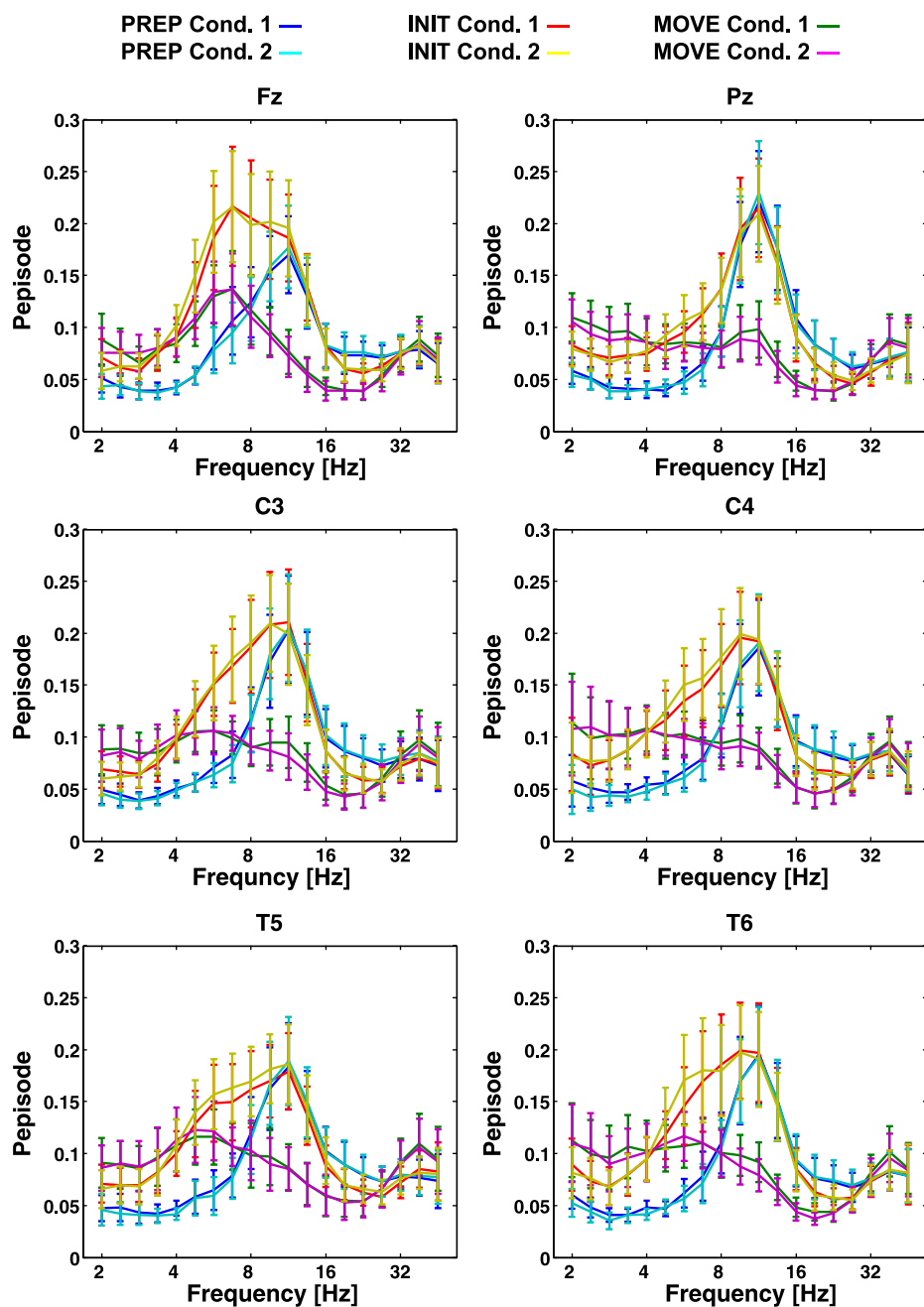


Fig. 5. Average proportion of oscillatory activity across conditions during preparatory (PREP), movement initiation (INIT), and movement execution (MOVE) phases. Error bars represent 95% confidence intervals. At electrode Fz, in both conditions (1 and 2), a strong increase in 4- to 8-Hz (theta) activity was observed during INIT and MOVE. Eight- to 13-Hz (μ) rhythmic activity at this electrode decreased during MOVE. At electrode Pz, small increases in theta were observed during INIT and MOVE, relative to PREP. μ activity decreased during MOVE. At electrode C3, in both conditions, μ activity was observed during PREP and INIT and decreased with MOVE. Increases in theta activity happened simultaneously during INIT and MOVE. At electrode C4, in both conditions, μ activity was observed during PREP and INIT and decreased with MOVE. Increases in theta activity happened simultaneously during INIT and MOVE. At electrode T5, for both conditions, theta activity increased during INIT and MOVE, relative to PREP. During INIT, theta activity was greater during condition 2. μ activity at this electrode decreased during MOVE. At electrode T6, for both conditions, theta activity increased during INIT and MOVE, whereas μ decreased during MOVE.

P_{episode} values. This estimates how large the oscillation would have been on each trial if evoked potentials were the sole contributor to our result. The P_{episode} values in the theta band for the “estimated evoked” signal (which were matched to the trial-by-trial durations of the INIT phase) were then subtracted from the initial theta-band P_{episode} values for each trial. We truncated the subtracted P_{episode} values at zero to avoid negative numbers. Difference values were then compared between condition 1 and condition 2 with a paired-samples *t*-test to determine whether a difference between reaching type remained. After conservatively removing any detected oscillations that could be due to evoked activity, we obtained the same difference: there was more theta activity in condition 2 than in condition 1, and the significance was improved [$t(181) = -5.33, P < 10^{-6}$]. Thus the central result cannot be

explained away as being entirely due to effects that are observable in the ERP. This includes phase-locked oscillations as well as discrete evoked potentials that happen to arise in an approximately rhythmic pattern.

Dorsal stream region. We considered the parietal electrode cluster (located near the dorsal stream) a control region to determine whether the topography of theta activity changes as the set of regions within the sensorimotor network changes. Condition 1 and 2 reaching are both reliant on the dorsal stream (Franz et al. 2009; Hesse and Franz 2009; Murata et al. 1996); thus theta activity should not differ between conditions at this site, because both types of reaching rely on its activation. The ANOVA revealed a main effect of phase [$F(1.58, 39.58) = 32.31, P < 0.01$], which was explained by post hoc pairwise comparisons as INIT > MOVE > PREP (see Fig. 5). All

Table 1. Changes in theta and mu oscillatory activity for each condition during INIT and MOVE, relative to PREP

Electrode clusters	Theta						Mu					
	INIT			MOVE			INIT			MOVE		
	1	2	1/2	1	2	1/2	1	2	1/2	1	2	1/2
Frontal	↑	↑		↑	↑							
Left motor	↑	↑		↑	↑		–	–		↓	↓	
Right motor	↑	↑		↑	↑		–	–		↓	↓	
Left ventral	↑	↑	+	↑	↑							
Right ventral	↑	↑		↑	↑							
Dorsal	↑	↑		↑	↑							

Arrows indicate an increase (↑) or decrease (↓) in oscillatory activity, whereas a minus sign (–) indicates no change ($P < 0.05$) during movement initiation (INIT) and movement execution (MOVE) relative to the preparatory phase (PREP). A plus sign (+) indicates when the synchronization or desynchronization of oscillatory activity is significantly greater for *condition 2* compared with *condition 1* (1/2).

phases were significantly different from one another ($P < 0.01$; Fig. 6B). The main effect of reaching type and interaction did not reach significance.

Theta activity as a function of region. Because frontal-midline theta is the main topographic pattern of theta activity that has been reported, we wanted to evaluate our hypothesis that it is largest in amplitude at anterior sites, potentially explaining why it has received more attention than theta oscillations with different topographies. Thus we collapsed P_{episode} across condition and reaching type and conducted a one-way ANOVA with the within-subjects factor region [5]. There was indeed a significant main effect [$F(3.21, 80.16) = 9.89, P < 0.01$], with the greatest proportion of theta activity present at the frontal cluster, consistent with the bulk of human EEG-recorded theta having been reported here. Post hoc pairwise comparison *t*-tests revealed that the frontal cluster differed significantly from the left temporal and parietal areas ($P < 0.05$); the other comparisons were not significant.

Mu oscillatory activity. We also analyzed the average P_{episode} within the mu band to determine whether the paradigm was as successful as previous sensorimotor studies at eliciting mu desynchronization. We conducted a 2×3 repeated-measures ANOVA with factors reaching type and phase at the left and right motor clusters, which is where we expected to see the greatest mu activity. We hypothesized that mu activity should desynchronize the most in this region during MOVE, when the reaches are being executed. Furthermore, if mu activity reflects principally an idling state there should be no difference between reach type, because mu desynchronization should simply reflect an override of that state in both conditions. However, if neural synchrony in the mu band has a more functional purpose, then differences between the conditions may be evident. In support of the latter conjecture, there was a main effect of phase for both left [$F(1.25, 31.17) = 49.64, P < 0.01$] and right regions [$F(1.57, 39.30) = 39.14, P < 0.01$]. The rank order was INIT > PREP > MOVE. However, only during the MOVE phase was mu activity significantly less than during either INIT or PREP ($P < 0.01$) at both left and right regions; INIT and PREP phases were not significantly different from one another (Fig. 6, C and D). There was no main effect of reach type at either region, and the two-way interaction at the right motor region was not significant. The two-way interaction between reach type and phase was significant at the left region [$F(1.70, 42.49) = 3.77, P < 0.05$]. Post hoc paired-samples *t*-tests revealed that mu activity was significantly lower during MOVE for *condition 2* [$t(25) = 2.26, P < 0.05$; Fig. 6C].

DISCUSSION

The aim of this study was to test whether the sensorimotor integration model of theta activity extends to humans. Results reveal that rhythmic theta-band activity synchronizes in humans whereas mu activity desynchronizes during sensorimotor behavior. Theta activity increased significantly during initiation (INIT) and movement (MOVE) relative to preparation (PREP) and reached its greatest proportions during the initiation phase. At the left ventral site during initiation, theta activity was significantly greater for *condition 2* than *condition 1*. Mu activity on the other hand, decreased significantly during movement, replicating the standard mu-rhythm pattern, yet was lower in presence in *condition 2*. These results suggest that network-specific theta synchronization in conjunction with mu desynchronization may represent broadly applicable rhythmic mechanisms for integration, including sensorimotor function, in the human brain.

Theta activity and sensorimotor function. Although EEG studies have rarely reported cortical theta-band activity during purely sensorimotor tasks, our results are consistent with those that have analyzed theta-band power, finding increased theta-band power during the planning phase of a catching task (Tombini et al. 2009), during the planning and execution phases of a choice-reaction task (Perfetti et al. 2011), and, intracranially, during motor imagery for sensorimotor planning (Hinterberger et al. 2008). Our results are also consistent with local field potential (LFP) recordings in monkeys, which found increased theta-band activity over motor cortex during movement planning and execution (Mehring et al. 2003; Rickert et al. 2005). In the present study, the BOSCM method allowed us to confidently claim that the signal in the theta band is in fact rhythmic, in turn suggesting that these recent theta-band findings also may have included rhythmic theta oscillations. Together, the results suggest that Bland's theta-based sensorimotor integration model can be extended to both nonhuman primate and human neocortical regions that presumably participate in the sensorimotor network.

Bland's theta sensorimotor integration model revisited. Bland's model derives from earlier animal studies of hippocampal theta activity during gross voluntary motor behaviors, but not more automatic behaviors (Black and Young 1972; Vanderwolf 1969; Yoshii et al. 1966). Our results reveal that theta activity in humans is also associated with voluntary motor behavior that is not restricted to learning and memory relevant function. Relative to baseline (preparation), theta ac-

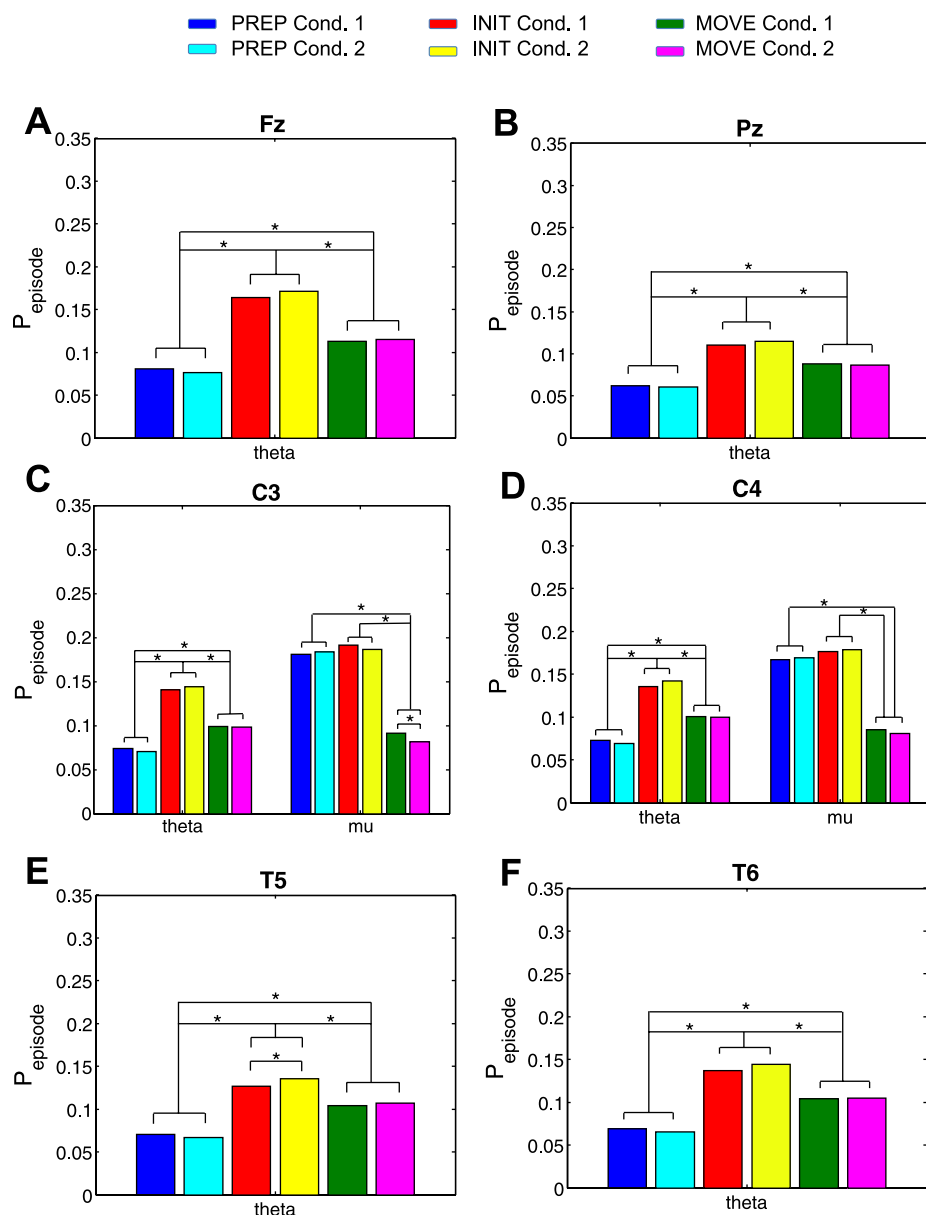


Fig. 6. Summary of the chief findings. Average $P_{episode}$ (amount of time occupied by oscillations as a function of frequency) is plotted as a function of condition for theta and mu bands (averaged across frequencies sampled within each band) at the respective locations analyzed (theta: Fz, Pz, C3, C4, T5, and T6; mu: C3 and C4). $*P < 0.05$.

tivity increased significantly in our task during initiation and movement, providing strong support for the suggestion that human cortical theta activity may be physiologically and functionally related to hippocampal theta activity in animals (Mitchell et al. 2008). Furthermore, Bland's model was motivated by observations that two types of theta activity occur during sensorimotor behavior. Type 1 is the originally described, movement-related theta activity that has a higher frequency, whereas type 2 is immobility-related theta activity that occurs in the absence of movement at a lower frequency (Bland et al. 2007). Although a substantial shift in frequency is not readily apparent in the $P_{episode}$ plots (although visual inspection of Fig. 5 suggests that peak frequency might depend to some degree on electrode location), theta activity does change systematically across the three phases of the task, just as type 2 theta activity transitions to type 1 during movement onset in animals.

The present paradigm successfully elicited theta activity in the absence of any "higher" cognitive or memory demands,

and results are consistent with Bland's model of hippocampal theta activity indexing a functional mechanism for sensorimotor integration (Bland 1986; Bland and Oddie 2001; Bland et al. 2007). A more general view of the role of theta oscillations may be that they facilitate precisely timed coordination amongst brain regions, which may or may not include the hippocampus (Burgess and Gruzelier 1997; Jensen and Tesche 2002; Klimesch et al. 2001; Payne and Kounios 2009; Womelsdorf et al. 2010).

It is important to note, however, that these results do allow for alternative interpretations. Namely, theta oscillations may not be a mechanism, but rather a by-product of a neurophysiological state conducive to sensorimotor integration. Whether any oscillatory signal has a mechanistic function should be included as a caveat to all oscillation research, because it is possible that rhythms are epiphenomena that reflect a change in the state of the network. Thus, although our results do not provide unequivocal evidence that theta oscillations are a central mechanism of sensorimotor integration, they offer sup-

port for a hypothesis derived from a model that does assume this (Bland 1986).

Theta activity within the relevant sensorimotor network: condition 1 vs. condition 2. The most compelling evidence for theta activity's involvement in sensorimotor integration is that the topography of theta activity changes as the cortical circuitry required to execute a behavior changes. Frontal and motor electrodes did not display differences in the amount of theta activity between *condition 1* and *condition 2* reaching, which is understandable given that both regions would be expected to contribute to sensorimotor integration to a similar degree in both conditions. Likewise, the parietal region did not display differences in the amount of theta activity between conditions, consistent with evidence that both types of reaching rely on the dorsal stream (Franz et al. 2009). During the initiation phase, theta activity was greater for *condition 2* at the left temporal region (located near ventral stream areas), corroborating behavioral, neuropsychological, and neuroimaging reports that perceptual brain mechanisms in the ventral stream are recruited when planning perceptually driven hand actions (Armstrong and Singhal 2011; Cohen et al. 2009; Goodale et al. 1991; James et al. 2003; Milner et al. 2001; Singhal et al. 2006). Thus, as the sensorimotor network shifts to include ventral regions, theta activity increases at the ventral site, during the phase when perceptual mechanisms are recruited.

Has theta activity been previously overshadowed in sensorimotor tasks? To our knowledge, theta activity has only recently been reported in human sensorimotor tasks and may have been previously overlooked. The time courses of these rhythms were visualized within the time-frequency spectrogram (Fig. 3) as well as the raw trace (Fig. 4): ~500 ms before the auditory cue to move, mu rhythmic activity dominates the signal, giving way to theta oscillations at the onset of the movement. As mentioned in the Introduction, we suggest that the visual impact of the mu rhythm may have garnered researchers' attention, and theta activity may not have been as easily observed. Motivated by Bland's model, however, we identified both human theta and mu activity in a sensorimotor task with little or no demand on learning.

Just as mu activity may have previously overshadowed frontal-midline theta activity, frontal-midline theta activity (even in memory and higher cognitive studies) may have overshadowed more posterior theta activity. Task-dependent theta activity at posterior locations may be harder to see if it is invoked at more transient times within experimental tasks, and a difference in source, therefore, might be easiest to see when comparing closely related tasks that vary in their underlying sensorimotor networks, as is the present case.

Theta activity and integration. A role for theta activity in sensorimotor integration may seem somewhat removed from alternate theories of frontal-midline theta activity indexing cognitive (Aftanas and Golocheikine 2001; Banquet 1973; Brookings et al. 1996; Ishihara and Yoshii 1967; Mitchell et al. 2008; Mizuki et al. 1982; Mundy-Castle 1957; Smith et al. 2001), learning, and memory processes (Caplan and Glaholt 2007; Gevins et al. 1997; Jensen and Tesche 2002; Krause et al. 2000; Onton et al. 2005). However, for arguably all reported behavioral correlates of theta activity (both animal and human), integration of information in various brain regions is demanded. Theta oscillations may reflect a mechanism for integration more generally, beyond the domain of sensorimotor

behaviors, and may serve to coordinate brain activity in a range of tasks for which integration is crucial. This includes learning and memory tasks at one end of the spectrum and sensorimotor tasks at the other. Although these functions may not be cleanly dissociable in practice, theories of theta activity in memory tend to be connected to findings that suggest theta activity has a local action, phase-coding sequential information and windowing LTP/LTD. In contrast, theories of an integrative significance for theta activity implicate long-range coordination and do not require memory or learning. Results of the present study challenge theories pertaining only to learning, memory, and cognitive functions, and it is plausible that the two roles coexist.

Theta activity may also reflect a refinement of sensorimotor and other behaviors. Animal research has shown that although disruption of the hippocampal theta rhythm may sometimes abolish sensorimotor behaviors (Bland and Vanderwolf 1972), it can also impair performance on goal-directed tasks, (Cornwell et al. 2008; Hasselmo et al. 2002; Winson 1978) and greatly reduce the rate and the extent to which conditioned associations are learned (Berry and Thompson 1979; Griffin et al. 2004; Seager et al. 2002). LFP research has also shown that theta activity in the motor cortex of monkeys correlates with intended movement direction (Rickert et al. 2005), which suggests theta activity may optimize performance by coding precise task details. In humans, increased theta power was found to correlate with improved performance on a repetitive catching task (Tombini et al. 2009), lending further support to this theory.

Mu and sensorimotor function. The mu rhythm has been the chief rhythm implicated in sensorimotor function (Niedermeyer and Lopes da Silva 2005), and our results are consistent with literature demonstrating bilateral mu desynchronization during movement. However, mu activity desynchronized more during *condition 2* than *condition 1* reaching, over the left motor region. Although mu desynchronization reflects activation of specific motor areas during movement (Pfurtscheller et al. 1997), it may also be sensitive to additional task demands (Pineda 2005). Our results demonstrate that mu suppression is a sensorimotor, and not just a motor phenomenon, because sensory input influenced the degree of desynchronization. Results are also consistent with the theory of mu activity as an analog of the mirror neuron system (Altschuler et al. 1997; Rizzolatti and Craighero 2004), a proposed mechanism for perception-action coupling. Because mu desynchronization occurs even when actions are observed or imagined (Pfurtscheller et al. 2006; Woodruff and Maaske 2010), additional desynchronization in *condition 2* may reflect a combined effect of both motor cortical activation and recruitment of perceptual mechanisms that are likely similarly engaged during motor imagery or imagined movement.

Higher frequency rhythms. Although this study focused on low-frequency rhythms (theta and mu), higher frequency oscillations in the beta and gamma ranges have also been implicated in nonhuman and human sensorimotor behavior (Donoghue et al. 1998; Engel and Fries 2010; Fukuda et al. 2010; Mehring et al. 2003; Murthy and Fetz 1992; Neuper and Pfurtscheller 2001; Perfetti et al. 2011; Schalk et al. 2008; Szurhaj and Derambure 2006; Tzagarakis et al. 2010; Wilson et al. 2010; Zhang et al. 2008; Zhuang et al. 2010). Thus a full model of the role of rhythmic activity in sensorimotor integra-

tion will need to address how multiple frequencies contribute differentially to behavior.

Conclusion. Theta oscillations synchronized while the mu rhythm desynchronized during a purely sensorimotor task. Both theta and mu activity responded to changes in the underlying sensorimotor network, suggesting a connection between animal and human electrophysiology. These findings support the notion that theta activity reflects underlying sensorimotor activities, whereas mu activity likely reflects levels of cortical activation during a sensorimotor task. If theta activity is a mechanism not only of sensorimotor integration but also of integration more generally, this may explain the broad range of complex cognitive tasks previously known to induce theta rhythms.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

L.C.C., A.S., M.H. and J.B.C. conception and design of research; L.C.C. performed experiments; L.C.C. analyzed data; L.C.C., A.S., M.H. and J.B.C. interpreted results of experiments; L.C.C. prepared figures; L.C.C., A.S., and J.B.C. drafted manuscript; L.C.C., A.S., and J.B.C. edited and revised manuscript; L.C.C., A.S., and J.B.C. approved final version of manuscript.

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