Cortical theta–gamma coupling governs the adaptive control of motor commands

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Motor control requires the adaptive updating of internal models to successfully target desired outcomes. This adaptive control can be proactive, such that imminent actions and corresponding sensorimotor programmes are anticipated prior to movement, or reactive, such that online error correction is necessary to adjust to sudden changes. While substantial evidence implicates a distributed cortical network serving adaptive control when behavioural changes are required (e.g. response inhibition), the neural dynamics serving such control when the target motor commands are to remain intact are poorly understood. To address this, we developed a novel proactive–reactive cued finger tapping paradigm that was performed during magnetoencephalography by 25 healthy adults. Importantly, to ensure condition-wise differences in adaptive cueing were not attributable to changes in movement kinematics, motor selection and planning processes were held constant despite changes in task demands. All data were imaged in the time-frequency domain using a beamformer to evaluate the effect of proactive and reactive cues on movement-related oscillations and subsequent performance. Our results indicated spectrally specific increases in low (i.e. theta) and high (i.e. gamma) frequency oscillations during motor execution as a function of adaptive cueing. Additionally, we observed robust cross-frequency coupling of theta and gamma oscillatory power in the contralateral motor cortex and further, the strength of this theta–gamma coupling during motor execution was differentially predictive of behavioural improvements and decrements during reactive and proactive trials, respectively. These data indicate that functional oscillatory coupling may govern the adaptive control of movement in the healthy brain and importantly, may serve as effective proxies for characterizing declines in motor function in clinical populations in the future.

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Abbreviations: BESA = brain electrical source analysis; DICS = dynamic imaging of coherent sources; MEG = magnetoencephalography; M1 = primary motor

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Introduction

A basic tenant of volitional motor control is that desired movement kinematics are transformed into discrete plans to successfully execute and terminate motor actions. After repeated exposure to a particular action or movement sequence, an internal model is generated within the sensorimotor system, and this is continuously and adaptively updated to fulfill task demands. Such motor control can be proactive, such that internal models of intended actions are anticipated prior to movement cues, or it can be reactive, whereby these models are adjusted on the fly to account for ongoing changes in the goal parameters. Previous studies have primarily interrogated the proactive and reactive control of movement through the use of stop-signal or Go/No-Go task paradigms (i.e. response inhibition), whereby participants are instructed to respond to an expected cue (i.e. proactive) and to inhibit their response to an unexpected cue (i.e. reactive). Generally, these studies have used a variety of approaches (e.g. functional magnetic resonance imaging, lesion studies, local field potential recordings) to demonstrate better behavioural outcomes (e.g. shorter stop-signal reaction times, higher stopping accuracy), indicative of better reactive inhibitory control that is concomitant with the recruitment of an extensive cortical and subcortical network (e.g. greater relative power, increased network connectivity, shorter connectivity pathways) including hubs in bilateral M1, supplementary motor and parietal cortices. In contrast, increases in the beta range following movement offset are prevalent slightly anterior to the contralateral M1, and may simply reflect the return of beta oscillatory power to idling levels. Alternatively, this post-movement increase in power may reflect the functional inhibition of the motor system during motor termination, and/or sensory reafference to the motor cortex. Other spectral changes necessary for the execution of motor actions include lower (i.e. theta) and higher frequency oscillations (i.e. gamma). While the precise role of movement-related theta and gamma oscillatory responses are not well understood, transient increases in these responses may serve as temporal coordinators and robust execution signals for motor action in the contralateral M1 for theta and gamma, respectively. Interestingly, while peri-movement oscillations in the alpha and beta range have been shown to be especially pertinent to higher order planning and movement selection factors, including response certainty and complexity, these oscillatory responses are less affected by the actual movement parameters themselves (e.g. force applied, frequency of movements). In contrast, high-frequency gamma activity seems to be particularly susceptible to changes in the kinematics, concomitant with alterations related to cognitive load when the movement to be performed is identical. For example, recent evidence suggests that the spectral properties of movement-related gamma activity (e.g. power and/or
frequency) are robustly modulated by increased cognitive demand, including increased response interference and the re-orienting of attention.\textsuperscript{32–36} Thus, oscillatory dynamics in the gamma range may provide valuable information regarding proactive and reactive control when the motor plan and selection processes are held constant. Herein, we developed a novel proactive and reactive finger tapping paradigm that was performed during magnetoencephalographic (MEG) imaging to evaluate the dynamic neural mechanisms serving the adaptive control of voluntary movement. Specifically, participants completed a single flexion-extension of the right index finger each time a red dot reached a target interval denoted in blue that surrounded the 12 o’clock position of a clock-like array (proactive condition). In the reactive condition, participants were presented with the same stimulus features as in the proactive condition, although when the red dot was a fixed distance away from the target interval (\textasciitilde 150 ms), the interval would shrink and shift to one of four locations within the original target interval’s overall span. Unlike previous work where movement parameters changed as a function of reactive cueing (e.g. inhibiting a pre-planned motor response, engaging different muscle groups, etc.), participants were instructed to respond identically, regardless of task condition. This allowed for more straightforward interpretations of adaptive cueing mechanisms (e.g. proactive versus reactive cues), as the to be performed movement was identical across both conditions. Importantly, our results reveal a dynamic coupling of cortical oscillations (i.e. theta and gamma) during motor execution in the contralateral M1 and further, robustly link the strength of cross-frequency coupling in M1 to the behavioural outcomes serving cue-related adaptations to control voluntary movements.

Materials and methods

Participants

Twenty-five healthy adults (12 females, $M_{\text{age}}$ = 25.34 years, range 21–32 years old, all right handed) were recruited for this study. Exclusionary criteria closely followed that described in previous papers (e.g. diagnosed neurological or psychiatric disorder, medical illness affecting CNS function, history of head trauma or loss of consciousness, current substance use/dependence, ferromagnetic implants).\textsuperscript{37,38} Written informed consent was obtained following a full description of the study in accordance with the guidelines of the University of Nebraska Medical Center’s Institutional Review Board.

MEG data acquisition and experimental paradigm

Our MEG data acquisition approach closely followed that described in previous papers using a MEGIN (MEGIN, Helsinki, Finland) 306-sensor instrument recorded at 1 kHz sampling rate (0.1–330 Hz acquisition bandwidth).\textsuperscript{39–43} Participants were seated in a nonmagnetic chair with their head positioned within the MEG helmet-shaped sensor array. To evaluate the proactive and reactive control of movement, we developed a novel finger tapping paradigm where participants were asked to perform the same flexion-extension of the right index finger to expected or unexpected stimulus targets. In the proactive condition, participants were instructed to maintain fixation on a centrally located crosshair while a red dot moved in a clock-like pattern towards a blue target interval that was fixed near the 12 o’clock position, and performed a single flexion-extension of the right index finger when the red dot was within the blue target interval (see Proactive in Fig. 1). This dot completed a full rotation around the clock-like circle (without tick marks or numbers) every 5 s, and was meant to serve as a pacing mechanism. For the reactive condition, participants were presented with the same proactive stimulus features of the clock-like design, however, when the red dot reached a fixed distance away from the original blue interval (\textasciitilde 150 ms), the target’s location (i.e. the blue interval) would shrink and shift within the original interval to one of four fixed locations (see Reactive in Fig. 1). This distance of \textasciitilde 150 ms prior to the original target onset was carefully chosen to ensure participants did not anticipate the shift and new location of the target and thus, did in fact exhibit a reactive behavioural response. However, response instructions were identical regardless of the interval’s location (i.e. respond once when the red dot was within the blue target interval). Participants completed 135 proactive and 85 reactive trials and target interval locations were presented in a pseudorandom order. For a video demonstration of the experimental paradigm, see Supplementary Video. 1. Of note, this ratio of trials per experimental condition was based on previous literature evaluating proactive and reactive processing\textsuperscript{9,11,44} which largely employs a 2:1 ratio of proactive to reactive trials, respectively to elicit the traditionally executed reactive behavioural response. The total time to complete the experiment was \textasciitilde 18 min. Pairwise statistical tests of response distance from target onset and coefficient of variation were conducted to evaluate behaviour as a function of proactive or reactive motor control. All MEG data were individually corrected for head motion and subjected to noise reduction using temporal signal space separation.\textsuperscript{45,46}

Structural MRI processing and MEG coregistration

Prior to the MEG measurement, four coils were attached to the participant’s head and the locations of these coils, in addition to the three fiducial points and scalp surface, were determined with a 3D digitizer (Fastrak 3SF0002, Polhemus Navigator Sciences, Colchester, VT, USA). Once the participant was positioned for MEG recording, an electric current with a unique frequency label (e.g. 322 Hz) was fed to each of the coils to induce a measurable magnetic field that would allow each coil to be localized with respect to the sensor array throughout the recording session. All MEG measurements were then transformed into a common
coordinate system and each participant’s MEG data were coregistered with T1-weighted structural magnetic resonance images prior to source space analyses using brain electrical source analysis (BESA) MRI (Version 2.0; BESA GmbH, Gräfelfing, Germany). Structural MRI data were aligned parallel to the anterior and posterior commissures and transformed into standardized space, along with the functional data, after beamforming (see below). Further details of our structural MRI processing and MEG coregistration pipeline can be found in recent papers.37,38

MEG preprocessing, time-frequency transformation and sensor-level statistics
Cardiac and ocular artefacts (e.g. blinks, eye movements) were removed from the data using signal-space projection and the projection operator was accounted for during source reconstruction.47 Epochs were of 4500 ms duration, with 0 ms defined as movement onset and the baseline being the −2000 to −1500 ms window. Epochs containing artefacts were rejected based on a fixed threshold method, supplemented with visual inspection. On average, 72 trials per participant and condition remained after balancing trial numbers across task conditions (i.e. pseudorandom omission of ~50 proactive trials throughout the entire experimental run) and subsequent artefact rejection.

Statistical analyses at the sensor level closely followed that described in previous papers.39-43,48 Specifically, following artefact rejection, epochs were transformed into the time-frequency domain using complex demodulation,49 and the resulting spectral power estimations per sensor were averaged over trials to generate time-frequency plots of mean spectral density. These sensor-level data were normalized to the baseline period (i.e. −2000 to −1500 ms time period). The specific time-frequency windows used for source reconstruction were determined by statistical analysis of the sensor-level spectrograms involving non-parametric permutation testing (i.e. 10,000 permutations) across all participants’ trials, task conditions and gradiometers.50,51

MEG source imaging
Source reconstruction of cortical oscillatory networks were computed using the dynamic imaging of coherent sources (DICSs) beamformer,52 which uses the cross-spectral density matrices to calculate noise-normalized source power for the entire brain volume (i.e. per voxel) using baseline periods of equal duration and bandwidth.53 Normalized source power was computed over the entire brain volume per participant at 4.0 × 4.0 × 4.0 mm resolution for the time-frequency periods identified through statistical analysis of the sensor-level data.
The resulting 3D brain images were averaged across all participants and task conditions to assess the neuroanatomical basis of the significant oscillatory responses identified through the sensor-level analysis, and to allow identification of the peak voxels per oscillatory response. Voxel time series data were then extracted from each participant’s data per condition using previously published methods.\(^{37,38}\) Once the voxel time series data were extracted, we computed the envelope of the spectral power within the frequency range used in the beamforming analysis. From this time series, we computed the relative (i.e. baseline-corrected) response time series of each participant per task condition at the single-trial level (see Cross-frequency coupling section below). MEG preprocessing and imaging used the BESA (Version 7.0) software. Further details of our source analysis pipeline can be found in our recent publications.\(^{38-40,48}\)

To examine the effect of proactive and reactive stimulus cueing on movement-related neural dynamics, we conducted paired sample \(t\)-tests between experimental conditions for each oscillatory response computed using DICS reconstruction methods (i.e. pseudo \(t\)-values). All pairwise testing was conducted using JASP. Additionally, to complement traditional frequentist hypothesis testing approaches, Bayesian analyses using zero-centred Cauchy distributions were also conducted in JASP to evaluate evidence for the data favouring the null/alternative hypotheses.

**Cross-frequency coupling and statistical analyses**

We also interrogated the functional coupling of relevant oscillatory responses modulated by adaptive cueing in the motor network (i.e. theta and gamma oscillatory power). First, we extracted relative single-trial voxel time series data (i.e. baseline corrected) from the peak voxels per oscillatory response during movement onset (i.e. \(-125\) to \(125\) ms for theta; \(-100\) to \(100\) ms for gamma) to conduct condition-wise multi-level models (MLMs) in R following standard data evaluation and trimming procedures (i.e. excluded cases exceeding 2.5 standard deviations from the participant’s mean). Specifically, we defined relative theta oscillatory power (continuous), task condition (factor with two levels) and their interaction as fixed effects, with subject and trial number defined as nested random effects to predict relative gamma oscillatory power at the single-trial level. Next, we aimed to directly link the strength of theta–gamma cross-frequency coupling in the motor cortex to behavioural performance on the task. Specifically, we computed the predicted gamma oscillatory power using the regression equation modelling significant theta–gamma power-to-power coupling at the single-trial level (see above). The resulting predicted relative gamma power reflects M1 gamma oscillatory power accounting for observed levels of theta power. Next, we ran an MLM with predicted gamma power (continuous), task condition (factor with two levels) and their interaction as fixed effects, with subject and trial number as nested random effects to predict the response distance from target onset (ratio score). Importantly, MLMs were conducted using the lme4 package in R and corrected for multiple comparisons using Tukey’s multiple comparison test.

Finally, recent evidence suggests that the nesting of higher frequency oscillations (i.e. gamma) within lower frequency signatures (i.e. theta) may not only be functionally coordinated by neural amplitudes, but also, by dynamic phase–amplitude interactions.\(^{54}\) Thus, for completeness, we evaluated whether theta–gamma phase–amplitude coupling (PAC) was present in the current dataset and further, whether it was modulated by reactionary motor control. Thus, we implemented the event-related phase–amplitude coupling method proposed by Voytek and colleagues,\(^{55}\) which expands upon traditional estimations of PAC in electrophysiological data to extract the correlation between higher frequency amplitudes and lower frequency phases per time point, thus not obscuring the temporal evolution of task-dependent PAC. We calculated the correlation of gamma (i.e. 70–80 Hz) power with theta (i.e. 4–8 Hz) phase at each time point in our experimental epoch (i.e. \(-2000\) to \(2500\) ms) for each condition separately (i.e. proactive versus reactive) using voxel time series extracted from the contralateral M1. The resulting PAC values range from 0 to 1, with larger values indicative of greater theta–gamma PAC in M1. Next, we conducted pairwise \(t\)-tests of task condition and Bayesian statistics to evaluate whether M1 theta–gamma PAC differed by adaptive cueing during motor execution (i.e. \(-125\) to \(125\) ms window) using JASP.

**Data availability**

Data from this study will be made available to qualified researchers upon reasonable request to the corresponding author.

**Results**

**Behavioural performance**

All 25 participants were able to successfully complete the quasi-paced finger tapping paradigm during MEG (Fig. 1). To evaluate the proactive and reactive control of motor performance on the task, we assessed measures of reaction time (i.e. response distance from target interval onset) and the coefficient of variation to assess the variability in behavioural performance, given the quasi-paced nature of the task instructions (see Experimental paradigm). Specifically, we computed ratio scores for both behavioural metrics to account for the difference in interval size between proactive and reactive conditions (e.g. response time distance from target onset/length of total target interval). Thus, all behaviours are expressed as per cent distance and/or variability from the onset of the blue target interval. Interestingly, participants responded significantly slower (\(t(24) = 11.05, P < 0.001\)) and with greater response time variability (\(t(24) = 3.04, P = 0.006\)) relative to the onset of the blue target interval for reactive trials compared with proactive trials (Fig. 1).

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\(^{37}\)\(^{38}\)\(^{39}\)\(^{40}\)\(^{48}\)\(^{54}\)\(^{55}\)
Sensor-level analysis

Time-frequency analyses indicated significant peri- and postmovement oscillatory responses in the theta (4–8 Hz), alpha (10–14 Hz), beta (20–28 Hz) and gamma (70–80 Hz) ranges. These responses were robust in gradiometers near the contralateral sensorimotor strip across all participants and both experimental conditions ($P < 0.001$, Fig. 2). Specifically, transient increases in theta and gamma oscillatory activity coincided closely with movement onset (theta: −125 to 125 ms; gamma: −100 to 100 ms), while decreases in alpha and beta activities were more temporally sustained surrounding the movement (i.e. −250 to 250 ms for alpha and beta). Finally, there was a robust synchronization in the beta range (16–26 Hz) that was detected during the 400–900 ms window following motor execution.

Oscillatory signatures of proactive and reactive movement

To identify the neural origins of oscillations seen at the sensor level, these windows were imaged using a beamformer. The resulting maps indicated that all five oscillatory responses reliably localized to the left M1 cortex contralateral to movement, regardless of experimental condition (Fig. 2). As described in the methods, we next extracted peak oscillatory activity from each respective grand-averaged cluster (i.e. across all participants and task conditions) in the M1 cortex for proactive and reactive trials separately to examine the effect of adaptive control of movement using pairwise comparisons and Bayesian statistics. Movement-related theta and gamma oscillatory activities were significantly stronger in response to reactive trials compared with proactive ones (Fig. 3), while event-related decreases in the alpha and beta range were unaffected by reactive cueing (theta: $t(19) = −2.27, P = 0.033$; alpha: $t(23) = −0.59, P = 0.558$; beta: $t(23) = 1.01, P = 0.321$; gamma: $t(23) = −2.87, P = 0.009$). Similarly, post-movement beta rebound (PMBR) responses following motor execution exhibited no differences as a function of task condition ($t(24) = −0.34, P = 0.735$). In fact, there was moderate evidence for the null hypothesis for each oscillatory response that was unaffected by the different task conditions, providing further evidence that reactive cueing does not modulate movement-related oscillations in the alpha and beta range (alpha: BF$_{01} = 3.97$, error % = 0.040; beta: BF$_{01} = 2.94$, error % = 0.0001; PMBR: BF$_{01} = 4.49$, error % = 0.030).

Cross-frequency coupling differentially predicts proactive and reactive movements

Given the spectrally specific alterations in both low (i.e. theta) and high (i.e. gamma) frequency oscillations as a function of proactive and reactive movement cueing, we evaluated the dynamic coupling of these oscillations within the M1 cortex. Importantly, there is converging evidence from several lines of work implicating the functional coupling of theta and gamma oscillations to support local and network-level neuronal communication during cognitive and sensory processing. Thus, to examine the specific impact of theta–gamma coupling during proactively and reactively cued simple finger movements, we conducted an MLM in R using single-trial data. As described in the methods, we extracted the time series of the peak voxel in left M1 and computed the spectral envelope for theta and gamma oscillatory responses at the single-trial level. Theta oscillatory power (continuous), task condition (two levels) and their interaction were treated as fixed effects, with subject and trial number as a nested random effect to predict gamma oscillatory power in the motor cortex. Our results indicated a significant main effect of theta power on gamma power, such that increases in theta power were predictive of increases in gamma power, indicative of significant power-to-power cross-frequency coupling during movement execution in left M1 ($F(2173) = 6.86, P = 0.001$; Fig. 3). In contrast, there were neither main effects of task condition nor a significant theta by condition interaction ($P > 0.501$) on gamma oscillatory power. For completeness, we next evaluated whether adaptive cueing modulated dynamic coupling of theta and gamma oscillations via phase–amplitude interactions, as opposed to the power-to-power interactions described above. As described in the methods, we implemented the event-related phase-amplitude coupling approach and conducted pairwise testing as a function of task condition. Our results indicated no significant differences in theta–gamma phase–amplitude coupling in M1 during motor execution, with moderate evidence for the null hypothesis observed ($M_{proactive} = 0.15$, $SD_{proactive} = 0.03$; $M_{reactive} = 0.14$, $SD_{reactive} = 0.02$; $t(24) = 1.20, P = 0.241$, BF$_{01} = 2.48$, error % = 0.00007).

Finally, we assessed whether the strength of theta–gamma power-to-power coupling in left M1 was predictive of behavioural performance on our motor task. To address this, we computed the predicted gamma power using the regression equation derived from our theta–gamma power-to-power coupling relationship (see model above). Briefly, because we did not observe any significant effect of condition, nor a theta by condition interaction in our MLM, we used the regression equation solely interrogating the predictive capacity of theta oscillatory power on gamma oscillatory power, as the regression coefficients did not differ from one another (see Materials and methods). Thus, we conducted a linear mixed effects model of predicted gamma power (i.e. indicative of theta–gamma power-to-power coupling; continuous variable), task condition (two levels) and their interaction as fixed effects, with subject and trial number as a nested random effect to predict response distance from target onset. Importantly, we observed a significant main effect of predicted gamma power (i.e. gamma activity predicted by theta activity in M1), such that increases in predicted gamma power during movement onset were predictive of closer response distances (i.e. faster responses; $F(2263) = 6.86, P = 0.009$). Additionally, as expected based on our behavioural analyses, there was a significant main effect of condition,
such that response distances from target were significantly longer for reactive trials compared with proactive ones ($F(3015) = 512.61, P < 0.001$). Finally, there was a significant predicted gamma power by condition interaction, such that during proactive trials, higher levels of predicted gamma power in the motor cortex were associated with increased response distances, while for reactive trials, greater predicted gamma power (i.e. greater theta–gamma coupling) was predictive of faster response times relative to the onset of the target interval ($F(3139) = 4.51, P = 0.034$; Fig. 4).

Notably, this interaction effect also held when gamma power was included as a covariate of no interest in the MLM.

**Discussion**

Using a novel proactive–reactive movement paradigm and advanced oscillatory analyses, we interrogated the functional coupling of motor cortical oscillations serving the adaptive control of voluntary movements. Specifically, we observed robust decrements in task performance, such that during reactive trials (i.e. an unexpected change in target interval location), participants responded more slowly and were more variable compared with the expected, proactively cued targets. In regard to the brain, during movement onset, we observed significant increases in low- (i.e. theta) and high- (i.e. gamma) frequency oscillatory activity during performance of reactive trials compared with proactive ones, while peri- and post-movement oscillatory activity in the alpha and beta range were unaffected by conditional cues. Finally, our novel finger tapping task elicited robust cross-frequency power-to-power coupling in the left M1 contralateral to movement, such that during motor execution, theta–gamma coupling was strong and further, increases in theta–gamma cross-frequency coupling were predictive of better task performance during adaptive motor control.

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**Figure 2 Sensor- and anatomical-space movement-related oscillations.** (Left): Time-frequency spectrograms locked to the onset of the movement (0 ms) for two sensors near the left sensorimotor cortex. The x-axis denotes time (in ms) and the y-axis represents frequency (in Hz). Relative power (i.e. percent change from baseline $-2000$ to $-1500$ ms) is expressed according to the colour scale bars inset in the top right of each spectrogram. (Right): Significant movement-related oscillations were imaged using a beamformer. Strong decreases in alpha (10–14 Hz) and beta (20–28 Hz) activity occurred 250 ms prior to and following movement, and these localized reliably to the left M1. In contrast, robust increases in theta (4–8 Hz) and gamma (70–80 Hz) activity were observed in the left M1 during movement onset ($-125$ to $125$ and $-100$ to $100$ ms for theta and gamma, respectively).
Below, we discuss the implications of these novel findings for understanding the proactive and reactive control of voluntary movement.

Previous investigations of proactive and reactive control of movement have employed a variety of experimental paradigms (e.g. stop-signal task, Go/No-Go) to examine movement selection and inhibition processes. These paradigms generally involve manipulating conditional cues unexpectedly (e.g. presented 2.5% of the time) and require participants to select a different movement (e.g. move a different finger) or alternatively, to inhibit the pre-planned movement. Importantly, these studies indicate that when movement cues are abruptly changed and participants must inhibit and/or significantly alter the parameters of the movement, behavioural performance is often degraded. For example, classic stop-signal paradigms tend to elicit key behavioural outcomes, including increased error rates to STOP trials, longer stop-signal response times (i.e. time needed to abort a pre-planned response) and even shorter response times to STOP trials when the action was completed erroneously. In contrast, for paradigms requiring motor responses to be altered based on a conditional cue (e.g. change in movement direction, different muscle groups engaged), response times tend to increase, indicative of poorer task performance. In contrast to these studies, the paradigm used in the current study enabled motor planning and selection processes to remain constant despite changing task demands, and thus facilitates a more direct interpretation of the findings. Interestingly, we found significant declines in behavioural performance during unexpected (i.e. reactive) cue trials, such that participants were slower to respond and much more variable in their responses (i.e. greater coefficient of variation) compared with the expected, proactively cued trials. Importantly, our results corroborate the previous work suggesting that reactive or unexpected cues directly affect motor outcomes compared with proactive ones. However, since prior work also involved changes to the movement (i.e. response inhibition, movement direction), the current findings are able to more directly link the alterations in performance to the reactive versus proactive dimension.

In regard to the brain, our novel proactive-reactive motor task elicited robust oscillatory activity in the theta, alpha and gamma bands and further, we observed frequency-specific alterations in motor cortical oscillations as a function of task condition. Specifically, we observed stronger theta and gamma oscillations during motor execution in reactive compared with proactive trials, while peri-movement decreases in the alpha and beta range were unaffected by task condition. While the precise role of theta and gamma oscillations in motor control still requires careful consideration, emerging data indicates an important, temporally defined role in the execution of motor commands. For example, theta oscillations have long been seen as temporal coordinators and organizers of sensory information. This specific role appears to be ubiquitous across sensory cortices and may be further propagated to serve as coordinators of the precise timing of motor actions in the contralateral M1. In contrast, gamma oscillations in the motor cortex were primarily thought to reflect pro-kinetic signals that are particularly sensitive to basic movement parameters such as the force, frequency and pacing of the performed action. However, recent work by our laboratory and others have...
In regard to the motor system, studies have suggested that motor function and attentional reallocation, demonstrating alterations in movement-related gamma power and/or frequency with increased cognitive interference and attentional reallocation, suggesting that gamma oscillations in the contralateral M1 are susceptible to higher order control mechanisms, especially when the specific movement remains constant across changing cognitive demands. Critically, this idea of cognitively controlled, movement-related gamma synchrony is strengthened by the current data, as our task was designed to control for precise movement kinematics in order to fully disentangle the cueing mechanisms serving adaptive motor control.

Our most important finding was likely the dynamic, single-trial coupling of theta and gamma oscillations during motor execution in the contralateral M1 cortex. Specifically, single-trial analyses indicated that increases in theta oscillatory power robustly predicted increases in gamma oscillatory power in the same region and further, gamma power differentially predicted trial-by-trial behavioural outcomes as a function of task condition. Such cross-frequency coupling of neural oscillations may serve an important mechanistic role in coordinating the local- and network-level communication among neuronal pools oscillating at disparate rates. In particular, such functional coupling tends to give rise to a nesting of faster oscillators (e.g. gamma) that are temporally coordinated with and modulated by the phase and/or amplitude of slower oscillations (e.g. theta) to further govern behavioural performance, albeit the dynamic coupling observed in the current study was specific to power-to-power dynamics rather than phase–power interactions between lower and higher frequency oscillators.

For example, the coupling of theta and gamma oscillations both locally and across the cortex has been shown to be critical for a variety of cognitive processes including memory, cognitive interference, associative learning, and motor function. In regard to the motor system, studies have shown substantial theta–gamma coupling in the rat motor cortex during rest and while moving (e.g. treadmill running) and further, this phenomenon appears to be temporally synced with movement initiation. Importantly, our study is the first to evaluate theta–gamma cross-frequency coupling within the motor cortex during adaptive motor control. Additionally, while holding the actual movement constant, we demonstrated a condition-specific modulation of behavioural performance, such that gamma oscillatory power estimated by the levels of theta power during motor execution significantly predicted key parameters of the behavioural response. Specifically, during proactive trials where the target interval was unexpected, increases in predicted gamma power were significantly predictive of slower response times. In contrast, during reactive trials where the target interval change was unexpected, increased predicted gamma power was predictive of faster response times, which suggests that greater theta–gamma cross-frequency coupling in the motor cortex leads to enhanced adaptive motor control when real time parameter adjustments are needed. While behavioural decrements in response to increased M1 theta–gamma coupling during proactive trials seems counterintuitive at first glance, such findings would be predicted based on prior work in healthy young and older adults. For example, a recent study in our

![Figure 4 Theta–gamma cross-frequency coupling modulates motor control.](image)
laboratory used an Eriksen Flanker paradigm during MEG to evaluate the role of motor cortical oscillations on the well-established age-related decline in visual selective attention function. The results demonstrated that M1 gamma power was a unique predictor of behavioural performance and further, in younger adults, elevations in M1 gamma power predicted faster reaction times regardless of task difficulty. In contrast, older adults did not exhibit this same behavioural benefit, and elevations in M1 gamma power were related to decrements in motor performance both in the presence and absence of visual interference, likely reflecting exhausted neural resources with increasing age. Such findings of elevated M1 gamma power contributing to behavioural benefits in times of increasing task difficulty compared with less difficult tasks are also corroborated by numerous studies in healthy young adults regarding response interference (e.g. multisource interference: Simon and Flanker stimuli) and attentional reorienting.

Conclusion

The current study was the first to identify the spectrotemporal dynamics serving adaptive motor control in the M1 cortex in healthy adults. Specifically, we developed a novel proactive–reactive movement paradigm and observed spectrally specific alterations in motor cortical oscillations during proactive and reactive movements and further, observed a dynamic coupling of theta and gamma oscillations during motor execution. Our study was also the first to directly link the strength of theta–gamma cross-frequency coupling to behavioural enhancements and decrements as a function of adaptive motor control. While the existing literature has provided substantial insight on internal model updating when major changes in the motor response are required (e.g. motor inhibition), the ability to adapt to more ecologically valid shifts in environmental parameters to maintain the same movement kinematics was poorly understood. Ultimately, our data provides novel mechanistic insight indicating that the adaptive control of movement is governed by strong theta–gamma cross-frequency coupling in the motor cortex. Essentially, during the updating of identical movement parameters, stronger coupling during reactive adaptation is necessary for improvements in behaviour, while stronger coupling during expected (i.e. proactive) trials is less essential and led to decrements in performance. Further, while the current study provided insight regarding the oscillatory dynamics serving specific behavioural modifications for reactionary motor control (i.e. coupling-related changes to response distances) future studies will benefit from also evaluating the impact of movement force in the context of proactive–reactive movements to more comprehensively characterize behaviour. Finally, in regard to mechanism, the observed theta–gamma power-to-power coupling observed in our study could be attributable, at least in part, to changes in GABAergic interneuronal pools. Importantly, previous work substantially implicates this GABA-mediated inhibitory drive in modulating local pyramidal cells, giving rise to a host of spectral profiles including the generation and modification of theta and gamma oscillatory activity. Thus, while GABA activity was not directly measured in the current study, future work in this area will be critical to fully unravel the nature of oscillatory coupling in the sensorimotor cortices during adaptive motor control.

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Competing interests

The authors report no competing interests.

Supplementary material

Supplementary material is available at Brain Communications online.

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