Journal Club

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The Oscillatory Nature of Movement Initiation

Cécilia Neige,[1,2*] Goldy Yadav,[3*] and Gerard Derosiere[3]

[1]Pôle Est, Centre Hospitalier Le Vinatier, F-69500 Bron, France, [2]Université Claude Bernard Lyon 1, Centre National de la Recherche Scientifique, Institut National de la Santé et de la Recherche Médicale, Centre de Recherche en Neurosciences de Lyon U1028 UMR5292, PsyR2 Team, F-69500, Bron, France, and [3]Cognition and Actions Laboratory, Institute of Neuroscience, Université Catholique de Louvain, Brussels, 1200, Belgium

Review of Hussain et al.

Initiating voluntary movements at appropriate times allows animals to interact optimally with the world. Given this, it is no surprise that neuroscientists have long aimed to understand the neural bases of movement initiation (Libet et al., 1983). An extra benefit of such research is that it may provide a foundation for developing interventions to improve symptoms of patients exhibiting impairments in movement initiation, such as those with Parkinson's disease or Tourette syndrome.

The execution of most voluntary movements relies on cortical cells in the primary motor cortex (M1), which project to the spine and connect with peripheral motor neurons. This corticospinal pathway provides a unique route through which the brain can initiate movements (Derosiere and Duque, 2020). Classical models in motor neuroscience posit that the initiation of a body movement occurs when corticospinal cells projecting to motor neurons innervating the related body part receive neural inputs sufficient to increase their activity to a triggering threshold (Schurger et al., 2012). Importantly, the basal level of corticospinal excitability will determine the likelihood that a given neural input will be sufficient to reach this threshold, and thus, to drive movement.

EEG recordings in humans have shown that activity in the primary motor cortex (M1), as in other cortical areas, fluctuates in an oscillatory pattern over time (Buzsaki, 2006). Two prominent EEG waveform oscillations that are considered to play a crucial role in goal-directed motor behaviors are the μ (8-12 Hz) and β rhythms (13-35 Hz) recorded over M1. Specifically, corticospinal excitability increases during the trough and rising phases of μ oscillations (Zrenner et al., 2018; Hussain et al., 2019) and at the peak and falling phases of β oscillations (Wischnewski et al., 2022; but for a lack of effect of the beta phase, see Hussain et al., 2019). Although the exact cause of these opposite effects of the μ and β phases on corticospinal excitability remains unknown, one possible explanation is that they are generated by distinct neural mechanisms. As such, the trough and rising phases of μ oscillations are associated with an increase in spiking frequency in motor cortices (Haegens et al., 2011) but do not involve any modulation in the activity of GABA interneurons (Bergmann et al., 2019). Conversely, the peak and falling phases of the beta rhythm are thought to be associated with a cyclic hyperpolarization of corticospinal cells mediated by a release of GABAergic activity (Rossiter et al., 2014; Hussain et al., 2022; Wischnewski et al., 2022). Still, despite the presence of different generators for these oscillations, the fascinating effects of the oscillatory phase on corticospinal output recently uncovered (Zrenner et al., 2018; Bergmann et al., 2019; Hussain et al., 2019; Wischnewski et al., 2022) raise the question as to whether specific phases represent critical temporal windows for releasing voluntary motor commands and initiating movements.

In work published recently in *The Journal of Neuroscience*, Hussain et al. (2022) addressed this key question. Healthy participants performed a self-paced movement task, in which they viewed a series of pictures and pressed a button with the left index finger to go to the next picture whenever they wanted. EEG and EMG of the left index finger muscle were recorded throughout the task, allowing the authors to record both oscillatory activity in M1 and the onset of muscle contraction, respectively.

To estimate the timing at which the motor command was released within M1, Hussain et al. (2022) first estimated each individual's cortico-muscular conduction time (i.e., from the right M1 to the left index finger muscle involved in the task), by applying single-pulse transcranial magnetic stimulation over the right M1 during rest. Such stimulation depolarizes corticospinal cells and ultimately evokes motor-evoked potentials (MEPs, recorded with EMG) in contralateral muscles, with a delay that usually varies between 18 and 25 ms, reflecting the cortico-muscular conduction time. The authors subtracted this estimated conduction time from the time of onset of muscle contractions measured with EMG during the task to estimate when the motor

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*C.N. and G.Y. contributed equally to this work.

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Correspondence should be addressed to Cécilia Neige at cecilia.neige@ch-le-vinatier.fr.

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command was released within M1 for each subject and each movement. After this, they extracted the phase angles of the μ and β frequencies in the EEG recording at the time of each motor command release. Finally, they assessed whether specific phase angles were associated with the release of the motor commands.

The study highlighted two major findings. First, motor commands were more often released during the falling phase of the contralateral beta activity (i.e., when activity went from peak to trough). Second, motor command release was not affected by the phase of the μ rhythm. In accordance with classical models of movement initiation, the authors concluded that the falling phase of the β frequency may coincide with the periodic synchronization of spiking activity in contralateral M1, which would bring corticospinal excitability closer to the triggering threshold and increase the propensity to initiate movements.

What might be the neural source of such a periodic synchronization of spiking activity in M1? As described above, β peaks are associated with a cyclic release of GABAergic activity (Rossiter et al., 2014; Hussain et al., 2022; Wischnewski et al., 2022). One possibility is that this cyclic release is generated by modulatory thalamo-M1 inputs (Takahashi et al., 2021): under the influence of fronto-basal ganglia circuits. Indeed, the inferior frontal gyrus and the presupplementary motor area both inhibit corticospinal output through basal ganglia circuits in various contexts, including during movement initiation (Obeso et al., 2013; van Campen et al., 2013). Interestingly, in some motor tasks, the inhibitory influence of these areas is cyclically released every 50 ms (Picazio et al., 2014), suggesting that (dis)inhibitory signals can be transmitted at a β frequency from frontal structures to corticospinal cells. Hence, one possibility is that the inferior frontal gyrus and/or the presupplementary motor area produce a "pulsed disinhibition" of corticospinal cells at the β frequency through fronto-basal ganglia-thalamo-M1 circuits, ultimately involving M1 GABAergic interneurons. Together, this circuitry would contribute to synchronizing spiking activity periodically in the motor output pathway, increasing the propensity to initiate movements at β peaks.

Of note, such a cyclic depolarization of corticospinal cells might not only increase corticospinal excitability but also decrease the cortico-muscular conduction time. In line with this idea, MEP latency is shorter during the peak of the β frequency (Torrecillos et al., 2020). This is of key importance to the study by Hussain et al. (2022), given that, as explained above, the average individual MEP latency was exploited to estimate the timing at which the motor command was released within M1 for each movement. Given the effect of the beta phase on MEP latencies, one could argue that the authors' estimation involved some time lag with respect to the actual timing of the motor command release, especially for commands released during the peak of the β frequency. However, the effect of the beta phase on MEP latencies is quite subtle, of the order of 0.4-0.8 ms (Torrecillos et al., 2020), while the duration of a full β cycle is of the order of 50 ms. Even for higher-frequency oscillations, such as γ (i.e., from 40 to 100 Hz), the duration of a full cycle is of the order of 10-25 ms. Hence, it is sensible to assume that the putative misestimation mentioned above was too subtle to affect the findings of the present study. Overall, the approach developed by Hussain et al. (2022) to identify the timing of motor command release is novel and may prove useful for future studies aiming to examine the functional role of these oscillations in movement initiation.

Strikingly, the phase of the μ frequency did not affect the propensity to initiate movements in this study. Yet, as mentioned earlier, corticospinal excitability rises cyclically during the trough and rising phases of the μ frequency. Why isn't the propensity to initiate movements higher while corticospinal output increases during these μ phases? This could perhaps be related to the fact that movement initiation implies (if not requires) a release of GABAergic activity in the motor cortex (Reynolds and Ashby, 1999), while GABAergic activity remains unchanged during the trough and rising phases of the μ rhythm (Bergmann et al., 2019). Another, complementary explanation, though speculative, could be that other motor circuits exhibit a concomitant decreased excitability during μ trough and rising phases. A proportion of corticospinal cells projecting to motoneurons originates outside M1, mostly in secondary motor areas (Dum and Strick, 1991). Therefore, while the excitability of M1-originating corticospinal cells indeed rises during μ trough and rising phase (Bergmann et al., 2019), it is plausible that the excitability of cells originating in secondary motor areas decreases, leading to a null net input on motoneurons and, ultimately, to a lack of effect of the μ phase on movement initiation.

In conclusion, the work by Hussain et al. (2022) investigates the functional role of cortical oscillatory phases in movement initiation. The authors show that motor command release coincides preferentially with restricted phases of the β, but not of the μ, frequency in contralateral M1. The study should prompt future work to further elucidate the functional role of neural oscillations in movement initiation and complex human motor behavior.

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