**EEG oscillations: how are they modulated during different phases of repetitive movements?**

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ABSTRACT

Voluntary movements are planned through the relative timing between sub-movements of movement sequences as part of the motor program. Different movement phases are characterized by specific amplitude modulation of cortical oscillations. The latter represent neurophysiological correlates of specific synchronization or desynchronization of different neuronal groups. In this NeuroForum, we review recent evidence regarding the temporal relation between neurophysiological correlates of different phases of a repetitive motor task using electroencephalography and source localization using individualized MRI.

Schmidt’s (1975) concept of generalized motor programs or *schema* has been an enduring theory in motor control. Since Summer’s (1975) supposition and subsequent electrophysiological support (Carter et al. 1984), it is widely accepted that the brain stores the relative timing between sub-movements of movement sequences as part of the motor program. Any discrepancy between timing and sequencing the components of a motor task disrupts the appropriate interaction with our physical and social environment. In this way, the brain can synchronize its’ own movements in relation to external events. The spatial involvement of different neural networks has been well-documented with functional imaging studies during various movements (Jahanshahi et al. 2010; Bortoletto and Cunnington 2010; Ariani et al.2015). However, empirical evidence highlighting the role of different neural networks and their temporal relation to different elements of a motor program is limited.

Previous data have shown that amplitude modulations of cortical oscillations during different movement phases represent neurophysiological correlates of synchrony/desynchrony states of specific neuronal groups (Neuper and Pfurtscheller, 2001). These cortical activities are time-locked to the event and they are called event-related desynchronization (ERD) (Pfurtscheller, 1977) and event-related synchronization (ERS) (Pfurtscheller, 1992). Notably, event-related responses allow detailed insights into the time course of brain activation, whereas frequency analysis allows the detection of brain networks and therefore sheds light on how brain areas interact with each other (Pollok, 2006).

In a recent study, Seeber et al. (2016) investigated the temporal relation between neurophysiological correlates of different phases of a repetitive motor task using high temporal resolution electroencephalography (EEG) recordings. A sample of 18 subjects performed rhythmic right hand movements while they were presented with blue dot stimuli blinking three times indicating the desired 0.67 or 1.5 Hz cadences. Participants performed the movements at the required cadence without the stimuli present. Structural MRI T1 scans were acquired for each participant to be used with EEG recordings to generate source models of cortical oscillations in different phases of the rhythmic movements (Seeber et al. 2016).

One of the main novelties of the study by Seeber et al. (2016) was that they were focused on two different elements of the cortical activities during the repetitive movements: 1) sustained amplitude envelopes (AE) corresponding to (ERD/ERS); and 2) movement phase-related amplitudes (MPAs) that correspond to the dynamic changes during different movement cycle phases. Sustained amplitude AE and dynamic movement AE were measured by low and high-pass filtering at 0.3 Hz after Morlet wavelet decomposition. These EEG patterns were investigated in terms of time courses, frequency spectra, time frequency plots in the right and left regions of interest (ROIs), which were identified as the centres of β oscillations (18-24 Hz) (Seeber et al. 2016).

Interestingly, Seeber et al. (2016) found that these two cortical activities showed different spectral and spatial patterns during rhythmic movements. Indeed, sustained ERD/ERS were characterized by suppression of α (10-12 Hz) and β1 (18-24 Hz) oscillations and amplitude increase of γ (60-80 Hz) oscillations. These amplitude modulations were mostly evident at the onset of the movement, beginning over 2.5 seconds prior to movement initiation, and remained sustained during the movement. These modulations showed a marked lateralization on the contralateral somatosensory cortex of hand area, especially for β1 and γ. The effect was particularly evident during the faster movement cadence.

On the contrary, MPAs showed a marked activity in the β2 (24-30 Hz) frequency range compared to α and γ. The amplitude modulation of these oscillations reached a peak at the onset of the movement cycle and, then, it showed changes phase-locked with the rhythmic flexion and extension of right fingers or thumb. β2 modulations were mainly present in bilateral sensorimotor regions and were higher during slower cadence of movement. β2 was also evidence in the right prefrontal cortex, particularly during faster cadence movements. β2 preceded but overlapped with α MPA while β2 and γ were divergently modulated. α MPAs showed dynamic co-modulations involving prefrontal, frontal and sensorimotor areas during the different steps of the movement cycle (Seeber et al. 2016).

The findings by Seeber et al. (2016) provide evidence for existence of two large networks, which are simultaneously involved in different sub-components of rhythmic movements. Importantly, there is a greater difference between the stronger lateralization of sustained ERD/ESD activities compared to the involvement of bilateral hemispheres in MPAs. This aspect together with the different frequency ranges that underlie sustained and dynamic activity lead support to two networks that have different but complementary roles in the context of timing and sequencing of rhythmic movements.

In line with the literature, the ERD/ERS results showed the well-known α and β desynchronization and γ synchronization on the sensory motor cortex representing the right hand around 2 seconds before the onset of the movement (Chrone 1998a, 1998b). Multiple studies have implicated ESD/ERS elements in the motor preparation (Bauer et al. 2014). Therefore, the findings by Seeber et al. (2016) highlight that distinct sustained cortical activity may be responsible for motor processing due to the combination of inhibitory inputs (α and β oscillations) and facilitator input (γ activity). This would be consistent with the common view of a causal link of sensorimotor cortical oscillations and accurate motor performance (Rao and Ballard 1999).

Notably, the innovative methods and novel findings of this study regard the characterization of MPAs, which are electrocortical networks not deeply known. The MPAs represent a dynamic network, which changes the related synchrony of neuronal populations in a phase-locked mode of the movement cycle. Therefore, it could be argued that these cortical activities are the neurophysiological correlate of two essential aspects of a repetitive movement: the timing and the sequencing. Interestingly, they have a peculiar spectral pattern (the β2 frequency) as well as spatial pattern (bilateral sensorimotor cortex, prefrontal cortex and supplementary motor area).The specific spatial pattern of MPAs is in overlap with the sensorimotor resting state network, which was described through fMRI techniques (Raichle 2010). This network may be linked with intrinsic brain activity which is focused on sensory information processing for interpreting and, then, responding to and predicting environmental demands (Raichle, 2010). In support of this notion, MPAs involved bilateral sensorimotor regions.

Seeber and colleagues (2016) investigated MPAs in the absence of overt external cues. The sensory information processed and integrated during the task were the somatosensory information generated by the hand and fingers during the movement and visual input from the moving fingers. Therefore, MPAs likely represent the integration of this sensory information during repetitive movements. Indeed, it is well known that high β have been involved in the prediction, integration and top-down control of sensorimotor input triggered by movements (Davis et al, 2012). Seeber et al. (2016) suggested that prefrontal cortex and, then, right sensorimotor MPAs with β2 spectrum may represent a further top down control during movements performed with a frequency of 1.5 Hz. Notably, the movements performed at 0.67 Hz exhibited a different β2 spatial pattern involving, firstly, bilateral hands regions and, then, central sensorimotor regions and SMA.

The findings of Seeber et al. (2016) further highlighted the importance of prefrontal regions in the top-down control of sensorimotor internal information in a context of complex repetitive movement. Notably, connections between prefrontal regions and subcortical areas (as basal ganglia and thalamus) as well as cerebellum are essential in this complex activity which lead to repetitive movements requiring sequencing and coordination (Houk et al., 1995) including timing to repetitive movements after cessation of auditory tones (Jahanshahi et al. 2010). Working memory function is linked with this complex motor function. Indeed, performing complex motor sequences requires storing instructions about the motor tasks. In line with this, Seeber et al. (2016) found α MPAs in bilateral sensorimotor areas, SMA and bilateral parietal areas. It is well known that this cortical activity is linked to working memory processing (Crespo-Garcia et al. 2013). Finally, Seeber et al. (2016) found γ activities in the left-hand region and left SMA, especially during faster movements. These cortical activities resulted conversely modulated by the high β MPA confirming the different roles of these oscillations on movements. It is likely that the γ was involved in excitation while β had an inhibitory function (Hermann, 2016).

Although there were many important findings and innovative methods in the study by Seeber *et al.* (2016), there were also several limitations. Firstly, the authors hypothesized that their findings might be applicable to both lower and upper extremities. However, rhythmic feet movements were not investigated within the same study with the same people. Previous research from the same group has demonstrated different profiles between sustained and dynamic gait, which did include changes sustained beta ERD and high γ during the gait cycle. However, changes in low γ were also found with gait while no α changes were found such as was demonstrated in the upper limbs. Although this different oscillatory profiles could underlie differences between gait and upper limb movements, the current study by Seeber *et al.* (2016) does not clarify similarities and differences between upper and lower limb rhythmic movements.

Secondly, the study was focused on a very simple sequence of repetitive movements as opening and closing the right hand or simple repetitive thumb movements. Consequently, the application of these findings to complex real-world sequences of voluntary movements, which involve several muscles and body regions, cannot be resolved. It is an experimental setting which was very useful to clarify aspects of motor programming but further studies on movements involving both sides of the body are needed to clarify the integration of different neuronal groups in a natural environment. Furthermore, the rhythm of the studied movements were performed following blinking cadence of a dot. Therefore, we are not able to conclude about neurophysiological correlate of self-paced movements.

Thirdly, the study failed to provide any evidence how these oscillatory networks may be modulated by varying the demands of the sustained or dynamic network outside of manipulating cadence of movements. In fact, the authors combined movements of hand and thumb rather than investigating differences that might characterize subtle yet important differences. The findings and impact of this study would have been greater if the authors demonstrated that manipulating the task complexity (i.e. repetition of different sequences of movement) resulted in measurable differences in both the sustained and dynamic networks. Furthermore, the oscillatory models described in the study by Seeber *et al.* (2016) would have provided more valuable information if functional connectivity was measured by coherence, phase lag index and/or phase-amplitude measures that would have captured how these oscillations are systematically co-modulated in relation to the phase in movement.

In conclusion, Seeber et al. (2016) provide novel evidence for two brain networks involved in performing repetitive finger movements. The MPAs (α, β, γ) that dynamical change during different movement cycles are a novel network involved in finger movements. Unlike the sustained activity network, the dynamic network characterized by the MPA may capture complexity of the sequences in repetitive movements, including motor as well as sensory and cognitive aspects. The temporal modulations in specific neural networks that were found during different phases of the movement cycle could provide evidence for neural representations of sub-movements of movement programs (Schmidt 1975; Summers 1975). Future studies should investigate whether varying sub-movements will result in distinct temporal patterns in specific neural networks. Additionally, many neurological diseases including neurodegenerative disorders like Parkinson’s disease are characterized by impairment of complex movement sequences. Therefore, investigations of the dynamic neural network characterized by MPAs could provide essential insight into the temporally modulations in distinct neural networks that characterize pathological movement impairments.

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