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Electrophysiological correlates of cortico-subcortical interaction: A cross-frequency spectral EEG analysis

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Abstract

Objective: Several studies have provided evidence for the notion that the coupling between slow and fast frequency in the EEG spectrum indicates cortico-subcortical cross-talk (CSC-ct). In addition, findings for increased limbic activation due to reduced cortical inhibition have recently been acquired. To get further insights into these mechanisms, the current study investigated whether CSC-ct would decrease as a function of increased slow (SW) or fast wave (FW) activity.

Methods: Resting state EEG recordings were obtained from 46 healthy, right-handed participants. CSC-ct was quantified by computing cross-frequency correlations between the power in the slow and fast frequency range. CSC-ct was compared between groups with relatively low and high SW activity and groups with relatively low and high FW activity.

Results: Relatively reduced SW, but not FW activity was associated with a significant coupling between slow and fast frequency EEG. Furthermore, relatively enhanced resting state SW activity was paralleled by slow and fast frequency EEG decoupling.

Conclusions: These findings are in line with the notion that increased subcortical drive can go accompanied by reduced CSC-ct.

Significance: Cross-frequency EEG analyses might provide a unique approach to obtain novel insights into cortico-subcortical interactions in relation to affective and cognitive behavior.

Keywords: Beta; Coupling; Cortex; Delta; EEG spectrum; Functional connectivity; Limbic system; Theta

1. Introduction

Robinson's contribution in *Clinical Neurophysiology* (1999;110:1427–1434) on the technical, physiological, and psychological significance of frequency bandwidths in EEG evoked potentials hallmarked the onset of a new field of research, wherein different EEG rhythms in the cortical EEG reflect the different subcortico-thalamic-cortical projections. Robinson (1999) showed that the event-related brain potentials are comprised of frequency bandwidths that originate from different neural arousal systems in awake humans. Through recording the EEG responses to auditory tones and using narrow-band filters he was able to demonstrate the relatively distinct nature of the 4, 7 and 10 Hz component waves in the auditory evoked potentials. Neurological studies had already shown that stimulation of brain-stem ascending reticular activating system (ARAS) elicits 1–4 Hz (delta) cortical responses (Guyton, 1976), whereas stimulation of the limbic system evokes 7 Hz (theta) activity (Gray, 1982). In addition to demonstrating a relationship between 4 Hz activity and the ARAS, Robinson argued that the thalamus could have been responsible for producing the 10 Hz oscillations.

Comparative research has provided evidence for dominant EEG rhythms to shift with brain complexity. Whereas the reptile brain is suggested to be an arousal system oscillating in the delta range (Gaztelu et al., 1991), lower mammals have an additional limbic system that is

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associated with theta oscillations (Klimesch, 1999). Finally, primates are geared with a cortical mantle, which oscillates in the 8–12 Hz (alpha) and the 13–30 Hz (beta) frequency range (Knyazev and Slobodskaya, 2003). This is in line with Basar's (1998) notion on the evolutionary accounts of brain development stating that only the human EEG contains the entire delta to beta frequency spectrum. Thus, in addition to temporal EEG, analyses in the frequency domain might yield insights in physiological properties that can be linked to the different arousal systems and provide possible insights into how these systems communicate.

Moreover, studying the relations between the different frequency bandwidths could reveal some of the dynamics of these interacting systems. Knayzev et al. (2004), for instance, argued that the delta and alpha system operate in close conjunction during behavioral regulation. Evidence for this assumption was provided earlier by Robinson (1999), who observed a negative relationship between 4 Hz (i.e. delta-theta activity) and 10 Hz (i.e. alpha) activity that was attributed to thalamic inhibition of the brain-stem ascending reticular activating system (ARAS).

Interestingly, the negative relationship observed by Robinson fits John Hughlings Jackson's (1958) visionary principle of descending inhibition (DI), which states that the cortical system executes inhibitory control over lower brain structures. Exemplary in this context is a functional neuroimaging study, which showed that the voluntary control of negative feelings is associated with enhanced prefrontal cortex (PFC) activity and reduced amygdala activity (Ochsner et al., 2002). Moreover, Anderson et al. (2004) recently discovered that the involvement of prefrontal cortex in the active suppression of unwanted memories was accompanied by reduced hippocampal activation and impaired retention. On basis of the evidence above, DI might be considered an example of cortico-subcortical cross-talk (CSC-ct) as reflected in the coupling between frontal slow (SW) and fast wave (FW) activity. In agreement, Knyazev and Slobodskaya (2003) showed that the coupling between the slow and fast frequency range predicts behavioral inhibition. In concordance, Schutter and Van Honk (2005) found cortisol, a stress-hormone associated with behavioral inhibition and anxiety, to be linked to the coupling between SW and FW activity. Moreover, the administration of testosterone, a steroid associated with behavioral activation and fearlessness (Van Honk et al., 2004), induces increased SW activity and decoupling of SW and FW activity (Schutter and Van Honk, 2004). Notably, testosterone acts on steroid responsive networks in the limbic system (Hermans et al., 2004; Wood, 1996) and the findings by Schutter and Van Honk (2004) can therefore be explained in terms of subcortically driven reductions in CSC-ct resulting in behavioral activation. This also provides an alternative electrophysiological explanation for increased disadvantageous risky decision making in the Iowa gambling task after administrating testosterone to healthy volunteers (Van Honk et al., 2004). Successful performance in the Iowa gambling task depends on avoidance of initially rewarding, but eventually disadvantageous decks of cards (Bechara et al., 1994). In agreement, Schutter and Van Honk (2005) demonstrated that increased ratios between SW and FW activity predicted risky disadvantageous decision-making. Thus, relatively increased SW compared to FW activity might reflect reduced cognitive control that should be paralleled by increased subcortical motivational drive and reduced CSC-ct.

To seek further evidence for these presumptions, we investigated the role of SW and FW and their distinct contribution to CSC-ct on basis of the following hypotheses: If the subcortical system is controlling CSC-ct during relaxed wakefulness, subjects with relatively high SW activity will show SW–FW decoupling, whereas significant SW–FW coupling will be observed in subjects with relatively low SW activity. If, on the other hand, the cortical system is controlling CSC-ct, subjects with relatively high FW activity will display significant SW–FW coupling, while SW–FW decoupling will be observed for subjects with relatively low FW activity.

2. Methods

2.1. Subjects

Forty-six healthy right-handed volunteers (35 females) aged between 18 and 24 years were recruited at Utrecht University, The Netherlands. All participants were medication free, except for the females taking oral contraceptives, had at least 12 years of education and written informed consent was obtained. All volunteers were unaware of the aim of the study and were paid for participation. The study was approved by the local ethical committee of the Faculty of Social Sciences.

2.2. Resting state EEG recording

EEG was recorded from 32 scalp locations according to the International 10–20 EEG System using Ag-AgCl-tipped electrodes (sampling rate: 256 Hz). Electro-oculogram (EOG) was recorded from a bipolar montages from the sub- and supra-orbital regions of the right eye and the outer canthi of the eyes. Raw EEG recordings were made with the ActiveTwo system (BioSemi, Amsterdam, The Netherlands) relative to the common mode sense (CMS). By physically integrating the first amplifier stage with a sintered Ag–AgCl electrode, extremely low-noise recordings free of interference can be achieved. The Active-electrode is a sensor with very low output impedance. The ground consisted of the active CMS active and passive driven right leg (DRL) electrode that form a feedback loop driving the subject's average potential as close as possible to the analog-to-digital converter (i.e. the amplifier 'zero')