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Frontal preparatory neural oscillations associated with cognitive control: A developmental study comparing young adults and adolescents

Kai Hwang [a,b,c,d,*], Avniel S. Ghuman [b,d,e], Dara S. Manoach [f,g], Stephanie R. Jones [h], Beatriz Luna [b,c,d]

[a] Helen Wills Neuroscience Institute, University of California Berkeley, Berkeley, CA, United States
[b] Department of Psychiatry, University of Pittsburgh, Pittsburgh, PA, United States
[c] Department of Psychology, University of Pittsburgh, Pittsburgh, PA, United States
[d] Center for the Neural Basis of Cognition, Carnegie Mellon University and University of Pittsburgh, Pittsburgh, PA, United States
[e] Department of Neurological Surgery, University of Pittsburgh, Pittsburgh, PA, United States
[f] Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School, Boston, MA, United States
[g] Athinoula A. Martinos Center for Biomedical Imaging, Charlestown, MA, United States
[h] Department of Neuroscience, Brown University, Providence, RI, United States

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ABSTRACT

Functional magnetic resonance imaging (fMRI) studies suggest that age-related changes in the frontal cortex may underlie developmental improvements in cognitive control. In the present study we used magnetoencephalography (MEG) to identify frontal oscillatory neurodynamics that support age-related improvements in cognitive control during adolescence. We characterized the differences in neural oscillations in adolescents and adults during the preparation to suppress a prepotent saccade (antisaccade trials—AS) compared to preparing to generate a more automatic saccade (prosaccade trials—PS). We found that for adults, AS were associated with increased beta-band (16–38 Hz) power in the dorsal lateral prefrontal cortex (DLPFC), enhanced alpha- to low beta-band (10–18 Hz) power in the frontal eye field (FEF) that predicted performance, and increased cross-frequency alpha-beta (10–26 Hz) amplitude coupling between the DLPFC and the FEF. Developmental comparisons between adults and adolescents revealed similar engagement of DLPFC beta-band power but weaker FEF alpha-band power, and lower cross-frequency coupling between the DLPFC and the FEF in adolescents. These results suggest that lateral prefrontal neural activity associated with cognitive control is adult-like by adolescence; the development of cognitive control from adolescence to adulthood is instead associated with increases in frontal connectivity and strengthening of inhibition signaling for suppressing task-incompatible processes.

Introduction

The ability to generate a task compatible response while suppressing prepotent and incompatible responses is a core component of cognitive control (Aron, 2007; Garavan et al., 2002; Ridderinkhof et al., 2004). This may be achieved through proactive, preparatory control processes (Aron, 2011; Braver, 2012) that modulate response related neural activities in preparation for an action (Cai et al., 2011; Connolly et al., 2002; DeSouza et al., 2003; Lavallee et al., 2014; Sacchet et al., 2015; Worden et al., 2000). Cognitive control has a protracted development through adolescence, in parallel with several circuit and systems level maturational processes (Luna et al., 2015). Initial developmental fMRI studies using tasks that require response inhibition show disparate results often implicating immaturity in prefrontal cortical systems (Bunge et al., 2002; Durston et al., 2002; Rubia et al., 2006, 2007; Velanova et al., 2009). Thus probing the neurodevelopmental differences in frontal preparatory processes is critical for understanding limitations in cognitive control during adolescence.

The antisaccade task (AS), which requires one to suppress a prepotent visually guided saccade in favor of a voluntary guided saccade to the opposite location, has been used to investigate the neural basis of preparatory cognitive control (Everling and Fischer, 1998). Non-human primate studies indicate that neural activities in oculomotor regions such as the frontal eye field (FEF), the supplementary eye field, and the superior colliculus (SC) during the preparatory period of the AS task predict correct versus incorrect AS task performance (Everling et al., 1998, 1999; Everling and Munoz, 2000; Schlag-Rey et al., 1997). Evidence indicates that top-down signaling modulates activity of saccade neurons in the FEF and the SC (Everling et al., 1998; Everling and Munoz, 2000), reducing the excitability of saccade neurons and/or adjusting the saccade generation threshold (Munoz and Everling, 2004). One possible source of this top-down signal is the prefrontal cortex (PFC), where the task-rule (AS vs. PS) information is actively maintained (Buschman et al., 2012; Johnston and Everling, 2006b).

* Corresponding author at: 132 Barker Hall, University of California Berkeley, California, CA 94720, United States.
E-mail address: kai.hwang@berkeley.edu (K. Hwang).

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AS performance improves through adolescence as reflected in an increased rate of correct inhibitory responses (Alahyane et al., 2014; Fischer et al., 1997; Fukushima et al., 2000; Klein and Foerster, 2001; Kramer et al., 2005; Luna et al., 2004; Munoz et al., 1998). Our developmental fMRI studies using the AS suggest that increased engagement of frontal regions such as the FEF and ACC (Ordaz et al., 2013; Velanova et al., 2008), as well as strengthening of prefrontal top-down connectivity (Hwang et al., 2010), may support developmental improvements in AS performance (Hwang and Luna, 2012). However, in addition to developmental changes in activation magnitudes, we do not understand the differences in the temporal and spectral dynamics of neuronal activities that may underlie developmental changes in frontal processes, limiting our ability to probe neurobiological mechanisms.

Magnetoencephalography (MEG), which measures electrophysiological activities generated by neuronal dynamics at a high temporal resolution, allows us to probe neuronal dynamics underlying the *preparatory* processes critical for AS performance and how preparatory activities change with age. MEG characterizes synchronous neural oscillations that have been hypothesized to support the coordination of brain functions for cognitive control (Buschman et al., 2012; Canolty and Knight, 2010; Cohen, 2011; Fries, 2015; Sacchet et al., 2015). Particularly relevant to cognitive control are beta and alpha rhythms. Beta rhythms (19–40 Hz; Buschman et al., 2012) can be generated by glutamatergic excitation in the deep layers of cortical columns (Roopun et al., 2010) or via top down inputs to supragranular layers that activate deep layer pyramidal neurons through their distal dendrites (Jones et al., 2009), which in turn send efferents to subcortical and other cortical regions (Douglas and Martin, 2004), supporting top-down control of sensory and motor processes for goal-directed behaviors (Buschman et al., 2012; Buschman and Miller, 2007; Gross et al., 2006; Picazio et al., 2014; Saalmann et al., 2007; Swann et al., 2009). Alpha-band activity (6–16 Hz; Buschman et al., 2012) has been found to reflect functional inhibition (8–14 Hz; Jensen and Mazaheri, 2010; Jones et al., 2010; Klimesch et al., 2007), as it is negatively correlated with neural spiking rate (Haegens et al., 2011) and increases during suppression of attention (Belyusar et al., 2013; Handel et al., 2011; Thut et al., 2006; Worden et al., 2000). A recent study shows alpha band synchrony between pre-frontal and primary sensory cortex increases in non-attended representation soon after an attentional cue as a means to inhibit distracting sensory stimuli, while beta band synchrony increases closer to stimulus processing, presumably to facilitate accurate sensory processing and motor response (Sacchet et al., 2015). Therefore, proactive cognitive control may be achieved by beta-band oscillations for top-down processes and alpha-band activity for suppressing task-incompatible processes.

In our initial MEG AS study (Hwang et al., 2014) on adult subjects, we found that beta-band power in the DLPFC and alpha-band power in the FEF during the preparatory period increased for the AS task. Further, trial-by-trial prestimulus FEF alpha-band power was positively correlated with successful saccadic inhibition. Compared to the PS task, the AS task enhanced cross-frequency amplitude coupling between beta-band activity in the DLPFC and alpha-band activity in the FEF. These results suggest that frontal task-related oscillatory neurodynamics reflect top-down control signaling (DLPFC beta-band activity), functional inhibition of saccade-related neural activity (FEF alpha-band activity), and inter-regional coordination of task-control signal communication (cross-frequency coupling between the DLPFC and the FEF).

Oscillatory neural activities undergo significant changes during adolescence (Uhlhaas et al., 2009, 2010) and aging (Ziegler et al., 2010). Therefore a better understanding of alpha-band and beta-band oscillatory dynamics could provide important insights into how the PFC, FEF, and its interactions support AS task performance through adolescence. In the present study, we examined differences between adults and adolescents in beta-band activity, alpha-band activity, and beta-alpha coupling to identify frontal neural processes specific to age-related improvements in cognitive control. Given our earlier fMRI results (Hwang et al., 2010; Ordaz et al., 2013), we predicted that adolescents would demonstrate adult level beta-band oscillatory activity in DLPFC but immature FEF alpha-band activity, and weaker cross-frequency coupling between FEF and DLPFC.

Methods

Participants

We recruited 48 healthy volunteers with no history of psychiatric or neurological illness in either themselves or a first-degree relative. Of the 26 adults and 22 adolescents, we report data from 20 adults (10 male) aged 20 to 30 years ($M = 26.11$ years, $SD = 3.41$) and 17 adolescents (8 male) aged 14 to 16 years ($M = 15.74$ years, $SD = 0.94$). Data from 11 participants were excluded due to the following reasons: two adults and one adolescent because of MEG sensor noise that could not be removed, one adult because of excessive eye blinks, three adults and three adolescents because of an insufficient number of noise-free trials, and one adolescent because of a history of psychiatric disorder discovered after completing the experiment. The study was approved by the University of Pittsburgh Institutional Review Board, and all participants or their legal guardians gave written informed consent. Subjects were compensated for their participation. Findings from the adult participants were reported in our previous publication (Hwang et al., 2014).

Behavioral paradigm

Participants performed a total of 210 AS and 210 PS trials distributed across eight MEG runs. AS and PS trials were presented in blocks within each run to minimize task-switching effects known to alter behavioral performance and neural activity (Akaishi et al., 2010; Lee et al., 2010). The sequence of AS and PS blocks was pseudo-randomized within each run to ensure that the same task block did not repeat more than once. Each run included 10 or 11 task blocks, with five trials per block. A short resting block was inserted between task blocks. Each trial started with a preparatory period where an instructional cue ("cue") was presented for 1.5 s. A red "x" fixation in AS trials instructed subjects to look to the opposite location of the target, while a green "x" fixation instructed subjects to make an eye movement to the target. The preparatory period was followed by a "response period," in which the visual stimulus ("target") was presented for 1.5 s. The target was a solid yellow circle (size ~1°, luminance 42.22 cd/m^2), presented on the horizontal meridian at one of four unpredictable eccentricities ($\pm 6.3°$ and $\pm 10.6°$ from center fixation). A 1.2- to 1.6-s jittered white fixation mark was presented between trials. During data acquisition, visual stimuli were projected on a screen located one meter in front of the participant.

Crucial to this paradigm is that the target location is not revealed during the preparatory period to prevent the planning of a determined saccade. Therefore, by comparing preparatory activity between AS and PS trials, we could identify neurodynamics specific to proactive control processes, independent of motor signals associated with saccade execution. Our analyses focused on the preparatory period (starting 1.5 s before target onset), as previous non-human primate electrophysiology studies indicate that neural activity during the preparatory period is predictive of AS task performance (Everling et al., 1999; Everling and Munoz, 2000).

Data acquisition

All MEG data were acquired using an Elekta Neuromag VectorView MEG system (Elekta Oy, Helsinki, Finland) comprising 306 sensors arranged in triplets of two orthogonal planar gradiometers and one magnetometer. MEG data were acquired continuously with a sampling rate of 1000 Hz in a three-layer magnetically shielded room. We measured