International Journal of Psychophysiology 115 (2017) 133–141

Contents lists available at ScienceDirect

International Journal of Psychophysiology

journal homepage: www.elsevier.com/locate/ijpsycho

Genetic influences on functional connectivity associated with feedback processing and prediction error: Phase coupling of theta-band oscillations in twins

Şükrü Barış Demiral [a,b,*], Simon Golosheykin [a], Andrey P. Anokhin [a]

[a] Washington University School of Medicine, St. Louis, MO, USA
[b] National Institutes of Health, Bethesda, MD, USA

ARTICLE INFO

Article history:
Received 24 November 2015
Received in revised form 25 November 2016
Accepted 28 December 2016
Available online 31 December 2016

Keywords:
Feedback
EEG
Prediction error
Genetics
Brain oscillations
Neural synchrony
Connectivity
Phase coherence

ABSTRACT

Detection and evaluation of the mismatch between the intended and actually obtained result of an action (reward prediction error) is an integral component of adaptive self-regulation of behavior. Extensive human and animal research has shown that evaluation of action outcome is supported by a distributed network of brain regions in which the anterior cingulate cortex (ACC) plays a central role, and the integration of distant brain regions into a unified feedback-processing network is enabled by long-range phase synchronization of cortical oscillations in the theta band. Neural correlates of feedback processing are associated with individual differences in normal and abnormal behavior, however, little is known about the role of genetic factors in the cerebral mechanisms of feedback processing. Here we examined genetic influences on functional cortical connectivity related to prediction error in young adult twins (age 18, n = 399) using event-related EEG phase coherence analysis in a monetary gambling task. To identify prediction error-specific connectivity pattern, we compared responses to loss and gain feedback. Monetary loss produced a significant increase of theta-band synchronization between the frontal midline region and widespread areas of the scalp, particularly parietal areas, whereas gain resulted in increased synchrony primarily within the posterior regions. Genetic analyses showed significant heritability of frontoparietal theta phase synchronization (24 to 46%), suggesting that individual differences in large-scale network dynamics are under substantial genetic control. We conclude that theta-band synchronization of brain oscillations related to negative feedback reflects genetically transmitted differences in the neural mechanisms of feedback processing. To our knowledge, this is the first evidence for genetic influences on task-related functional brain connectivity assessed using direct real-time measures of neuronal synchronization.

1. Introduction

Evaluation of action outcome plays a key role in the organization of adaptive goal-directed behavior (Anokhin, 1974), such that a discrepancy between the predicted and actual outcome (prediction error, or negative feedback) leads to updating of action-outcome associations and enables subsequent behavioral adaptations. The present study is focused on one important component of these processes, namely processing of negative versus positive feedback (monetary loss and gain outcomes in a gambling task).

Studies using event-related brain potentials (ERPs) have identified a number of electrophysiological signatures of feedback processing. In the first study of this kind, Haschke et al. (1987) investigated neural correlates of the mismatch between the intended and actually achieved result of an action using ERP responses to external feedback stimulus informing the participants about the correctness of their choice. They found striking differences between ERPs elicited by positive and negative feedback, with error feedback producing both negative-going and positive-going potential shifts, while positive feedback elicited a positive-going wave only. Subsequent studies have further characterized the difference between ERP responses to negative and positive feedback stimuli using a variety of paradigms such as time estimation (Miltner et al., 1997) and gambling tasks (Gehring and Willoughby, 2002). Converging evidence from these and many other ERP studies suggests that a discrepancy between the negative and positive outcomes producing a net negative ERP deflection that was variably termed as feedback-ERN, medial frontal negativity (MFN), or feedback-related negativity (FRN; see Fig. 1). Studies using reinforcement learning paradigms have also shown that FRN reflects outcome expectation failure, rather than subsequent behavioral adjustment; the latter was associated with the P3 component immediately following FRN (Chase et al., 2011).

Extensive human and animal research has shown that evaluation of action outcome is supported by a distributed network of brain regions,

* Corresponding author at: Laboratory of Neuroimaging (LNI), National Institute on Alcohol Abuse and Alcoholism (NIAAA), National Institutes of Health, 10 Center Drive, Room B2L124, Bethesda, MD 20892-1013, USA.
E-mail address: sukru.demiral@nih.gov (Ş.B. Demiral).

http://dx.doi.org/10.1016/j.ijpsycho.2016.12.013

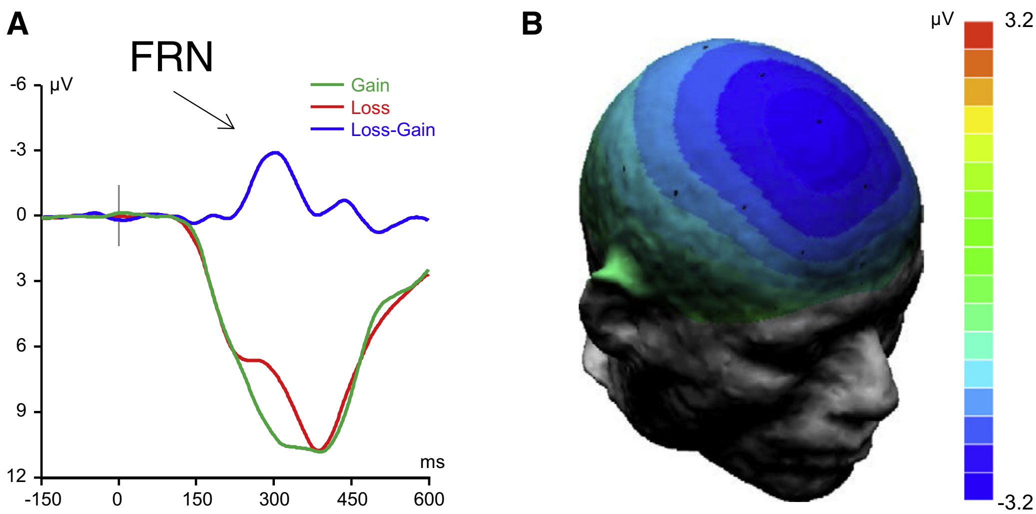

Fig. 1. Event-related brain potentials (ERPs) elicited by gains and losses in the monetary gambling task. A. Grand-averaged waveforms for loss trials (red), gain trials (green), and the difference wave (blue) showing the feedback-related negativity (FRN). B. Scalp potential map showing topographical distribution of the FRN. The ERP signal is bi-mastoid referenced, and −200 ms–0 ms baselined.

in which the anterior cingulate cortex (ACC), and the dopamine system play a central role (Anokhin, 1974; Bush et al., 2000; Rushworth and Behrens, 2008; Schultz and Dickinson, 2000; Ullsperger et al., 2014). Studies using source localization (reviewed in Walsh and Anderson (2012)) and multimodal imaging with simultaneous EEG and fMRI registration (Hauser et al., 2014) have localized the FRN source in the anterior cingulate cortex (ACC), although some evidence also suggests the involvement of basal ganglia (Foti et al., 2014), but see Cohen et al., 2011.

According to the functional systems perspective (Anokhin, 1974), goal-directed behavior is subserved by a dynamic integration of neural activity in diverse brain regions involved in action planning, execution, and evaluation of the result. How can such a large-scale and rapid communication between spatially segregated brain regions be achieved? The theory of spatiotemporal organization of brain processes (summarized in Livanov (1977)) posits that synchronized (coherent) neural oscillations constitute a neurobiological basis of dynamic functional connectivity, and enable the integration of disparate brain regions into a unified functional network. According to Livanov's theory, an important condition for the transmission of excitation in the cerebral cortex is the temporal coordination of the functional state (excitability) of interacting but spatially distributed neuronal groups, which is achieved by phase coupling of their excitability cycles reflected in neural oscillations (Livanov, 1977). Numerous studies in humans and animals provided a strong support for this perspective and showed that synchronization of neural oscillations represents a fundamental neurophysiological mechanism of integrative brain activity underlying cognition and behavior (Buzsaki and Draguhn, 2004; Fries, 2005; Jacobs et al., 2007; Livanov, 1977; Palva et al., 2005; Varela et al., 2001). Human studies have consistently shown connectivity between the prefrontal regions with widespread cortical areas during complex cognitive tasks, although patterns of connectivity showed some task specificity (Livanov, 1977; Livanov et al., 1964).

Of particular importance, theta-band oscillations play an important role in long-range communication among distant brain regions. Increased spatial coherence in the theta band was observed during a variety of cognitive and behavioral paradigms in animal and human experiments, leading to a conclusion that theta-band synchrony serves as a basic mechanism of long-range neuronal communication (Benchenane et al., 2011; Cavanagh et al., 2012; Cohen, 2011; Livanov, 1977; Livanov et al., 1964; Nigbur et al., 2012; Womelsdorf et al., 2010b). For instance, studies using EEG spectral power analysis and time-frequency decomposition found increased activity in the theta-band (3–7 Hz) power in response to negative feedback and performance errors compared to positive feedback (Cavanagh et al., 2010; Cohen et al., 2007; Luu et al., 2004; Marco-Pallares et al., 2008; Womelsdorf et al., 2010a).

In addition, a number of recent studies investigating spatial synchronization of neural oscillations related to action outcome processing found that negative feedback leads to a transient increase in theta band synchronization between the medial prefrontal cortex, dorsolateral prefrontal cortex, central, and parietal areas (Cavanagh et al., 2010; Luft et al., 2013; van de Vijver et al., 2011). A study using arrays of surgically implanted microelectrodes in humans has shown that theta oscillations, which are related to error processing, are generated in the area 24 of the dorsal ACC (Wang et al., 2005). Importantly, this study also provided evidence for ACC-neocortical interaction as indicated by a transient increase in the phase locking of their synaptic activity in the theta range, suggesting that the ACC theta forms part of a larger network involving widespread cortical locations in other cortical areas (Wang et al., 2005). Another study using implanted electrodes showed interaction between the medial prefrontal cortex and the nucleus accumbens during feedback processing (Cohen et al., 2009). These data are consistent with fMRI studies indicating co-activation of ACC with widespread cortical regions during cognitive control (Liddle et al., 2001). Furthermore, the strength of theta-band synchronization was related to white matter connectivity between the ACC and other regions (Cohen, 2011). In summary, these studies suggest that FRN triggers a formation of a widespread frontoparietal cognitive control network where the dynamic connectivity is achieved by a transient phase synchronization of theta oscillations.

There is increasing evidence that individual differences in neural synchrony are associated with individual differences in cognition and behavior, both normal and abnormal. In our previous study, the strength of frontoparietal coherence in the theta band during the performance of both verbal and non-verbal cognitive tasks predicted individual differences in general cognitive abilities (Anokhin et al., 1999). A recent study has shown that stronger theta synchronization during feedback processing in a learning task is associated with better learning performance revealing individual differences in feedback processing (Luft et al., 2013). Furthermore, the theory of spatial organization of brain processes (Livanov, 1977) proposed that abnormal local and spatial synchronization of neuronal oscillations may result in disruptions in neuronal communication and coordinated activity of brain regions supporting complex cognition and behavior and thus play an important role in the etiology of neuropsychiatric disorders. This hypothesis was