NeuroImage 157 (2017) 13–26

Contents lists available at ScienceDirect

NeuroImage

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

Development of the error-monitoring system from ages 9–35: Unique insight provided by MRI-constrained source localization of EEG

George A. Buzzell[a,*], John E. Richards[b], Lauren K. White[c], Tyson V. Barker[a], Daniel S. Pine[d], Nathan A. Fox[a]

[a] Department of Human Development and Quantitative Methodology, University of Maryland, College Park, MD 20742, United States
[b] Department of Psychology, University of South Carolina, Columbia, SC 29208, United States
[c] Department of Child and Adolescent Psychiatry, The Children's Hospital of Philadelphia, Philadelphia, PA 19104, United States
[d] Emotion and Development Branch, Intramural Research Program, National Institute of Mental Health, Bethesda, MD 20814, United States

ARTICLE INFO

Keywords:
Error-monitoring
ERN
Source-localization
Development
Adolescence
Posterior cingulate

ABSTRACT

The ability to self-detect errors and dynamically adapt behavior is a cornerstone of higher-level cognition, requiring coordinated activity from a network of neural regions. However, disagreement exists over how the error-monitoring system develops throughout adolescence and early adulthood. The present report leveraged MRI-constrained EEG source localization to detail typical development of the error-monitoring system in a sample of 9–35 year-olds (n = 43). Participants performed a flanker task while high-density EEG was recorded; structural MRIs were also acquired for all participants. Analysis of the scalp-recorded EEG data revealed a frontocentral negativity (error-related negativity; ERN) immediately following errors for all participants, although the topography of the ERN varied with age. Source localization of the ERN time range revealed maximal activity within the posterior cingulate cortex (PCC) for all ages, consistent with recent evidence that the PCC provides a substantial contribution to the scalp-recorded ERN. Activity within a network of brain regions, including dorsal anterior cingulate, PCC, and parietal cortex, was predictive of improved performance following errors, regardless of age. However, additional activity within insula, orbitofrontal cortex and inferior frontal gyrus linearly increased with age. Together, these data suggest that the core error-monitoring system is online by early adolescence and remains relatively stable into adulthood. However, additional brain regions become embedded within this core network with age. These results serve as a model of typical development of the error-monitoring system from early adolescence into adulthood.

Introduction

Achieving goal-directed behavior and maintaining task performance requires the online monitoring of performance in order to detect errors. The neural basis of such error monitoring is observable in scalp-recorded EEG as a fronto-central negativity for error vs. correct responses, termed the error-related negativity (ERN; Falkenstein et al., 1990; Gehring et al., 1993). Studies have demonstrated that ERN magnitude is predictive of immediate error correction (Gehring et al., 1993), as well as improved performance on subsequent trials (Maier et al., 2011), consistent with the notion that error monitoring facilitates task performance. Additionally, an extensive body of research has linked individual differences in error-related processing to psychopathology, extending interest in error monitoring into the clinical domain (see Olvet and Hajcak, 2008). Prior research has generally supported the view that ERN magnitude increases throughout adolescence and into early adulthood (for a review, see Tamnes et al., 2013). However, the neuroanatomical basis of such age-related changes in error monitoring, during the time range of the ERN, remains ambiguous. Specifically, it is unclear whether the development of error-monitoring, as measured by the ERN, is associated with changes within a relatively focal and well-defined source, such as cingulate cortex, or reflects differential activation across a network of neural regions. Answering such questions has recently been made possible by advances in electroencephalogram (EEG) source localization techniques that individually model the brain and skull, and could substantially inform increasingly complex models of error-monitoring and related processes (e.g. Shenhav et al., 2013; Weinberg et al., 2016). However, advanced source localization methods have not yet been applied to the study of error-monitoring system development.

Functional magnetic imaging (fMRI) studies have demonstrated that error processing is associated with widespread activation across a

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[*] Correspondence to: Benjamin Building, 3942 Campus Dr., College Park, MD 20742, United States.
E-mail address: gbuzzell@umd.edu (G.A. Buzzell).

http://dx.doi.org/10.1016/j.neuroimage.2017.05.045
Received 11 February 2017; Accepted 19 May 2017

broad network of neural regions (Taylor et al., 2007). Namely, the dorsal-anterior and posterior cingulate cortex (dACC and PCC, respectively), insula, operculum, ventral and lateral prefrontal cortex, and lateral parietal cortex have all been linked to error processing in prior fMRI investigations (for a review, see Taylor et al., 2007). The dACC in particular, has been the focus of extensive research into error processing, demonstrating sensitivity to errors in both fMRI (Carter et al., 1998; Holroyd et al., 2004; Kerns et al., 2004) and single-unit recording (Ito et al., 2003; Amiez et al., 2005) investigations. Consistent with this notion, the majority of source localization studies in both children and adults have reported focal activation within the dACC (for a review, see Agam et al., 2011). However, as noted by Agam et al. (2011), a careful reading of the literature reveals that although many studies describe peak ERN source activity as occurring within the dACC, approximately half of the foci of these studies lay posterior to the ACC-PCC border, and a more appropriate label for these ERN sources would be “PCC”. Critically, a recent report that employed MRI-constrained source-localization of the ERN, along with a distributed-source solution, identified maximal ERN-source activity within the posterior cingulate cortex (PCC), as opposed to the dACC (Agam et al., 2011). Additionally, given that several other neural regions are known to be activated by errors (Taylor et al., 2007), it is possible that the methods that have typically been employed previously for source localization (dipole modeling with standard head models) have obscured important nuances in understanding networks involved in error monitoring.

While the ERN magnitude is believed to increase throughout adolescence and into early adulthood (Tamnes et al., 2013), prior source localization investigations of ERN development have reported a primary source within dACC that does not change as a function of age (Mathewson et al., 2005; Ladouceur et al., 2007; Santesso and Segalowitz, 2008). Thus, the same region of cingulate cortex may generate the ERN throughout adolescence and adulthood, with changes in amplitude resulting only from changes in the efficiency of this neural region. However, it is well established that widespread areas of the brain, particularly regions underlying higher cognitive functions, undergo substantial reorganization over the course of adolescence and into adulthood (Sowell et al., 1999b; Gogtay et al., 2004; Tamnes et al., 2010). Additionally, analyses of executive functioning development have demonstrated dramatic changes in network dynamics with increasing age (Fair et al., 2007, 2009). Therefore, it is possible that age-related changes in the magnitude of the scalp-recorded ERN are not driven by changes within a relatively focal and well-defined source, such as the cingulate cortex, but instead reflects differential activation across a network of neural regions. It is possible that previous investigations missed such effects, given the use of a “dipole fitting” procedure, in which the number and possible location of sources are strongly influenced by the decisions of the experimenter (for details, see Michel et al., 2004). Additionally, none of the previous developmental investigations employed realistic modeling of the brain and skull, a factor that can substantially influence source localization accuracy (Vorwerk et al., 2014; Cho et al., 2015), especially within a developmental context (Reynolds and Richards, 2009; Richards and Xie, 2015).

Development of the error-monitoring system during adolescence and early adulthood is of particular interest, given that this period is marked by an increased risk for various forms of psychopathology, including anxiety disorders, depression, psychopathy, impulse-control disorders and schizophrenia (Pine et al., 1998; Kessler et al., 2007; Merikangas et al., 2010). Critically, several forms of psychopathology that emerge in adolescence have been linked to either increases or decreases in the ERN (Gehring et al., 2000; Hall et al., 2007; Olvet and Hajcak, 2008; McDermott et al., 2009). Further, competing models exist for explaining the link between the ERN and specific forms of psychopathology, such as anxiety (Moser et al., 2013; Weinberg et al., 2016). An improved estimation of the neural source(s) generating the scalp-recorded ERN would not only help to inform more general models of error monitoring and the ERN, but also shed light on the relation between the ERN and specific forms of psychopathology. Moreover, a model of typical error-monitoring system development during adolescence and adulthood would provide a valuable reference for future studies investigating the development of psychopathology related to this system.

The current study employed MRI-constrained source localization of the ERN in order to relate variation in age from early adolescence through early adulthood to variation in functioning of the error-monitoring system. Consistent with either the prevailing view (Ullsperger et al., 2014), or recent research (Agam et al., 2011), we hypothesized that changes in the ERN would be primarily explained by a source within either the anterior or posterior cingulate, respectively. However, given the dramatic cortical reorganization that is reflected in adolescence and early adulthood, an alternative possibility is that changes in the ERN arise from changes in distributed source activity outside of cingulate cortex.

Method

Participants

Forty-three participants ranging in age from 9.89 to 35.09 years (*M* age = 18.65, SD = 6.18, 23 females) completed the study. The participants consisted of 17 Caucasians, 13 African-Americans, 12 Asians, and one Hispanic; a one-way ANOVA model indicated no significant differences in age across the ethnic categories, $F(3,39) = 1.80$, $p = .163$. Of note, the primary analyses of this study treated age as a continuous variable. Nevertheless, where appropriate, participants were divided into four roughly equal groups (quartile split based on age) for display purposes and exploratory analyses. The four age groups were as follows: group one ($n = 10$) had an age range of 9.89–13.63 years (*M* age = 11.79, 6 females); group two ($n = 11$) had an age range of 14.18–15.96 years (*M* age = 15.02, 7 females); group three ($n = 11$) had an age range of 16.92–22.80 years (*M* age = 20.35, 5 females); group four ($n = 11$) had an age range of 22.95–35.09 years (*M* age = 26.81, 5 females).

Participants were healthy volunteers recruited from the local DC-metropolitan area and received monetary compensation for their participation. Inclusion criteria for participants included an IQ > 70 and normal physical health. The minimum IQ for participants included in the current sample was 91 (*M* = 113.77, SD = 11.34); critically, IQ did not correlate with age ($p = .285$). Additionally, participants were free of psychopathology as determined by a structured interview; the Schedule School-Age (K-SADS- PL; Kaufman et al., 1997) was used for participants 17 and younger and the Structured Clinical Interview for DSM-IV- TR Axis 1Disorders (SCID; First, Spitzer, Gibbon and Williams, 2002) for participants 18 and older. All participants over the age of 18 provided written informed consent; for participants under the age of 18, parents signed consent and youth signed assent. All procedures were approved by the Institutional Review Boards of the University of Maryland (UMD) and the National Institute of Mental Health (NIMH). Data from an additional 3 participants were collected, but not used, as the result of artifact-laden EEG (n = 1), an error during EEG recording (n = 1), or low behavioral accuracy (accuracy < 70%; n = 1).

Procedure

Participants performed a modified flanker task (Eriksen and Eriksen, 1974) at UMD while EEG data were collected; fiducial anatomical and electrode landmarks were digitized for each participant. Additionally, structural MRIs were collected for all participants at NIMH for the purpose of creating subject-specific head models for current source reconstruction. Participants also performed the flanker task while at NIMH and functional data were collected. Results of the