NeuroImage 184 (2019) 599–608

Contents lists available at ScienceDirect

NeuroImage

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

# Integrating high-density ERP and fMRI measures of face-elicited brain activity in 9–12-year-old children: An ERP source localization study

Pan Liu [a,*], Xiaoxiao Bai [b], Koraly E. Pérez-Edgar [a]

[a] Department of Psychology, Child Study Center, The Pennsylvania State University, University Park, PA, 16802, USA
[b] Social, Life, and Engineering Sciences Imaging Center, The Pennsylvania State University, University Park, PA, 16802, USA

ARTICLE INFO

*Keywords:*
Face processing
Dot-probe
fMRI
ERP
Source analysis
Children

ABSTRACT

Social information processing is a critical mechanism underlying children's socio-emotional development. Central to this process are patterns of activation associated with one of our most salient socioemotional cues, the face. In this study, we obtained fMRI activation and high-density ERP source data evoked by parallel face dot-probe tasks from 9-to-12-year-old children. We then integrated the two modalities of data to explore the neural spatial-temporal dynamics of children's face processing. Our results showed that the tomography of the ERP sources broadly corresponded with the fMRI activation evoked by the same facial stimuli. Further, we combined complementary information from fMRI and ERP by defining fMRI activation as functional ROIs and applying them to the ERP source data. Indices of ERP source activity were extracted from these ROIs at three *a priori* ERP peak latencies critical for face processing. We found distinct temporal patterns among the three time points across ROIs. The observed spatial-temporal profiles converge with a dual-system neural network model for face processing: a core system (including the occipito-temporal and parietal ROIs) supports the early visual analysis of facial features, and an extended system (including the paracentral, limbic, and prefrontal ROIs) processes the socio-emotional meaning gleaned and relayed by the core system. Our results for the first time illustrate the spatial validity of high-density source localization of ERP dot-probe data in children. By directly combining the two modalities of data, our findings provide a novel approach to understanding the spatial-temporal dynamics of face processing. This approach can be applied in future research to investigate different research questions in various study populations.

## 1. Introduction

Individual variation in processing socioemotional information (e.g., facial expressions) is a critical contributor to both typical and atypical socioemotional development in children (MacLeod et al., 1986). Experimental data and clinical insights both suggest that biases that enhance attention to social cues, such as angry faces, may exacerbate risk for psychopathology (particularly anxiety) and maintain clinical states (Britton et al., 2012; Pérez-Edgar et al., 2010; Pérez-Edgar et al., 2014; White et al., 2009). This study investigated the neural circuitry associated with the processing of threatening and neutral faces as presented in a standard attention paradigm. Specifically, we integrated event-related potential (ERP) and functional magnetic resonance imaging (fMRI) data collected from parallel dot-probe tasks in a sample of 9–12-year-old children. By using high-density ERP source localization techniques, we examined the spatial correspondence between the ERP source activity and fMRI activation evoked by the same faces. Further, by integrating the temporal information from the ERP data and the spatial information contributed by the fMRI data, we were able to better depict the spatial-temporal characteristics of face processing in school-age children. Coupling the spatial distribution and chronometry of processing may help us better understand the neural underpinnings of face-related processing, which is important for discerning typical developmental mechanisms and identifying individual variation that may relate to psychopathology.

The dot-probe paradigm has been typically used to measure attention processing biases, especially related to threat, in both children (Bar-Haim et al., 2007; Britton et al., 2012; Liu et al., 2018; Monk et al., 2006; Monk et al., 2008; Price et al., 2014; Telzer et al., 2008) and adults (Fani et al., 2012; Hardee et al., 2013; Mogg and Bradley, 1999). In this paradigm, each trial presents a pair of faces (threat-neutral or neutral-neutral) followed by an arrow-probe replacing one of the faces. The participant

* Corresponding author.
*E-mail addresses:* pliu261@gmail.com (P. Liu), baixx013@gmail.com (X. Bai), kxp24@psu.edu (K.E. Pérez-Edgar).

https://doi.org/10.1016/j.neuroimage.2018.09.070
Received 23 January 2018; Received in revised form 17 September 2018; Accepted 25 September 2018
Available online 27 September 2018
1053-8119/

identifies the direction of the arrow as quickly and as accurately as possible via a button press. The processing bias is quantified by subtracting reaction times (RTs) in response to probes replacing the threat face (congruent trials) from RTs to probes replacing the neutral face (incongruent trials) in threat-neutral face pairs. This paradigm is also commonly combined with neuroscience approaches, such as ERP and fMRI, to provide biomarkers of threat-related processes (Britton et al., 2012; Monk et al., 2006, 2008; Price et al., 2014; Fu et al., 2017; Hardee et al., 2013; Liu et al., 2018; Thai et al., 2016). Indeed, biomarkers of attentional processing biases have proven to be more reliable psychometrically, and are better predictors of risk, than the initial RT-based bias measures (Brown et al., 2014; White et al., 2016).

ERP/EEG and fMRI studies are typically carried out in parallel within the developmental neuroscience literature, with limited attempts to integrate data from the two units of analysis. Two studies have compared ERP source localization and fMRI activation data modulated by the same task, examining children's early reading acquisition (Brem et al., 2009, 2010) and semantic processing (Schulz et al., 2008). Both studies reported significant spatial convergence between ERP and fMRI data. In addition, individual structural MRI images have been combined with EEG/ERP source localization data to construct individual-specific head models for more precise localization in children, adolescents, and adults (Bathelt et al., 2014; Buzzell et al., 2017; Ortiz-Mantilla et al., 2011). In a similar vein, source localization of resting-state EEG data has been combined with resting-state fMRI in epileptic children to locate the neural generators of epileptic spikes (Elshoff et al., 2012; Groening et al., 2009). To our knowledge, however, no study has taken the approach of combining ERP and fMRI to explore the neural correlates of face processing in children. By taking advantage of the high temporal resolution of ERP *and* the refined spatial characterization from fMRI, this novel approach could significantly advance our understanding of the neural mechanisms underlying children's emotion-related processing.

In the dot-probe literature, several studies have used Low Resolution Electromagnetic Tomography to conduct source localization for task-generated ERP data from adults. One study found that the early visual components, C1, evoked by the face-pair (~90 ms post-stimulus), and P1, evoked by the face-pair or the probe (~130 ms), were localized within the striate and extrastriate visual cortices, respectively (Pourtois et al., 2004). Another study (Mueller et al., 2009) found that an enhanced P1 elicited by angry-neutral versus happy-neutral faces possibly originated from the right fusiform gyrus in anxious adults. Finally, a P1, which was larger when evoked by probes replacing neutral faces (incongruent) versus angry faces (congruent), originated from the anterior cingulate cortex (ACC; Santesso et al., 2008). These results are compatible with fMRI findings in dot-probe studies, noting that ACC activation or ACC-related connectivity were reported in the incongruent versus congruent condition in adults (Carlson et al., 2009) and youth (Fu et al., 2017; Price et al., 2014).

However, none of the current ERP source localization findings have been directly compared and integrated with fMRI activation evoked by the same paradigm. In addition, we do not know if localization patterns differ in children, even with the same task parameters used in adult studies. This is critical, as both attentional biases in processing socio-emotional information and anxiety symptoms typically first emerge in childhood (Dudeney et al., 2015; Kessler et al., 2005). Therefore, it is important to directly integrate ERP and fMRI data from a parallel dot-probe paradigm in the same sample to specify the spatial-temporal dynamics of children's processing of emotional faces.

Studies linking fMRI to EEG/ERP are also important from a methodological perspective. ERP/EEG studies are more economical than fMRI research and much easier to implement in children, especially when studying task-modulated processes (Pérez-Edgar and Bar-Haim, 2010). Localizing the neural generators of high-density ERP data might provide a feasible alternative to fMRI when attempting to characterize the spatial dimension of neural functions. However, we must first establish the spatial validity of ERP source localization by examining convergence with the spatial distribution indicated by fMRI data. The question of method convergence has become more salient with the advent of the National Institute on Mental Health's (NIMH) Research Domain Criteria (RDoC) initiative (Insel et al., 2010; Cuthbert and Kozak, 2013), which seeks to examine psychological constructs across multiple units of analysis (e.g., behavioural, neural, physiological, genetic, molecular). This work requires that we verify the coincidence (or lack thereof) of measures generated across units of analysis.

Consistent with the RDoC initiative, and building on the developmental neuroscience literature, this study has three research goals:

First, we examine the spatial correspondence between high-density ERP source localization and fMRI activation, by comparing the two units of data modulated by a parallel dot-probe paradigm from a sample of 9- to 12-year-old children.

Second, we aim to demonstrate the neural correlates of children's face processing by synthesizing the spatial information from the fMRI data with temporal information from the ERP data. In particular, we initially defined fMRI activation evoked by the faces as functional ROIs. These ROIs were then applied to the source localization data time-locked to three *a priori* ERP peaks (i.e., time points) elicited by the same faces. We were then able to examine any differences in temporal dynamic patterns of activation between the three time points within each functional ROI.

Third, this study will provide a foundation for implementing a simultaneous ERP-fMRI approach in children, a more advanced tool for future research. Simultaneous data collection may help us better understand the spatial-temporal characteristics of the neural underpinnings of face processing and other psychological processes.

There is limited existing data on ERP-fMRI convergence with the dot-probe task in children. As such, this is an initial exploratory examination of convergence patterns. Nonetheless, given the previous ERP source localization findings in the adult dot-probe data (Pourtois et al., 2004; Santesso et al., 2009) and its compatibility with other fMRI dot-probe data, we expected good correspondence between the ERP sources and fMRI activation modulated by the dot-probe paradigm. Moreover, a previous MEG study exploring adults' facial expression processing (Sato et al., 2015) found that the source of their MEG signals achieved maximum activity 150–200 ms after the face onset, in areas involving the middle temporal visual area, fusiform gyrus, and superior temporal sulcus. In contrast, maximum activity in the later window of 300–350 ms was observed in the inferior frontal areas. Based on these data, we expected that the temporal dynamic patterns characterized by the ERP source activity in children might also differ across functional ROIs defined by the fMRI activation. For instance, ERP source activity might achieve its initial maximum in the posterior, visual-sensory regions first, followed by later activation in the anterior, frontal regions.

## 2. Material and methods

### 2.1. Participants

Participants were a cohort of 118 9-12-year-old children ($M_{age}$ = 10.98, SD = 1.04, 58 male) drawn from a larger attentional bias modification (ABM) training project examining the relations between temperament, ABM, and anxiety (Liu et al., 2018).[1] All participants were recruited from the area surrounding State College, PA. The present study incorporated the baseline/pre-training data from the larger project. From this sample, 74 participants with useable dot-probe ERP data were selected for the source localization analysis (selection criteria specified below). For the dot-probe fMRI data, children with head motion exceeding 3 mm or behavioural accuracy <75% were excluded from analysis. Eventually, 99 children contributed useable fMRI data collected

[1] Children in the larger study were characterized for the temperamental trait of behavioural inhibition (BI), ranging across the full BI spectrum from low to high. The current findings did not vary as a function of BI.