



# Motivated attention and family risk for depression: Neuronal generator patterns at scalp elicited by lateralized aversive pictures reveal blunted emotional responsivity



Jürgen Kayser<sup>a,b,c,\*</sup>, Craig E. Tenke<sup>a,b,c</sup>, Karen S. Abraham<sup>a</sup>, Daniel M. Alschuler<sup>a</sup>,  
Jorge E. Alvarenga<sup>a</sup>, Jamie Skipper<sup>c</sup>, Virginia Warner<sup>c,d</sup>, Gerard E. Bruder<sup>a,b</sup>,  
Myrna M. Weissman<sup>b,c,d</sup>

<sup>a</sup> Division of Cognitive Neuroscience, New York State Psychiatric Institute, New York, NY, USA

<sup>b</sup> Department of Psychiatry, Columbia University College of Physicians & Surgeons, New York, NY, USA

<sup>c</sup> Division of Epidemiology, New York State Psychiatric Institute, New York, NY, USA

<sup>d</sup> Mailman School of Public Health, Columbia University, New York, NY, USA

## ARTICLE INFO

### Keywords:

Depression risk  
Emotional lateralization  
Event-related potential (ERP)  
Late positive potential (LPP)  
Source localization  
Visual half-field paradigm

## ABSTRACT

Behavioral and electrophysiologic evidence suggests that major depression (MDD) involves right parietotemporal dysfunction, a region activated by arousing affective stimuli. Building on prior event-related potential (ERP) findings (Kayser et al. 2016 *NeuroImage* 142:337–350), this study examined whether these abnormalities also characterize individuals at clinical high risk for MDD. We systematically explored the impact of family risk status and personal history of depression and anxiety on three distinct stages of emotional processing comprising the late positive potential (LPP). ERPs (72 channels) were recorded from 74 high and 53 low risk individuals (age 13–59 years, 58 male) during a visual half-field paradigm using highly-controlled pictures of cosmetic surgery patients showing disordered (negative) or healed (neutral) facial areas before or after treatment. Reference-free current source density (CSD) transformations of ERP waveforms were quantified by temporal principal components analysis (tPCA). Component scores of prominent CSD-tPCA factors sensitive to emotional content were analyzed via permutation tests and repeated measures ANOVA for mixed factorial designs with unstructured covariance matrix, including gender, age and clinical covariates. Factor-based distributed inverse solutions provided descriptive estimates of emotional brain activations at group level corresponding to hierarchical activations along ventral visual processing stream. Risk status affected emotional responsivity (increased positivity to negative-than-neutral stimuli) overlapping early N2 sink (peak latency 212 ms), P3 source (385 ms), and a late centroparietal source (630 ms). High risk individuals had reduced right-greater-than-left emotional lateralization involving occipitotemporal cortex (N2 sink) and bilaterally reduced emotional effects involving posterior cingulate (P3 source) and inferior temporal cortex (630 ms) when compared to those at low risk. While the early emotional effects were enhanced for left hemifield (right hemisphere) presentations, hemifield modulations did not differ between risk groups, suggesting top-down rather than bottom-up effects of risk. Groups did not differ in their stimulus valence or arousal ratings. Similar effects were seen for individuals with a lifetime history of depression or anxiety disorder in comparison to those without. However, there was no evidence that risk status and history of MDD or anxiety disorder interacted in their impact on emotional responsivity, suggesting largely independent attenuation of attentional resource allocation to enhance perceptual processing of motivationally salient stimuli. These findings further suggest that a deficit in motivated attention preceding conscious awareness may be a marker of risk for depression.

## 1. Introduction

Dysfunctions in emotion processing and regulation are considered to be a core deficit of mood disorders (e.g., Gross and Munoz, 1995;

Rive et al., 2013). These deficits involve abnormal activations of brain regions that largely overlap with those identified by affective neuroscience as key modules for emotional processing and self-awareness, which include amygdala, striatum, nucleus accumbens, anterior insula,

\* Corresponding author at: New York State Psychiatric Institute, Unit 50, 1051 Riverside Drive, New York, NY 10032, USA.  
E-mail address: [kayserj@nyspi.columbia.edu](mailto:kayserj@nyspi.columbia.edu) (J. Kayser).

<http://dx.doi.org/10.1016/j.nicl.2017.03.007>

Received 26 January 2017; Received in revised form 16 March 2017; Accepted 20 March 2017

Available online 22 March 2017

2213-1582/ © 2017 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

orbitofrontal, ventromedial, prefrontal, anterior cingulate, and posterior cingulate cortex (e.g., Davidson et al., 2000; Pessoa, 2008; Phan et al., 2002; Phillips et al., 2003a, 2003b; Price and Drevets, 2012). Behavioral, autonomic and electrophysiologic evidence suggest that major depressive disorder (MDD) is characterized by hypoactivation of right parietotemporal cortex, a region which is critically involved in the detection of stimulus significance and mediation of concomitant arousal processes (e.g., Bruder et al., 1997; Bruder, 2003; Caltagirone et al., 1989; Gadea et al., 2011; Gainotti, 1987; Heller, 1993; Heller and Nitschke, 1997; Heller et al., 1998; Jaeger et al., 1987; Keller et al., 2000; Liotti et al., 1991; Liotti and Tucker, 1992, 1995; Tranel and Damasio, 1994).

Electrophysiological measures of ongoing brain activity, particularly ERPs, provide a convenient means to dissect consecutive stages of cognitive-affective processing. A large number of studies have demonstrated that a broad, long-lasting late positive potential (LPP), which is characterized by a mid-centroparietal scalp topography emerging around 200–300 ms after stimulus onset, is greater for arousing emotional (pleasant or unpleasant) than nonarousing neutral stimuli (e.g., for reviews, see Hajcak et al., 2012; Olofsson et al., 2008). The affective LPP modulation, which survives stimulus repetition (habituation) effects (e.g., Ferrari et al., 2017), is closely related to stimulus arousal rather than valence properties (e.g., Cuthbert et al., 2000; Schupp et al., 2000). This supports the idea of an increased orientation and allocation of attentional resources to stimuli that intrinsically engage motivational brain circuits (motivated or emotional attention), thereby boosting further processing of emotional stimuli (e.g., Bradley, 2009; Pourtois et al., 2013; Vuilleumier and Driver, 2007).

Several ERP studies have reported right-lateralized emotional effects involving the LPP, but also earlier ERP components over occipitotemporal and temporoparietal regions (e.g., Junghöfer et al., 2001; Kayser et al., 1997, 2000, 2016; Keil et al., 2001, 2002), which is of interest for at least two reasons. First, these findings provide direct, electrophysiologic evidence in healthy populations in support of theoretical models postulating a differential involvement of the two hemispheres during affective states and affective processing (e.g., for reviews see Campbell, 1982; Davidson, 1995; Demaree et al., 2005; Gainotti, 1989; Heller, 1993). Specifically, these ERP findings corroborate the hypothesis of a right hemispheric advantage for the perception of emotionally-arousing stimuli (e.g., Caltagirone et al., 1989; Gainotti, 1987; Heller, 1993; Tranel and Damasio, 1994). Second, ERP and MEG studies in clinically-depressed patients have shown marked reductions of amplitude and asymmetry in response to emotional compared with neutral stimuli (e.g., Foti et al., 2010; Kayser et al., 2000; Moratti et al., 2008), implicating a functional deficit in MDD involving the right temporoparietal junction (rTPJ; e.g., Liotti and Tucker, 1995; Tucker, 2015). The rTPJ has been recognized as a key region for detecting affective significance within a network involving cortical (anterior insula, anterior cingulate cortex) and subcortical (amygdala, striatum) structures for detecting emotional and reward saliency (Corbetta and Shulman, 2002; Lutz et al., 2015). Blunted electrophysiological responses involving right temporoparietal cortex to emotionally-arousing stimuli in MDD may even constitute a biomarker of treatment success. In a pre-/post-treatment design with 25 MDD patients receiving the serotonergic/noradrenergic antidepressant mirtazapine for four weeks, baseline hypoactivation of rTPJ and bilateral dorsolateral prefrontal cortex (dlPFC) during emotional picture presentation normalized with successful treatment (Domschke et al., 2015). These effects emerged as early as 150 ms after stimulus onset, suggesting dysfunctional processing (rTPJ) and top-down regulation (dlPFC) of emotional stimuli at a preconscious level. Similar pre-/post-treatment effects were reported for 19 MDD patients receiving 4-week electroconvulsive therapy or no intervention (Zwanzger et al., 2016). Furthermore, reduced LPP responses to emotional (pleasant and unpleasant) versus neutral pictures were observed for patients with current MDD, particularly for those with an early onset (i.e., first depressive episode before the age

of 18), whereas patients with a current anxiety disorder did not differ from healthy controls (Weinberg et al., 2016). This suggests that blunted ERPs to salient stimuli may represent a specific phenotype for unipolar depression that is more pronounced with early onset of the disorder.

A related question is whether these abnormalities in brain function also represent a marker of risk, or endophenotype, for major depression, in which case this biomarker should precede onset of the disorder and not be a result of the mental illness itself (e.g., Gottesman and Gould, 2003). Offspring and grandchildren of depressed patients are at increased risk for developing depressive and anxiety disorders (e.g., Talati et al., 2013; Weissman et al., 2016a). In agreement with EEG findings at rest for MDD patients (e.g., Bruder et al., 1997), descendants of probands with MDD, compared to those without, had greater alpha activity over right than left parietal regions, presumed to indicate reduced right parietal activation (Bruder et al., 2005, 2007). Furthermore, structural imaging measures suggested greater cortical thinning over right posterior cortex in children at high versus low risk (Peterson et al., 2009), and alpha was inversely related to cortical thickness, although not directly to alpha asymmetry (Bruder et al., 2012). While these findings are intriguing, the relationship of resting to task-related alpha (e.g., Tenke et al., 2015), or between structural and functional brain measures, is complex and as of yet not fully understood, necessitating the use of more targeted paradigms and measures. A recent MEG study employing the steady-state visual evoked fields technique reported a robust emotional modulation of rTPJ activity in 15 healthy women and 20 clinically-depressed women without a family history of depression; however, this modulation was markedly reduced in 8 depressed patients having at least one parent with a recurrent MDD diagnosis (Moratti et al., 2015). The difference between patient groups persisted after separately controlling for severity of current depressive symptoms, dosage of antidepressive medication, current age, or age of onset, suggesting that the demonstrated familial and likely genetic component of MDD (e.g., Guffanti et al., 2016; Sullivan et al., 2000; Weissman et al., 2005, 2016b; Wickramaratne and Weissman, 1998) also affects motivated attention. Several ERP studies have provided evidence that familial risk of MDD is associated with diminished attention to affective signals (e.g., Gibb et al., 2016; Kujawa et al., 2015; Nelson et al., 2015, 2016; Weinberg et al., 2015), including reduced LPP responses to emotional faces in children of mothers with a history of depressive disorders (Kujawa et al., 2012).

Most affective ERP studies employed visual stimuli from the *International Affective Picture System* (IAPS) for manipulation of emotional content, which affords stimulus selection on the basis of normative ratings for pleasure and arousal (e.g., Bradley and Lang, 2007; Lang et al., 2005). However, other stimulus characteristics (e.g., content, complexity, luminance, contrast, spatial frequency, color) not controlled for by these ratings will substantially influence early and late ERP components (e.g., Bradley et al., 2007; Delplanque et al., 2007; Wiens et al., 2011), which further complicates and potentially confounds the distinction between emotional and cognitive processing (Kayser et al., 1997, 2016). Importantly, any differences in stimulus characteristics will also impact on the study of functional hemispheric asymmetries, including emotional lateralization. To avoid these issues, we developed set of highly-controlled stimuli (pairs of pictures depicting facial areas of patients with skin diseases *before* and *after* surgical treatment), which largely isolate emotional content (negative valence, high arousal) from other stimulus features (see Fig. 1 in Kayser et al., 2016). These stimuli were used during a passive viewing paradigm with separate presentations to the right or left hemifield to directly probe lateralized hemispheric activity (e.g., Young, 1982). Furthermore, we have routinely used temporal principal components analysis (PCA) as a convenient, data-driven means to analyze cognitive and affective ERPs (e.g., Donchin and Hefley, 1978; Kayser and Tenke, 2003). For healthy adults, we found (1) enhanced LPP amplitudes for negative compared to neutral stimuli, and (2) earlier hemispheric asymmetries of emo-

متن کامل مقاله

دریافت فوری ←

**ISI**Articles

مرجع مقالات تخصصی ایران

- ✓ امکان دانلود نسخه تمام متن مقالات انگلیسی
- ✓ امکان دانلود نسخه ترجمه شده مقالات
- ✓ پذیرش سفارش ترجمه تخصصی
- ✓ امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله
- ✓ امکان دانلود رایگان ۲ صفحه اول هر مقاله
- ✓ امکان پرداخت اینترنتی با کلیه کارت های عضو شتاب
- ✓ دانلود فوری مقاله پس از پرداخت آنلاین
- ✓ پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات