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## Emotional prediction: An ALE meta-analysis and MACM analysis

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## ABSTRACT

The prediction of emotion has been explored in a variety of functional brain imaging and neurophysiological studies. However, an overall picture of the areas involved this process remains unexploited. Here, we quantitatively summarized the published literature on emotional prediction using activation likelihood estimation (ALE) in functional magnetic resonance imaging (fMRI). Furthermore, the current study employed a meta-analytic connectivity modeling (MACM) to map the meta-analytic coactivation maps of regions of interest (ROIs). Our ALE analysis revealed significant convergent activations in some vital brain areas involved in emotional prediction, including the dorsolateral prefrontal cortex (DLPFC), ventrolateral prefrontal cortex (VLPFC), orbitofrontal cortex (OFC) and medial prefrontal cortex (MPFC). For the MACM analysis, we identified that the DLPFC, VLPFC and OFC were the core areas in the coactivation network of emotional prediction. Overall, the results of ALE and MACM indicated that prefrontal brain areas play critical roles in emotional prediction.

## 1. Introduction

Human beings live in an uncertain world, which leads to a huge loss, and ultimately affects their physical and mental health. Humans, however, do not process external environment stimuli passively, but continuously generate top-down predictions about them (Kveraga, Ghuman, & Bar, 2007). Pre-awareness of emotional information conveyed by others enables individuals to act appropriately in social exchanges (Lin et al., 2012; Peng, De, Yuan, & Zhou, 2012; Ran, Chen, Pan, Hu, & Ma, 2014).

An increasing number of studies have explored the neural underpinnings underlying emotional prediction. For example, Nitschke, Sarinopoulos, Mackiewicz, Schaefer, and Davidson (2006) have demonstrated that the prediction of a negative emotional stimulus triggers brain areas involved in the experience of negative emotion. This find is consistent with the functional magnetic resonance imaging (fMRI) result that predictable unpleasant stimuli relative to predictable neutral stimuli result in activation of mainly anterior insula, striatum, thalamus, hypothalamus, amygdala, cingulate cortex and prefrontal areas (Herwig, Abler, Walter, & Erk, 2007). While some reports have observed enhanced neural responses in supracallosal anterior cingulate cortex, ventrolateral prefrontal cortex, insula, and amygdala for predictable emotional events (both positive and negative) compared to unpredictable ones (e.g. Onoda et al., 2008), several other studies reported a reversed pattern of activation in insula and amygdala for predictable negative emotional stimuli compared with unpredictable ones (e.g. Sarinopoulos et al., 2010). Such discrepancies may arise from differences in experimental task and stimuli. For instance, in the study of Onoda et al. (2008), participants were instructed to detect an auditory cue. However, a visual cue was employed in the study of Sarinopoulos et al. (2010).

Our recent study have showed decreased activity in the right dorsolateral prefrontal cortex for predictable fear faces and increased activity in the left for predictable happy faces, suggesting that positive and negative emotional prediction may be two distinct

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processes (Ran, Chen, Zhang, Ma, & Zhang, 2016a). There has been a growing recognition that altered prediction of future negative emotional events may be a key aspect of anxiety disorders (Eysenck, 1997; Grillon, 2008). For example, evidence from functional MRI data suggests that brain activation on the right insula is significantly higher in high trait anxiety compared to anxiety normative individuals during aversive prediction (Simmons et al., 2011). Moreover, it is found that heightened anxiety in generalized anxiety patients is associated with increased activation in middle frontal areas and the insula when they anticipate encountering negative emotional stimuli (Schlund, Verduzco, Cataldo, & Hoehnsaric, 2012). More recently, some researchers have reported that greater activation in the bilateral anterior insula was observed in posttraumatic stress disorder (PTSD) versus control subjects during prediction of unpleasant (combat-related) images (Aupperle et al., 2012; Simmons et al., 2013).

Although a wealth of research has investigated the neural correlates of emotional prediction, an overall picture of the areas involved this process remains unexploited. Therefore, the present study adopted a meta-analysis approach of brain imaging studies to identify human brain areas associated with emotional prediction. We adopted an activation likelihood estimation (ALE) meta-analysis because it can accommodate the large amounts of data generated across multiple studies (Eickhoff et al., 2009; Eysenck, 1997; Laird et al., 2005). In addition, a meta-analytic connectivity modeling (MACM) was employed to analyse the co-occurring network of emotional prediction (Eickhoff et al., 2011; Laird et al., 2013; Robinson, Laird, Glahn, Lovallo, & Fox, 2010).

## 2. Materials and methods

### 2.1. Literature search and selection

Relevant studies were identified through a systematic online database search for peer-reviewed articles published before October 2016 on PubMed Database, ISI Web of Knowledge and Google Scholar. Searches were conducted with the keywords “fMRI” or “positron emission tomography (PET)”, in combination with one or two of the following search terms: “prediction”, “anticipation”, “expectation”, “inference”, “foresight”, “prospection”, “forecasting”, “preparation”, “emotion”, “expression”, “happy faces”, “aversive pictures”, “negative emotion”, “positive emotion”, “angry faces” and “fear faces”.

The search yielded 36 potential studies that were further assessed according to the following requirements: (1) the subjects in the selected studies were healthy individuals; (2) the coordinates in the studies were in Talairach or in Montreal Neurological Institute (MNI) space; (3) the studies applied whole-brain general-linear-model-based analyses. A total of 18 imaging studies were included in the final meta-analysis (Table 1). These studies included six experimental contrasts: Predictable > Unpredictable, Unpredictable > Predictable, Predictable negative > Unpredictable negative, Predictable positive > Unpredictable positive, Unpredictable negative > Predictable negative, Unpredictable positive > Predictable positive. Some studies contributed more than one experimental contrast. For example, the study of Ueda et al. (2003) included two experimental contrasts.

### 2.2. Activation likelihood estimation meta-analysis approach

An activation likelihood estimation (ALE) meta-analysis (Eickhoff et al., 2009) was conducted using the GingerALE software (version 2.3, <http://www.brainmap.org/ale/>). Applying the ALE analysis, the reported coordinates of brain areas involving in emotional prediction were converged across different experiments. Give that various emotional predictions might activate different brain areas, we converged the coordinates of the areas associating with negative (angry, fearful and aversive) and positive (happy) emotional prediction. To determine statistical significance, we run a permutation test of randomly distributed foci with 5000 simulations (Feng, Luo, & Krueger, 2015). The ALE-maps had a threshold at a false discovery rate (FDR) of  $p < 0.05$

**Table 1**

All studies entered into the meta analysis are listed, including year, first author, neuroimaging, number of subjects and experimental contrast.

Year	First author	Neuroimaging	Number of subjects	Experimental contrast
2003	Ueda	fMRI	15	Predictable negative > Unpredictable negative, Predictable positive > Unpredictable positive
2004	Simmons	fMRI	28	Unpredictable > Predictable
2006	Bermpohl	fMRI	17	Predictable positive > Unpredictable positive
2006	Simmons	fMRI	32	Unpredictable > Predictable
2007a	Herwig	fMRI	12	Unpredictable > Predictable
2007b	Herwig	fMRI	34	Unpredictable > Predictable
2007c	Herwig	fMRI	16	Predictable > Unpredictable
2008	Onoda	fMRI	18	Predictable > Unpredictable
2010	Schienle	fMRI	30	Unpredictable negative > Predictable negative
2010	Sarinopoulos	fMRI	40	Unpredictable negative > Predictable negative
2011	Clauss	fMRI	42	Predictable > Unpredictable
2011	Brühl	fMRI	14	Unpredictable > Predictable
2012	Barbalat	fMRI	26	Unpredictable negative > Predictable negative
2014	Lutz	fMRI	46	Unpredictable > Predictable
2014	Greenberg	fMRI	25	Unpredictable > Predictable
2016	Ran_EXP 1	fMRI	24	Predictable negative > Unpredictable negative, Unpredictable negative > Predictable negative
2016	Ran_EXP 2	fMRI	25	Predictable positive > Unpredictable positive, Unpredictable positive > Predictable positive
2016	Dzafic	fMRI	28	Predictable > Unpredictable; Unpredictable > Predictable

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