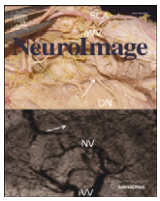
NeuroImage 57 (2011) 1608–1616

Contents lists available at ScienceDirect

NeuroImage

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



Ventral striatal and medial prefrontal BOLD activation is correlated with reward-related electrocortical activity: A combined ERP and fMRI study

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ARTICLE INFO

Article history:
Received 7 February 2011
Revised 8 April 2011
Accepted 13 May 2011
Available online 23 May 2011

Keywords:
Reward
Striatum
fMRI
Erp
Feedback negativity
Feedback related negativity

ABSTRACT

Functional magnetic resonance imaging (fMRI) research suggests that the ventral striatum (VS)/nucleus accumbens, medial prefrontal cortex (mPFC), and broader mesocorticolimbic dopamine system mediate aspects of reward processing from expectation of reward to pleasantness experienced upon reward attainment. In parallel, research utilizing event-related potentials (ERP) indicates that the feedback negativity (FN) is sensitive to reward vs. non-reward feedback and outcome expectation. The FN has been source localized to the mPFC and dorsal striatum, and converging evidence suggests that the FN reflects reward processing in the mesocorticolimbic system. However, the extent to which ERP and fMRI measures of reward processing are correlated has yet to be explored within the same individuals. The primary aim of the current study was to examine the convergence between fMRI (i.e., VS and mPFC) and ERP (i.e., FN) measures of reward processing in forty-two participants who completed counterbalanced fMRI and ERP sessions while performing the same monetary gambling task. For the *Win>Loss* comparison, fMRI activation in the mesocorticolimbic reward circuit including the VS and mPFC was positively correlated with the FN. Here, we demonstrate that monetary gains activate the VS, mPFC, caudate, amygdala, and orbital frontal cortex, enhance the FN ERP component within 300 ms post feedback, and that these measures are related. Thus, fMRI and ERP measures provide complementary information about mesocorticolimbic activity during reward processing, which may be useful in assessing pathological reward sensitivity.

Introduction

The mesocorticolimbic dopamine (DA) system, which includes dopaminergic projections from the ventral tegmental area to both the ventral striatum (VS)/nucleus accumbens and dorsal striatum (i.e., caudate and putamen) as well as orbital frontal cortex (OFC), medial prefrontal cortex (mPFC), and amygdala, has long been implicated in reward processing (Nestler and Carlezon, 2006). In functional magnetic resonance imaging (fMRI) studies, the VS responds to drugs (Breiter et al., 1997; Drevets et al., 2001), attractive faces (Senior, 2003), erotic images (Sabatinelli et al., 2007a; Walter et al., 2008), favorable social interactions (Zink et al., 2008), monetary rewards (Knutson and Bossaerts, 2007), and pleasant tastes (O'Doherty et al., 2002). The VS responds in anticipation of reward (Knutson et al., 2001a, 2001b; O'Doherty et al., 2002) and other striatal areas including the caudate mediate the relationship between action and reward outcome (Tricomi et al., 2004; Zink et al., 2004). Reward attainment (Knutson et al., 2001b; O'Doherty et al., 2002) and outcome monitoring (Kringelbach, 2005) recruit the mPFC. Finally, the subjective feeling of hedonia is associated with OFC activation (Kringelbach, 2005; Kringelbach et al., 2003). Thus, components of the mesocorticolimbic DA system mediate reward processing from seeking to gratification.

Complementary evidence from scalp-recorded event-related potentials (ERPs) has revealed that the "feedback negativity"[2] (FN; peaking at 300 ms) is sensitive to positive vs. negative outcomes such as monetary rewards (Gehring and Willoughby, 2002; Miltner et al., 1997). Variation in FN amplitude is thought to reflect the early, binary evaluation of outcomes as either better or worse than expected. The FN is larger in response to unexpected outcomes (Hajcak et al., 2007;

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[2] This ERP component is referred to alternately as the feedback error-related negativity, medial frontal negativity, or feedback negativity. These names are derived from the observation of a relative negative deflection in the ERP for unfavorable outcomes. Taking the "loss minus win" difference yields negative values at frontocentral recording sites. Recent evidence, however, suggests that the FN may actually reflect a positivity to favorable outcomes (Foti et al., 2011; Holroyd et al., 2008), although we have opted to use the "loss minus win" convention (as opposed to "win minus loss") in figures here to be consistent with the existing literature.

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doi:10.1016/j.neuroimage.2011.05.037

Holroyd et al., 2003; Potts et al., 2006), tracks the relative valence of outcomes within the immediate context (Holroyd et al., 2006, 2004a), and is insensitive to outcome magnitude (Hajcak et al., 2006; Sato et al., 2005; Yeung and Sanfey, 2004). One challenge in using the FN to study reward processing, however, is the issue of component overlap. In particular, the FN overlaps in time with the parietally-maximal P300, a component which is also sensitive to subjective probability and expectation violations (Courchesne et al., 1977; Duncan-Johnson and Donchin, 1977). In principle, apparent variation in FN amplitude could actually reflect variation in the P300. In a prior study, we applied temporospatial principal components analysis (PCA) to parse the ERP waveform and isolate the FN from overlapping responses (Foti et al., 2011). One advantage to this approach is that it improves the accuracy of source localization techniques, allowing for a better estimate of potential neural generators of ERP components (Dien, 2010b). In fact, in our data the PCA-derived FN localized to the dorsal striatum (Foti et al., 2011), whereas in previous work using traditional scoring techniques the FN has primarily been localized to the mPFC (i.e., anterior cingulate cortex Gehring and Willoughby, 2002; Miltner et al., 1997; Potts et al., 2006), although others have localized the FN to the dorsal striatum (Martin et al., 2009).

Together, these lines of evidence suggest that activity in both the mPFC and the striatum (dorsal and ventral) may contribute to the FN, but to date there have been no direct comparisons of fMRI and ERP measures of reward-related activity. Data from fMRI and ERP measures reflect distinct physiological processes—changes in cerebral blood flow associated with neuronal activity and synchronized changes in postsynaptic potentials, respectively. Studies have often found linear relationships between fMRI and ERP measures (Logothetis, 2003; Mathalon et al., 2003; Sabatinelli et al., 2007b), which suggests common neural activity across methods, and yet in principle it is also possible for fMRI and ERP measures to be orthogonal to one another within the same experimental task (Nunez and Silberstein, 2000). Here, we explicitly assess the relationship between fMRI (i.e., mPFC and VS) and ERP (i.e., FN) measures of reward sensitivity. In a counterbalanced order, participants completed fMRI and ERP versions of a simple gambling task in which they could win or lose money on each trial (Foti and Hajcak, 2009; Hajcak et al., 2006). We predicted that the *win>loss* contrast would yield activation in VS, mPFC, and additional mesocorticolimbic structures (Knutson et al., 2001b) and an enhanced amplitude of the reward-related FN ERP at frontocentral electrode sites (Hajcak et al., 2006). Critically, given that both measure neural reactivity to reward, we expected that *win>loss* differences measured by fMRI (i.e., mPFC and VS) and ERP (i.e., FN) would be positively correlated with each other. Furthermore, based on our previous source localization work summarized above (Foti et al., 2011), we hypothesized that a PCA-derived measure of the FN would better correlate with fMRI activity than scores derived from a window measurement.

Methods

Participants

Forty-five (male = 27) consenting adults between the ages of 19 and 25 ($M = 21.11$, $SD = 1.27$) participated in the study. Forty reported being right-handed and five reported being left-handed. Potential participants were screened for metal. Participants were monetarily compensated for their time. The Institutional Review Board of Stony Brook University approved this study. Participants completed fMRI and ERP testing sessions in a counterbalanced order (23 completed the fMRI session first)[3]. Two participants had poor quality EEG data, defined as having fewer than 20 artifact-free trials per condition (Marco-Pallares et al., 2011). Grubbs' (1969) test was performed on key study variables to identify outliers; one participant had significantly deviant fMRI VS data ($z = 5.04$, $p < 0.05$). These three participants were excluded from respective subsequent analyses, leaving 42 (25 male) individuals with both ERP and fMRI measures.

Gambling task (fMRI)

The experiment was programmed and run with E-prime (Psychology Software Tools, Pittsburg, PA). An MRI-compatible 60 Hz projector with a 1024 × 768 resolution, reflected stimuli onto a mirror attached to the head coil. Each trial began with a white fixation cue presented in the center of a black screen (500 ms). Next, a screen displayed two doors side-by-side for 4000 ms. Participants were instructed that behind one of the doors there was a monetary prize (+$0.50) while behind the other door there was a loss (−$0.25). Participants used a MRI-compatible response box to make their choice of door. Note, participants were told that if they did not choose while the doors were on the screen, that the computer would choose a door at random. Then, after another brief fixation cue (500 ms), a feedback screen was displayed (1000 ms) where a green '↑' indicated a correct guess, while a red '↓' indicated an incorrect guess. A blank black screen jittered intertrial interval occurred between each trial ($M = 4000$ ms, *Min.* = 1500 ms, *Max* = 14000 ms). The task was 10 min and 5 s in duration and consisted of 60 trials with 30 predetermined wins and losses presented in a pseudorandom order. That is, unknown to participants, left or right door responses did not influence whether or not a trial was a win or loss. Prior to the collection of functional imaging data participants completed two practice trials containing examples of a win and a loss.

Functional image acquisition and analysis

A 3 Tesla Siemens Trio whole body scanner was used to acquire 242 T2*-weighted whole-brain volumes with an EPI sequence sensitive to BOLD signal using the following parameters: TR = 2500 ms, TE = 22 ms, flip angle = 83°, matrix dimensions = 96 × 96, FOV = 224 × 224 mm, slices = 40, slice thickness = 3.5 mm, and gap = 0. Standard preprocessing procedures were performed in SPM8, including image realignment corrections for head movements, slice timing corrections for acquisition order, normalization to standard 2 × 2 × 2 mm Montreal Neurological Institute space, and spatial smoothing with a Gaussian full-width-at-half-maximum 8 mm filter. First-level single subject SPMs were created from a model, which specified the onset of loss (i.e., ↓) and win cues (i.e., ↑).

Gambling task (ERP)

The ERP version of the gambling task was administered using Presentation software (Neurobehavioral Systems, Inc., Albany, California, USA) to control the presentation and timing of all stimuli. The task was designed to proceed in a similar manner to the fMRI version, with the timing of stimuli within each trial as follows: (i) the graphic of two doors was presented until a response was made, (ii) a fixation mark was presented for 1000 ms, (iii) a feedback arrow was presented for 2000 ms, (iv) a fixation mark was presented for 1500 ms, and (v) 'Click for the next round' was presented until a response was made. To familiarize participants with the task, they first completed five practice trials.

ERP data acquisition and analysis

The continuous EEG was recorded using a custom cap (Cortech Solutions, Wilmington, North Carolina, USA) and the ActiveTwo BioSemi system (BioSemi, Amsterdam, Netherlands). The signal was preamplified at the electrode with a gain of 1; the EEG was digitized at

[3] Values for all extracted fMRI activations and PCA scores did not differ between the two testing orders (all p's ≥ 0.30).