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Anterior cingulate activity to monetary loss and basal ganglia activity to monetary gain uniquely contribute to the feedback negativity

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HIGHLIGHTS

- The feedback negativity is a composite of two signals: loss-related theta activity in the anterior cingulate cortex, and gain-related delta activity with a potential source in the striatum.
- Symptoms of internalizing psychopathology relate specifically to reduced gain-related delta activity and not loss-related theta activity.
- Gain-related delta activity may specifically be effective for quantifying impaired reward sensitivity and basal ganglia dysfunction in clinical populations.

ABSTRACT

Objective: The feedback negativity (FN) is an event-related potential that differentiates unfavorable versus favorable outcomes. Although thought to reflect error-related activity within the anterior cingulate cortex, recent work indicates the FN may also reflect reward-related activity that has been linked to the basal ganglia. To date, it remains unclear how to reconcile these conflicting perspectives.
Methods: We decomposed the FN by applying time–frequency analysis to isolate activity unique to monetary losses and gains. The FN was recorded from 84 individuals during a laboratory gambling task.
Results: Two signals contributed to the FN elicited by unpredictable outcomes: theta activity (4–7 Hz) was increased following monetary loss, and delta activity (<3 Hz) was increased following monetary gain. Predictable outcomes elicited delta but not theta activity. Source analysis revealed distinct generators, with loss-related theta localized to the anterior cingulate cortex and gain-related delta to a possible source in the striatum. Symptoms of depression, anxiety, and stress reactivity were specifically associated with blunted gain-related delta.
Conclusions: The FN may be a composite of loss- and gain-related neural activity, reflecting distinct facets of reward processing.
Significance: Gain-related delta activity may provide unique information about reward dysfunction in major depression and other internalizing psychopathology.

1. Introduction

Decision-making is guided by feedback about the consequences of our actions: favorable outcomes suggest a course of action to be pursued, whereas unfavorable outcomes indicate the need for adjustments. Event-related potential (ERP) studies of feedback pro-

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cessing have focused on the feedback negativity (FN), an early component that differentiates unfavorable outcomes (i.e., errors, monetary loss) compared to favorable outcomes (i.e., correct responses, monetary gain) (i.e., correct responses, monetary gain; Gehring and Willoughby, 2002; Miltner et al., 1997). The differentiation in FN amplitude between favorable and unfavorable outcomes peaks at approximately 300 ms and at frontocentral electrodes, and source localization techniques have identified a likely neural generator in the anterior cingulate cortex (ACC; Gehring and Willoughby, 2002; Miltner et al., 1997; Potts et al., 2006; Ruchsow et al., 2002); converging evidence of an ACC source is also found from simultaneous ERP and functional magnetic resonance imaging (fMRI) recordings (Hauser et al., 2014). The FN has been discussed in terms of reinforcement learning, such that variation in FN amplitude reflects phasic changes in mesencephalic dopamine signals to the ACC when outcomes are better or worse than expected (Holroyd and Coles, 2002). Consistent with this perspective, FN amplitude is increased for unpredicted compared to predicted outcomes (Hajcak et al., 2007; Holroyd et al., 2003).

Critically, the FN has often been interpreted as an ERP response specifically elicited by monetary loss and error feedback, thereby reflecting a process which tracks the occurrence of unfavorable outcomes (Heldmann et al., 2008; Holroyd and Coles, 2002; Holroyd et al., 2003). That is, the FN has typically been viewed as a negative deflection in the ERP waveform that is increased for monetary loss and is either reduced or absent for monetary gain. Recent work, however, converges upon the opposite viewpoint: variation in FN amplitude may instead be largely driven by neural activity on gain trials. In particular, it has been suggested that both monetary gain and loss feedback elicit a common N2, and monetary gain feedback also elicits a distinct positive-going deflection (Baker and Holroyd, 2011; Holroyd et al., 2011, 2008). Functionally, the N2 is thought to index the conflict associated with unpredicted outcomes rather than valence per se, whereas the reward positivity reflects dopaminergic signals to positive outcomes (Baker and Holroyd, 2011). Because these components typically have extensive temporal and spatial overlap, they both contribute to observed FN amplitude and are difficult to distinguish using traditional time-domain ERP analysis.

Complementing these data, several studies have shown that when the FN is scored using temporospatial principal components analysis (PCA), it is isolated as an absolute positivity that is increased for gains compared to losses (Carlson et al., 2011; Foti and Hajcak, 2009; Foti et al., 2011b) – in accordance with the reward positivity identified by Baker and Holroyd (2011). The advantage of applying PCA in this manner is that it maximizes the separation between the FN and other overlapping ERP components, particularly the P300. In contrast to previous work attributing the FN to activity in the ACC, source localization of this PCA-derived reward response has revealed a possible source in the striatum (Foti et al., 2011b), a part of the core neural network involved in reward processing (Liu et al., 2011). In a follow-up study utilizing both ERPs and fMRI recorded in separate sessions, FN amplitude correlated directly with the gain-related hemodynamic response in the striatum, orbitofrontal cortex, and medial prefrontal cortex (Carlson et al., 2011); FN amplitude also correlated with midbrain gray matter volume, an association which was mediated by functional activity in the striatum (Carlson et al., 2014). Further, a recent study using simultaneous ERP and fMRI recordings observed that trial-by-trial variation in FN amplitude was associated with BOLD signal within the striatum, cingulate, and medial prefrontal cortex – and that this association with reward circuit activity was specific to gain trials (Becker et al., 2014).

Reframing the FN as a response to monetary gain – a neurobiological index of hedonic capacity – makes it well-suited to studying individual differences in reward sensitivity. Indeed, a recent study demonstrated that FN amplitude relates to individual differences in both behavioral and self-report indicators of reward sensitivity (Bress and Hajcak, 2013). As a neural measure of reward sensitivity, the FN has also been applied to the study of abnormal reward processing in relation to psychopathology. FN amplitude on gain trials is increased among problem gamblers, indicating hypersensitivity to reward (Hewig et al., 2010). On the other hand, FN amplitude is blunted among adults and children with current depressive symptoms, indicating reduced reward sensitivity (Bress et al., 2012, 2013b; Foti and Hajcak, 2009; Liu et al., 2014). The FN appears to be an effective tool for capturing trait and state differences in reward processing, and it may potentially be a useful biomarker for quantifying impaired reward sensitivity in relation to psychiatric illness.

A remaining challenge is how best to reconcile these two distinct conceptualizations of the FN as either an error signal elicited by unfavorable outcomes or a reward signal elicited by favorable outcomes. One possibility is that both accounts are accurate, and that both loss- and gain-related neural activity contribute to the scalp-recorded FN. Emerging evidence from time–frequency decompositions of the FN suggests that this may be the case. Unlike traditional time-domain ERP analyses, this approach is capable of isolating neural signals with distinct frequency characteristics, even if the signals have considerable temporal and spatial overlap (Bernat et al., 2005; Harper et al., 2014). When applied to ERPs elicited by monetary feedback, two distinct effects in the time range of the FN are apparent. On the one hand, activity in the theta frequency band (4–7 Hz) is increased for monetary loss; on the other, activity in the delta frequency band (<3 Hz) is increased for monetary gain (Bernat et al., 2008, 2011; Cohen et al., 2007; Nelson et al., 2011). In the time-domain ERP waveform, the delta response would manifest as a positive-going peak that is increased (i.e., more positive) on gain trials, and the theta response would manifest as a negative-going peak that is increased (i.e., more negative) on loss trials. When entered as simultaneous predictors of time-domain FN amplitude, both the delta and theta responses yield significant effects, indicating that they reflect relatively independent processes that each contribute to the observed FN (Bernat et al., 2008, 2011). These findings potentially provide a conceptual and empirical bridge between the two opposing viewpoints of the FN, demonstrating how unique sources of loss- and gain-related neural activity may contribute to the ERP response – and how they may be quantified separately using time–frequency analysis.

In the current study, we sought to build upon this preliminary evidence by applying time–frequency analysis to an FN dataset recorded in a relatively large sample during a simple gambling task. The FN in this dataset was previously scored using temporospatial PCA (Foti and Hajcak, 2009) as well as a standard time-window measure (Foti and Hajcak, 2012), but the frequency characteristics were not considered. We focused the current analysis on two key questions: First, we examined the likely neural generators of the theta- and delta-band responses, with the goal of potentially reconciling inconsistent source localization results in the FN literature. Loss-related theta activity has been linked to a source in the ACC (Vaidyanathan et al., 2008), which is consistent with several reports localizing the time-domain FN to the ACC (Gehring and Willoughby, 2002; Miltner et al., 1997; Potts et al., 2006; Ruchsow et al., 2002). Of particular interest here is the possibility that gain-related delta activity may be localized to a source in the striatum (Becker et al., 2014; Carlson et al., 2011; Foti et al., 2011b). To the extent that the FN may represent a composite of anterior cingulate and basal ganglia activity, time–frequency analysis may be an effective technique for isolating activity emanating from these two distinct neural generators.

Second, we considered how time–frequency analysis might shed additional light on our understanding of the link between abnormal