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Patterns and reliability of EEG during error monitoring for internal versus external feedback in schizophrenia☆,☆☆

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ABSTRACT

Background: Accurately monitoring one's performance on daily life tasks, and integrating internal and external performance feedback are necessary for guiding productive behavior. Although internal feedback processing, as indexed by the error-related negativity (ERN), is consistently impaired in schizophrenia, initial findings suggest that external performance feedback processing, as indexed by the feedback negativity (FN), may actually be intact. The current study evaluated internal and external feedback processing task performance and test-retest reliability in schizophrenia.
Methods: 92 schizophrenia outpatients and 63 healthy controls completed a flanker task (ERN) and a time estimation task (FN). Analyses examined the ΔERN and ΔFN defined as difference waves between correct/positive versus error/negative feedback conditions. A temporal principal component analysis was conducted to distinguish the ΔERN and ΔFN from overlapping neural responses. We also assessed test-retest reliability of ΔERN and ΔFN in patients over a 4-week interval.
Results: Patients showed reduced ΔERN accompanied by intact ΔFN. In patients, test-retest reliability for both ΔERN and ΔFN over a four-week period was fair to good.
Conclusion: Individuals with schizophrenia show a pattern of impaired internal, but intact external, feedback processing. This pattern has implications for understanding the nature and neural correlates of impaired feedback processing in schizophrenia.

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1. Introduction

Schizophrenia is a debilitating disorder characterized by difficulties in social and occupational functioning and diminished engagement in productive and pleasurable activities (Barch and Dowd, 2010, Blanchard et al., 2011). Accurately monitoring one's performance on daily life tasks, and integrating internal and external performance feedback are necessary for guiding productive behavior (Falkenstein et al., 1990, Gehring et al., 1993, Holroyd and Coles, 2002). Internal and external feedback monitoring have been investigated through event-related potential (ERP) measures in healthy participants and, to a lesser extent, in people with schizophrenia. While research has consistently shown that patients with schizophrenia show impairments in internal feedback monitoring, initial findings suggest that sensitivity to external feedback may be intact.

Internal feedback monitoring is indexed by the error-related negativity (ERN), an ERP component involved in monitoring actions and detecting errors (Falkenstein et al., 1990, Gehring et al., 1993, Simons, 2010). It is typically studied using simple choice reaction time tasks (e.g., flanker, go/nogo, and Stroop tasks). The ERN is evident as a larger negative deflection at frontocentral sites peaking at approximately 50 ms following erroneous responses compared to the correct response negativity (CRN), a smaller negative-going component following correct responses. Studies examining the ERN/CRN also typically report on the error positivity (Pe), a parietal positive-going deflection in the waveform that is evident following the ERN and typically peaks at around 300 ms (Falkenstein et al., 2000). The Pe is thought to index error awareness (Endrass et al., 2007, Nieuwenhuis et al., 2001).

On the other hand, external feedback monitoring is indexed by the feedback negativity (FN), which is elicited when participants need to rely on external feedback (e.g., positive or negative performance feedback, monetary gain or loss) to know whether a response results in a

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☆☆ Ethical standards: The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional guides on the care and use of laboratory animals.

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good or bad outcome. The FN is often studied using simple gambling or guessing paradigms, and it reflects a relative negativity at frontocentral recording sites at approximately 300 ms that is larger following unfavorable outcomes compared to favorable outcomes (Hajcak et al., 2006, Sato et al., 2005, Yeung and Sanfey, 2004). Although it is called feedback *negativity*, this difference wave may actually reflect a reward-related positivity that is absent or suppressed following non-rewards (Foti et al., 2011, Proudfit, 2015).

Many studies have found blunted ERN in schizophrenia compared to controls across different types of tasks (e.g., Foti et al., 2012, Horan et al., 2012, Kansal et al., 2014, Morris et al., 2006, 2008). Further, patients typically demonstrate normal CRN and Pe (Alain et al., 2002, Horan et al., 2012, Mathalon et al., 2002, Morris et al., 2008). Thus, the diminished differentiation between ERN and CRN in patients may reflect impaired early self-monitoring and internal error processing, whereas later response evaluation (Pe) seems to be intact. Some studies have reported that diminished ERN is associated with more severe negative symptoms and poorer real-world functioning (Foti et al., 2012, 2013).

While individuals with schizophrenia consistently demonstrate impairments in processing internal feedback as indexed by the ERN, there is some evidence for intact sensitivity to external performance feedback as indexed by FN. Thus far, only two studies have investigated FN in schizophrenia and both found that it was comparable to healthy control participants. One study (patient n = 32) used a time estimation task and a passive gambling task to assess external feedback processing, as well as the flanker task to assess internal feedback processing. Patients showed intact FN on both external feedback tasks accompanied by diminished ERN on the flanker task (Morris et al., 2011). Another study by our group (patient n = 35) found that patients and controls demonstrated comparable FN differentiation between reward and non-reward feedback using a gambling task, also accompanied by impaired ERN in patients on the flanker task (Horan et al., 2012). The findings of comparable FN between groups could reflect an intact ERP component in schizophrenia. Alternatively, it could reflect limited statistical power, or limited reliability in FN measurement.

While these initial studies found a differential pattern of results across ERN and FN tasks in schizophrenia, we sought to replicate and extend these previous findings in three ways. First, we recruited substantially larger samples than the prior studies that examined FN. Second, the current analyses applied more data-driven and precise temporal principal components analysis (PCAs) to ERP data recorded during the flanker task (ERN) and a time estimation task (FN), with the goal of more clearly distinguishing the ERN and FN from overlapping neural responses. Third, we evaluated the reliability of these measures in patients by assessing the stability of the ERN and FN across two testing sessions spaced four weeks apart. As an additional step, we investigated whether ERN and FN were correlated with clinical symptoms and functional outcome in patients.

2. Methods

2.1. Participants

Ninety-two outpatients with schizophrenia and 63 control subjects participated in this study. All participants were assessed at baseline (Session 1) and patients only were reassessed at a 4-week follow-up (Session 2). Patients met criteria for schizophrenia disorder based on the Structured Clinical Interview for DSM-IV Axis I Disorders – Patient Edition (SCID-I/P) (First et al., 1996). Exclusion criteria for patients included: substance dependence in the last six months or abuse in the last month; not currently experiencing a mood disorder episode; loss of consciousness for more than one hour; an identifiable neurological disorder; or insufficient fluency in English. Eighty-three patients were medicated at clinically determined dosages with 71 receiving atypical antipsychotic medications, 8 receiving typical antipsychotic medications, 4 receiving both types of medication, and 9 not taking medication, and all patients were clinically stable (no hospitalizations in the past three months, no medication changes in the past six weeks, and no changes in housing status in the past two months).

Healthy controls were recruited through postings on websites, and were matched to the patient group on gender, age, and ethnicity. They were excluded for neurological disorder or head injury, psychotic disorder in a first-degree relative, or insufficient fluency in English. They were also excluded (based on the SCID-I/P) for history of psychotic disorder, bipolar disorder, recurrent depression, lifetime history of substance dependence, substance abuse in the last months, or avoidant, paranoid, schizoid, or schizotypal personality disorder, based on the Structured Clinical Interview for DSM-IV Axis II Disorders (SCID-II) (First et al., 1994). Given that benzodiazepines have been found to attenuate the ERN (De Bruijn et al., 2004, Johannes et al., 2001, Riba et al., 2005), all participants were queried to ensure they were not taking benzodiazepines on testing days prior to testing. All participants provided written informed consent in accordance with approval from the Institutional Review Board at the VA Greater Los Angeles Healthcare System. This study was part of a larger research project from which results for a different experimental task have been reported previously (Reddy et al., 2016); none of the ERP data has been reported elsewhere.

2.2. ERP paradigms

2.2.1. ERN flanker task

Internal performance feedback was assessed using an arrow version of the flanker task (Eriksen and Eriksen, 1974, Hajcak et al., 2005). On each trial, five horizontally aligned arrowheads were presented at central fixation. Participants were instructed to press the right mouse button if the center arrow was facing to the right and to press the left mouse button if the center arrow was facing to the left. In half of the trials the center and flanking arrows were compatible ("<<<<<" or ">>>>>") and half were incompatible ("<<><<" or ">><>>"); the order of compatible and incompatible trials was random. All stimuli were presented for 200 ms followed by an inter-trial interval (ITI) that varied randomly from 2300 to 2800 ms.

Participants completed 20 practice trials during which they were instructed to be both as accurate and fast as possible. The task consisted of 11 blocks of 30 trials (330 trials total) with each block initiated by the participant. To encourage both fast and accurate responding, participants received feedback based on their performance at the end of each block. If performance was 75% correct or lower, the message "Please try to be more accurate" was displayed; performance above 90% correct was followed by "Please try to respond faster"; otherwise, the message "You're doing a great job" was displayed.

2.2.2. FN time estimation task

External performance feedback monitoring was assessed using a modified version of a time estimation task (Miltner et al., 1997). On each trial, participants were presented with an auditory cue (1000 Hz tone, 65 dB) and instructed to estimate when exactly one second had elapsed following the cue by pressing the left mouse button. A fixation mark ('+') appeared in the center of the screen during the estimation period. Following the button press, a happy or sad cartoon face appeared, with a happy face (positive feedback) indicating their response fell within the designated time window for that trial, and a sad face (negative feedback) indicating their response was outside the window. At the beginning of the task, the time window had an initial length of 400 ms centered around the one-second mark (i.e., 800–1200 ms following the auditory cue). The window was dynamically adjusted in order to maintain an approximate success rate of 50%. After each accurate response, the window was shortened by 20 ms, and lengthened by 20 ms for each inaccurate response. Stimuli were presented as follows: a 50 ms auditory cue, a fixation mark was presented until a response was made and then 1200 ms afterward, a feedback face was presented for 1500 ms followed by a fixation mark for 2500 ms.

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