Error-Related Brain Activity as a Biomarker for Cocaine Relapse

Addiction is characterized by the observation that substance-dependent individuals continue to use substances despite the negative consequences, such as social, interpersonal, or physical problems. The ability to adequately monitor negative consequences in behavior, referred to as error processing, is necessary for optimal behavioral performance to guide one's behavior toward one's long-term goals (eg, maintain abstinence from substance use). It has been previously reported that cocaine-dependent individuals show a decreased sensitivity to errors and this has been attributed to reduced activation in the anterior cingulate cortex (ACC; Kaufman *et al*, 2003). Likewise, electrophysiological research has shown that the error-related negativity (ERN)—which represents the brain's automatic detection of an error—is reduced in cocaine users compared with healthy controls (Franken *et al*, 2007). It has been theorized that a reduced ERN is a representation of the notion that errors are perceived as less meaningful or motivationally relevant in substance-dependent individuals (Hajcak, 2012). This may underlie their persistence of drug taking despite the clear adverse consequences. Additionally, it is conceivable that these brain dysfunctions associated with error processing also have a role in drug relapse.

Error processing is typically measured using reaction time tasks with high chances to make errors, such as the Go-Nogo task or Eriksen flanker task. To examine the predictive role of error processing in drug relapse, we measured event-related potentials (ERPs) in response to an Eriksen flanker task in cocaine-dependent patients during their first week of detoxification treatment (Marhe *et al*, 2013). In this task, letter strings are presented and participants are required to respond as quickly and accurately as possible to a target letter. This task is frequently used to measure error processing, as participants easily make mistakes on this task. First, the results confirmed that the ERN amplitude was indeed reduced in cocaine-dependent patients as compared with non-dependent controls. Most interestingly, ERN amplitude predicted cocaine use after treatment, over and above other relevant predictors measured at baseline such as substance use severity and subjective cocaine craving. A reduced ERN at baseline was associated with a higher number of days of cocaine use at 3-month follow-up. Another recent study using functional magnetic resonance imaging found that the reduced error-related brain activity in areas such as the dorsal ACC, thalamus, and insula is associated with cocaine relapse after treatment (Luo *et al*, 2013). The results of both these studies indicate that cocaine-dependent patients exhibiting underactive error-related brain activity are more at risk of relapse.

Error-related brain activity might serve as a biomarker helping to identify patients vulnerable for relapse already early in treatment. Although there is knowledge on the underlying brain processes of error processing (Kaufman *et al*, 2003; Luo *et al*, 2013), further investigation of the underlying neural circuitry and neurochemistry using neuroimaging and (combined) pharmacological approaches will further advance this research area. Regarding the results of Marhe *et al* (2013), it could be beneficial in the future to routinely assess the ERN amplitude in cocaine-dependent patients at the start of detoxification treatment. The idea to use electroencephalography (EEG) as a screening instrument has gained interest, specifically for ERP components that have good psychometric properties, such as the ERN (Hajcak, 2012; Hoffmann and Falkenstein, 2012). In addition, EEG is a noninvasive, relative inexpensive, and accessible biomarker. Therefore, it would be very feasible to use this measure in large-scale (genetic) studies. Future studies should reconfirm the association between the ERN and drug relapse and further examine the sensitivity and specificity of the ERN as a predictor of cocaine relapse. Ultimately, treatment programs could be tailored to the patient's need to improve outcomes.

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Parkinson's Disease Biomarkers: Resources for Discovery and Validation

Parkinson's disease (PD) is currently diagnosed using clinical features. While experienced neurologists can typically diagnose PD with 70–90% accuracy, there are many situations early in the course of the disease when clinical diagnosis is less precise. There is a paucity of objective measures that could be employed to improve the diagnosis, stratify patients by subtypes, and track underlying disease progression. Development of innovative new therapies that slow or stop the progression of the disease would be accelerated by such objective biomarkers. Various imaging modalities including specific dopaminergic markers and