Clinical Neurophysiology 125 (2014) 1417–1426

Contents lists available at ScienceDirect

Clinical Neurophysiology

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

Neural correlates of performance monitoring in daily and intermittent smokers

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ARTICLE INFO

Article history:
Accepted 4 December 2013
Available online 11 December 2013

Keywords:
Performance monitoring
Error-related negativity
Event-related potentials
Smoking
Substance dependence

HIGHLIGHTS

- This is the first study to measure inhibitory control and event-related potentials (ERP) measures of performance monitoring in nondaily, non-dependent smokers.
- Monitoring and regulation of behavior, which is important for adaptive and optimal performance, is impaired in persons with substance dependence.
- Increased Error Positivity ERP response in nondaily smokers reflects cognitive processes that may prevent the transition to dependent smoking.

ABSTRACT

Objectives: Despite efforts that have increased smoking regulation, cigarette taxation, and social stigma, cigarette smoking remains the leading cause of preventable death worldwide, and a significant personal and public economic burden. In the U.S., intermittent smokers comprise approximately 22% of all smokers and represent a stable, non-dependent group that may possess protective factors that prevent the transition to dependence. One possibility is that intermittent smokers have intact CNS frontal regulatory and control mechanisms that enable resistance to nicotine-induced changes.
Methods: The present study measured inhibitory control using a flanker task and a go–nogo continuous performance tasks in daily dependent smokers, intermittent non-dependent smokers, and nonsmokers. Event-related potential (ERP) measures of were concurrently recorded to measure performance monitoring via Event-Related Negativity (ERN) and error positivity (Pe) components during error trials for each task.
Results: In both tasks, behavioral and ERN measures did not differ between groups; however, amplitude of the Pe component was largest among intermittent smokers.
Conclusions: Thus, intermittent smokers differed from both daily smokers and nonsmokers on error processing, potentially revealing neuroprotective cognitive processes in nicotine dependence.
Significance: A better understanding of factors that mediate behavioral regulation may provide novel treatment approaches that help individuals achieve controlled smoking or cessation.

1. Introduction

Difficulty regulating behavior and monitoring performance outcomes plays a significant role in the development and maintenance of addiction (Chiu et al., 2008; de Wit, 2009; Sokhadze et al., 2008). Drug dependent individuals have difficulty inhibiting the response to drugs or drug cues, especially during withdrawal (Li and Sinha, 2008). A compromised self-regulatory system in dependent smokers may drive relapse rates to be as high as 50% in the first week and 95% in the first year following cessation, despite a desire to quit by nearly 70% of individuals (CDC, 2011a; Hughes, 2007). Smokers report reduced self-control, increased impulsiveness, and inability to resist temptation, all of which may contribute to relapse (Coggins et al., 2009). Impairments on laboratory tasks of inhibitory control and executive function are evident in abstinent states, even following three months of cessation, compared to

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1388-2457/$36.00
http://dx.doi.org/10.1016/j.clinph.2013.12.001

satiated states, which may contribute to failed cessation efforts (Billieux et al., 2010; Dawkins et al., 2009; Harrison et al., 2009). In chronic smokers during abstinence, imaging studies show neuroadaptation of frontostriatal brain regions involved in regulating inhibitory control, as evidenced by reduced frontal grey matter volumes and densities, increases in neural response to drug cues, and reduced anterior cingulate metabolic activity compared to nonsmokers (Feil et al., 2010). The ability to regulate cognitive processes and adjust behavior for optimal performance requires online monitoring of actions and subsequent outcomes (Ridderinkhof et al., 2004). In smokers, reduced neural response following error commission suggests potential difficulties in performance monitoring that may potentiate relapse or continued smoking despite negative health consequences (Franken et al., 2010; Luijten et al., 2011b).

A subset of smokers report feeling in control of their smoking behavior, an absence of withdrawal symptoms, and higher cessation rates (Coggins et al., 2009; Shiffman, 1989; Shiffman et al., 1990). These self-reported "some day" smokers, also referred to as "chippers" or intermittent smokers (ITS), comprise 22% (9.9 million) of the U.S. smoking population and this number is believed to be increasing (CDC, 2011b; Shiffman et al., 2012). Their ability to avoid dependence cannot be attributed to differences in smoking topography (e.g., number of puffs, puff duration, inter-puff/cigarette interval) or changes in blood–nicotine concentration (Brauer et al., 1996; Coggins et al., 2009; Shiffman, 1989). Compared to daily, dependent smokers, long-term ITS report having an internal locus of control and greater self-control compared to regular smokers (Coggins et al., 2009; Kassel et al., 1994; Shiffman and Paty, 2006). Surprisingly, the neurocognitive factors that allow ITS to avoid dependence have received remarkably little attention.

Behavioral measures of inhibitory control have not been investigated previously in ITS. The Eriksen Flanker Task targets selective inhibition and conflict control, where participants must respond quickly to identify the middle letter (or arrow) in trials when it is flanked by congruent or incongruent letters (or arrows). The Go/No-go continuous performance task targets sustained attention and behavioral control where participants must inhibit a prepotent motor response to a frequently occurring "Go" stimulus when an infrequent 'No-go' stimulus is presented. These tasks reflect the ability to control behavior prior to motor initiation, such as inhibiting smoking-related cues or the automaticity of reaching for a cigarette when it is available, respectively, and may be especially relevant in the planning and single instances of drug seeking or use. Overall, studies of inhibitory control in smokers have produced mixed results, finding that smokers had impaired accuracy in some (Luijten et al., 2011a: Go/No-go task) but not all studies (Dinn et al., 2004): Go/No-go task, Stroop Color-Word task; Franken et al., 2010: Flanker task; Luijten et al., 2011b: modified Flanker task). Impaired performance on measures sensitive to behavioral control, such as the Stop Signal task (Billieux et al., 2010) and the Go/No-go and Anti-saccade tasks (Spinella, 2002) has been found to correlate with increased smoking rate and dependence.

The medial frontal cortex and associated regions are involved in monitoring unfavorable outcomes, response errors and conflict, and decision uncertainty (Ridderinkhof et al., 2004). Event-related potential (ERP) recordings during performance of the inhibitory control tasks provide an evaluation of online performance monitoring and behavioral modification when errors are detected. The Error-Related Negativity (ERN) and Error Positivity (Pe) ERP components are believed to index performance monitoring in tasks that induce cognitive and response conflicts. The ERN is a negative-voltage potential with a fronto-central scalp distribution that occurs approximately 50–100 ms following the commission of an error (Gehring et al., 1993). The Pe is a positive-voltage potential with a fronto-central or centro-parietal scalp distribution that occurs approximately 200–400 ms following an erroneous response (Arbel and Donchin, 2009; Overbeek et al., 2005). The ERN is associated with automatic error detention or conflict monitoring, whereas the Pe is associated with the awareness and motivational significance of an error (Arbel and Donchin, 2009; Falkenstein et al., 2000; Gehring et al., 2012; Nieuwenhuis et al., 2001; Overbeek et al., 2005; Pontifex et al., 2010; Shalgi et al., 2009; Yeung et al., 2004). Generation of the ERN has been localized to the dorsal anterior cingulate cortex (ACC) with potential contributions from the pre-supplementary motor area and the lateral prefrontal cortex, whereas the less-understood Pe may be comprised of a fronto-central waveform originating from the medial frontal cortex and a late centro-parietal waveform generated by the superior parietal cortex and rostral ACC (Arbel and Donchin, 2009; Gehring et al., 2012; Herrmann et al., 2004; Overbeek et al., 2005; Pontifex et al., 2010). Recent studies support that the Pe co-varies with the stimulus-locked P300 ERP, associated with attentional salience and novelty detection (Polich, 2007; Ridderinkhof et al., 2009; Shalgi et al., 2009).

Ascending dopaminergic projections, which densely innervate the medial frontal cortex, release the primary neurotransmitter responding to errors in reward prediction. Phasic dopamine changes may play a role in adjusting behavior to improve task performance via reinforcement learning principles (Overbeek et al., 2005). The ERN has been consistently found to be sensitive to dopamine neurotransmission, however the role of dopamine has been less certain for the P3 and Pe response (Gehring et al., 2012; Overbeek et al., 2005). There has been some support of dopaminergic mediation of frontal P300 (P3a), but studies have found no influence of dopamine on the Pe response (Gehring et al., 2012; Overbeek et al., 2005; Polich and Criado, 2006). In substance dependence, frontostriatal dysregulation can impair the selection and maintenance of task/goal-relevant information while suppressing inappropriate responses or representations (Dawkins et al., 2009; Feil et al., 2010). Specifically, substance dependence is associated with impairments in the dorsolateral prefrontal cortex (involved in attention, goal identification, and selection) and the ACC (involved in assessment of consequences and error detection) (Feil et al., 2010; Goldstein and Volkow, 2002), which may contribute to deficits in inhibitory control and performance monitoring.

Imaging studies support that substance abuse populations have shown decreased error-related activity in the anterior cingulate cortex, a region believed to be involved in ERN and Pe generation (Gehring et al., 2012; Olvet and Hajcak, 2008). Studies of drug users have found disrupted ERN response in regular users cocaine (Franken et al., 2007), and alcohol (Schellekens et al., 2010) and disrupted Pe/P300 in users cannabis (Fridberg et al., 2013), cocaine (Franken et al., 2007), and alcohol (Polich and Ochoa, 2004; Rodriguez Holguin et al., 1999). Fridberg et al. (2013) found no ERN differences between controls and chronic cannabis users. In participants at risk for alcoholism, smoking was found to moderate the P300 such that smoking accounted for more variance of the decreased P300 than alcohol risk (Polich and Ochoa, 2004). Studies specific to smoking have found reduced amplitudes of the ERN (Luijten et al., 2011b) and Pe (Franken et al., 2010; Luijten et al., 2011b) in smokers compared to nonsmokers during inhibitory control tasks (Franken et al., 2010; Luijten et al., 2011b). However, Franken et al. (2010) found no ERN differences between controls and cigarette smokers. In an oddball task, increased P3a amplitude in response to the distractor shows that the P300 is sensitive to acute nicotine administration both in low-use and high-use chronic smokers, suggesting nicotine-dependent alterations in the brain mechanisms contributing to P300 generation (Polich and Criado, 2006). Finally, acute abstinence from smoking resulted