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Effects of smoking abstinence on reaction time variability in smokers with and without ADHD: An ex-Gaussian analysis

Scott H. Kollins^{a,*}, F. Joseph McClernon^b, and Jeff N. Epstein^c

^aDepartment of Psychiatry, Duke ADHD Program, 718 Rutherford Street, Durham, NC 27705, United States

^bDepartment of Psychiatry, Box 2701, Duke University Medical Center, Durham, NC 27710, United States

^cCincinnati Children's Hospital Medical Center, Cincinnati, OH 45206, United States

Abstract

Smoking abstinence differentially affects cognitive functioning in smokers with ADHD, compared to non-ADHD smokers. Alternative approaches for analyzing reaction time data from these tasks may further elucidate important group differences. Adults smoking ≥ 15 cigarettes with ($n = 12$) or without ($n = 14$) a diagnosis of ADHD completed a continuous performance task (CPT) during two sessions under two separate laboratory conditions—a 'Satiated' condition wherein participants smoked up to and during the session; and an 'Abstinent' condition, in which participants were abstinent overnight and during the session. Reaction time (RT) distributions from the CPT were modeled to fit an ex-Gaussian distribution. The indicator of central tendency for RT from the normal component of the RT distribution (μ) showed a main effect of Group (ADHD < Control) and a Group $\times$ Session interaction (ADHD group RTs decreased when abstinent). RT standard deviation for the normal component of the distribution (σ) showed no effects. The ex-Gaussian parameter τ , which describes the mean and standard deviation of the non-normal component of the distribution, showed significant effects of session (Abstinent > Satiated), Group $\times$ Session interaction (ADHD increased significantly under Abstinent condition compared to Control), and a trend toward a main effect of Group (ADHD > Control). Alternative approaches to analyzing RT data provide a more detailed description of the effects of smoking abstinence in ADHD and non-ADHD smokers and results differ from analyses using more traditional approaches. These findings have implications for understanding the neuropsychopharmacology of nicotine and nicotine withdrawal.

Keywords

ADHD; Smoking; Nicotine dependence; Reaction time; Neuropsychology

1. Introduction

Abstinence from cigarette smoking has been shown to disrupt a range of cognitive processes including attention (Gilbert et al., 2004), working memory (Mendrek et al., 2005), and response inhibition (Powell et al., 2004); and these changes have been hypothesized to increase the

Conflict of interest

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probability of smoking behavior because resumed smoking reverses these adverse effects (Heishman, 1998; Heishman et al., 1994).

Recently, we reported that cognitive processes, especially those associated with reaction time variability (reaction time standard deviation; RTSD), are more disrupted in smokers with ADHD following smoking abstinence, compared to non-ADHD smokers (McClernon et al., 2008). No effects of group or condition were observed for mean RT. However, both ADHD and non-ADHD smokers exhibited greater RT variability following overnight abstinence (main effect of condition); and RT variability increased significantly more during abstinence for the ADHD group (Group $\times$ Condition interaction). Since reaction time data are typically positively skewed, Gaussian summary statistics such as means and standard deviations, which are based on normal distributions, provide inaccurate estimates of central tendency and variability if values are distributed non-normally. Since the degree of skew may be exaggerated among individuals with ADHD (Hervey et al., 2006; Leth-Steensen et al., 2000), indicators that rely on a normal distribution may be inaccurately describing RT data among individuals with ADHD and excluding relevant information that may define ADHD performance. In turn, the manner in which smoking abstinence influences traditional measures of RT distributions may not accurately reflect the underlying psychopharmacological phenomenon.

An alternative approach for analyzing RT variability that takes into account this skew has been proposed in which the distribution of RTs are modeled using an ex-Gaussian curve (Leth-Steensen et al., 2000). The ex-Gaussian curve represents the sum of the independent Gaussian (normal) distribution and exponential random variables, the latter portion of which makes up the positive skew of the distribution curve (Burbeck and Luce, 1982). The ex-Gaussian distribution has three parameters: μ , the mean of the normal component; σ , the standard deviation of the normal component; and τ , a value describing both the mean and the standard deviation of the exponential component.

Based on this approach for describing RT distributions, it has been demonstrated that τ represents a more sensitive measure of RT variability in individuals with ADHD (Hervey et al., 2006; Leth-Steensen et al., 2000). In these studies, individuals with ADHD performed similarly to non-ADHD controls in terms of μ and σ but were highly discrepant from normal controls on the ex-Gaussian τ measure indicative of periodic, excessively long RTs (Leth-Steensen et al., 2000). Given that our previous findings reported on Gaussian indicators of RT, a more precise characterization of how smoking abstinence differentially affects RT using ex-Gaussian approaches is warranted. Such an approach may provide more detailed information on the neuropsychopharmacology of nicotine and nicotine withdrawal and how these differ in ADHD and non-ADHD smokers. The purpose of the present study, therefore, was to conduct a secondary analysis of previously published data to determine how smoking abstinence differentially affects ex-Gaussian parameters of reaction time distributions in smokers with and without ADHD.

2. Methods

Characteristics of the sample and details of the procedure have been published previously (McClernon et al., 2008). Briefly, smokers with ($n = 12$, mean age = 31.8 years, mean years of smoking = 13.3) and without ADHD ($n = 14$, mean age = 32.8, mean years of smoking = 14.8) and with no additional Axis I or II DSM-IV psychopathology completed a baseline session to familiarize them with the testing battery and environment. After the baseline sessions, participants attended two experimental sessions that differed only in that one was conducted after overnight abstinence (after 10 P.M.) from smoking (Abstinent condition) and the other was conducted after smoking as usual (Satiated condition). The order of conditions was randomly assigned and counterbalanced.

Sessions started between 7 and 9 A.M. During the Satiated condition, participants were permitted to smoke during breaks, while no smoking was permitted during the Abstinent condition. Smoking status was verified via salivary nicotine levels and expired air carbon monoxide (CO) levels. Saliva and breath samples were collected from all participants at each session.

Performance variables from the Conners Continuous Performance Test (Conners, 1994) were the primary outcome measures for the present analysis. The CPT was completed on an IBM-desktop computer in a quiet setting with minimal distractions. Three hundred sixty (360) total letters appeared on the computer screen, one at a time, each for approximately 250 ms. The 360 trials were presented in 18 blocks of 20 trials each. The blocks differed only in the interstimulus intervals (ISI) between letter presentations, which lasted 1, 2, or 4 s.

Participants were instructed to press the spacebar when any letter except the letter “X” appeared on the screen. The event rate, or percentage of trials when letters other than “X” appeared, was 90% across all ISI blocks. Reaction time was measured from the point at which any letter other than “X” appeared on the screen until the spacebar was depressed. Only successful non-“X” trials, or trials where the participant correctly pressed the spacebar when presented with a target stimulus were included for RT data analysis. The total Conners’ CPT task takes approximately 14 min to complete.

RTSYS 1.0 (Heathcote, 1996) is a DOS-based statistical program used for the analysis of RT data. The RTSYS program uses a theoretical distribution comprised of the combination of a Gaussian distribution in the initial or left side of the distribution curve, and an exponential distribution on the latter or right side of the distribution curve as a model of RT distribution. This type of distribution has been shown to create a better fit than traditional Gaussian distributions for RT (Luce, 1986). Specifically, it can more easily account for the positively skewed distribution commonly seen in reaction time data. This theoretical distribution, the ex-Gaussian, represents the sum of the independent Gaussian (normal) distribution and exponential random variables that comprise the positive skew of the curve. The ex-Gaussian distribution has three parameters: μ , the mean of the normal component; σ , the standard deviation of the normal component; and τ , a single value that describes both the mean and the standard deviation of the exponential component. The parameters of μ and τ share a linear additive relationship such that their sum equals the overall mean of the distribution. The τ component characterizes the positive skewness of the distribution. The RTSYS program uses each RT response recorded for successful Go trials during the CPT administration for each participant to calculate μ , σ , and τ for each individual.

Distributions were censored for excessively fast RTs, which are thought to occur through anticipation (Ulrich and Miller, 1994). It has been demonstrated that the non-decision portion of simple reaction time is at least 100 ms (Luce, 1986). As such, any responses that occurred less than 100 ms following presentation of a stimulus were omitted from analysis. RTSYS interprets any converged value of σ or τ less than $\text{mean}/100$ as indicating a failure and sets all ex-Gaussian parameters as missing.

Probability density plots for all RTs were generated using the kernel estimation procedures in Stata. To illustrate Group and Condition differences, these functions were estimated separately by group for each condition (Satiated vs. Deprived) and for short (<600ms) and long (>600ms) RTs. Mean data for each of the distributional parameters were analyzed using two way mixed-model ANOVA with group (ADHD vs. non-ADHD) as the between subjects factor and condition (Abstinence vs. Satiated) as the within subjects factor.

3. Results

CO levels were consistent with overnight abstinence with mean CO (ppm) levels of 10.64 and 12.50 for control and ADHD groups, respectively. On the Satiated day, mean CO levels were 29.86 and 32.92 in the control and ADHD groups, respectively. Results of salivary nicotine analyses were consistent with CO levels. On the Abstinent day, mean salivary nicotine levels (ng/ml) were 17.14 and 0.42 for control and ADHD groups, respectively. On the Satiated day, salivary nicotine levels were 531.30 and 584.81 for the control and ADHD groups, respectively. For both CO and salivary nicotine, there were main effects for condition (F -values = 27.99–53.63, $p < 0.001$), but no main effect for group and no Condition $\times$ Group interaction (McClernon et al., 2008).

Significant main effects of group were observed for μ , the parameter representing central tendency of RT for the Gaussian component of the distribution ($F = 7.76$; $p < 0.01$). Smokers with ADHD exhibited faster RTs under both conditions compared to the non-ADHD smokers. Fig. 1a illustrates these findings. For σ , the indicator of variance for the Gaussian component of the RT distribution, there were no main effects of group or condition. There was a trend ($p = 0.053$) for a significant Group $\times$ Condition interaction for the σ variable (Fig. 1b). For the τ indicator, there was a significant main effect for group ($F = 5.64$; $p < 0.05$), a significant main effect for condition ($F = 15.16$; $p < 0.001$), and a significant Group $\times$ Condition interaction ($F = 9.90$; $p < 0.01$). The ADHD group showed significantly higher values of τ compared to the control group and both groups showed an increase in τ under Abstinent conditions. The extent of the change in τ in the Abstinent condition was greater for the ADHD group (Fig. 1c).

Fig. 2 illustrates probability density plots for RTs under each condition and further illustrates the findings from Fig. 1. As can be seen, in the normal component of the distribution, represented in the top two panels, RTs for the ADHD group were faster (shown by a leftward shift in the distribution). For the exponential component of the distribution, shown in the bottom two panels, the ADHD group exhibited a higher probability of exhibiting very long RTs and this tendency was exacerbated when Deprived (Abstinent). In fact, in the Deprived condition, the proportion of long RTs (>1000 ms) was more than five times greater for the ADHD group compared to the control group (.027 vs. .005, respectively; data not shown).

4. Discussion

These findings extend our previous work and more precisely characterize both the effects of smoking abstinence on RT variability; and group differences between smokers with and without ADHD. Our previous study reported that, using traditional Gaussian measures of reaction time variability and central tendency, that abstinence increased reaction time variability across groups. Also, smokers with ADHD showed non-significant but *slower* mean reaction times across conditions. The present findings indicate that ADHD smokers actually exhibit significantly *faster* reaction times in the Gaussian component of the RT distribution (μ) (see Fig. 2) and that there are no significant differences between the ADHD and non-ADHD groups with respect to the effects of smoking abstinence on RT variability in the Gaussian component of the distribution. Examination of the ex-Gaussian component of the distribution, however, reveals significant effects of both group and state on τ , as well as a significant Group $\times$ Condition interaction.

Several limitations are worth noting. Due to the small sample size of this study, our findings should be regarded as preliminary. Also, the ex-Gaussian approach to characterizing reaction time data may not be as precise as other more flexible approaches that are available in standard statistical packages. It is worth noting that we selected the ex-Gaussian approach primarily on

the basis of its demonstrated ability to distinguish individuals with ADHD from those without the disorder. In spite of these limitations, several interesting interpretations can be offered.

One interpretation of these findings is that the increase in tau does not signify an overall increase in RT variability but rather indicates a pattern of relatively typical RT variability with periodic excessively long RT trials interspersed. These long RT trials have been hypothesized to be the occasions where individuals with ADHD demonstrate attentional lapses (Hervey et al., 2006; Leth-Steensen et al., 2000). If this interpretation is correct, it would help to more accurately characterize the effects of smoking abstinence on cognitive functioning in both ADHD and non-ADHD individuals. In other words, nicotine abstinence may increase the likelihood of attentional lapses (measured as periodic long and variable RTs) in both ADHD and non-ADHD smokers, but to a greater degree in those with ADHD.

Nicotine addiction and ADHD share common neural circuitry (McClernon and Kollins, 2008) and future studies can clarify the neural underpinnings of abstinence-induced deficits in attentional functioning among smokers with ADHD. Decreases in brain activation in dorsal anterior cingulate gyrus (dACG) have been associated with attentional lapses (Weissman et al., 2006) and individuals with ADHD have been shown to lack normal, anti-correlated activation between this region and brain areas involved in non-goal directed cognition (i.e., default mode network) (Castellanos et al., 2008). Thus, we would hypothesize that smoking abstinence disrupts dACG activation and connectivity to a greater degree in ADHD smokers which may account for their more frequent attentional lapses. This hypothesis could be tested using fMRI methods and demonstrates the usefulness of the ex-Gaussian approach taken here in terms of generating new perspectives on cognitive performance.

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Fig. 1.

Mean and standard error for reaction time distribution components by group and condition. (a) Values for mu, the mean of the normal component of the RT distribution. (b) Values for sigma, the standard deviation of the normal component of the RT distribution. (c) Values for tau, a parameter describing the ex-Gaussian (skew) component of the RT distribution. F -values for main effects and interactions are presented for each component.

Fig. 2.

Probability density plots for RTs. Top panels represent (from left to right) distributions for short RTs (<600 ms) for Satiated and Deprived conditions, respectively. Bottom panels represent (from left to right) distributions for long RTs (>600ms) for Satiated and Deprived conditions, respectively. See text for additional details.