Event-Related Potentials as an Index of the Attentional Effects of Nicotine

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April 2005
Abstract

Evidence indicates that, in addition to habitual and social factors, smokers are motivated to use nicotine because of increased attention, weight maintenance, and relaxation. To investigate the relationship between nicotine use and enhanced attention, the electroencephalogram (EEG) was used within a double-blind, placebo-controlled design. Accordingly, either nicotine gum or a placebo was randomly administered to smokers in each of their two testing sessions. EEG and event-related potential (ERP) data was collected while participants first, viewed a movie with the sound turned off while auditory tones were presented via headphones and subsequently, while responding to rare stimuli from the same series of tones. The amplitudes and latencies of the P3a, P3b and MMN components were of specific interest. It was expected that earlier latencies and larger amplitudes for both the P3b and MMN waves would provide evidence for facilitation of nicotine on the attentional process.

Event-Related Potentials as an Index for the Attentional Effects of Nicotine

Attention involves focusing awareness on a narrow range of stimuli or events. In a way, attention works as a filter, in that it screens out irrelevant information and allows a select amount of stimuli to enter our conscious awareness. Problems with attention constitute a vital field of study because they are found in varying intensities in the entire population. These attentional deficits are especially prominent in those with behavioural disorders, particularly Attention Deficit Hyperactivity Disorder and Tourette’s syndrome.

If stimuli are to be remembered or learned from, it is almost always necessary to pay attention to them. Thus, the attentional process either directly or indirectly influences most aspects of cognitive functioning (Samuels & Davis, 1998; Stanhope, McLenaghan & Dourish, 1995). Various attempts at improving attention, and in turn, cognitive functioning, have been made. Several of these studies have included the use of pharmacology, especially nicotine. Nicotine administration or smoking has been found to result in cognitive enhancements in a variety of studies (for a review see Pritchard, Sokhadze & Houlihan, 2004). Consistent with these investigations, this study will explore the effects of nicotine on attention. It is expected that upon administration of nicotine attention will be enhanced and cognitive function will be augmented.

Attention appears to be essential to our innate ability to perceive, think and
behave. Even in the early writings of James (1920), he suggests that several varieties of attention are necessary to our human existence. Selective attention, divided attention, pattern recognition, sustained attention and visual search are the varieties that James (1920) contrasts and many other researchers have proposed others. For the purpose of this study, selective attention and sustained attention are of specific interest. Selective attention, according to Tecce (1972), is a process that allows an individual to select relevant information from an environment and to ignore irrelevant information. Therefore, selective attention implies that one stimulus is attended to while others are ignored. Sustained attention/vigilance requires one to focus his/her attention on a selected stimulus for an extended period of time.

Selective and sustained attentional processes are modulated by the cholinergic system (Mirza & Stolerman, 2000). Within this system there are two distinct types of receptors, muscarinic receptors and nicotinic receptors. Nicotinic receptors play a central role in the early processing of stimulus evaluation and are activated by acetylcholine (Mirza & Stolerman, 2000). Woods, Alho and Algazi (1992) suggest that attention affects early cognitive processes by filtering irrelevant sensory information. Therefore, nicotinic receptors may be a vital component in the modulation of attention.

Nicotine is a naturally occurring substance that improves cognitive functioning by mimicking the effects of acetylcholine on nicotinic receptors (Howson et al, 2004; Engeland, Mahoney, Mohr, Ilivitsky & Knott, 2002; Houlihan, Pritchard, Guy & Robinson, 2002). The most commonly reported improvements after smoking/nicotine administration have included faster reaction times (RT) and improved accuracy (for reviews see Pritchard et al, 2004; Sherwood, 1993; Heishman, 1998).

Nicotine is the principal psychoactive chemical in tobacco and acts as a central nervous system stimulant. Therefore, when studying the effects of nicotine on cognitive processes, cigarette smokers are generally recruited as subjects. Studying a population of non-smokers is usually avoided due to the possibility of side effects such as nausea or headaches. Upon repeated exposure to nicotine, smokers develop a tolerance to many of the negative side effects of nicotine that naïve persons do not. Thus, regular smokers are usually preferred to naïve participants when studying the cognitive effects of nicotine.

There are a number of considerations that must be made when testing a population of only smokers. This includes developing a control group that can manage individual differences in smoking style and behaviour, the differing amount of nicotine inhalation when smoking and lifestyle choices made by smokers as opposed to non-smokers. Many studies that test only a smoking population deal with these issues of individual differences by requiring participants to abstain from nicotine overnight (Trimmel & Wittberger, 2004; Houlihan, Pritchard, Guy & Robinson, 2002). This method however, precipitates new problems in that deprivation from nicotine may cause participants to experience withdrawal symptoms. Nicotine deprivation can result in the deterioration of cognitive abilities (for a review see Heishman, 1998). Additionally, deprivation followed by an acute administration of nicotine can result in the participant showing a dramatic improvement in cognitive ability. This improvement may be due to a direct effect of nicotine (facilitation) but may also be the result of relief from withdrawal. It is therefore, very difficult to determine if nicotine facilitation
is the result of true effects of nicotine on the cognitive process. Heishman (1998) suggests that true enhancement is most clearly demonstrated in non-smokers or regular smokers that are not deprived of nicotine. When testing a smoking population, it is possible to minimize the impact of withdrawal by testing a participant no more than thirty minutes post-nicotine administration (Pritchard, 1989). Under these testing circumstances, the participant is referred to as minimally deprived. Studies that used minimally deprived smokers as participants suggest that improvements in accuracy and reaction time are the result of an increase in attention (Jacobson, D’Souza, Mencel, Pugh, Skudlarski & Krystal, 2004a; Trimmel & Wittberger, 2004; Rezvani & Levin, 2001).

Improvements in attention are frequently tested with Conner’s Computerized Continual Performance Task (Rezvani & Levin, 2001; White & Levin, 1999). This test measures attention in both adults and children by counting errors of commission (responding when inappropriate) and errors of omission (failing to respond when appropriate). Errors of omission correspond to attentional lapses and prolonged response times, which are consistent with problems regarding sustained attention. Rezvani and Levin (2001) tested the effectiveness of nicotine on non-smokers by measuring performance on Conner’s CPT. They found that nicotine, unlike a placebo, significantly reduced the number of errors of omission, thus suggesting that nicotine improved sustained attention.

Conner’s CPT, in conjunction with other methods, has also been used as a diagnostic tool to determine attentional capacity in suspected ADHD cases (Nichols & Waschbusch, 2004). In addition, Wilens et al (1999) employed Conner’s CPT to measure the effects of nicotine on attentional modulation in ADHD patients. Following nicotine administration, patients were more able to focus and sustain their attention and as a result, regulate their behavior. Using similar methods, Levin, Conner, Keith and Silva (1998a) also demonstrated the attentional enhancements subtended by nicotine in ADHD patients.

Nicotine administration has also been shown to help Tourette’s syndrome patients in alleviating attentional deficits (Howson et al, 2004; Silver, Shytle, Philipp, Wilkinson, McConville & Sanberg, 2001). Howson et al (2004) administered nicotine to children via a transdermal nicotine patch and found that it not only increased control over tic symptoms but also helped attenuate the behavioural and emotional symptoms that are frequently associated with Tourette’s. In this study, self-reports and parental ratings also indicated that problems with attention were lessened. Nicotine was also administered by transdermal patch in Silver et al (2001). This study found that nicotine, as compared to a placebo, alleviated emotional and behavioural symptoms, which only then allowed increased control over tics. Resulting from these inquiries involving ADHD and Tourette’s populations, Health Canada has approved a low-dose transdermal patch to be used in children and adults with these disorders (Howson et al, 2004).

The most promising method implicated in the investigation of nicotine’s effect on cognitive function uses event-related potentials (ERPs) in addition to RT. ERPs represent the changes in neural activity that result from the presentation of stimuli. They are derived from the electroencephalogram (EEG) and can be time-locked to the stimuli that are presented. Analysis of the polarity, amplitude, latency and scalp distribution of ERP waves allow the isolation of actual neuroelectric brain responses to stimuli. Specifically, ERP
analysis represents a reliable way of examining the brain activity related to attention (for a review see Pritchard, Sokhadze & Houlihan, 2004).

Nicotine improved reaction time (RT) in a variety of studies that used ERPs to investigate short-term memory, response preparation and response selection (Houlihan, Pritchard & Robinson, 1996; 1999; 2001; Ilan & Polich, 1999). While RT is shortened after nicotine administration, there is no indication that short-term memory is accessed more rapidly. Instead, it is suggested that nicotine may improve RT by enhancing other cognitive processes, specifically, attention (Houlihan et al, 2001). Those that have directly examined attention with ERPs have done so by examining the P300 component.

A relatively novel approach to exploring the role of nicotine on attention involves the mismatch negativity (MMN) component. The MMN is an event-related potential that reflects the brain’s response to any discriminable change in a series of repetitive auditory stimuli. Therefore, the MMN is generated when a deviant tone is heard in a series of standard tones. The deviant tone can differ from the standard tone in frequency, amplitude, intensity, duration or any combination of these. Any physical deviance in the stream of auditory stimuli will elicit an MMN, regardless of attention to the stimuli. Therefore, the MMN component is elicited even in the absence of attention and is thus considered preattentive (Jacobsen, Schroger & Alter, 2004b; Naatanen, 2000; 2003; 2004).

The only study that has measured the effects of nicotine on the MMN was done by Engeland et al (2002). This investigation measured nicotine’s effect on memory in Alzheimer’s disease (AD) patients by administering it via a transdermal patch. Memory was measured by manipulating the inter-stimulus interval (time elapsed between the onset of one stimuli to the onset of the next) and by using the MMN as a dependent measure. With nicotine, it was asserted that sensory memory lasted longer than with a placebo. These preliminary findings are significant to AD patients because the ability to encode information into short- and long-term memory is directly related to sensory memory capabilities. It is also significant because it illustrates the effectiveness of the MMN component in studying cognitive processes.

The P300 component has been used to explore the effects of nicotine on cognitive processes as well (for a review see Pritchard et al, 2004). The P300 is characterized by a positive wave over the parietal area that peaks approximately 300 ms after the onset of an attended rare stimulus in a series of standards. The amplitude of the P300 is inversely related to the probability of the rare stimuli. Thus, when listening to a series of tones, the amplitude of the P300 will be greatest in response to rare stimuli (Pritchard, 1989). Extremely deviant rare stimuli that is attended to will result in a component called P3a. This is an aspect of the P300 but is typically seen earlier (shortened latency) and is usually more frontally distributed. Generally, the P3a is understood to represent a shift in the focus of attention in response to extremely different stimuli but does not require further processing. The element that distinguishes the P300 and the P3a from the MMN is attention. A rare stimulus will elicit a P300 only in the presence of attention whereas a MMN can be elicited without attention. Because of this difference, the time-course of stimulus processing to attended stimuli (P300 and P3a) will be compared to that of unattended stimuli (MMN) in this study. It is expected that the differences found between these groups will reveal relevant information
about the sequence of stimulus processing when attention is manipulated.

In this study, factors of amplitude, latency and location of elicitation of the MMN, P300 and P3a will be used as measures of the attentional processes of regular smokers. Two conditions will be used in this study, one that asks the participant to ignore a sequence of auditory stimuli and one that asks the participant to attend to the sequence. The P300 and P3a will be present in the attend condition only while the MMN should be present in both conditions. Under the influence of nicotine, it is expected that the latency of the MMN, P300 and P3a will be shortened in the attend condition. Overall, it is expected that ERP data will show that nicotine improves sustained and selective attention. This will be interpreted if components appear sooner, with larger amplitudes and in some cases, such as with the P3a, if components do not appear at all.

Method

Participants

Nine St. Thomas University undergraduate students (2 male) ranging in age from 19 to 28 (mean 21.88 years) participated in this study. They were recruited via email invitation according to their response on a previously administered Internet based survey on smoking behavior and personality. Participants were contacted only if they reported smoking at least ten cigarettes per day for a minimum of two years and gave permission to be contacted regarding possible participation in future studies.

Participation was entirely voluntary and all participants were notified that they were free to withdraw at any time without penalty. They were compensated with course credit where applicable. They each participated in two separate testing sessions where after providing written consent (see appendix A), they were asked to complete a confidential self-report health questionnaire (see appendix B). Participants who reported an underlying neurological disorder, the use of central nervous system altering medications, or a hearing impairment were excluded from testing as these conditions could impair the resulting ERPs.

EEG Recording

EEG was recorded using a Neuroscan NuAmps amplifier. Recordings were from 38 Sn electrodes embedded in an electrode cap that follows an extended 10-20 International system (American Electroencephalographic Society, 1991). The electrodes in the cap were referenced to the tip of the nose and an electrode was placed just above the clavicle to record heart rate. Vertical EOG was recorded from electrodes placed above and below the left eye and horizontal EOG was recorded from electrodes placed to the outer side of each eye. The ground electrode was embedded in the electrode cap and was located between the FPz and Fz electrodes. Data was recorded at a sampling rate of 500 Hz. According to standard EEG recording techniques (Picton et al, 2000) testing took place in a dark, sound-attenuated room, where the participant sat in a comfortable chair with a set of headphones over his/her ears.

Experimental Design

This study employed a double-blind experimental technique. Thus, each participant was required to report for testing on two separate occasions. Participants were randomly assigned either nicotine or
placebo gum for their first session and the opposite administration in their second. The nicotine gum and placebo were similar in size, flavour and appearance and the administration order was kept secret until after all data collection and ERP scoring had been completed.

*Nicotine Gum and Proper Chewing Technique*

Nicotine was administered orally in the form of 4-mg nicotine polacrilex (gum). The 4 mg dose was chosen because it has been shown to be most effective in eliciting performance effects in research populations of regular smokers (Sherwood, 1993). The placebo gum was also administered orally but did not contain nicotine. The nicotine and placebo gum were both coated with one drop of Tabasco sauce and wrapped in a piece of Juicy Fruit gum. The drop of Tabasco sauce was used to mimic the heat of nicotine in the placebo gum (Sherwood, Kerr & Hindmarch, 1991) and the Juicy Fruit was used to mask any remaining flavour differences.

A standard chewing technique of one bite per thirty seconds for twenty minutes (Hindmarch, Kerr & Sherwood, 1990) was used to ensure that the nicotine was absorbed similarly between participants and in a controlled fashion. The chewing instructions were clearly explained to all participants. Auditory tones were also played to remind the participants to chew at according to the prescribed schedule. Before the chewing process began, participants were connected to the EEG. This allowed the investigator to observe the EEG recordings and ensure that the chewing was compliant with the technique (high frequency waves are extremely evident when jaw muscles are activated).

*Tasks and Stimuli*

This study involved the completion of two simple tasks. In both tasks, a series of four hundred auditory tones were presented through a set of headphones. Each tone was 100 ms in duration, had a 10 ms rise/fall time and an SOA of 1 sec. Within this paradigm, standard tones (1000 Hz) were presented with an 80% probability. Slightly deviant tones (1128 Hz) and highly deviant tones (2000 Hz) were also presented, each with a 10% probability. All tones were presented in pseudorandom order so that at least two standard tones occurred between each deviant.

In the first task (passive attention), the participant watched a movie with the sound turned off and was instructed to ignore the auditory stimuli. In the second task (active attention), the participant did not see the movie but instead was asked to respond to the slightly deviant tone by pressing a button on a response pad. During this second task, instructions emphasized response speed but also highlighted the importance of accuracy.

*Procedure*

After providing consent, the participant was asked to exit the building to smoke one of his/her own cigarettes. This was done to create a timing baseline of when nicotine was last used for all participants. This precaution also made certain that deprivation effects did not confound the data (Hindmarch et al, 1990). After smoking, the participant was asked to complete a health questionnaire and a mood questionnaire (see Appendix C). The mood questionnaire contained questions related to affect and also the possible side effects of nicotine. Following the completion of the questionnaires, he/she was prepared for EEG recording.

Forty-five minutes after smoking the cigarette, the half-life of nicotine, the participant was given a piece of gum to chew according to specific instructions. He/she chewed the gum for a total of twenty minutes, until the nicotine should have reached peak levels in the body (Hindmarch
et al, 1990; Phillips & Fox, 1998). As a result, EEG recording did not begin until after the nicotine from the gum had reached peak levels in the participant’s brain.

After completing the passive component of the testing session, the participant completed the mood questionnaire again and was asked about any physiological side effects he/she may have been experiencing. Subsequently, he/she completed the active task and filled out the mood questionnaire for a third and final time. The entire recording session took, on average, thirty minutes. This indicates that the nicotine from the gum should not have reached its half-life before the end of the testing procedures (Sherwood et al, 1991).

Upon completion of the recording session, the investigator explained the study to the participant and gave him/her a debriefing sheet that summarized the experiment (see Appendix D for debriefing form and Figure 1 for a visual representation of the timeline of the procedure).

Data Analysis

Data from two participants was excluded from analysis. One participant failed to complete the study, as she was experiencing heat discomfort. This subjective experience of being extremely warm may have been a side effect of the nicotine but it may also have simply been due to the high temperature of the recording room. The other participant, whose data was excluded, responded to an incorrect deviant tone during the active task.

For the remaining participants, EOG reduction was conducted on the continuous EEG using a Neuroscan regression-based algorithm. EEG recordings were epoched from 50 ms pre-stimulus to 700 ms post-stimulus. Trials containing residual EEG that exceeded ± 75 µV were not included in the averaging process. Artefact-free averages were computed for each LOCUS (electrode location), DRUG (nicotine gum and placebo gum), TASK (active/attend and passive/non-attend) and DEVIANCE (highly deviant, slightly deviant and standard).

The N100 component was analyzed for each average at six electrode locations (F3, Fz, F4, FC3, FCz and F4). Peak amplitudes and latencies were computed at these sites within the latency window of 75ms to 150ms. Repeated measures analyses of variance (ANOVA) were computed for the factors of DRUG (nicotine vs placebo), TASK (attend vs non-attend), DEVIANCE (standard, slight and extreme) and LOCUS.

The P3a component was analyzed for the averages collected during the active task and only for the extremely deviant tones. Peak amplitudes and latencies for three electrodes (F3, Fz and F4) were included in the ANOVAs that examined the relationship between DRUG (nicotine vs placebo) and LOCUS. The latency window used for the P3a component (200ms to 350ms) was earlier than that used for the P3b (300ms to 500ms).

The P3b component is generally more pronounced over the parietal lobe, thus the P3, Pz and P4 electrodes were the only electrode locations included in this analysis. The ANOVA used for the P3b component included only the averages for the targets (active condition, slightly deviant) and compared DRUG (nicotine vs placebo) and LOCUS.

MMNs were also computed by subtracting the slightly deviant wave from the standard wave and the extremely deviant wave from the standard wave. The peak amplitudes of the MMNs were labeled at the maximum negative voltage found within the latency window of 100 ms to 250 ms post-stimulus. ANOVAs were also computed for this component over nine electrode locations (F3, Fz, F4, FC3, FCz, FC4, C3, Cz and C4) and took into consideration DRUG (nicotine
vs placebo), TASK (active vs passive), DEVIANCE (slight vs extreme only) and LOCUS.

In addition to ERP analysis, response time (RT) and accuracy data were analyzed across all participants for the active attention task in which participants were asked to respond to a target (slightly deviant tone). These factors were analyzed using paired t-tests to determine whether nicotine significantly affected behavioral performance. As well, each question on the mood questionnaires was analyzed across DRUG and TIME conditions with a repeated measures ANOVA.

**Results**

*Mood Questionnaire*

The mood questionnaire was scored according to the placement of an ‘X’ along a line that measured 10 centimetres. Subsequent analyses of the responses on these mood questionnaires indicate that only the question pertaining to relaxation state was significantly affected by nicotine ($M_{nicotine}=6$, $M_{placebo}=7$). Of the other nine questions (see Appendix C), none were significantly affected by DRUG.

*Behavioral Data*

**Response Accuracy.**

Accuracy of response to the target tone during the active attention task was not significantly affected by DRUG. The mean accuracy in the nicotine condition was 84.5 (out of 96). The mean accuracy in the placebo condition was 84.2 (out of 96).

**Reaction Time.**

Analysis of RT data indicates that nicotine did not facilitate response selection. In fact, the mean RT time for the nicotine condition ($M=496$ ms) was longer than for the placebo condition ($M=464$ ms).

*Event-Related Potentials*

**N100 Component.**

A main effect of LOCUS on N100 latency was found $F(5,20)=6.613$, $p=0.021$, $\varepsilon=0.3954$. The latencies were earliest for FC3 at $M=108$ ms and FCz at $M=109$ ms (see Table 1 for complete list of latencies). Also for latency, an interaction effect was found between the factors of TASK and DEVIANCE $F(2,8)=8.557$, $p=0.028$, $\varepsilon=0.6507$ (Figure 2 & Figure 3). Subsequent post hoc analysis of this interaction indicated that the main effect for latency was in the active attention task $F(2,8)=5.487$, $p=0.042$, $\varepsilon=0.842$. The latency for the extremely deviant tones ($M=104$ ms) was earlier than that for the slightly deviant ($M=114$) and the standard tones ($M=111$ ms).

Also, another interaction effect on latency of the N100 was found between the factors of TASK and DRUG $F(1,4)=7.964$, $p=0.048$ (Figure 4). However, post hoc analysis of this relationship failed to establish any main effects between any of these four variables. This failure to find any main effects is most likely the result of very small differences between the means for each of the variables.

A main effect of LOCUS on N100 amplitude was found $F(5,20)=4.271$, $p=0.034$, $\varepsilon=0.5501$. The amplitudes for the N100 were largest for Fz at $M=4.604$ µV, FC3 at $M=4.603$ µV and FCz at $M=4.604$ µV (see Table 1 for complete list of amplitudes). Also for amplitude, an interaction was found between the factors of TASK and DEVIANCE $F(5,20)=4.271$, $p=0.034$, $\varepsilon=0.5501$ (Figure 5). Subsequent post hoc analysis of this interaction indicated that the main effect was for the passive attention task $F(2,8)=10.173$, $p=0.006$, $\varepsilon=0.773$. Within the passive attention task, the extremely deviant tones
elicited a larger amplitude (M=-5.117) than the slightly deviant (M=-3.254) and standard tones (M=-2.601).

**MMN Component.**

Analysis of the MMN component showed a main effect of DEVIANCE on latency $F(1,6)=11.615$, $p=0.014$ (Figure 6 & Figure 7). The MMN latency for the slightly deviant tones had a mean value of 219 ms while the latency for the extremely deviant tones was significantly earlier (M= 190 ms).

Similarly, analysis showed a main effect of DEVIANCE on amplitude $F(1,6)=9.704$, $p=0.021$ (Figure 7 & Figure 8) as well. The MMN amplitudes for the slightly deviant tones were on average -5.471µV while the mean amplitudes for the extremely deviant tones were smaller (M= -3.627 µV). Another main effect was found confirming that TASK had an effect on the amplitude of the MMN component $F(1,6)=6.076$, $p=0.049$ (Figure 9). The MMN amplitude was larger for the active task (M= -4.92 µV) than it was for the passive task (M= -4.178 µV).

An interaction effect was also found for the MMN amplitude between DEVIANCE and DRUG $F(8,48)=21.360$, $p=0.004$ (Figure 10 & Figure 11). Post hoc analysis investigating this interaction indicated that there was both a main effect of DEVIANCE on the amplitude of the MMN within the nicotine condition $F(1,6)=34.558$, $p=0.001$ and of DRUG on the amplitude of the MMNs for the extremely deviant tones $F(1,6)=7.689$, $p=0.032$. For the DEVIANCE effect, the mean amplitude for the extremely deviant tones was -5.617µV, which was significantly larger than the mean amplitude for the slightly deviant tones (M= -3.684µV). For the DRUG effect, the mean amplitude within the nicotine condition for the extremely deviant tones (M= -5.617µV) was larger than within the placebo condition (M= -4.223µV).

**P300 Components.**

A main effect of LOCUS of P3a latency was found $F(2,10)=6.084$, $p=0.03$, $\varepsilon=0.7773$. The P3a latencies were 305 ms at F3, 307 ms at Fz and 310 ms at F4. No other significant effects were found for this component.

The P3b component was analyzed over the three parietal electrodes and a main latency effect of DRUG was found $F(1,6)=5.882$, $p=0.05$ (Figure 12 & Figure 13). As compared to placebo administration (M= 390 ms), the latency of the P3b with nicotine administration was earlier (M= 374 ms). There were no other significant effects were found for this component.

Discussion

The purpose of this study was to examine various ERPs to investigate the attentional effects of nicotine. The results of this investigation suggest that nicotine may facilitate the attentional process in three very different ways. Firstly, enhanced amplitudes found for the MMN component indicate that attention may be facilitated by improvements in sensory memory storage. Secondly, though nicotine did not shorten the latency or heighten the amplitude of the P3a component, this effect may still indicate that the vigilance type of attention (James, 1920) was improved with nicotine administration. Thirdly, nicotine also appeared to significantly improve the latency of the P3b, which is implicated in stimulus evaluation. Each of these improvements will be discussed in more detail.

The MMN component reflects automatic sensory memory storage. It is also one of the earliest ERPs that measure
the brain responses involved in the attentional process, especially the switching of attention to novel stimuli in the environment (Naatanen, 2000). In an auditory modality, whenever a tone is heard, its physical characteristics are stored in sensory memory for a short period of time. The characteristics of all subsequent tones are compared against those that are stored in sensory memory. The MMN is elicited whenever the brain detects a difference between the characteristics of the current tone and that which is stored in memory. As such, the amplitude of the MMN is considered a reflection of how well the physical characteristics of the tones are held in sensory memory storage.

In this study, nicotine administration enhanced the amplitude of the MMN. Therefore, it appears that with nicotine, participants were more able to store information in sensory memory. Therefore, they were more able to access that information when it was needed. Similar results were found by Engeland et al (2002), however there were many important differences between that study and the one that is currently being discussed. Engeland et al (2002) was interested in investigating how nicotine could alleviate some of the memory-related symptoms involved in Alzheimer’s Disease (AD). Therefore, they only included participants who were diagnosed with AD and interestingly, only those who were not regular smokers. Additionally, route of nicotine administration differed as Engeland et al (2002) administered nicotine via a transdermal nicotine patch. Regardless of these differences, many of the same effects of nicotine on the MMN component (mainly increased amplitude) were observed in both studies, suggesting that nicotine may be beneficial to not only clinical populations, but also a general population.

In addition to the sensory memory enhancements, this study also indicates that nicotine administration promoted performance on a vigilance task. The P3a component is elicited when a stimulus is so novel that it demands attention and draws concentration away from a narrow range of stimuli. Thus, in effect, the P3a denotes a participant becoming distracted by a novel stimulus. Due to the properties of this component, the fact that nicotine did not significantly affect the P3a may indicate that it acted as a protective factor against probable distraction. As a result, it is possible that nicotine makes a person more able to focus his/her attention, thus improving attentional capacity in a way that was not previously expected. These results are consistent with much of the literature, which finds that nicotine administration does not impact the latency or the amplitude of the P3a. In addition, Haarar and Polich (2000, as cited in Pritchard et al, 2004) actually found that the amplitude of the P3a was smaller with nicotine, which even further suggests that the drug may act as a protective factor against attentional distraction.

This may explain nicotine administration’s paradoxical effect on ADHD and Tourette’s patients (Howson et al, 2004; Silver et al, 2001). Since nicotine is a stimulant drug, it is counterintuitive that it would ‘calm’ people with these types of disorders. However, the results of this study indicate that it is possible that ADHD and Tourette’s symptoms are alleviated with nicotine by allowing the patients to better focus their attention on the tasks at hand and less apt to become distracted by novel events. This effect of nicotine is extremely beneficial for these types of people; however, the effect may not be desirable for other groups. For example, a reduced sensitivity to novel events would not be helpful for such occupations as an air traffic
controller or security guard. Thus, the effect of nicotine on the P3a component suggests that its use may be efficacious for some groups of people but relatively dangerous for others.

The other main effect of nicotine administration that was observed in this study is evidenced by the earlier P3b latencies that were found. The P3b component is elicited when a participant is asked to intently listen for a rare stimulus in a stream of standards. Thus, when a person is paying attention to a stream of stimuli, the P3b is found at the point in time where he/she becomes consciously aware that they perceived the meaningful stimulus. As such, the P3b component is often thought to reflect stimulus evaluation and possibly awareness of deviance.

In this study, the latency of the P3b in response to targets (slight deviance in the active attention task) was significantly earlier with nicotine administration. This effect is consistent with many other studies that have looked at the effects of nicotine on the P3b (Pritchard et al, 2004; Woods et al, 1992). While this appears to suggest that the stimulus evaluation and recognition phase of responding to the target tones was executed more quickly for the nicotine condition than the placebo condition, it cannot be conclusively determined. This is because a question is raised when looking at the P3b and RT data together. Theoretically, if the P3b happens earlier, then the RT should also be earlier. This is because a relatively standard amount of time elapses between stimulus evaluation and response execution. This was not the case with the results found in this study. Though P3b latency was shortened, this effect seemed to be absorbed in the time frame between stimulus evaluation and response execution. Therefore, it appears that some other process between these two phases required more time with nicotine administration than is normally required (placebo administration). It is possible that with nicotine, though participants are able to recognize the meaningful stimulus more quickly, they are less impulsive to press the response button and to commit to response execution. However, this effect may be the result of having a small sample size and thus, reduced power. A larger sample size in future studies may cause this lack of RT effect to reverse.

Regardless of the small sample size that was used in this study, the results found imply that nicotine administration has a significant impact on the attentional process. Many literature reviews pertaining to the cognitive effects of nicotine have agreed that it appears to improve performance on a variety of tasks. However, there has been much debate over whether these effects are the result of true nicotine enhancement or simply relief from the withdrawal state that many nicotine studies induce (Pritchard et al, 2004; Pritchard, Robinson & Guy, 1992, Heishman, 1998; Wasnes & Warburton, 1983). Importantly, the current study eliminated this problem, as it did not require a period of abstinence from the drug. As such, there can be little debate over whether the effects of nicotine in this study indicate true attentional enhancement.

The implications of this study are widespread. Not only did the results confirm many of the initial hypotheses, but they also confirmed the results of several other clinically motivated studies (Howson et al, 2004; Engeland et al, 2002). As this investigation was focussed on a general population of regular smokers, the results suggest that nicotine’s facilitation of attention can be generalized beyond clinical populations of Alzheimer’s, ADHD and Tourette’s patients onto a more normal population. Additionally, as this study used only minimally deprived participants, it can be concluded that the results found are
attributable to a true nicotine enhancement rather than simply the relief of nicotine withdrawal.

References

Attention and Nicotine


Figure 1

**Timeline of Events for Testing Session**

1. Informed Consent (beginning of session)
2. Smoking of one cigarette
3. Health and Mood Questionnaire
4. EEG preparation
5. Gum chewing
6. EEG Recording
   a. Attend task
   b. Mood Questionnaire
   c. Non-Attend Task
7. Mood Questionnaire
8. Debriefing
9. End of session
Figure 2

*N100 Latency – DEVIANCE/TASK Interaction Bar Graph*
Figure 3

*N100 Latency – DEVIANCE/TASK Interaction Grand Average*
Figure 4

*N100 Latency – DRUG/TASK Interaction Bar Graph*
Figure 5

*N100 Amplitude – DEVIANCE/TASK Interaction Bar Graph*
Figure 6

*MMN Latency – DEVIANCE Bar Graph*
Figure 7

*MMN Active Extreme - Attend.avg—
MMN Active Slight - All.avg—

**Attention and Nicotine**

**MMN Latency & Amplitude – DEVIANCE Grand Average**
Figure 8

*MMN Amplitude – DEVIANCE Bar Graph*
Figure 9

*MMN Amplitude – TASK Bar Graph*
Figure 10

MMN Amplitude – DRUG/TASK Interaction Bar Graph
Figure 11

**MMN Amplitude – DRUG/TASK Interaction Grand Average**

![Graph showing MMN Amplitude for Active Extreme - Nicotine and Active Slight - Placebo](image-url)
Figure 12

*P3b Latency – DRUG Bar Graph*
Figure 13

*P3b Latency – DRUG Grand Average*
### Table 1

*N100 – LOCUS Latency Values*

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Appendix A

CONSENT FORM

Study Title: The Attentional Effects of Nicotine on Brain Waves.
Investigator: Amanda Clark - gtnqg@stu.ca
Supervisor: Dr. Michael Houlihan – mhoulihan@stu.ca
(506) 460-0336
Ethics Contact: Dr. Ian Fraser – fras@stu.ca
(506) 460-0322

Introduction:
We would like to invite you to take part in a study that will examine the attentional effects of nicotine on your brain waves. Your participation in this study is completely voluntary; if you decide not to take part it will not affect the quality of your education and you are free to withdraw at any time without penalty. If you do choose to withdraw, you reserve the right to request the destruction of all information gathered pertaining to your participation. Participation in this study requires you to come to the lab on two separate occasions. This form will detail any risks or inconveniences that you might experience as a result of participation. Please discuss any questions you may have with the investigator before signing this form.

Purpose of the Research: This study will measure the effects of nicotine on your brain waves by using an electroencephalogram (EEG). The EEG is used because it is able to extract certain characteristics from your brain waves that allow the researchers to better understand the processing of information in your brain. This study will focus on attention and how your brain reacts to tasks where you will have to selectively attend to certain stimuli.

Requirements of the Study: Before setting up the EEG equipment, you will be required to go to a designated smoking area on campus to smoke one cigarette. When you finish smoking, you will be prepared for EEG recording.

The EEG will record your brain activity by affixing a cloth cap to your head that contains several electrodes. To increase the conductivity of the electrodes a jelly-like substance will be used between the electrodes of the cap and your scalp. A blunt syringe will be used to put the substance between the electrodes and your scalp. This syringe will not pierce the skin but some people (about 5%) will experience some mild discomfort, as the syringe will be used to push aside any hair that may be lying between the electrodes and the scalp.

Once prepared for EEG recording you will be given a piece of gum to chew. This gum may or may not contain any nicotine. The gum may have a slightly aversive taste. You will listen to an audio recording instructing you when and how to chew the gum. This is required because a particular chewing technique is necessary to ensure correct absorption of the nicotine from the gum. Please attempt to follow the chewing instructions as closely as possible.

You will also be asked to fill out a completely confidential health questionnaire. This questionnaire will inquire about your use of medication and your health history.
During EEG recording, you will be asked to complete two simple tasks while listening to a series of tones. First, you will watch a video with the sound turned off, while having a series of auditory tones presented to you through headphones. Later, you will be required to press a response button when you hear a tone with certain characteristics.

Who can participate: Potential participants include people who are regular smokers (15 cigarettes per day) who have relatively normal hearing. In order to qualify as a regular smoker, you must actually inhale as you smoke a cigarette.

Who cannot participate: People with an underlying neurological disorder, those on medications that affect brain function, and those who have a severe hearing problem will be excluded.

Risks and discomforts: There is a mild risk of discomfort from the electrodes and the electrode gel. The gel washes out of your hair and you will be able to do this before leaving the lab. There is also a risk of nausea if this is the first time that you have had nicotine in your body. If, for example, you smoke but do not inhale, you may not be accustomed to the effects of nicotine. In this situation, there is a moderate risk of developing mild nausea symptoms, but they will be short-lived. Though unlikely, there may also be risks that we have not foreseen, such as an allergic reaction to the nicotine gum or the jelly-like substance. Please indicate all known allergies in the space provided on the health questionnaire.

Compensation: There will be no cost to you for participating in this study. None of your legal rights are waived, and the investigators and the university still have their professional and legal responsibilities. In return for your participation, you will be compensated with 4 of the 4 bonus points that you are eligible for in your Introductory Psychology class.

Confidentiality: All data collected from you during participation in this study will be held in complete confidence. Any paper-based data will be kept in a locked filing cabinet inside a locked research lab. All EEG recordings will be kept on a restricted access computer that is located in the locked research lab.

Questions or problems: You have the right to ask questions about this study at any time. Please contact Amanda Clark at (506) 460-0337, or Dr. Michael Houlihan (PhD) at (506) 460-0336.

Participant Consent
I have read the information on this consent form and have had the chance to ask questions which have been answered to my satisfaction before signing my name. I understand the nature of the study and I understand the potential risks of participation. I understand that I have the right to withdraw from the study at any time without it affecting me in any way. I freely agree to participate in this research study.

_________________________  _________________
Name of Participant (Print)    Signature of Participant    Student ID

Date: ____________________  Time: _______________
If you are interested in receiving the final results of this study please check the adjacent box. Please also indicate an appropriate email address where this information can be sent.

STATEMENT BY PERSON PROVIDING INFORMATION ON STUDY

I have explained the nature and demands of the research study to the participant named above.

Name (Print)____________________________ Position ______________

Signature: ______________________________
HEALTH QUESTIONNAIRE

All of the information contained in this questionnaire will be kept strictly confidential and will be used only for screening purposes. If you wish, you may choose not to answer any of the following questions.

Gender:  Male    Female  
Date of Birth (dd/mm/yy): _______________  Weight: ________

Do you inhale when you smoke?       YES   NO

Have you had, or do you currently have, any of the following conditions?  
(Please circle “YES” or “NO”)

- Diabetes       YES   NO
- Asthma         YES   NO
- Epilepsy       YES   NO
- Circulation problems       YES   NO
- Heart Condition       YES   NO
- Stroke       YES   NO
- Paralysis       YES   NO
- Hearing Loss       YES   NO
- Visual Problems       YES   NO
- Attention Deficit Hyperactivity Disorder       YES   NO
- Neurological deficits       YES   NO
- Learning disabilities       YES   NO
- Have you ever suffered from head trauma?       YES   NO
- Are you currently taking any medication?       YES   NO
  if yes please indicate: ______________________

Are you pregnant or attempting to become pregnant?       YES   NO
Are you currently under a doctor’s care for any medical condition?       YES   NO

Please indicate any allergies that you may have in the space provided below.

____________________________________________________________________________________
Appendix C

MOOD QUESTIONNAIRE

Name: ___________________________  Date: ________________________

Time: ___________________________

Please indicate how you feel by marking an ‘X’ along the line below.

Do you feel jittery?
Not at All ------------------------------- Extremely

Do you feel relaxed?
Not at All ------------------------------- Extremely

Do you feel nauseous?
Not at All ------------------------------- Extremely

Do you feel euphoric?
Not at All ------------------------------- Extremely

Do you feel drowsy?
Not at All ------------------------------- Extremely

Do you feel anxious?
Not at All ------------------------------- Extremely

Do you feel alert?
Not at All ------------------------------- Extremely

Do you feel energetic?
Not at All ------------------------------- Extremely

Do you feel tense?
Not at All ------------------------------- Extremely
DEBRIEFING FORM

Study Title: Event-Related Potentials: An Index for the Attentional Effects of Nicotine.
Investigator: Amanda Clark - gtnqg@stu.ca
Supervisor: Dr. Michael Houlihan – mhoulihan@stu.ca; (506) 460-0336
Ethics Contact: Dr. Ian Fraser – fras@stu.ca; (506) 460-0322

You have just participated in a study that examines how nicotine affects attentional processes as evidenced by changes in your brain waves. The tasks that you completed attempted to manipulate your attention to auditory tones by asking you to either focus your attention on the video and ignore the tones, or to pay attention to them by responding to the tones that were different in pitch (frequency). We will be able to determine certain things about your attentional process by contrasting the way that your brain reacted to the tones that you ignored and the tones that you paid attention to. Your brain activity will also be examined at a later date when we compare the recordings from the session when you received nicotine to that from the session where you received a placebo.

You will not be identified as a study participant in any reports or publications of this research. If, for any reason, you wish to have your data removed from the study, please contact one of the researchers involved in this study.

Thank you for your participation. If you have any further questions or concerns at any time, please contact Amanda Clark or Dr. Michael Houlihan (PhD) using the contact information indicated above.

For further reading on this subject, see the following:
