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Effect of Smoking on Cognitive Functioning in Young Saudi Adults

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEF 1,2 **Shahid Bashir**
ABDEF 3 **Faisal Alghamdi**
ABCDF 3 **Ahmed Alhussien**
ABCDEF 3 **Meshal Alohal**
ABEF 3 **Abdullah Alatawi**
BE 3 **Tariq Almusned**
DE 1 **Syed Shahid Habib**

1 Department of Physiology, Faculty of Medicine, King Saud University, Riyadh, Saudi Arabia
2 Berenson-Allen Center for Noninvasive Brain Stimulation, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, U.S.A.
3 Faculty of Medicine, King Saud University, Riyadh, Saudi Arabia

Corresponding Author: Shahid Bashir, e-mail: sbashir10@gmail.com

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Background: Smoking is the predominant form of tobacco consumption and is growing worldwide, particularly in the younger generation in the Middle-East. We aimed to determine the effects of tobacco smoking on cognitive functions among young Saudi adults.




Material/Methods: We recruited a group of cigarette smokers (N=22) and a group of controls (non-smokers) (N=30) from apparently healthy male volunteers aged 18–29 years. Cognitive function was assessed by using the Cambridge Neuropsychological Automated Battery (CANTAB). The cognitive functions outcome variables were the response time (attention-switching task [AST]), and the percentage of correct response (pattern recognition memory [PRM] task). Clinical, demographic, blood markers (brain-derived neurotrophic factor (BDNF) and apolipoprotein E) were assessed between groups.

Results: The 2 groups were matched for age and educational status. In comparison to the control group, smokers showed significant cognitive impairments in AST-Latency ($p=0.001$), AST-Congruent ($p=0.001$), and AST-Incongruent condition ($p=0.001$). There was not significant difference in BDNF APOE serum level between the 2 groups.

Conclusions: These results indicate that attention and alertness were significantly impaired in smokers compared to non-smokers.

MeSH Keywords: **Memory • Mild Cognitive Impairment • Nicotine • Smoking Cessation**

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Background

Health authorities report that 6 million smokers in the Kingdom of Saudi Arabia (KSA) spend SR11 billion annually to satisfy their urge for nicotine [1]. Smokers in the KSA are mainly 17–40 years old [1–3]. Researchers report that smoking causes lung cancer and chronic respiratory and cardiovascular diseases, and is a risk factor for infections of the respiratory tract, adverse postoperative events, osteoporosis, delayed wound healing, diabetes, reproductive disorders, and duodenal and gastric ulcers [4–6]. All these characteristics of smoking show that it is a serious and chronic condition that occurs in a substantial part of the population.

Nicotine dependence is currently included in the Diagnostic and Statistical Manual of Mental Disorders fourth edition (DSM-IV-TR) as a 'substance use disorder' [7].

The nicotine in cigarettes has a function similar to that of acetylcholine, which is a neurotransmitter found in most brain areas, modulating cognition via cortico-subcortical circuitry [8]. Due to the function similarity, nicotine has an effect on these receptors, including prefrontal cortices, amygdalo-hippocampal formation, and nucleus accumbens [8–10], which support daily cognitive tasks, including memory, attention, decision-making, and reward systems [11–13]. However, the role of nicotine in cognition is controversial [14]. Chronic use of nicotine could be detrimental to cognitive functions. We used the Cambridge Neuropsychological Test Automated Battery (CANTAB), which is a computerized standard software, to assess cognitive functions according to the age and sex of participants. We used Attention-Switching Task (AST) and Pattern Recognition Memory (PRM) to assess cognitive functions, because memory and attention are main parameters used in assessing cognition in smokers [15].

Brain-derived neurotrophic factor (BDNF) is one of the factors affecting the growth and survival of neurons; it is correlated with the number of cigarettes smoked, and has pro-atherothrombotic effects [16]. Apolipoprotein E (APOE) is reported to be elevated in people who smoke heavily and is a predictor of squamous metaplasia in the lung [17]. Another study found that elevated levels of APOE in smokers is correlated with amyloid levels in the brain, which increases the risk for Alzheimer disease [18].

Based on what is known about modulatory influences of nicotine on cognition, and on the above-described studies in young smokers, we hypothesized that smoking is associated with deficits in cognitive function among young people.

Material and Methods

Subjects

This cross-sectional study was conducted in the Department of Physiology, College of Medicine, King Saud University, Riyadh, Saudi Arabia during the period Nov 2015 to May 2016. We matched subjects by age, sex, ethnicity, and socioeconomic status to estimate the impact of cigarette smoking on cognitive functions.

A detailed interview of the participants was conducted for study enrollment. All participants were questioned regarding cigarette smoking and use of other tobacco products. We excluded subjects based on a detailed history obtained regarding any drug intake, diseases such as seizures, and psychiatric problems.

Our study had 2 groups. The smoking group consisted of 22 male volunteers, with mean age 24.4 ± 5.30 (Mean \pm SD) years who were considered as regular cigarette smokers for at least 1 year and who smoked at least 1 cigarette per day. These 22 cigarette smokers were matched with a group of 30 non-cigarette smokers (control) who had never smoked, who were healthy male volunteers with mean age 23.31 ± 2.68 (Mean \pm SD) and were matched with the smoking group for age, sex, ethnicity, and socioeconomic status. This control group primarily consisted of university students, as well as technicians, secretaries, research assistants, and receptionists. The Institutional Review Board, King Khalid University Hospital and College of Medicine, King Saud University, approved the study.

Methods

Blood sampling

Venous blood samples were collected from all participants and were stored at -70°C until assayed. Blood samples were analyzed for brain-derived neurotrophic factor (BDNF) and apolipoprotein E (APOE) levels. Plasma BDNF and APOE concentrations were measured by competitive enzyme immunoassay using Human BDNF and APOE ELISA kits, following manufacturer's instructions (Elabsciences Biotechnology Co., Ltd., China). Pre-coated antibody specific to BDNF and APOE reacted with samples and standards. Following blocking and incubation, BDNF- and APOE-specific antibodies were used. Both BDNF and APOE peptide and targeted peptide in samples interacted competitively with the BDNF and APOE antibodies.

Cognitive function

Neuropsychological testing was performed using CANTAB (Cambridge Neuropsychological Test Automated Battery)

Table 1. Anthropometric data of smoking groups and control group.

Parameters	Control group (n=30)	Smoking group (n=22)	P value
Age	21.8±1.73	22.9±3.75	0.190
BDNF	610±401	397±328	0.103
APOE	635±370	718±417	0.525

Vales are presented in Mean ±SD; NS – non-significant.

Table 2. Comparison of cognitive functions between smoking group compared to their matched control group.

Parameters	Control group	Smoking group	p-value
AST-Latency	411±58.3	591±128.3	0.001
AST-Congruent	393±51.3	565±128.9	0.001
AST-Incongruent	430±70	619±137.8	0.001
PRM	91.8±7.9	88.5±7.4	0.101

Vales are presented in Mean ±SEM.

research suite software (version 6. 0.37, Cambridge Cognition). The entire battery required 25–30 min to complete. The participants were made to sit comfortably on a chair and were asked to respond to test items by pressing the response button with the index finger of the dominant hand.

Attention-switching task (AST)

AST measured the participant’s ability to switch attention between the direction of an arrow and its location on the screen and to ignore task-irrelevant information in the face of interfering or distracting events. This test was designed to measure top-down cognitive control processes involving the pre-frontal cortex. This test is a sensitive measure of frontal lobe and ‘executive’ dysfunction. The test displayed an arrow, which can appear on either side of the screen (right or left) and can point in either direction (to the right or to the left). Each trial displayed a cue at the top of the screen that indicates to the participant whether they have to press the right or left button according to the “side on which the arrow appeared” or the “direction in which the arrow was pointing”. Some trials displayed congruent stimuli (e.g., arrow on the right side of the screen pointing to the right) whereas other trials displayed incongruent stimuli, which required a higher cognitive demand (e.g., arrow on the right side of the screen pointing to the left).

Pattern recognition memory (PRM)

This is a test of visual pattern recognition memory in a 2-choice forced discrimination paradigm. A sequence of visual patterns was presented in the center of the screen. These patterns were

designed so that they cannot easily be given verbal labels. In the recognition phase, the participants were required to choose between a pattern they had already seen and a novel pattern.

Statistical analysis

AST test outcome measures include response latencies and error scores, which reflected the participant’s attention-switching ability and the interference of congruent and incongruent task-irrelevant information. The PRM task allows measurement of the numbers of correct patterns selected, and statistical analysis measuring the probability of an error after a correct or incorrect response. Statistical analysis was performed using SPSS software (version 22.0; SPSS Inc., Chicago, IL). Comparison of quantitative data between the smoking group and the control group was performed using *t* tests for normally distributed data and the Mann-Whitney test for skewed data. Two-tailed statistics were used and statistical significance was set at $P < 0.05$. Pearson correlations were used as needed.

Results

Table 1 summarizes the anthropometric variables including age, BDNF, and APOE. The control group consisted of 30 participants with mean age 23.31±2.68 (Mean ±SD) years and the smoking group consisted of 22 participants with mean age 24.4±5.30 (Mean ±SD) years.

Table 2 summarizes the comparison of the cognitive function test parameters of smokers and their matched control group.

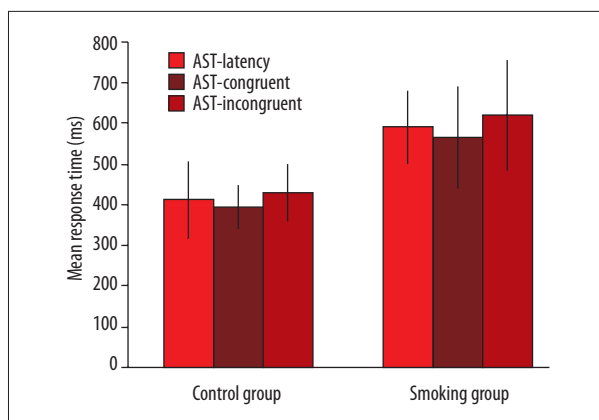


Figure 1. Comparison of cognitive functions between smokers compared to their matched control group for attention-switching task (AST) latency, AST-congruent, and AST-incongruent conditions.

There was a decline in the cognitive function parameters, including AST-Latency; 411 ± 58.3 in the control group vs. 591 ± 128.3 in smokers ($p=0.001$); AST-Congruent in control group was 393 ± 51.3 vs. smokers 565 ± 128.3 ($p=0.001$); AST-Incongruent in control 430 ± 70 vs. smokers 619 ± 137.8 ($p=0.001$) (Figure 1); PRM control 91.8 ± 7.9 vs. smokers 88.35 ± 7.4 ($p=0.101$).

Discussion

In the present study, we determined the effects of smoking on cognitive functions among young Saudis. We found that smoking impaired the cognitive performance compared to their matched control group. The impairment was statistically significant for attention, reaction time, and memory tasks. These domains of cognition were selectively tested because their use is supported by the literature and use of only selected domains decreases the testing time, thereby reducing participant exhaustion and resultant confounding effects. However, we did not observe a significant difference in the PRM paradigm, perhaps due to preservation of memory functions in smokers. Confounders such as sleep, vision problems, drinking coffee, or smoking half an hour before testing were studied. The finding of associations between smoking and relative

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cognitive problems is concordant with several previous studies in young people [19–21] but extends these findings to include dissociable domains tapped by well-validated translational cognitive tests. This study is the first of its kind in the Middle-East that investigated the effect of smoking on cognitive function.

Functional outcomes in smokers can be improved by smoking cessation [22]. Cognitive effects of smoking tobacco and drinking alcohol have been examined in other research, which found a cognitive decline but normal BDNF level. However, smoking severity is associated with low BDNF level [23]. Smoking is decreases cognition in patients with Parkinson disease, even after quitting [24]. Smokers who were matched for education, age, income, and sex had significant impairment in cognition, spatial working memory, sustained attention, and executive planning and had inappropriate behavior involving risk-taking as compared to non-smokers [15].

The limitations of our study are small its sample size and cross-sectional design. Large-scale prospective studies with more detailed assessments are required to determine the true links between smoking and cognitive impairment. Smoking is continuously spreading among youth worldwide and has been growing in popularity in the Middle-East.

Conclusions

Smoking impairs cognitive functions, expressed in our data by the significant increase in latency, as well as congruent and incongruent condition, of smokers compared to their matched controls in AST, which may be due to early frontal lobe and ‘executive’ dysfunction. Evidence of the harm caused by smoking justifies effective policies such as factual and visible health warnings on all tobacco products and advertising. Investment in research and policy initiatives to understand and control cigarette smoking needs to become a public health priority.

Competing interest

The authors declare that they have no competing interests.

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