Degree of dependence influences the effects of smoking on psychomotor performance and working memory capacity

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ABSTRACT

الأهداف: استكشاف التأثير المتغير لدرجة الاعتماد على التدخين على كل من الأداء النفسي الحركي وقدرة الذاكرة العملية.

الطريقة: أُجريت هذه الدراسة العشوائية المقارنة الاستطلاعية في فرع الأدوية – كلية الطب – الجامعة المستنصرية – بغداد – العراق وذلك خلال الفترة من يناير إلى فبراير 2011م. لقد قام طلاب الطب الذكور في المرحلة الثالثة بالإجابة على استبيان فيغرستورم لإدمان النكوتين، وبعد ذلك أُخذت عينة عشوائية من 32 طالب وقُسمت إلى 3 مجموعات كالتالي: 10 طلاب غير مدخنين (درجة: 0)، و11 طالب قليل التدخين (درجة: 5 أو أقل)، و11 طالب شديد التدخين (درجة: 6 أو أكثر). وقد استعملت بطارية ليدز للقياس النفسي الحركي لقياس الوقت التفاعلي الحركي وانصهار الوميض، بينما قيست قدرة الذاكرة العملية بواسطة فحص إن باك الحاسوبي.

النتائج: لقد شوهد تحسناً كبيراً في الترتيب التصاعدي لاندماج الومضات بين شديدي التدخين بالمقارنة مع غير المدخنين (p=0.005, CI: 0.99–6)، وقليلي التدخين (p=0.053, CI: 0.39–4.5). إلا أن نتائج شديدي التدخين أظهرت تراجعاً كبيراً في اختبار الذاكرة العملية ثري باك وذلك بالمقارنة مع نتائج غير المدخنين (p=0.006, CI: 4–25.8)، ونتائج قليلي التدخين (p=0.009, CI: 3–24.4). ولم تظهر هناك أي تغييرات ذات دلالة إحصائية بين المجموعات الثلاث بالنسبة للترتيب التنازلي لاندماج الوميض، ومكونات الوقت التفاعلي الحركي، و اختبار الذاكرة العملية تو وثري باك.

خاتمة: أظهرت الدراسة بأن التدخين الشديد (عالي النيكوتين) يعزز درجة اليقظة، ولكنه يضعف قدرة الذاكرة العملية.

Objectives: Exploration of the variable effect of the degree of smoking dependence on psychomotor performance and working memory capacity.

Methods: This is a randomized, controlled, prospective study conducted in the Department of Pharmacology, College of Medicine, Al-Mustansiriya University, Baghdad, Iraq from 15 January 2011 to 25 February 2011. After third stage male medical students completed the Fagerstrom Test for Nicotine Dependence questionnaire, we randomly selected a sample of 32 students and divided them into 3 groups: 10 participants with zero score (non-smokers), 11 participants with a score of 5 or less (light smokers), and 11 participants with a score of 6 or more (heavy smokers). Choice reaction time and flicker fusion were measured by the Leeds psychomotor performance test battery, and working memory capacity was measured by the N-back working memory test.

Results: We found significant improvement in ascending flicker fusion test in heavy smokers in comparison with non-smokers (p=0.005, confidence interval [CI] 0.99-6), and light smokers (p=0.053, CI 0.39-4.5). Heavy smokers significantly deteriorated in the 3-back task in comparison with non-smokers (p=0.006, CI 4-25.8), and light smokers (p=0.009, CI 3-24.4). No significant changes were seen between groups in the descending critical flicker fusion, the components of choice reaction time, and in 1-, 2-back working memory tests.

Conclusion: Heavy smoking (high nicotine) enhances arousal, but impairs working memory capacity.

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Tobacco is a leading cause of death in the world, responsible for one in 10 deaths among adults. Today, every 6 seconds someone dies from tobacco

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caused disease. While tobacco use is declining in developed countries, it is increasing dramatically in developing countries.[1] Animal and human studies have shown that nicotine in cigarettes is responsible for the addictive properties of tobacco.[2] There is inconsistency in the results of studies regarding the effects of smoking on psychomotor performance and working memory, some studies show improvement, while others show deterioration in the effects.[3,4] Researchers in the field explain the variability in the results obtained from these studies as follows: first, cognitive effects of acute nicotine administration (to non-smoker or abstinent smoker) differ from the chronic use of cigarette smoking.[5] Secondly, medicinal nicotine improves symptoms in patients with Alzheimer's and Parkinson's diseases,[6,7] but chronic smoking is found to cause neurodegeneration and increased risk of occurrence of these conditions.[8,9] Thirdly, response to working memory tests differs between adolescent and adult-onset smoking.[10] Finally, the importance of the degree of dependence demonstrated in previous studies, which shows significant improvement in cognitive processing after smoking in previously abstinent heavy, but not light smokers.[11] A recent study by Nesic et al[12] showed that the degree of dependence on smoking had substantial effects on cognitive flexibility. Our study compares non-smokers, light smokers, and heavy smokers according to the Fagerstrom Test for Nicotine Dependence (FTND), which incorporate other aspects of smoking behavior in addition to the number of cigarettes, and may be more appropriate to detect the differences between low- and high-dependent smokers.[13] The aim of our study is to compare the 3 groups regarding critical flicker fusion (CFF), which measures the degree of arousal,[14] and the choice reaction time (CRT), which measures the level of attention,[3] and the *N*-back task, which measures working memory capacity.[15]

Methods. This is a randomized, controlled, prospective study conducted in the Department of Pharmacology, College of Medicine, Al-Mustansiriya University, Baghdad, Iraq between 15 January 2011 and 25 February 2011. The principles of Helsinki Declaration were followed in the study, an independent scientific committee revised and approved the study, and informed consent was obtained from the participants.

After third stage male medical students completed the FTND questionnaire, we randomly selected a sample of 32 students and divided them into 3 groups: 10 participants with zero score (non-smokers), 11 participants with a score of 5 or less (light smokers), and 11 participants with a score of 6 or more (heavy smokers).[16] Exclusion criteria included the following: evidence of eye disease, diabetes, hypertension, and history of drug therapy within 7 days. The intake of beverages was forbidden on the day of the test.

The choice reaction time (CRT), which is measured by the Leeds psychomotor test battery, is used as an indicator of sensorimotor performance, assessing the ability to attend and respond to a critical stimulus. Participants are required to place the index finger of their preferred hand on a central starting button and are instructed to extinguish one of 6 equidistant red lights, illuminated at random, by pressing the response key in front of the light as quickly as possible.[17] The CRT components (total, recognition, and motor) are repeated 5 times by the participants, then the mean is calculated and recorded. Recognition reaction time (RRT) is the recorded time between the onset of the stimulus (appearance of random red light) to the lifting of the finger of the participant from the start button. The motor reaction time (MRT) indicates the movement component of this task, and is the time between the participant lifting his finger from the start button and touching the response button. Total reaction time (TRT) is the sum of RRT and MRT.[18]

The CFF assesses the integrative capacity of the CNS and, more specifically, the ability to discriminate discrete bits of sensory information. In this, the participants are required to discriminate flicker from fusion and vice versa, in a set of 4 light-emitting diodes arranged in a 1-cm square. The diodes are held in foveal fixation at a distance of 1 m, individual thresholds are determined by the psychophysical method of limits on 5 ascending (flicker to fusion), and 5 descending (fusion to flicker) scales. A decrease in the CFF threshold is indicative of a reduction in the overall integrative activity in the CNS.[19,20]

The *N*-back task uses the visual working memory task proposed by Jaeggi et al,[21] where squares at 8 different locations were presented sequentially on a computer screen at a rate of 3 seconds (stimulus length, 500 ms; interstimulus interval, 2,500 ms). A response was required whenever one of the presented stimuli matched the one-presented *n* positions back in the sequence. In the 1-back condition, the target was any square position that is identical to the square position immediately preceding it. In the 2-back, the target was square position similar to another square position 2 trials back. The 3-back is square position identical to another square position 3 trials back. Participants made responses manually by pressing the letter "A" of a standard keyboard with their left index finger for visual targets. The computer automatically measured the accuracy rate (number of successful responses). The participants were allowed to practice both the psychomotor test battery and the *n*-back task to become familiar with it before the beginning of the trial.

Statistical analysis. The results are expressed as mean ±SD for the number of observations, while expressed as percentage for the accuracy rate in the *N*-back task. Statistical analysis was carried out using the Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, USA) version 11.5. Comparison between groups was carried out using ANOVA test, post hoc analysis by Tukey test for the significance between groups, 95% was assumed for the confidence interval (CI) and *P*-value.

Results. Thirty-two participants enrolled in the study, 10 non-smokers, 11 light smokers, and 11 heavy smokers, with a mean age of 22.4±1.01. We found significant differences between the groups regarding the FTND score and number of cigarettes per day. **Table 1** shows the mean±SD of the 3 groups (non-smokers, light smokers, and heavy smokers) regarding the CRT (total, recognition, and motor reaction time); CFF threshold (ascending, descending); and working memory test (1-back, 2-back, and 3-back working memory tests). The CRT improved in light smokers, and then deteriorated in heavy smokers in comparison with non-smokers, but these changes did not reach a significant level (**Table 2**). Heavy smokers showed significant improvement in ascending CFF test (**Table 2**) in comparison with non-smokers (p=0.005, CI 0.99-6), and light smokers (p=0.053, CI 0.39-4.5), but there were no significant changes between the groups regarding descending CFF. In the 1-back memory task, the groups showed nearly the same scoring (**Table 1**), in the 2-back, heavy smokers scored lower than the other 2 groups, but this change was not significant. Heavy smokers significantly deteriorated in the 3-back task in comparison with non-smokers (p=0.006, C.I. 4-25.8), and light smokers (p=0.009, CI 3-24.4).

Table 1 - Comparison between non-smokers, light smokers, and heavy smokers regarding the choice reaction time (total, recognition, motor); critical flicker fusion threshold (ascending, descending); and working memory capacity test (1, 2, 3-back).

Cognitive test	Non-smokers (n=10)	Light smokers (n=11)	Heavy smokers (n=11)
Choice reaction time (ms)			
Total reaction time	604.2±54.8	597.8±46.2	620.6±42.3
Recognition reaction time	398.6±64.5	374.0±33.0	390.1±34.6
Motor reaction time	205.6±48.6	223.8±40.5	230.4±55.4
Critical flicker fusion threshold (Hz)			
Ascending	31.1±1.6	32.5±2.6	34.6±2.4
Descending	32.4±2.7	32.2±4.0	33.4±3.8
Working memory capacity (%)			
1-back	98.6±2.9	98.4±5.1	93.1±10.6
2-back	83.6±10.2	82.1±9.5	76.1±12.9
3-back	75.2±10.9	74.0±12.1	60.2±6.4

Numbers represent mean±SD, choice reaction time measured in milliseconds (ms), critical flicker fusion frequency measured in Hz, working memory capacity represent accuracy rate (%)

Table 2 - The *p*-value and confidence interval (CI) for the 3 participating groups (non-smokers, light-smokers, and heavy smokers).

Cognitive test	Non-smokers versus light smokers		Non-smokers versus heavy smokers		Light smokers versus heavy smokers	
	P-value	95% CI	*P*-value	95% CI	*P*-value	95% CI
Choice reaction time (ms)						
Total reaction time	0.950	-45.2-58	0.714	-35.2-68.0	0.511	-27.6-73.2
Recognition reaction time	0.443	-24.6-73.8	0.907	-40.8-57.6	0.687	-31.9-64.2
Motor reaction time	0.670	-34.2-70.6	0.480	-27.8-77.3	0.945	-44.5-57.8
Critical flicker fusion threshold (Hz)						
Ascending	0.338	-1.0-3.9	0.005*	0.99-6.0	0.053*	0.39-4.5
Descending	0.990	-3.7-4.1	0.821	-2.9-4.8	0.733	-2.6-4.9
Working memory capacity (%)						
1-back	0.999	-7.5-7.8	0.208	-2.3-13.1	0.210	-2.2-12.7
2-back	0.947	-10.4-13.4	0.287	-4.5-19.3	0.430	-5.7-17.5
3-back	0.960	-9.7-12.1	0.006*	4-25.8	0.009*	3.0-24.4

ANOVA test used for the comparison between groups, post hoc analysis carried out using the Tukey test.
*represents significant difference between groups

Discussion. Our results show a significant increase in the ascending CFF in heavy smokers in comparison with non- and light-smokers, but at the same time there is a significant deterioration in the same group regarding the 3-back working memory task.

Previous studies show that cigarette smoking increases CFF threshold, and it is well known that nicotine contained within cigarette smoke is a psychomotor stimulant and acts as sympathomimetic.[22] Nicotine enhances arousal by the following mechanism: increasing norepinephrine secretion in the brain, stimulating the sympathetic ganglia, and peripherally increasing epinephrine secretion through stimulation of the adrenal medulla.[23] All the above indicate that the nicotine arousal mechanism is hardly subjected to desensitization because of the different routes of stimulation to the CNS. Studies that show improvement in working memory after nicotine administration or cigarette smoking usually use either nicotine-naïve individuals, or show the effects of acute nicotine administration following a prescribed period of deprivation among chronic smokers.[24] Studies that have examined the cognitive impact of chronic cigarette smoking show that it impairs working memory capacity.[25]

Researchers in the field of neuroscience show that optimum working memory requires optimum concentrations of dopamine and norepinephrine.[26] Dopamine action in the prefrontal lobe (neural circuit for working memory) follow an inverted U-shape function, high or low dopamine levels may impair working memory.[27] Regarding norepinephrine, studies show that moderate levels of this neurotransmitter improve working memory, while high concentrations of norepinephrine impair working memory capacity.[28] Nicotine action in the brain also follows the inverted U-shape theory, because high doses of nicotine have been shown to impair psychomotor performance and working memory.[9,29] Nicotine increases the level of dopamine and norepinephrine in the frontal lobe above the optimum level, and this may impair working memory.[30] Recently, researchers have shown that the balance between nicotine neuroprotection and toxicity depends on the dose,[31] and chronic nicotine intake is associated with significant changes in gene expression and neuronal morphology in the prefrontal cortex, specifically during the adolescent period.[32]

Because of the small sample size, this study is considered a preliminary study that needs further verification with studies with larger sample sizes and different tests that are more objective in measuring psychomotor performance and working memory capacity. The implications of our results for future research include further neurobiological and imaging studies that differentiate between light and heavy smokers.

In conclusion, our study shows that heavy smoking and high nicotine dose enhances arousal, but impairs working memory capacity in comparison with non- and light-smokers.

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