

A Study of the Effect of Cigarette Smoking On Cognitive Parameters In Human Volunteers

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Abstracts: Introduction: Nicotine, one of the major alkaloids of cigarette smoke, is known to stimulate the CNS. It was thought worthwhile to study effect after single cigarette smoking on some cognitive functions. These effects may be important in relation to increasing incidence of conditions where cognitive functions are deranged e.g. Alzheimer's disease. Materials and Methods: The design of the study was open. Cognitive tests, blood pressure and heart rate recording were done in a group of subjects (n=34) who smoked a cigarette. The tests were performed twice in individual subjects; one before and other after smoking a cigarette (in control group (n=30) the two tests were performed after a resting period of 5 minutes). To study cognitive functions, following parameters were included: Forward Digit Span Test, Word List Memory Test, Benton Visual Retention Test, Mental Arithmetic Test, Motor Co-ordination Test, Digit Letter Substitution Test and Paragraph Cancellation Test (details of the tests will be elaborated during presentation). Results: In the subjects who smoked a cigarette heart rate, systolic, diastolic and mean blood pressure exhibited significant rise. In these subjects, scores of various cognitive tests showed statistically significant improvement as compared to the control group (detail data will be furnished during presentation). Conclusion: In the present study, smoking a cigarette has shown definite improvement in cognitive functions like short-term memory, alertness, visual retention, calculation skill and motor co-ordination. No attempt is made in the present study about the effect of repeated smoking. The tolerance to these effects cannot be ruled out presently. The present results need further exploration from point of view of therapeutic utility. [Dumatar C et al. NJIRM 2011; 2(3) : 71-76]

Key Words: cigarette smoking, cognitive parameters

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Introduction: Tobacco, *Nicotiana tobacum*, is a native plant of the American continent. Cigarette smoking is dangerous from point of dependence. Nicotine is one of the major alkaloids of cigarette smoke. Recognizing the health hazards of tobacco, most countries of the world have promulgated various laws enforcing the cigarette manufacturing companies to display health warnings on packages and advertisement of cigarettes. Despite the understandings about hazardous effects, tobacco smoking is prevalent in large populations. Naturally, this leads to the question: Why people smoke and become habituated for smoking? There must be some inherent properties of nicotine (content of cigarettes) responsible for it. Nicotine markedly stimulates the CNS. The smoker feels alert; there is some muscle relaxation too. There are indications that nicotine improved attention and performances of memory tasks in both animals and humans. Data on human studies is based in the form of response to questionnaire by the subjects who were in habit of smoking in most of the

studies. It was thought worthy to study the effect of tobacco on cognitive function in more objective way. So, study was conducted in subjects who were occasional smokers to study the effects after single cigarette smoking. It was considered worthwhile to study the effect on occasional smokers. It would be of interest to demonstrate acute effects of smoking. From this point, the present study was proposed.

Medical literature is emphasizing on the increasing incidence of conditions where cognitive functions are deranged. Alzheimer's disease draws attention of many. If at all, smoking shows some acute promising effects, nicotine can be a good candidate to study from point of view of utility in such disorders. Nicotine substitutes and modified delivery system may promise to avoid the hazardous effects of smoking and other modalities of nicotine use. With such future possibilities the present study was proposed simply to understand the acute effects of cigarette smoking.

Material and Methods: A total of 64 medical students & doctors of male sex voluntarily participated in the study. Age of the subjects ranged from 20 to 40 yrs and the weight from 50 to 70 kg. All subjects were in good health as determined by medical history and physical examination. Subjects were excluded if they had any history of vision abnormalities or skeletal muscular disorders or injuries or anxiety disorders or peripheral vascular diseases or serious psychiatric condition or chronic respiratory or acute respiratory episode in recent past & subjects having blood pressure (BP) greater than 150/100. Experiments were conducted between 5.30 p.m. to 9.30 p.m. and subjects were not allowed to smoke at least 1 hr prior to the experiment. None of the subjects had taken any drug for at least last 7 days. Not more than five subjects participated per day. Subjects were exposed to battery of various tests in sequence. They were given details about each test, clarifying all doubts. Subjects were given trial before the test wherever required. Keeping in view the time required to conduct the test, only nine tests were conducted in an individual subject, which may throw light on various aspects of mental, psychomotor and cognitive performance.

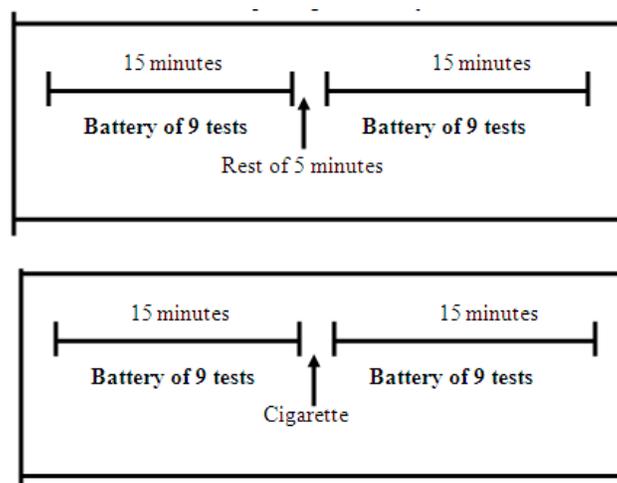
During pilot-study assessment about time required for each test was done. As the design of the study included administration of tests before and after smoking a cigarette, and as nicotine from cigarette has immediate effect, the tests were repeated immediately after smoking a cigarette. As the effect of nicotine from one cigarette lasts 10 – 15 minutes, not more than nine tests were considered appropriate. The sequence of various tests was arranged in such a way that there is minimum possibility of interference of one test on another. Following sequence of the battery of tests was followed¹⁻⁶:

1. Forward Digit Span Test
2. Word List Memory Test
3. Mental Arithmetic Test
4. Motor Co ordination Test
5. Digit Letter Substitution Test
6. Paragraph Cancellation Test
7. Benton Visual Retention Test

In addition to the above tests heart rate and blood pressure were recorded.

mm of mercury or any cardiac condition causing documented hemodynamic compromise were excluded from the study.

Experimental design: Subjects who had no exposure to smoking cigarettes were included in the Control group. Subjects who had earlier exposure to smoking cigarettes were included in the Cigarette group. In the control group, battery of tests was done in the subjects who were non-smokers, then giving a rest interval of 5 minutes and repeating the battery of tests.



In the cigarette group, battery of tests was done in the subjects who were smokers, then subject was asked to smoke a cigarette, which he normally used to smoke, and repeat the battery of tests. All brands of cigarette available in the market were made available.

Every test was administered twice in both the groups. The test material for repeat exposure was prepared in such a way that there would not be interference of initial test.

Thus, the design of the study was open and comparison of cigarette group with control group.

Method used in the study: Forward Digit Span Test was done as described by Matarazzo¹, Word List Memory Test as describe by Rey², Mental Arithmetic Test as describe by Ida sue Baron et al³, Motor Co ordination Test as describe by Avram et al⁴, Digit Letter Substitution Test as describe by Natu and Agarwal⁵, Paragraph Cancellation Test as

describe by Natu and Agarwal⁵, Benton Visual Retention Test as describe by Benton⁶ was used.

Statistical analysis: Scores of various parameters during initial tests in control group and cigarette group were analysed by unpaired 't' test to see homogeneity of the population. Scores of various parameters in each group during initial tests and subsequent tests were analysed by paired 't' test. Any difference in this comparison in control group would be indicative of effect of repeat test. The difference in cigarette group would be indicative of effect of cigarette smoking, provided there is lack of difference in repeat test in control group.

Result: Subjects who had no exposure to cigarette smoking during the study represented the control group. Subjects who had exposure to single cigarette smoking during the study represented the experimental group.

A total of 30 non-smokers and 34 smokers completed the study. Smokers had a history of smoking of at least 6 months, with current use <10 cigarettes per day and a score <2 (maximum = 10) on the Fagerström test for nicotine dependence indicating that the subjects were not addicted to nicotine. Result are describe in following Table

Table 1: Hear Rate and Blood Pressure comparison in both group before and after test

Test	Control group (n = 30)		Cigarette group (n = 34)	
	Initial test	Subsequent Test	Initial test	Subsequent Test
Heart rate	79.97 ± 2.58	80.23 ± 2.71	80.25 ± 2.55	81.38 ± 1.92*
B.P Systolic	122.33 ± 2.17	122.27 ± 2.02	122.75 ± 2.82	124.25 ± 2.49****
Diastolic	80.67 ± 2.8	80.73 ± 2.7	81.0 ± 3.02	82.75 ± 3.2****

Mean ±S.D; *p<0.05; **p<0.02; ***p<0.01; ****p<0.001

Table 2: Cognitive test result comparison in both group before and after test

Test	Control group (n = 30)		Cigarette group (n = 34)	
	Initial test	Subsequent Test	Initial test	Subsequent Test
1 Forward	5.07	5.13 ±	4.74 ±	5.35 ±

	Digit Span Test	± 0.94	1.01	1.16	0.95****
2	Word List Memory Test	5.83 ± 1.42	5.80 ± 1.45	5.56 ± 1.48	6.24 ± 1.67**
3	Mental Arithmetic Test	30.50 ± 10.61	31.17 ± 10.64	39.85 ± 20.43	34.62 ± 18.79****
4	Motor Co-ordination test	322.83 ± 85.90	328.47 ± 91.73	354.32 ± 82.15	423.26 ± 106.74***
5	Digit Letter Substitution Test	8.37 ± 6.49	59.73 ± 8.98	57.97 ± 7.74	61.44 ± 6.67****
6	Paragraph Cancellation Test	109.43 ± 18.69	116.27 ± 25.57*	108.09 ± 26.91	124.21 ± 24.28****
7	Benton Visual Retention Test	8.20 ± 1.37	8.07 ± 1.34	8.09 ± 1.46	8.65 ± 1.32***

Mean ±S.D; *p<0.05; **p<0.02; ***p<0.01; ****p<0.001

Table 3: Effect of cigarette smoking

	Test	Effect of Cigarette Smoking
I	Heart Rate	Increase
	Blood Pressure	Increase
II	Forward Digit Span Test	Improvement
	Word List Memory Test	Improvement
	Mental Arithmetic Test	Improvement
	Motor Co-ordination Test	Improvement
	Digit Letter Substitution Test	Improvement
	Paragraph Cancellation Test	Improvement
	Benton Visual Retention Test	Improvement

Discussion: Tobacco, *Nicotiana tobacum*, is a native plant of the American continent. Consumption of tobacco started in the early 16th century and it has progressively increased over the centuries despite the well established hazards of smoking⁶. Nicotine is the principle and most potent psycho-pharmacologically active component of cigarette smoke⁷. Smokers are more likely to suffer

from fatal ischaemic heart disease⁸, Buerger's disease⁹, cancer and chronic obstructive pulmonary disease⁸. Cigarette smoking is the most dangerous dependence producing drug¹⁰. Recognizing the health hazards of tobacco, most countries of the world have promulgated various laws enforcing the cigarette manufacturing companies to display health warnings on packages and advertisements of cigarettes. Despite all these efforts, people still continue to smoke cigarettes. Probably, this may be due to peer pressure and social acceptability.

Nicotine markedly stimulates the CNS¹¹. The smoker feels alert, yet there is some muscle relaxation. Nicotine readily crosses the blood brain barrier stimulating the nicotinic acetylcholine receptors (nAChR). The stimulation of the presynaptic nAChRs on ACh neurons increases the acetylcholine release as well as its metabolism¹². Many neurons in the brain express the neuronal nicotinic receptors at which nicotine acts and, as a result, nicotine stimulates other pathways. These pathways include the noradrenaline-secreting neurons of the locus ceruleus which project to the forebrain, many of the acetylcholine-secreting neurons found in the hippocampus and cortex which secrete the excitatory amino acid, glutamic acid, and the inhibitory amino acid, γ -aminobutyric acid¹³. It seems likely that stimulation of the receptor located on glutamate-secreting terminals facilitates release of the glutamate, and that stimulation of NMDA receptors located on the dopamine-secreting neurons in the ventral tegmental area (VTA) results in increased burst firing of the neurons, and thus an enhanced dopamine response to nicotine¹⁴. The administration of a nicotine bolus causes increased dopamine release in the nucleus accumbens¹⁵. It also seems likely that the effects of nicotine on acetylcholine-secreting neurons may be implicated in the increase in arousal and attention sometimes associated with smoking¹⁵. In addition, the stimulatory effects on both acetylcholine and glutamate secretion in the hippocampus and cerebral cortex may mediate the improved cognitive function which has been reported for nicotine¹³. In a study of 600 adult smokers, 53% agreed strongly and 38% agreed mildly with the statement 'smoking can help people relax', whilst only 2% disagreed strongly¹⁰.

In most of the studies, data was collected in form of questionnaire from the subjects who were in habit of smoking. In the present study it was aimed to study the effect of tobacco on cognitive function in more objective way. The study was conducted in subjects who were occasional smokers to establish the effects, if any, after single cigarette smoking. The tests used in the study were those, which were well established in most cognitive studies. As the aim was to study the objective effects, only 64 subjects could participate in the study. The protocol was to compare the performances on various tests after smoking a cigarette against the performance of a control group of subjects. The limitations of this open design are obvious. Placebo-control study would have been a better design. De-nicotinised cigarette would have served the purpose of proper placebo. Because of non-availability of such material presently, placebo-control study could not be planned. As the smokers would have known that the cigarette is de-nicotinised¹⁶, it would not have served the purpose in blind study. Knowing the hazards of smoking, non-smokers were neither included nor were induced to smoke during the study.

As the central effects of nicotine from cigarette are produced within 7 seconds, tests were conducted immediately after smoking a cigarette. Also, since the nicotine level in blood falls back to pre-smoking level within 15 minutes not more than 9 tests were considered appropriate.

In our study, smoking has been shown to increase heart rate and both systolic and diastolic blood pressure. Nicotine is known to produce these effects through stimulation of nicotinic receptors in autonomic ganglia and adrenal medulla¹⁷. Stimulation of autonomic ganglia leads to sympathetic stimulation and of adrenal medulla to secretion of adrenaline. These effects lead to increase in heart rate and systolic and diastolic blood pressure. In Motor Co-ordination Test, to draw a zigzag line in the restricted area without making any error measures the alertness and fine motor co-ordination movements. Mean number of units traversed as well as errors committed (touching adjacent lines) was taken into consideration during scoring¹⁸. In our study, after smoking a cigarette there was improvement in the

score of the test, but it remained unaltered in control group suggesting nicotine improves alertness and fine motor co-ordination tasks. Results of a double blind study of cigarette smoking on a 1-hour computer based simulation of driving suggest that cigarette smoking may improve driving performance and enhance cognitive and psychomotor function¹⁹. Caffeine in coffee has been shown to improve the score in this test in a double blind study¹⁸. Generalized alertness may be responsible for the seen effects.

In Forward digit span test the subject was asked to repeat the pronounced digit series in forward order. This test measures retention and short-term memory. After smoking a cigarette, the score was increased, but it remained unaltered in control group suggesting that nicotine has improved short-term memory.

Word list memory test measures learning and short-term recall. After smoking a cigarette, the number of words recalled increased, but it remains unaltered in control group suggesting that nicotine has improved learning and short-term memory in this test too.

Benton Visual Retention Test measures visual perception, immediate retention and non-verbal recall, again, indicating short-term memory. After smoking a cigarette, the number of figures recalled increased, but it remained unaltered in control group suggesting that nicotine has improved short-term memory based on visual perception.

Mental arithmetic test measures problem solving capacity, calculation skill and attention. After smoking a cigarette, the duration of time required to complete the task was decreased, but it remained unaltered in control group suggesting that nicotine has improved the performance. Problem solving capacity, calculation skill and attention appear to be improved by cigarette smoking.

Digit Letter Substitution test includes process of understanding the task, speed of going to key and decision of using an appropriate letter for the digit. Alertness and good coordinating capacity is needed for good performance of this test. After smoking a

cigarette, there was increase in the number of digits substituted, but it remained unaltered in control group suggesting nicotine improved alertness and co-ordination.

Paragraph Cancellation Study also tests a particular function. Vowels like a, e, i, o, u and double letters appearing in the paragraph were targets for cancellation. Thus, while doing this test subject carries a concept of vowels and double letters and tries to search accordingly in the paragraph. Considering the speed of completing the task during scoring, one actually tests individual's capacity of perception, recognition, attention and ability of sorting out each letter befitting with the criteria for cancellation. Nicotine did not appear to improve these functions in our study in terms of total cancelled letters. In terms of percent accuracy of cancellation, nicotine appears to improve the performance. This shows that smoking may improve quality of performance of a work. This may be due to increase in general alertness.

In the literature, the tests exploring other cognitive function showed that there is consistent improvement in performance after smoking. It is important to note that nicotine improved attentional performance and reduced errors of omission on Conners' continuous performance test (CPT) with chronic transdermal nicotine in Alzheimer's disease subjects in a double-blind, placebo controlled, cross-over study²⁰.

Caffeine in coffee has been shown to improve performance in a double blind study in mental arithmetic test²¹ and digit letter substitution test^{18,21}. However, improvement in total number of cancelled letters and percent accuracy of cancellation was observed in both caffeine and placebo group^{18,21}. Thus, there appear qualitatively different effects of caffeine as compared to nicotine. Generalized alertness by both the compounds cannot explain the observed effects.

Conclusion: In the present study, smoking a cigarette has shown definite improvement in cognitive functions like short-term memory, alertness, visual retention, calculation skill and motor co-ordination. No attempt is made in the present study about the effect of repeated

smoking. The tolerance to these effects cannot be ruled out presently. The present study needs further exploration from point of view of therapeutic utility.

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