EFFECT OF SMOKING ON NEUROCOGNITIVE FUNCTION

Soundariya K[1], Deepika V[2], Venkatesh SP[3]

[1] Associate Professor, Department of Physiology, Sri Manakula Vinayagar Medical College and Hospital, Puducherry- 605107, India
[2] Assistant Professor, Department of Physiology, Sri Manakula Vinayagar Medical College and Hospital, Puducherry- 605107, India
[3] Assistant Professor, Department of Surgery, Indira Gandhi Medical College and Research Institute, Puducherry – 605009, India

Abstract: **Background and Objectives**: Decline in cognitive function is a debilitating health problem at an older age. Identification of the modifiable risk factors at an earlier age may promote good cognitive health in later age. Cigarette smoking is a modifiable risk factor whose negative impact on respiratory and cardiovascular health is well addressed. However, research on the effect of smoking on cognition had shown inconclusive results. Hence the present study aimed to study the impact of smoking on neurocognition in the individuals in the age group of 20-50 years. **Methods**: A total of 150 study participants in the age group of 20-50 years were recruited for the study. They were divided into smokers and nonsmokers. Cognitive function was evaluated by AddenBrooke's Cognitive Examination – Revised (ACE-R), which included MMSE (Mini Mental State Examiation) as a part of it component. Fagerstrom Nicotine dependence scale (FNDS) was used to measure the nicotine dependence among the smokers. Data were analysed using appropriate statistical tests. $p < 0.05$ was considered statistically significant. **Results**: The total cognitive scores of the smokers by ACE-R and MMSE were significantly lower than the nonsmokers ($p<0.001$). The cognitive scores were significantly lower in moderate smokers and in smokers with significant nicotine dependence. Cognitive scores had a statistically significant negative correlation with the pack years and with the nicotine dependence. **Conclusion**: Cigarette smoking significantly influences cognitive function and hence cessation of smoking at an earlier age may prevent the onset of cognitive impairment at older age.

Key Words: Cognition, Nicotine Dependence, Pack years, Smokers

Abbreviations : ACE-R , AddenBrooke's Cognitive Examination – Revised; FNDS , Fagerstrom Nicotine Dependence Scale; MMSE , Mini Mental State Examination

Author for correspondence: Dr. Soundariya K, Department of Physiology, Sri Manakula Vinayagar Medical College and Hospital, Madagadipet, Puducherry - 605107
Ph No: 9786895193, e- mail: soundariyapriya@yahoo.com

Introduction:

Smoking remains a serious global health threat and is one of the leading causes of preventable deaths worldwide. It harms nearly every organ of the body and has been attributed as a risk factor for a variety of conditions like respiratory diseases, cardiac diseases, vascular diseases and also cancer[1]. World Health Organization (WHO) report predicts that the annual death toll due to tobacco consumption could rise to over 8 million in the next two decades[2] and it has aimed at a 30% relative reduction in the prevalent current tobacco use in persons aged more than 15 years in the upcoming years[3].

Adequate cognitive functioning plays a vital role in leading an independent life. Cognitive decline is a debilitating health problem in the elderly people. With the increase in the life expectancy of the population, presence of cognitive impairment may significantly contribute to morbidity, thereby posing a strain on the caregivers of the family, health care facilities and also national income[4]. A preclinical phase of cognitive impairment may precede the onset of Alzheimer's disease by several years[5]. Hence it is imperative to identify the risk factors that affect the cognitive functioning. Cigarette smoking is a modifiable risk factor that may influence cognitive functioning.

Extensive research has attested the adverse effects of smoking on respiratory and cardiac function. However, only few studies have explored the impact of smoking on cognition. Literature search on the effect of smoking on cognition had revealed conflicting results. Early research indicates that nicotine content of the cigarettes may enhance the cognitive performance by enhancing regional cerebral blood flow [6,7]. However a meta analysis revealed a faster cognitive decline among current smokers than ex smokers or non smokers[8]. Identification of risk factors that contribute to

cognitive decline may help in the development of primary prevention strategies for promoting a good cognitive health in later life. Though the benefits of cessation of smoking in the elderly had been extensively studied, the degree to which smoking uniquely contributes to cognitive functioning has yet to be established. With a paucity of data on this aspect in the Indian context, the present study aimed to study the impact of smoking on neurocognition.

Material and Methods:

A total of 150 males in the age group of 20-50 years were recruited by house visits in the local area for the present cross sectional study. Known hypertensives, known diabetics, individuals on sedatives, anti psychotic drugs, age > 50 years, individuals with mental illness, vascular diseases were excluded from the study. As this test was a literacy based assessment, only literate adults with education ≥ 9 years were included for the study[9]. Subjects more than 50 years were not included to avoid the bias resulting from age related cognitive decline. Due to non availability of female smokers, the study participants were restricted to males. After obtaining permission from the institutional ethics committee, the procedure and purpose of the study were clearly explained to all the study participants. The study participants were divided into two groups as smokers and nonsmokers. Informed consent was obtained from all the study participants. The smokers were further divided based on their Pack years into Light (0-20) and Moderate smokers (20-40)[10].There were no heavy smokers with pack years >40. Adden Brooke's cognitive examination – Revised version (ACE-R) was used for cognitive assessment. This cognitive assessment included five domains, each representing a specific cognitive function like Attention(18), memory(26), fluency(14), language(26) and visuospatial ability(16), contributing to a total score of 100. The ACE-R also included Mini Mental state examination (MMSE) as a part of its component. Of the total 100 points, MMSE included 30 points. Higher scores indicate a better cognitive function. As per the guidelines for research purposes a score of ≤ 82 is considered to yield a 100% chance of having dementia. Fagerstrom Nicotine dependence scale, a 6 item self report questionnaire was used to assess the nicotine dependence in smokers. A score of 5 or more was considered as significant dependence, less than 4 as low to moderate dependence.

Statistical analysis was done using SPSS software version 23. Student t test was used to compare the scores between smokers and nonsmokers , between light and moderate smokers and the scores between smokers with low nicotine dependence and significant nicotine dependence. Pearson's correlation test was used to correlate between the smoking status by pack years, nicotine dependence and the cognitive scores. $p < 0.05$ was considered statistically significant.

Result:

In the present cross sectional study, of the total study participants, 63 were smokers and 87 were nonsmokers. Table 1 shows the baseline characteristics and the comparison of the cognition scores of ACE-R and MMSE between smokers and nonsmokers. The scores in the individual domains other than Fluency were significantly lower in smokers compared to non smokers ($p < 0.001$). Total scores of cognitive analysis by ACE – R and MMSE were again lower in smokers (84.11 ± 5.33, 25.90 ± 1.71) compared to the non smokers (91.91 ± 3.14, 28.43 ± 1.19), which was statistically significant ($p < 0.001$).

Table 1: Comparison of the baseline characteristics and cognitive scores of ACE-R and MMSE between smokers and nonsmokers.

Parameters	Nonsmokers	Smokers
n	87	63
Age	33.45 ± 8.08	34.49 ± 7.73
ACE-R		
Attention	16.79 ± 1.06	16.09 ± 1.02*
Memory	24.34 ± 1.56	22.84 ± 1.35*
Fluency	11.45 ± 1.39	11.25 ± 0.86
Language	23.75 ± 1.18	20.98 ± 2.40*
Visuospatial	15.67 ± 0.56	12.98 ± 1.67*
Total	91.91 ± 3.14	84.11 ± 5.33*
MMSE	28.43 ± 1.19	25.90 ± 1.71*

Values expresses as mean ± S.D. *$p < 0.001$, n = Number of participants, ACE – R – AddenBrooke's Cognitive Examination Revised , MMSE – Mini Mental State Examination.

Table 2 shows the comparison of the total scores of cognition by ACE-R and MMSE between

Light and Moderate smokers. Moderate smokers (80.10 ± 3.86) had lower scores than the Light smokers (85.97 ± 4.89), which was statistically highly significant ($p < 0.001$).The Nicotine dependence score among Light and Moderate smokers were 5 ± 1.78, 7.05 ± 1.93 respectively, which was significantly higher among the Moderate smokers.

Table 2: Comparison of the baseline characteristics and cognitive scores by ACE-R and MMSE between Light and Moderate smokers.

Parameters	Light Smokers	Moderate Smokers
n	43	20
Pack years	5.8 ± 4.59	23.67 ± 3.42*
ACE-R – Total	85.97 ± 4.89	80.10 ± 3.86*
MMSE	26.32 ± 1.68	25 ± 1.41*
FNDS Score	5 ± 1.78	7.05 ± 1.93*

Values expressed as Mean ± S.D. N = Number of participants, ACE – R – AddenBrooke's Cognitive Examination Revised, MMSE – Mini Mental State Examination, FNDS Score – Fagerstrom Nicotine Dependence Scale Score, *$p < 0.001$

Table 3 shows the comparison of the total scores of cognition by ACE-R and MMSE between smokers with low to moderate dependence and Significant nicotine dependence. The total cognitive scores of ACE-R and MMSE were significantly lower in individuals with significant nicotine dependence ($p< 0.001$).

Table 3: Comparison of the cognitive scores by ACE-R and MMSE between smokers with low to moderate and significant nicotine dependence

Parameters	Low to Moderate Dependence	Significant Dependence
n	19	44
Pack years	4.87 ± 6.55	14.33 ± 9.03*
ACE-R – Total	88.63 ± 3.46	82.15 ± 4.79*
MMSE	27.10 ± 1.37	25.38 ± 1.58*
FNDS	3.15 ± 0.89	6.72 1.35*

Values expressed as Mean ± S.D. * $p < 0.001$, n = Number of participants, ACE – R – AddenBrooke's Cognitive Examination Revised, MMSE – Mini Mental State Examination. FNDS Score – Fagerstrom Nicotine Dependence Scale Score

Table 4 shows the correlation between the Pack years, Nicotine dependence and Cognitive scores. Cognitive score had a negative correlation with the Pack years (-0.702) and with the nicotine dependence (-0.704), which were statistically highly significant ($p < 0.001$).

Table 4: Correlation of the Cognitive score with pack years and Nicotine dependence.

Variables	Cognitive score (ACE –R)	
	Coefficient	p Value
Pack years	- 0.702	0.001
Nicotine dependence	- 0.704	0.001

ACE – R – AddenBrooke's Cognitive Examination Revised

Discussion:

The present cross sectional study assessed the cognition of the study participants in the age group of 20-50 years, using ACE-R and MMSE, and studied the impact of smoking on cognition by comparing the cognitive scores between the smokers and the non smokers. Of the 63 smokers, 44 had significant nicotine dependence as measured by Fagerstrom nicotine dependence scale.

The results of the present study showed that the total scores of ACE-R and MMSE were significantly lower in smokers compared to the non smokers. Similar results were observed in another cross sectional study by Sudharkodhy S et al[11]. Two other longitudinal studies also support the findings of the present study. Anstey KJ and his colleagues observed that current smokers had a greater rate of cognitive decline over a period of 2-7 years compared to the non smokers[12]. Sabia S et al observed a faster global cognitive decline in middle aged smokers, in a cohort study[13]. However the result of the present study goes in contrast with the findings of Dumatar C who had shown a definite improvement in short term memory, alertness and motor coordination in smokers[14]. The contradiction could be explained with the fact that Dumatar C observed the acute effects of smoking on cognition. These conflicting results show that acute administration of nicotine may improve arousal and attention, through the nicotinic

cholinergic receptors activation[15]. Further the studies that had addressed the beneficial effects of nicotine as a cognitive enhancer, had been performed under the circumstances of smoking abstinence, where nicotine administration brought significant relief of the withdrawal symptoms and hence showed a cognitive enhancement[16]. However Almeida OP et al observed that chronic smokers lose a disproportionate quantity of gray matter density in the areas critical for cognitive function, over a period of two years[17].

The cognitive scores in the various domains like attention, memory, visuospatial ability and language were significantly lower in smokers compared to the nonsmokers. Heishman SJ et al in his metaanalysis revealed that nicotine enhances the motor abilities, attention and memory, however these changes were attributed as the acute effects of nicotine[18]. Hence this warrants more research in the form of longitudinal studies to clearly differentiate the acute and chronic effects of cigarette smoking. In the present study Moderate smokers had significantly lower cognitive scores than light smokers. However their Nicotine dependence was very high compared to the light smokers. Similar results were observed by Razani J et al, where heavy smokers performed poorly in executive functions[19].

In the present study, individuals with significant nicotine dependence had lower cognitive scores than the smokers with low to moderate nicotine dependence. Further cognitive scores showed a significant negative correlation with the level of nicotine dependence and smoking status as assessed by the number of cigarettes smoked per day. Chandra M et al in their study observed that nicotine dependence was a poor prognostic factor associated with dementia[20]. These results suggest that nicotine dependence may significantly influence the cognitive decline in the smokers.

Conclusion:

The results of the present study suggest that cigarette smoking may cause subtle reductions in the cognitive function even at an earlier age of 20 – 50 years. ACE-R and MMSE may be used as simple screening methods for early identification of mild cognitive impairment among smokers. Cessation of smoking at an earlier age may prevent the onset of cognitive impairment at older age.

References:

1. U.S. Department of Health and Human Services. The Health Consequences of Smoking: 50 Years of Progress. A Report of the Surgeon General. Atlanta(GA) : U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2014.
2. World Health Organization. WHO Global report: Mortality attributable to tobacco. Geneva (Switzerland). World Health Organization,2012;http://apps.who.int/iris/bitstream/10665/44815/1/9789241564434_eng.pdf; accessed August 10, 2015.
3. World Health Organization. WHO Global action plan for the prevention and control of non communicable diseases 2013–2020. Geneva (Switzerland). World HealthOrganization,2012;http://apps.who.int/iris/bitstream/10665/94384/1/9789241506236_eng.pdf ;accessed August 10,2015.
4. Kalaria RN, Maestre GE, Arizaga R, Friedland RP, Galasko D, Hall K, et al. Alzheimer's disease and vascular dementia in developing countries: Prevalence, management and risk factors. Lancet Neurol 2008; 7: 812-26.
5. Elias MF, Beiser A, Wolf PA, Au R, White RF, D'Agostino RB. The Preclinical Phase of Alzheimer Disease: A 22-Year Prospective Study of the Framingham Cohort. Arch Neurol 2000; 57(6): 808-813.
6. Ghatan PH, Ingvar M, Eriksson L, Stone-Elander S, Serrander M, Ekberg K,Wahren J. Cerebral effects of nicotine during cognition in smokers and non-smokers. Psychopharmacology (Berl). 1998; 136(2): 179-89.
7. Warburton DM. Nicotine as a cognitive enhancer. Prog Neuropsychopharmacol Biol Psychiatry 1992; 16(2): 181-91.

8. Anstey KJ, von Sanden C, Salim A, O'Kearney R. Smoking as a risk factor for dementia and cognitive decline: a meta-analysis of prospective studies. Am J Epidemiol 2007; 166(4): 367-78.
9. Mathuranath PS, Cherian PJ, Mathew R, George A, Alexander A, Sarma P. Mini mental state examination and the Addenbrooke's cognitive examination: effect of education and norms for a multicultural population. Neurol India 2007;55(2): 106–110.
10. Lee YH, Shin MH, Kweon SS, Choi JS, Rhee JA, Ahn HR, et al. Cumulative smoking exposure, duration of smoking cessation, and peripheral arterial disease in middle-aged and older Korean men. BMC Public Health 2011;11 :94.
11. Sudharkodhy S, Reddy m, Sneha R, Kutty K. Effect of Tobacco on Cognitive Function in Elderly People –A Pilot Study. J Clin Biomed Sci 2015; 5(1): 17-20.
12. Anstey KJ, von Sanden C, Salim A, O'Kearney R. Smoking as a risk factor for dementia and cognitive decline: a meta-analysis of prospective studies. Am J Epidemiol 2007; 166(4): 367-78.
13. Sabia S, Elbaz A, Dugravot A, Head J, Shipley M, Hagger-Johnson G, Kivimaki M, Singh-Manoux A. Impact of smoking on cognitive decline in early old age: the Whitehall II cohort study. Arch Gen Psychiatry 2012; 69(6): 627-35.
14. Dumatar C , Chauhan J. A study of the effect of cigarette smoking on cognitive parameters in human volunteers. NJIRM 2011; 2(3): 71-76.
15. Laviolette SR , Derek van der Kooy. The Neurobiology of Nicotine addiction: Bridging the gaps from molecules to behavior. Nature Reviews Neuroscience 2004; **5:** 55-65.
16. Ernst M, Heishman SJ, Spurgeon L, London ED. Smoking history and nicotine effects on cognitive performance. Neuropsychopharmacology 2001; 25(3): 313-9.
17. Almeida OP, Garrido GJ, Alfonso H, Hulse G, Lautenschlager NT, Hankey GJ, Flicker L. 24-month effect of smoking cessation on cognitive function and brain structure in later life. Neuroimage 2011; 55(4): 1480-9.
18. Heishman SJ, Kleykamp BA, Singleton EG. Meta-analysis of the acute effects of nicotine and smoking on human performance. Psychopharmacology (Berl) 2010; 210(4): 453-69.
19. Razani J, Boone K, Lesser I, Weiss D. Effects of cigarette smoking history on cognitive functioning in healthy older adults. Am J Geriatr Psychiatry 2004; 12(4): 404-11.
20. Chandra M, Anand KS. Assessment of nicotine dependence in subjects with vascular dementia. Int J Res Med Sci 2015; 3.

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