Advanced Medical Journal, Vol.8, No.2, P.8-15, 2023 https://doi.org/10.56056/amj.2023.212

Correlation between smoking and brain atrophy detected by cross sectional imaging

Aryan Wirya Marof *
Saeed Nadhim Younus **

Abstract

Background and objectives: Smoking have effect on many organs in human body, we are focusing on its relation with brain atrophy. We aimed to determine whether there is an association between smoking and brain atrophy by using certain parameters from CT scan or MRI of brain.

Methods: This is a case control study done from December 2019 to May 2021, a total of 100 cases of CT scans and MRI brain which is randomly selected reviewed by taking certain measurements like frontal horn index, Evans ratio, bicaudate index, huckman number, cella media.

Results: Brain atrophy group involved 50 cases and control non-atrophy group 50 cases both group with equal number of male and female, there is statistically significant difference between smokers with brain atrophy 30% and smokers with no brain atrophy 6% with p-value 0.027, also the mean duration of smoking among brain atrophy was 17.83 years while among non-atrophic brain was 9.83 years. Number of cigarettes smoked per day showed statistically significant difference as it was 21.07 cigarettes among smokers with brain atrophy versus 13.83 cigarettes in non –brain atrophy smokers.

Conclusions: Current brain imaging demonstrate that chronic tobacco smoking is associated with significant increase in prevalence of brain atrophy than non-smokers, smoking can be considered a risk factor for brain atrophy.

Key words: Brain atrophy; CT scan and MRI measurements ;Smoking**.**

Introduction

Nearly two billion humans globally use tobacco products, mainly in the form of cigarettes, tobacco associated illnesses resulting in four million deaths per year.[1] There is an extensive number of studies very clearly show the effect of chronic cigarette smoking on human cardiac vascular system, pulmonary function and its carcinogenic effect but only limited number of studies describe its effect on brain in general.[2-5] New studies show chronic cigarette smoking through numerous biomedical conditions may directly or indirectly compromise brain neurobiology and neurocognition.[6-9] Studies in middle-aged to older adults show that chronic smoking is related to increase of global brain atrophy with advancing age.[10-13] Chronic Tobacco smoking have both chemical and anatomical effect on brain in normal adults.Smokers show decrease level of concentration during working time than non smokers, also those start to smoke at earlier age show more impairment than those start smoking in later life.[14] In other studies, comparing non-smoker control NSC to smokers, poorer performance in smokers was found in auditory-verbal learning and/or memory, vocabulary expression, speed of processing information, visual search speed, risk

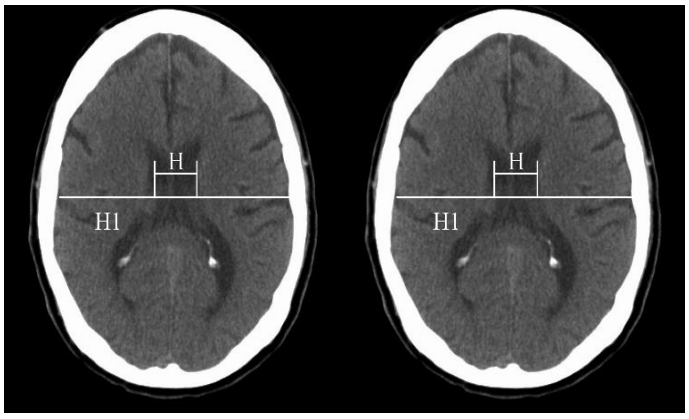
*MBCH, Radiology department, Rizgari teaching hospital, Erbil, Iraq.
**MBCH, DMRD, PHD, kHCMS, Scientific Counsel of Radiology, Erbil, Iraq.
Corresponding author: Aryan Wirya Marof. E-mail: aryanwm89@yahoo.com

taking behavior, working memory, processing speed and general intellectual abilities.[15-16]Many MRI studies show higher number of cigarettes was associated with increased ventricular volume in male and increased sulcal volume in female, inconsideration of age and vascular risk factors .[17] More new MRI studies used voxel-based morphological measures gray mater volume to assess the regional brain volumes and densities of the cortical gray matter, smokers show lower tissue densities with smaller volumes in bilateral anterior frontal lobe regions, insula, smaller volume of the left dorsal cingulate and lower gray matter density in the cerebellum than non smoker controls. Older age smokers show reduced gray matter density in right thalamus, left posterior cingulate gyrus, bilateral precentral and middle frontal gyri compared to non smoker controls.[18]Magnetic resonant- based DTI (diffusion tensor imaging) is also used for structural integrity of corpus callosum .[19]It is clear that smoking in middle age and older is associated with increased incidence of hyperintensities on MR imaging on T2-weighted and FLAIR in regional white matter [20]. This white matter hyperintensities are due to decreased cerebral blood perfusion [21] and affect neurocognitive dysfunction.[22] A single volume proton MR spectroscopy study show lower NAA (N-acetylaspartate) which is a marker for neuronal integrity in left hippocampus of chronic smokers in relation to non smokers, and Cho (Choline) which is a marker for cell membrane turnover/synthesis, were higher in this region which is related positively to packs per year.[23]Few published studies specifically show decrease whole brain perfusion in chronic smokers than non smokers, and perfusion was inversely related to number of packs per year.[24] There is significant number of cytotoxic compounds which damage neuronal or glial cells and promote oxidative damage, although nicotine is a principle bioactive in cigarette but all the neurocognitive and neurobiological changes are due to continuous exposure of cardiopulmonary, cerebrovascular, and brain parenchyma to nicotine and non-nicotine products[25] .Most experienced radiologist is able to determine brain atrophy qualitatively by looking at ventricular space dilatation, gray and white matter volume but quantitative examination is necessary to accurately identify these changes. There are many software can be used by CT or MRI for evaluation of brain atrophy and volume as a whole brain or regional but these methods require some degree of manual supervision. Although they are more precise but there use in routine daily practice require time and training. The aim of the study was to determine the correlation between cigarette smoking and brain atrophy.

Materials and methods

This is a case-control study. It was approved by the ethical committee of Kurdistan Board of Medical specialties. The study was performed on 100 patients who attended radiology department of Rizgary teaching hospital in Erbil city on those who have attending for brain study (CT – scan or MRI) from December 2019 to May 2021. In this study we reviewed 100 cases, aged 20- ≥ 60 years. Smokers in our study are those who use any product of tobacco at least once a day this in consistent with WHO[26] definition for smoker, non-smokers in our study are those neither ex-smoker nor passive smoker. Verbal and written consent were taken from each individual for the purpose of getting Data regarding demographic characteristics, smoking habit, duration of smoking, educational level, medication use, and co morbidities like hypertension, diabetes, stroke, were collected by self-administered questionnaires.The exclusion criteria are factors that affect brain atrophy

like hypertension, diabetes mellitus, trauma, stroke, tumor, multiple sclerosis, brain operation, psychiatric disease, dementia and some medication that affect brain atrophy like anticonvulsant. Regarding the age of both groups those more than 18 years are involved in the study. The CT scanner was a 16-detector row, the patients were put in supine position and scanning head, slice thickness 4 mm slices, 120–130 kV, 250 mAs.Magnetic resonant imaging was performed with1.5 tesla MRI a turbo spin-echo pulse sequence. The scanning parameters were as follows: TR/TE 3200/85 ms, FA (fractional anisotropy) 150, FOV was 22x22 cm, matrix size was 256x256, and slice thickness 4 mm.The brain atrophy parameters were measured on the CT scans or MRI. Based on the commonly used method described by Meese[27]. Each parameter was measured twice in order to increase accuracy and limit the "partial volume" effect.The calculated indices include:frontal horn index = bifrontal diameter to maximum width of the anterior horns of the lateral ventricles. (less than or equal to 3.7)[27] Huckman number = minimal bicaudate distance + maximum width to anterior horn of lateral ventricle (less than or equal to 45mm)[27]Frontal horn width to intercaudate distance ratio, FH/CC (normal value 2.2-2.6).[28]Bicaudate index = Minimum width of the lateral ventricles at level of caudate nucleus to the maximum skull width at the same level (normal value 0.09-0.12) .[28] Cella media index or schiersmanns index for assessment of ventricular size with respect to brain tissue and cerebral atrophy = biparital diameter of skull to maximum external diameter of lateral ventricle at cella media (normal value more than 4).[28]Evans index= maximum bi frontal horn of lateral ventricle to maximum skull diameter in same axial plain (normal less than 0.3).[28]



Figure(1): CT of the brain, cella media index: H1/H, frontal horn index A1/A
Bicaudate index: B/B1, Evan's index = A/C, Hackman number = A+B .

Data entered and analyzed using Statistical Package for Social Sciences version 25 (SPSS Inc., IBM Company, Chicago, Illinois, USA). Descriptive analyses were expressed as frequencies and percentages and the inferential results were compared between the subjects with different variables using a statistical significance level of ≤ 0.05 and analyzed using t-test and Pearson Chi square or Fisher's exact tests if necessary.

Results

The findings of Table (1) show that, there was a significant association between age groups and brain atrophy, most patients with no atrophy were younger than patients with brain atrophy, Chi square test was done and p-value 0.013. There was a significant statistical association between smoking and brain atrophy, a higher

percentage (30%) of patients with brain atrophy were smokers while only (12%) of patients with no atrophy were smoker. Chi square test was done with p-value 0.027.

Table (1): Association between age group, smoking and Atrophy.

Variable	Categories	Brain atrophy		p-value
		Yes	No	
age groups(yrs)	20 – 29	3 (6%)	7 (14%)	0.013
	30 – 39	8 (16%)	13 (26%)	
	40 – 49	20 (40%)	5 (10%)	
	50 – 59	10 (20%)	14 (28%)	
	≥ 60	9 (18%)	11 (22%)	
Smoking	Yes	15 (30%)	6 (12%)	0.027
	No	35 (70%)	44 (88%)	
Total		50 (100%)	50 (100%)	

The overall risk (odds ratio) of development of brain atrophy among smokers was three times higher than non-smokers (OR: 3.14), this was statistically significant and p-value was 0.027. In contrast, the OR of getting brain atrophy among non-smokers was less than one (0.79), avoiding the practice of smoking seems to be protective against development of brain atrophy (Table 2).

Table (2): Risk estimation (odds ratio) for development of brain atrophy among smokers and non-smokers.

Odds ratio (OR)	Value	95% Confidence Interval	
		Lower	Upper
Odds Ratio for atrophy (yes / no)	3.14	1.10	8.94
For cohort smoking = yes	2.50	1.05	5.91
For cohort smoking = no	0.79	0.64	0.98

The results of Table (3) reveal that, there was non-significant association between gender and atrophy, approximately half (50%) of participants in each group were male and the other half were female, p-value was (0.842). There was a non-significant association between type of smoking and brain atrophy; most of the smokers in each group were smoking cigarettes. More than half (53.3%) of patients with atrophy were smoking cigarettes, and (20%) of patients with atrophy were smoking argillah, and more than quarter (26.7%) of patients with brain atrophy were smoking both cigarette and argillah, and p-value was (0.497). There was a non-significant association between educational level and atrophy; the majority of the participants in both groups were either graduate or under-graduate. Thirty percent of patients with atrophy were graduated, while (56%) of patients with brain atrophy were under-graduated and only (14%) of patients with atrophy were illiterate, and p-value was (0.039).

Table (3): Association between general information and atrophy.

Variable	Categories	Brain atrophy		p-value
		Yes	No	
Gender	Male	25 (50%)	24 (48%)	0.841
	Female	25 (50%)	26 (52%)	

Type of smoking	Argillah	3 (20%)	0 (0%)	0.497
	Cigarette	8 (53.3%)	4 (66.7%)	
	Both	4 (26.7%)	2 (33.3%)	
Education level	Under-graduate	28 (56%)	24 (48%)	0.093
	Graduate	15 (30%)	24 (48%)	
	Illiterate	7 (14%)	2 (4%)	
Total		50 (100%)	50 (100%)	

Table (4) reveals that, there was statistically significant difference in smoking cigarettes per day between patients with brain atrophy and patients with no atrophy, patients with atrophy were smoking more cigarettes with mean of 21.07 cigarettes/day while patients with no atrophy were smoking cigarettes with average of 13.83 cigarettes/day, t-test was significant and p-value was 0.004. There was a statically significant difference in duration of smoking of patients with atrophy and with no atrophy, the duration of smoking among patients with atrophy was longer with an average of 17.83 years while the duration of smoking among patients with no atrophy was shorter with mean of 9.83 years, t-test was significant and p-value was 0.001.

Table (4): Age, cigarettes and duration of smoking in patients with and without atrophy.

Variable	Atrophy	N	Mean	Std. Deviation	p-value
cigarette per day	Yes	15	21.07	4.30	0.004
	No	6	13.83	5.41	
duration of smoking	Yes	15	17.53	4.94	0.001
	No	6	9.83	2.56	

Discussion

In this study examining smokers and non – smokers with and without brain atrophy we found that the incidence of brain atrophy among smokers was three times higher compared to non-smokers (OR: 3.14), after excluding other obvious factors that can cause brain atrophy directly or indirectly like diabetes mellitus, multiple sclerosis, stroke, brain operation, radiation or chemotherapy, brain tumors, intracranial hemorrhage, certain type of drug especially those used in seizure, alcoholic, psychiatric conditions and Alzheimer. This is consistent with a study done by Peng et al [29] who used CT-scan in middle-aged and older adults to show that chronic smoking is associated with an abnormal increase of global brain atrophy with advancing age. These studies use whole brain volumes and did not used major anatomical subdivisions (e.g., frontal gray matter/white matter). Another study by A Hayee et al[11] suggests smoking increases age-related brain atrophy. Moreover, nother study by Martin et al[30] shows smaller gray matter volume among smokers in comparison to non- smokers.

Moreover the t-test was significant when studying the number of cigarettes smoked per day with brain atrophy with average 21.07 cigarette per day compared to 13.83 cigarettes per day for smokers with no brain atrophy, This is in agreement with the Durazzo et al[31] who found that chronic smoking have novel evidence in age related volume loss with grater

smoking quantity was related to smaller volume. This is the same result with a study by Brody et al,[32] who found smaller gray matter volume and /or densities among smokers in comparison to non-smoker. They also found that the increase pack per year also related to decrease gray matter densities in pre frontal area. Longstreth et al[33] found that greater pack per year was associated with brain atrophy among elderly smokers. The duration of smoking with brain atrophy in our study mean 17.53 year which is t-test significant and p –value was 0.004. A smaller number of years of smoking with no brain atrophy in comparison with a study by Durazzo et al[31] grater rate atrophy over two years.In our study there was no difference in gender and brain atrophy p-value 0.842. Few studies have searched for gender related effects on brain atrophy particularly tobacco smoking which is contrary to Leonard et al[33] who observed different gray matter and white matter volume among males and females. Such a discrepancy among studies is due to the use of whole brain as variable Regarding the type of smoking, there was no statically significant different between smoking cigarettes and argilla. Although its specific effects on brain has not been studied, a study done in 2018 in Los Angeles found that argilla was more harmful than cigarette to the cardiovascular system. Also, no significant association between educational level and smoking with brain atrophy could be discerned, perhaps due to sample size.

Conclusions

In our study we found that chronic cigarette smoking is associated with whole brain atrophy according to certain quantitative brain atrophy parameters after excluding other inciting factors which make the result more representative. We can consider smoking to be a risk factor for brain atrophy and accelerate age related brain atrophy. And the number of smoking have direct relation with atrophy.

Conflicts of interest

The author reports no conflicts of interest.

References

1. De Marini DM. Genotoxicity of tobacco smoke and tobacco smoke condensate: a review. Mutat Res. 2004; 567(2-3): 447-74.
2. Ambrose JA, Barua RS. The pathophysiology of cigarette smoking and cardiovascular disease: An update. J Am Coll Cardiol. 2004; 43(10):1731-7.
3. Boudreaux ED, Francis JL, Taylor CL, et al. Changing multiple health behaviors: smoking and exercise. Prev Med. 2003; 36(4): 471-8.
4. Casasola GG, Marques JA, Sánchez-Alarcos JM, et al. Cigarette smoking behavior and respiratory alterations during sleep in a healthy population. Sleep Breath. 2002; 6(1): 19-24.
5. Bartal, M. Health effects of tobacco use and exposure. Monaldi. Arch. Chest Dis. 2001; 56(5): 545-54.
6. Bolego C, Poli A, Paoletti R. Smoking and gender. Cardiovascular research. 2002; 53(3): 568-76.
7. Garey KW, Neuhauser MM, Robbins RA, et al. Markers of inflammation in exhaled breath condensate of young healthy smokers. Chest. 2004; 125(1): 22-6.
8. Hawkins BT, Brown RC, Davis TP. Smoking and ischemic stroke: a role for nicotine? Trends Pharmacol Sci. 2002; 23(2): 78-82.
9. Bolego C, Poli A, Paolettim R. Smoking and gender. Cardiovasc. Res. 2002; 53: 568-76.

10. Durazzo TC, Meyerhoff DJ, Nixon SJ. Chronic cigarette smoking: implications for neurocognition and brain neurobiology. Int J Environ Res Public Health. 2010; 7(10): 3760-91.
11. Hayee A, Haque A, Anwarullah AK, et al. Smoking enhances age related brain atrophy--a quantitative study with computed tomography. Bangladesh Med Res Counc Bull. 2003; 29(3): 118-24.
12. Razani J, Boone K, Lesser I, et al. Effects of cigarette smoking history on cognitive functioning in healthy older adults. Am J Geriatr Psychiatry. 2004; 12(4): 404-11.
13. Swan GE, De Carli C, Miller BL, et al. Biobehavioral characteristics of non demented older adults with subclinical brain atrophy. Neurology 2000; 54: 2108-14.
14. Jacobsen LK, Krystal JH, Mencl WE, et al. Effects of smoking and smoking abstinence on cognition in adolescent tobacco smokers. Biol. Psychiat.2005; 57: 56-66.
15. Sabia S, Marmot M, Dufouil C, et al. Smoking history and cognitive function in middle age from the Whitehall II study. Arch. Intern. Med. 2008; 168: 1165-73.
16.Whalley LJ, Fox HC, Deary IJ, et al. Childhood IQ, smoking, and cognitive change from age 11 to 64 years. Addict. Behav. 2005; 30: 77-88.
17. Longstreth Jr WT, Arnold AM, Manolio TA, et al. Clinical correlates of ventricular and sulcal size on cranial magnetic resonance imaging of 3,301 elderly people. Neuroepidemiology. 2000; 19(1): 30-42.
18. Almeida OP, Garrido GJ, Lautenschlager NT, et al. Smoking is associated with reduced cortical regional gray matter density in brain regions associated with incipient Alzheimer disease. Am J Geriatr. Psychiatry 2008; 16: 92-8.
19. Paul RH, Grieve SM, Niaura R, et al. Chronic cigarette smoking and the microstructural integrity of white matter in healthy adults: A diffusion tensor imaging study. Nicotine Tob. Res.
2008; 10: 137-47.
20. Power MC, Deal JA, Sharrett AR, et al. Smoking and white matter hyperintensity progression: the ARIC-MRI Study. Neurology. 2015; 84(8): 841-8.
21. Marstrand JR, Garde E, Rostrup E, et al. Cerebral perfusion and cerebrovascular reactivity are reduced in white matter hyperintensities. Stroke. 2002; 33(4): 972-6.
22. Gunning-Dixon FM, Raz N. The cognitive correlates of white matter abnormalities in normal aging: a quantitative review. Neuropsychology. 2000; 14(2): 224-32.
23. Gallinat J, Lang UE, Jacobsen LK, et al. Abnormal hippocampal neurochemistry in smokers: evidence from proton magnetic resonance spectroscopy at 3 T. J Clin Psychopharmacol. 2007;27(1):80-4.
24. Kochanowicz J, Lewko J, Rutkowski R, et al. Influence of smoking cigarettes on cerebral blood flow parameters. Biol Res Nurs. 2015; 17(1):8-12.
25. Anbarasi K, Vani G, Balakrishna K, et al. Effect of bacoside A on membrane-bound
ATPases in the brain of rats exposed to cigarette smoke. J. Biochem. Mol. Toxicol. 2005; 19:
59-65.
26. World Health Organization. The WHO Framework Convention on Tobacco Control. WHO Document Production Services, Geneva, Switzerland, 2003. Available from: http://apps.who.int/iris/bitstream/handle/10665/42811/9241591013.pdf;jsessionid=2A3D16B0603464435085E73DF59F805A?sequence=1
27.Robert C, GleN A Bryll A, et al. Computed Tomography Assessment of Brain Atrophy in Centenarians. Int J Environ Res Public Health. 2019; 16(19): 3659.
28. Keats TE, Sistrom C. Atlas of Radiologic Measurement. Mosby. 2001.

29. Peng P, Wang Z, Jiang T, et al. Brain-volume changes in young and middle-aged smokers: a DARTEL-based voxel-based morphometry study. Clin Respir J. 2017; 11(5): 621-31.
30. Elbejjani M, Auer R, Jacobs DR, et al. Cigarette smoking and gray matter brain volumes in middle age adults: the CARDIA Brain MRI sub-study. Transl Psychiatry. 2019; 9(1): 78.
31. Durazzo TC, Meyerhoff DJ, Murray DE. Comparison of regional brain perfusion levels in chronically smoking and non-smoking adults. Int J Environ Res Public Health.2015; 12(7): 8198-213.
32. Brody AL, Mandelkern MA, Jarvik ME, et al. Differences between smokers and non-smokers in regional gray matter volumes and densities. Biol. Psychiatry .2004; 55; 77–84.
33. Longstreth WT, Diehr P, Manolio TA, et al. Cluster Analysis and Patterns of Findings on Cranial Magnetic Resonance Imaging of the Elderly. The Cardiovascular Health Study. Arch Neurol. 2001;58(4):635-640.