Original Research Article

# Effect of tobacco smoking on P300 event related potential in new beginners and chronic smokers

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## Abstract

**Background**: Identification of effect of smoking on P300 Event related potential which in turn represents basic characteristics of neurocognitive functioning which may help to elucidate the mechanism of tobacco dependence. **Objectives:** To study and compare effect of smoking on auditory P300 Event related potential in chronic smokers (Group I) and new beginners of smoking (Group II) before and immediately after cigarette smoking. **Materials and Methods:** Auditory P300 amplitude and latency were recorded in 50 Group I and 50 Group II male individuals in age group of 25 to 35 years before and immediately after smoking. 30 age and sex matched non smokers were taken as controls. **Results:** Group I had P300 of significantly lower amplitude and longer latency ($p<0.001$) compared to Group II and controls before smoking. Significantly reduced latency and increased amplitude of P300 ($p< 0.001$) was noticed in Group II immediately after smoking compared to Group I. In group I after smoking though increase in amplitude ($p< 0.01$) and reduced latency ($p< 0.05$) was noticed, still overall P300 was reduced in chronic smokers before or after smoking. **Conclusion:** Improvement in cognitive function though occurs immediately after cigarette smoking there occurs progressive decline in cognitive function with years of Chronic smoking. Reduced P300 may be a marker of risk for nicotine dependence.

**Key Words:** Auditory ERP; P300;Tobacco smoking.

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## INTRODUCTION

Tobacco smoking is the most prevalent type of dependence with numerous adverse effects on human health and is considered to be the leading preventable cause of death in the world.[1] Leaves of tobacco plant contains an alkaloid substance called nicotine which is found to be the addiction causing substance in cigarettes.[2,3] Majority of cigarette smokers report that smoking helps them to remain alert and increases their concentration which may contribute to addictive actions of nicotine.[1,4] Cigarette smoking by people is done in order to regulate emotions and relieve negative emotions and the most frequently given reasons for cigarette smoking is to reduce their stress and for relaxation.[5] Ability of nicotine in enhancing cognitive processing mechanism has led to greater understanding of the role of cholinergic mechanism in cognitive functioning.[6]The usual content of nicotine in one cigarette is 6-11mg,of which men usually inhale 1-2mg during smoking.[7]Effect of substance abusing and substance dependence on the functional integrity of CNS has been widely tested using quantitative neurophysiological test event related potentials study(ERPs) particularly p300.[8]Latency is an indicator of relative timing of stimulus evaluation process and amplitude indicates attention resource allocation. ERP P300 component quantified by their amplitude and latency measures reflects unique basic characteristics of neurocognitive brain function.[9] Previous studies have reported effect of chronic smoking on cognitive function but not much studies have been done to see acute effect. Our purpose of study was to examine acute and chronic

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effect of cigarette smoking on p300 ERP which indirectly represents cognitive performance and extent of influence of nicotine on cognitive performance in individuals of chronic smokers and new beginners of smoking.[10]

## MATERIAL AND METHODS

The study was undertaken in apparently healthy 50 Group I (Chronic smokers) and 50 Group II (New beginners of smoking) male subjects in age group of 25 to 35 years. 30 apparently healthy age and sex matched non smokers were taken as control group. The participants were selected randomly from the general population and informed consent was taken. Participants were screened for inclusion criteria and were excluded for exclusion criteria, like consumption of nicotine products within past few years other than smoking such as tobacco chewing, any neurological condition, head injury, any severe medical illness like cardiac diseases, pulmonary diseases, renal diseases, diabetes mellitus, hypertension, thyroid disease, medication and drug abuse, psychological disorders, alcohol consumption or any other condition which were likely to affect ERP were excluded. Subjects selected were right handed individuals with normal intelligence level. Smokers were selected based on as per the standard criteria of world health organization.[11] History of smoking was taken in detail regarding number of cigarettes smoked per day, brand of cigarettes to see for nicotine content in each cigarette, pattern of smoking, smoking duration etc., were taken and classified accordingly as new beginners and chronic smokers. Participants were asked to remain overnight deprivation from cigarette smoking, caffeine and alcohol.ERP was recorded during morning hours under constant conditions of temperature and humidity after allowing subjects to rest for 10 mins. ERP responses elicited by a auditory oddball task were measured at the mid-parietal site by using RMS EMG MK2 machine before and immediately after cigarette smoking according to their usual morning routine timing of their own regular cigarette puff. The auditory oddball paradigm is constituted by selective attention tasks. Subjects are given instructions to respond to click stimulus or ignore these stimuli which is given sequentially with predetermined perceptual features. Infrequent stimuli are considered as target events that is randomly embedded in a background of "standard" stimuli and must be physically or mentally responded by the subject. Standard events are the sounds that are more frequent and should be ignored. Target stimuli elicits a large positive potential having a maximum latency of 300–400 ms which increases in magnitude from medial frontal site to parietal scalp electrode sites.

## RESULTS

The results are tabulated (Table 1 and Table 2) and compared in terms of mean values and analysed. The statistical comparisons of the matching variables (age, height and weight) are inherently similar for all the groups and statistical evaluation was performed by using SPSS software. Statistical analysis was done for intra group comparisons by paired t test and intergroup comparisons by unpaired t-test. Multivariate analysis was done to assess the independent effect of smoking on P300. A 'p' value of 0.05 or less was considered for statistical significance and 'P' < 0.001 as highly significant.

**Table 1:** Comparision of mean latency (msec) among three groups

| Groups | No. | Before Smoking | After smoking | Mean diff | t value | P value |
|---|---|---|---|---|---|---|
| Gr I | 50 | 363.3±13.2 | 359.5±19.6 | 3.8 | 2.17 | 0.05 * |
| Gr II | 50 | 305.0±25.9 | 288.9±14.1 | 16.1 | 4.6 | 0.00 ** |
| control | 50 | 296.3±29.2 | - | - | - | - |
| | Gr I v/s Gr II | | t = 14.19, P = 0.00 ** | t = 14.78, P = 0.00 ** | | |
| Difference between groups | Gr I v/s Control | | t = 15.25, P = 0.00 ** | t = 12.71, P = 0.00 ** | - | |
| | Gr II v/s Control | | t = 1.93, P = 0.06, ns | t = 0.64, P = 0.53,ns | | |

**Table 2:** Comparision of mean amplitude (µ volt) among three groups

| Groups | No. | Before Smoking | After smoking | Mean diff | t value | P value |
|---|---|---|---|---|---|---|
| Gr I | 50 | 3.85±0.32 | 3.99±0.36 | 0.14 | 2.63 | 0.011 * |
| Gr II | 50 | 4.52±0.47 | 5.37±0.63 | 0.85 | 9.36 | 0.00** |
| control | 50 | 4.67±0.67 | - | - | - | - |
| | Gr I v/s Gr II | t = 8.39, P = 0.00 ** | t = 13.39, P = 0.00 ** | | | |
| Difference between groups | Gr I v/s Control | t = 7.77, P = 0.00 ** | t = 6.36, P = 0.00 ** | - | | |
| | Gr II v/s Control | t = 1.26, P = 0.21, ns | t = 5.38, P = 0.00 ** | | | |

Our study results showed significantly reduced mean amplitude and mean latency was significantly longer in chronic smokers compared to new beginners of smoking (P< 0.001) and non smokers group (P< 0.001) before smoking. No significant difference was found with mean P300 amplitude and latency in new beginners before smoking compared to non smokers. Immediately after smoking, this study found significant increase in mean P300 amplitude and significant decrease in P300 latency in chronic smokers compared to mean value of amplitude (P<0.01) and latency (P<0.05) before smoking in the same group .Though there was rise in amplitude and reduced latency after smoking still overall p300 was significantly less in chronic smokers compared to new beginners after smoking(P<0.001), and non smokers(P<0.001). Where as new beginners of smoking showed increase in mean amplitude and decrease in latency (P<0.001) which was found to be highly significant immediately after smoking compared to before smoking value and chronic smokers and when compared to non smokers significant increase in mean amplitude was noticed though nosignificant difference was noticed in mean latency. After smoking both group I and group II showed enhanced cognitive function but new beginners showed significant improvement in neurocognitive function compared to chronic smokers. However the overall P300 value before or after smoking was reduced in chronic smokers compared to new beginners or non smokers suggesting decline in neurocognitive function of brain with chronic smoking. The possibility whether decrease in latency and increase in amplitude in smokers immediately after smoking is due to effect of overnight withdrawal effect from smoking after a period of abstinence was not ruled out in this study.

## DISCUSSION

Cigarette smoking has its deleterious effect on all the systems of our body and smoking cessation greatly reduces its health related consequences. However people who are dependent on cigarette smoking report the beneficial effects of smoking on concentration, memory and work performance.[4] However whether the extent of enhancement of cognition remains the same immediately after smoking in chronic smokers than when he had begun smoking in his initial days of smoking is little understood. Our study results are consistent with other studies.

**Chronic smokers before smoking**

- ShahiraMostafa and hiscolleagues studied cognitive function in chronic smokers and found that P300 of lower amplitude and longer latency.[12]
- Anokhin P. and his co-workers in their study noticed significant reduction in P300 amplitude in regular smokers compared to nonsmokers.[13]
- Micheal C. *et al* observed significantly prolonged P300 latency in chronic and regular smokers compared to nonsmokers.[14]
- Haarer and Polich studied normal young adults who were daily smokers with those who smoked infrequently by using a visual task and found lowP300 target amplitude for regular compared to infrequent smokers either before and after tobacco smoking.[15]
- FigenG. *et al* found in their subjects, reduced P300 due to chronic tobacco smoking.[1]

**Acute effect of smoking**

- Hasenfratz *et al* observed increased P300 amplitude and decreased latency immediately afterSmoking.[16]
- Le Houzec *et al* reported that cigarette smoking did not have significant effect on N1 amplitude or latency, but P300 latency speeded up due to the effect of nicotine [17]
- Ilan and his co-workers using electrophysiological techniques have mainly focused on acute effects of smoking and observed that nicotine may facilitate cognitive performance and improve mood.[18]
- Stephen J *et al* in their study showed beneficial effect of acute nicotine exposure on cognitive performance which is the reason for initiation of smoking and also for maintenance of dependence on tobacco.[6]

**Acute effect of smoking**

Enhanced cognitive function seen after smoking could be attributed to the fact that, structural similarity of nicotine with acetylcholine has been shown to improve cognitive functioning and nicotinic acetylcholine receptors are distributed widely all over the brain, with highest density in regions like thalamus, basal ganglia, frontal region, cingulate, hippocampal brain regions, occipital region, and cortex of insula.[16]The most abundant receptor subtypes in the brain are α7 and high affinity to α4bβ2*receptors.[19] Following a puff of cigarette, within 10 to 60secs nicotine enters cerebral circulation and binds to the nicotinic acetylcholine receptors. Activation of these receptors increases extracellular release of dopaminein the nucleus accumbensin ventral tegmental area and this is known in mediating the rewarding effects of nicotine.[19] Studies have supported the factthat likely steps in mediating cognitive-enhancing effects of nicotine could be due to the release of glutamate, acetylcholine and Dopamine, norepinephrine, serotonin, GABA and release of dopamine mainly responsible for addictive

properties of nicotine. To a lesser extent, studies have supported the role of nAChR genes as related to cognitive performance.[19]

**Chronic effect of smoking:** However, in our study, in chronic smokers there was overall reduced p300 value compared to the other two groups before or after smoking. This shows that smoking cigarettes for years there occurs progressive decline in cognitive function and chronic exposure to nicotine produces neuroadaptive changes in brain mainly the anterior dorsolateral, mesial frontal cortex, limbic system which may lead to neurochemical changes or impairment of neurocognitive functioning.[1] Influence of dose-response relationship has been suggested between cigarette smoking, neurocognitive and neurobiological function.[13] The reasons behind the cognitive changes seen in chronic smokers still remains unclear. The mechanisms of nicotine in chronic smokers leading to declinein cognitive function may operate in a direct and/or indirect manner showed by Functional MRI studies.[13] This may be attributed to long term continuous exposure of the cardiovascular system, pulmonary system, cerebrovascular system and brain parenchymal tissue to dangerous toxic content of cigarette smoke.[13] Release of potentially toxic substances in the peripheral(including cytokines and interleukins) and central components (including nitric oxide) is related to direct toxic effect of nicotine after cigarette smoking on brain parenchyma.[20,21]Various cytotoxic compounds present in cigarette smoke such as carbon monoxide, free radicals species and their precursors, nitrosamines, phenolic compounds, and other polynuclear aromatic compounds, cause damage to neuronal or glial cell organelles and promote oxidative damage also cause decreased enzyme-based free radical scavenger.[13] It is certainly possible that cigarette smoking results in long term modulation of neurotransmitter concentrations[1]that is release of dopamine, norepinephrine and gamma-amino-butyric acid which are functionally altered**.**[22,23]and/or alterations inreceptor densities and receptor tolerancein the brain parenchyma that ultimately interfere with effective cognitive performance.[20,21] Functional neuroimaging studies investigating reason for decline in neurocognitive functioning in chronic smokers have shown it to be due to decreased global cerebral blood flow as well as hypoxia caused by chronic smoking as its result due to atherosclerosis, by causing abnormalities in vascular endothelial morphology and function thus altering cerebral perfusion.[13]ordue to hypoxia resulting from chronic obstructive lung disease associated with years of smoking.[24]

## CONCLUSION

In conclusion, response to acute cigarette smoking shows complex effects on the neurocognitive function of brain though showing improvement in cognitive function immediately after smoking but subsequently overall decline in cognitive function with progressed prolonged chronic smoking. Quitting smoking is possible in the new beginners which becomes difficult in chronic smokers as it brings alterations in brain tissue which leads to nicotine dependence.

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