Indian Journal of Basic and Applied Medical Research; March 2021: Vol.-10, Issue- 2, P. 20 – 27
DOI: 10.36848/IJBAMR/2020/26215.55558

Original article:

Evaluating the cognitive impairment using Event related potential - p300 in young Schizophrenics and its association with obesity

Mangani Mangalavalli.S[1] , Souganyadevi alias mahalakshmi[2], Arun Selvaraj[3],Deepika velusamy[4], V.Anebaracy[5]

[1,4] Department of Physiology, [2,3] Department of Psychiatry
Sri Manakula Vinayagar Medical College and Hospital, Madagadipet, Pondicherry- 605107.
[5]Department of Physiology, Sri Lakshmi Narayana Institute of Medical Sciences
Corresponding author: Mangani Mangalavalli.S

Abstract:

Schizophrenia is a psychological disease which is associated with significant disability, cognitive impairment and affects the overall working capacity of the individual. The cognitive impairment in Schizophrenics ranges from mild to severe. Auditory event related potential is considered as a valid tool to be used as a biomarker in Schizophrenia. Hence the present study aimed to study and compare the cognitive function in Schizophrenia and normal individuals. Further the prevalence of Basal metabolic rate (BMI) among Schizophrenic patients and its association with the latency and amplitude of the p300 wave forms was also correlated.p300 event related potential was done for 60 individuals, out of which 30 were Schizophrenic patients and 30 were normal controls. The BMI and the cognition p300 were compared between the Schizophrenic group and the normal control group. $p<0.05$ was considered to be statistically significant. The latency of p300 was significantly ($p<0.01$) prolonged (316.48±16.48 in Schizophrenia and 305.44±19.21 in controls) and the amplitude was significantly ($p<0.014$) shorter (3.01±0.59 in Schizophrenics and 3.54±1.15 in controls) in Schizophrenic group as compared to normal control group.BMI was also found to be higher (25.32±2.97 in Schizophrenia and 23.92±3.19 in controls) and was statistically significant ($p<0.041$). The BMI showed a positive correlation with the latency of p300 and a negative correlation with the amplitude of p300 in Schizophrenic patients and was statistically significant.(<0.001) Cognitive impairment can be detected much early during the prodromal period in Schizophrenics and appropriate treatment modalities can be planned. Keeping the BMI under normal range would also help to provide a healthy life for the Schizophrenic patients.

Key words: Schizpophrenia, BMI,Auditory event related Potential, Latency, Amplitude, p300

Introduction:

According to the World health organization, almost 20 million people are affected by Schizophrenia. It occurs quite early among men and is found to be associated with significant disability and affects the overall educational and working capacity of the individual.[1] Its highly pertinent that India has to talk about mental disorders.[2] Almost one in every six Indians need some form of mental health help.[3] Schizophrenia is considered as one of the mental disorders wherein there is a genetic predisposition and they exhibit a disturbance in processing the environmental

information especially in identifying and responding to any type of stimuli.[4] Schizophrenics generally suffer from cognitive impairment that can range from moderate to severe degree more so in the domains of attention, memory, verbal skills, speed at which they process information and their executive capability.[5,6] The cognitive impairment in Schizophrenics may be a pathophysiological feature of the disease itself, which are found to exist in first episode patients and also in first degree relatives.[7,8] Event related potentials (ERP) are considered as examples of biological traits which are characteristics that are heritable and are also electrophysiological trait marker for diagnosing Schizophrenia.[9] association of obesity with Schizophrenia is found to be 50% in Schizophrenic population.[10,11] The causation is of multifactorial in nature. The drugs used to treat Schizophrenia have the propensity for weight gain and can also cause other metabolic disturbances. Certain drugs like Olanzapine, Clozapine have shown almost 5 times increase in predisposition to metabolic disorders in just 3 years of treatment.[12] Patients with Schizophernia have unhealthy diet and poor life style because of the nature of the disease itself as well as their poor socioeconomic status, lower educational level, inadequate physical activity add on to the manifestation of obesity.[13] Obesity was found to be associated with impairment of neural activity while processing sensory and cognitive information. [14] Hence this study was undertaken to evaluate the association of obesity with p300 in Schizophrenics.

Materials and Methods:

This study was a hospital based cross sectional study conducted in research lab of department of Physiology, at Sri Manakula Vinayagar medical college and hospital, Pondicherry, India. Patients attending the Psychiatry outpatient department and who were diagnosed as Schizophrenics according to the ICD-10 DCR were taken up for the study. The sample size was calculated as 50, (25 in each group) based on open Epi software, version 3.01 with relative precision of 20% and a confidence interval of 95%. Schizophrenic patients who satisfy the inclusion criteria and willing to participate were included in the study after getting informed consent.Inclusion criteria: 1) Patients fulfilling the diagnostic criteria in ICD-10 DCR for Schizophrenia 2) adults of both sex and of age group (20-60years) 3) patient who consent to participate in the study.Exclusion criteria:1) Patient with acute exacerbation of Schizophrenia.2) Patients with any other coexisting psychiatric illness.3) Patient with any other co-morbid medical or surgical illness. 3) Unable to cooperate to undergo the study.

Methodology and data collection:

The study was started after obtaining approval from the Instituitional Ethical Committee.

1) The subjects were divided into two groups: control (n=25) and Schizophrenics (n=25). All the patients attending the OP/IP of the Department of Psychiatry will be evaluated for symptoms of Schizophrenia depending on their complaints for the study group and healthy individuals , not having any co morbidities and not on any medications, were included in the control group.

2) Patients were diagnosed as Schizophrenia based on fulfilling the diagnostic criteria in ICD-10 DCR.

3) Participants willing to participate in the study were taken up after obtaining the informed consent.

4) The basic anthropometric measurements like Height, Weight and Waist circumference were measured and Body mass index was calculated for all the participants. A detailed medical history and physical examination was done.

5) The cognitive status of the patient was assessed using event related potential (Auditory component) p300 wave recording. After placing the electrodes in the appropriate positions, an auditory stimulus will be given through a headphone. A continuous low intensity sound will be heard, which the subject have to listen. Meanwhile, intermittently a high pitched sound will occur at irregular time interval, which the subject has to count mentally in order to stay alert during the test. A baseline cognition assessment using P300 test will be done at rest.

Recording P300:

The procedure of recording p300 was explained verbally to the subjects. Using the auditory component of the Oddball paradigm, P300 was recorded, in which two different tones was given through a headphone and the subject is made to hear them- one is a low intensity frequent tone of 1KHz, and the other is a high pitched, rare tone of 2KHz. The tone will be heard at random intervals and occur at frequencies of 80% and 20% respectively. The subjects were asked to listen the rare type of tone and mentally count them. 300 stimuli were given at the rate of 1 stimuli/s. The resultant bioelectrical signals are picked by the scalp electrodes which are placed according to the 10-20 international system of electrode placement.The skin to electrode impedance must be kept as low as 5 KOhms by cleaning the skin thoroughly. The active electrode were at kept at the vertex(Cz) , the ground electrode is placed over the forehead (Fz) and two reference electrodes are placed over both the right and left mastoid processes and named as A1 and A2 respectively.[15]

4. Subjects must be kept alert and count the high pitched rare stimuli mentally. These signals were then recorded on the screen of EMG EP MKII equipment (Electromyography, Evoked potential machine, MK II model, Recorders and Medicare System Private Ltd., Chandigarh, India). The average of two recordings was taken up for the final measurement. The latency and amplitude of the P300 wave for the rare stimuli was considered for analysis. P300 wave amplitude was then measured taking the peak amplitude between 250-500 ms, post the stimulus. The time period between the stimulus onset and the peak amplitude was taken for the P300 latency. Basal recording of P300 was done for both the control and the study group. The delayed cognitive functioning will be assessed by the prolonged latency of the P300 wave in the Schizophrenics. The delay in the latency of occurrence of the P300 waves in Schizophrenics when compared with the healthy normal controls was taken as the value to assess the cognitive performance of the subjects.

Statistical analysis:

Data entry and statistical analysis were performed using Microsoft Excel and SPSS version 16 respectively. (SPSS, Inc, Chicago, IL, USA). The mean and standard deviation were calculated. Student's unpaired t-test was used to assess the difference between means. A p value <0.05 was taken as statistically significant. The association between obesity and cognition (p300) was done using Pearson's correlation analysis.

Results:

Table 1: P300 values and BMI of Schizophrenic patients and controls

	Group 1 (n=30)	Group 2 (n=30)	P value
Latency (ms)	305.44±19.21	316.48±16.48	0.01*
Amplitude (v)	3.54±1.15	3.01±0.59	0.014*
BMI	23.92±3.19	25.32±2.97	0.041*

Values expressed as mean ± SD; Latency in ms and amplitude in V

*p-Value less than 0.05 is considered as statistically significant.

**p-Value less than 0.001 is considered as statistically highly significant

Table 2: Pearson correlation between BMI and p300

Association between p300 (Latency and Amplitude) with BMI and FCT

	Latency (ms)		Amplitude(v)	
	r	P	r	p
BMI	0.66	<0.001**	-0.53	<0.001**
FCT	-0.55	<0.001**	0.59	<0.001**

**p<0.001 is statistically highly significant

Totally 60 patients were enrolled in the study.30 normal (control) individuals and 30 young Schizophrenic patients. It was seen in table 1 that the Latency of p300 waves was more in Schizophrenic patients 316.48±16.48. In normal individuals the latency of p300 waves was less 305.44±19.21 and the p value <0.01*. It was also noticed that the amplitude of the p300 waves were shorter in Schizophrenic patients 3.01±0.59 as compared to their normal counterparts 3.54±1.15. This difference was found to be statistically significant with p<0.014*.

Overweight and obesity was more prevalent among the Schizophrenic patients 25.32±2.97, while the normal group had a relatively lower average BMI 23.92±3.19 with many controls being normal weight. The p value was p<0.041* and was statistically significant.

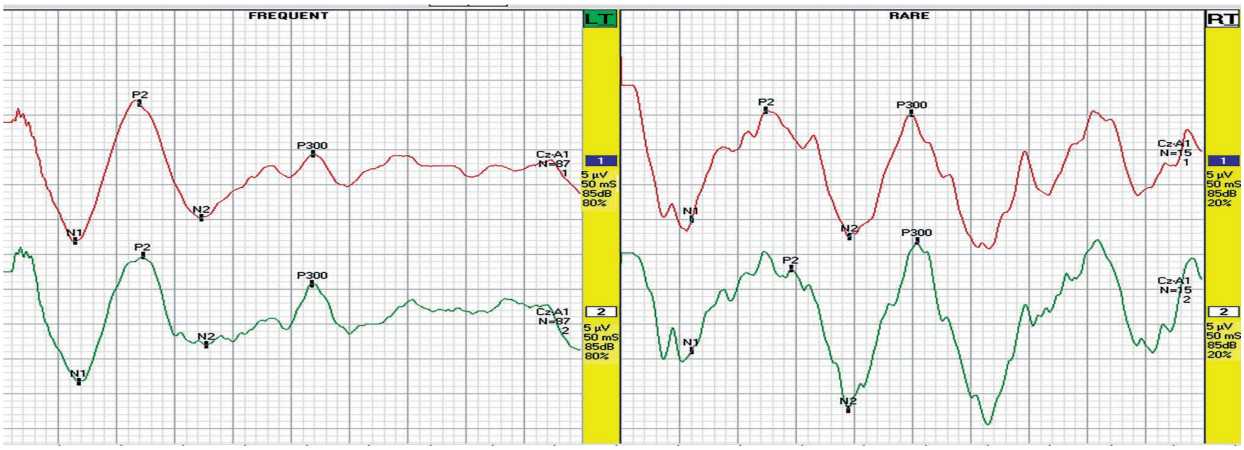

Figure 1. P300 Wave form for frequent and rare stimuli from a Schizophrenic patient

Table 2 shows the association between the latency and amplitude of p300 waves with obesity. There was a positive correlation between obesity and latency of p300 waves. The more prolonged the latency, the more was the BMI. In Schizophrenics the latency was longer and the BMI was also higher. The p value was <0.001** and was found to be statistically highly significant. There was found to be a negative correlation between the BMI and the amplitude of p300 waves. The lower the amplitude the more the BMI. In Schizophrenic patients the amplitude of the p300 waves were lower while the BMI was higher. This association was also found to be statistically significant with a p value of <0.001**.

Discussion:

Auditory event related potential is accepted as a valid tool in assessing the cognitive function of an individual. This electrophysiological test is getting growing importance in recent times as it has been proved that even mild cognitive impairment actually induces changes in the latency as well as amplitude of p300 wave.[16] Schizophrenia is known to be associated with cognitive impairment which is one of the key features.[17] It is observed that the cognitive impairment starts much before the onset of Schizophrenia and almost 98% of Schizophrenic patients showed some form of cognitive impairment ranging from mild to severe.[18]

Evidence suggests that reduced amplitude of p300 wave is most striking feature in Schizophrenia patients. P300 is also considered as an important biomarker in schizophrenia where in changes are very obvious during the transition phase from schizophrenic prodromal period to actual psychosis development.[19]

In our study, the latency of the p300 waves were prolonged and the amplitude of the p300 waves were shorter in Schizophrenic patients. In the normal control group, the latencies were shorter and the amplitudes were higher. The Schizophrenia patients were found to be obese as compared with the control group. Further it was also observed that the association of BMI with Schizophrenia had a positive correlation, wherein the longer the latency, the higher was the BMI.

Similar results were noted in a by Turetsky et al, showed that the amplitude of p300 wave can be used as a predictive biomarker for predictive risk and also used for treatment studies.[19] Reduced amplitude and prolonged

latency of p300 waves are noted as robust biological findings in schizophrenia in studies by Roth et al.[20] In yet another study by Georg Winterer et al, it was showed that there was significant reduction in the amplitude component of the temporoparietal p300 wave.[21] Jeon et al, demonstrated that there was significant increase in latency and shortening of amplitude of p300 waves in Schizophrenic patients as compared to the normal control group.[22] Alain et al, and Korostenskaja et al, demonstrated negative results with p300 and schizophrenia.[23,24].

DE Hert et al, and Coodin et al in their study showed that the prevalence of obesity among the Schizophrenic patients was higher as compared with the general population.[25,26] Annamali et al, showed that almost 50% of Schizophrenic patients were obese. [27] Tascilar et al showed that obesity caused cognitive impairment and decreased neurological activity along with prolonged latency and short amplitude of p300 waveform.[28]

In our study, it was demonstrated that the Latency was prolonged and amplitude was shortened in Schizophrenic patients and BMI was also higher among the Schizophrenic group as compared with the normal control group. There was a positive correlation between BMI and latency of p300 using Pearson correlation test. Longer the latency, higher the BMI. There was a negative correlation between the amplitude of p300 and BMI. The shorter the amplitude the higher the BMI among the Schizophrenic patients proving that obesity is more prevalent in the Schizophrenic patients and also shows statistically significant correlation with p300 in Schizophrenia.

Conclusion:

Normal cognitive functioning is essential for any person to understand the disease process and also to adhere to the treatment. In Schizophrenia there is cognitive impairment seen much before the onset of the disease. Obesity is also double the prevalence in Schizophrenia than in the general population. Auditory event related potential p300 can be used as a valid biomarker in early diagnosis of Schizophrenia. The early identification of cognitive impairment by p300 test and appropriate treatment modalities can go a long way in the prognosis of the Schizophrenic patients.ERP can be hence used as a method of research in the neuropsychiatric field and it has a promising future.[29]

References:

1. https://www.who.int/newsroom/factsheets/detail/schizophrenia#:~:text=Schizophrenia%20affects%2020%20million%20people,affect%20educational%20and%20occupational%20performance.
2. Afshan Y. India needs to talk about mental illness, The Hindu, 23 October. 2016 3.
3. The National Mental Health Survey of India, 2015–16, Insights, 31, December. 2016
4. Venables P. Input dysfunction in schizophrenia. In: Maher BA, editor. Progress in Experimental Personality Research. Academic Press; Orlando: 1964. pp. 1–47.
5. Green MF, Kern RS, Braff DL, Mintz J. Neurocognitive deficits and functional outcome in schizophrenia: are we measuring the “right stuff”? Schizophr Bull. 2000;26(1):119–136.
6. Goldberg TE, Goldman RS, Burdick KE, Malhotra AK, Lencz T, Patel RC, Woerner MG, Schooler NR, Kane JM, Robinson DG. Cognitive improvement after treatment with second-generation antipsychotic

medications in first-episode schizophrenia: is it a practice effect? Arch Gen Psychiatry. 2007;64(10):1115–1122.

7. Hill SK, Schuepbach D, Herbener ES, Keshavan MS, Sweeney JA. Pretreatment and longitudinal studies of neuropsychological deficits in antipsychotic-naive patients with schizophrenia. Schizophr Res. 2004;68(1):49–63.
8. Snitz BE, Macdonald AR, Carter CS. Cognitive deficits in unaffected first-degree relatives of schizophrenia patients: a meta-analytic review of putative endophenotypes. Schizophr Bull. 2006;32(1):179–194.
9. Van Beijsterveldt CEMBoomsma DI Genetics of the human electroencephalogram (EEG) and event-related brain potentials (ERPs): a review. Hum Genet. 1994;94319- 330
10. DE Hert M, Schreurs V, Vancampfort D, VAN Winkel R. Metabolic syndrome in people with schizophrenia: a review. World Psychiatry. 2009;8:15–22.
11. Annamalai A, Tek C. An overview of diabetes management in schizophrenia patients: office based strategies for primary care practitioners and endocrinologists. Int J Endocrinol. 2015;2015:969182.
12. De Hert M, Schreurs V, Sweers K, Van Eyck D, Hanssens L, Sinko S, Wampers M, Scheen A, Peuskens J, van Winkel R. Typical and atypical antipsychotics differentially affect long-term incidence rates of the metabolic syndrome in first-episode patients with schizophrenia: a retrospective chart review. Schizophr Res. 2008;101:295–303.
13. Ratliff JC, Palmese LB, Reutenauer EL, Liskov E, Grilo CM, Tek C. The effect of dietary and physical activity pattern on metabolic profile in individuals with schizophrenia: a cross-sectional study. Compr Psychiatry. 2012;53:1028–1033.
14. Tascilar ME, Turkkahraman D, Oz O, et al. P300 auditory event-related potentials in children with obesity: is childhood obesity related to impairment in cognitive functions?. Pediatr Diabetes. 2011;12(7):589-595.
15. Soundariya Krishnamurthy, Yuvarajan Sivagnaname, Gokul Chandu Gumallapu Identification of subclinical cognitive impairment in chronic obstructive pulmonary disease using auditory P300 event related potential. Monaldi Archives for Chest Disease 2019; 89:1039.
16. Medvidovic S, Titlic M, Maras-Simunic M. P300 evoked potential in patients with mild cognitive impairment. Acta Informatica Medica 2013;21:89-92.
17. Bowie CR, Harvey PD. Cognitive deficits and functional outcome in schizophrenia. Neuropsychiatr Dis Treat. 2006;2(4):531-536.
18. Tripathi A, Kar SK, Shukla R. Cognitive Deficits in Schizophrenia: Understanding the Biological Correlates and Remediation Strategies. Clin Psychopharmacol Neurosci. 2018;16(1):7-17.
19. Turetsky BI, Dress EM, Braff DL, et al. The utility of P300 as a schizophrenia endophenotype and predictive biomarker: clinical and socio-demographic modulators in COGS-2. Schizophr Res. 2015;163(1-3):53-62.
20. Roth WT Cannon EH,Some features of the auditory evoked responses in schizophrenics. Arch Gen Psychiatry. 1972; 27: 466-477.

21. Georg Winterer, MD; Michael F. Egan, MD; Thomas Raedler, MD; et al P300 and Genetic Risk for Schizophrenia,Arch Gen Psychiatry. 2003;60(11):1158-1167.
22. Jeon YW, Polich J. Meta-analysis of P300 and schizophrenia: patients, paradigms, and practical implications. Psychophysiology. 2003 Sep;40(5):684-701.
23. Alain C, Cortese F, Bernstein LJ, He Y, Zipursky RB (2001) Auditory feature conjunction in patients with schizophrenia. Schizophr Res 49: 179–91.
24. Korostenskaja M, Dapsys K, Siurkute A, Maciulis V, Ruksenas O, et al. (2006) Effects of risperidone on auditory information processing in neuroleptic-naïve patients with schizophrenia spectrum disorders. Acta Neurobiol Exp (Wars) 66: 139–144.
25. DE Hert M, Schreurs V, Vancampfort D, VAN Winkel R. Metabolic syndrome in people with schizophrenia: a review. World Psychiatry. 2009;8:15–22.
26. Coodin S. Body mass index in persons with schizophrenia. Can J Psychiatry. 2001 Aug;46(6):549-55.
27. Annamalai A, Tek C. An overview of diabetes management in schizophrenia patients: office based strategies for primary care practitioners and endocrinologists. Int J Endocrinol. 2015;2015:969182.
28. Tascilar ME, Turkkahraman D, Oz O, Yucel M, Taskesen M, Eker I, Abaci A, Dundaroz R, Ulas UH. P300 auditory event-related potentials in children with obesity: is childhood obesity related to impairment in cognitive functions? Pediatr Diabetes. 2011 Nov;12(7):589-95.
29. Winkler, I., Karmos, G.,& Nδδtδnen, R. (1996). Adaptive modeling of the unattended acoustic environment reflected in the mismatch negativity event-related potential. Brain Research, 742:239-252.

Date of Publishing: 05 March 2021
Author Declaration: Source of support: Nil, Conflict of interest: Nil
Ethics Committee Approval obtained for this study? YES
Was informed consent obtained from the subjects involved in the study? YES
For any images presented appropriate consent has been obtained from the subjects: NA
Plagiarism Checked: Urkund Software

DOI: 10.36848/IJBAMR/2020/26215.55558