# Letters to Editor

## Gender Differences in Auditory P300 Event-Related Potential in Indian Population

Sir,

Identification of biomarkers in mental illnesses is an important step toward developing reliable diagnostic tests, identifying people at risk, predicting the course and prognosis of illnesses, and developing an etiopathophysiologically valid psychiatric classification system. Event-related potentials (ERP) are voltage fluctuations in the electroencephalogram (EEG) that are time-locked to internal or external events (e.g., stimuli, response, decision).[1] ERPs have been used to study the neural basis of cognitive functions and the pathophysiological basis of psychiatric and neurologic diseases.[2] Recent evidence suggests that the P300 ERP component has great potential as an actionable biomarker in schizophrenia as it can help in diagnosis, differential diagnosis, predicting disease risk, predicting treatment response, and in new treatment development.[3] But, its use in real-world settings is limited by the lack of normative data in different populations and limitations in technical expertise.

A recent multisite study of the Consortium on the Genetics of Schizophrenia demonstrated that P300 measures could be reliably obtained from settings without EEG-specialized laboratories, extensive technical training, or onsite expertise in EEG assessment and analysis; a relatively simple, two-channel EEG system yielded 91% usable P300 data in less than 30 min across multiple sites. Furthermore, demographic factors, especially age, sex, and race, are important variables that affect P300 values.[4]

Age-related normative data for P300 in the Indian population has been published before.[5] However, gender differences in P300 have not been investigated in the Indian population. This study aimed to compare the latency and amplitude of P300 in males and females in the 20–25 years age group of the Indian population. This age group was selected as P300 waveforms have well-established adult form by this age, and this age group also represents the peak age of the onset of schizophrenia.[6,7]

This study was carried out at the Centre for Cognitive Neurosciences in a tertiary teaching hospital in India. The study was approved by the institute ethics committee. The sample consisted of auditory P300 ERP of healthy control participants from previous studies done at the department. A list was made of all previous studies, from 1999 to 2009, conducted at the department measuring P300. Only those studies in which the same auditory oddball paradigm was used were included. Healthy control participants in the age range of 20–25 years were selected from these studies.

P300 recordings of healthy control participants were analyzed for amplitude and latency. P300 amplitude was measured as the peak amplitude relative to a pre-stimulus baseline between 250 and 500 ms post-stimulus, and the P300 latency was measured relative to the stimulus onset and defined as the time period between stimulus onset and peak amplitude. In all these studies, P300 was recorded by an auditory oddball paradigm in which two types of tones were presented to the participants through a headphone; a frequent tone at 40 dB and a rarer louder target tone at 55 dB. Participants were instructed to recognize the rarer type of tone and press a button with the dominant hand each time they heard it. EEG filters were set at a high cutoff of 100 Hz and a low cutoff of 0.1 Hz. The frequency of the target tone was 2 kHz and its presentation probability was 20%, whereas the frequency of the frequent tone was 1 kHz, and the presentation probability was 80%. Signal averaging was done using EB Neuro Galileo NT (Firenze, Italy). Trials with significant artifacts, including eye blinks, eye movements, muscle artifacts, and skin potentials, were excluded manually before generating averaged ERP waveforms.

Data obtained were analyzed using the SPSS 17 version. Shapiro-Wilk's test showed that most of the variables were not normally distributed. Mann-Whitney U test was used to compare age, amplitude, and latency in the three central electrodes (frontal [Fz], central [Cz], and parietal [Pz]) across gender. The significance level was kept at $P < 0.05$ (two-tailed). There was no statistical difference in the age across the genders ($U = 95.5$, $P = 0.15$).

The amplitude and latency in Fz, Cz, and Pz electrodes were calculated in 34 participants—13 males and 21 females. Reliable data for Fz electrodes was found only in 12 males and 20 females. P300 latency in Fz, Cz,

**Table 1: Age and P300 amplitude (in microvolts (μV)) and latency (in milliseconds) across frontal (Fz), central (Cz), and parietal (Pz) locations**

| | Males ($n$=13)* | | Females ($n$=21)* | | U | $P$ | $\eta^2$ |
|---|---|---|---|---|---|---|---|
| | Mean±SD | Median (range) | Mean±SD | Median (range) | | | |
| Fz Latency | 344.11±23.49 | 346.88 (331.25-374.22) | 360.45±15.55 | 364.45 (280.47-393.75) | 73 | 0.07 | 0.105 |
| Cz Latency | 337.41±24.82 | 339.06 (303.91-372.27) | 350.5±13.41 | 356.64 (286.33-376.17) | 85 | 0.07 | 0.098 |
| Pz Latency | 331.25±28.13 | 329.3 (294.14-372.27) | 347.25±21.16 | 346.88 (292.19-389.84) | 71 | 0.02 | 0.159 |
| Fz Amplitude | 6.27±5.67 | 4.265 (1.6-21.7) | 7.82±3.9 | 7.67 (0.79-17.4) | 82 | 0.15 | 0.068 |
| Cz Amplitude | 8.93±5.85 | 6.81 (2.75-21.8) | 11.12±4.6 | 10.7 (4.85-25.1) | 92.5 | 0.12 | 0.072 |
| Pz Amplitude | 11.34±5.56 | 9.18 (4.23-21.4) | 14.57±6.16 | 13.5 (5.48-32.6) | 95 | 0.15 | 0.064 |

*Males $n$=12 and *Females $n$=20 for Fz amplitude and latency

and Pz electrodes showed a clear trend toward higher values in females in comparison to males, but no such difference was seen in amplitude [Table 1].

Previous studies regarding the influence of gender on P300 have shown mixed results. While earlier studies found no effect of gender on latency or amplitude, later studies showed a larger P300 amplitude in females.[8,9] Studies have also shown that P300 latencies vary as a function of age and gender. Segalowitz and Barnes (1993) reported larger P300 amplitudes in females in a young adolescent group, while in the older adolescent group (17 years), males showed larger amplitudes.[10] A recent systematic review exploring gender effects on auditory P300 revealed interesting findings.[11] 13 out of 31 studies reported larger P300 amplitudes in females. Only one study out of 24 studies reported longer P300 latencies in females, and all other studies found no gender-related effect on P300 latencies.[11] The study by Melynyte *et al.*, which found longer latencies in females, included only young female subjects (age range: 18–29 years), which is comparable to our sample.[12] More studies are needed in this specific age group with more sample size to test the consistency of this finding. Gender differences in P300 have been attributed to variations in processing strategies, anatomical differences such as larger corpus callosum in females, different neuronal maturity rates, and hemispheric asymmetry between males and females.[13]

Keeping in mind that our study sample was small, results from our study and previous studies suggest the need for gender-based P300 normative data for it to be clinically useful.

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**Conflicts of interest**
There are no conflicts of interest.

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