

## Research Article

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# Is cognitive processing affected in adults with hypospadias?: P300 study

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**Abstract:** Background: Hypospadias is a common urogenital system disorder. The frenulum, which is the most sensitive area of the glans penis, is not present in patients with hypospadias. This may lead to a failure in sexual and ejaculatory function, and cause emotional problems affecting cognitive processes.

**Aim:** We aimed to study auditory Event Related Potentials (ERP) in patients with hypospadias to understand the status of cognitive function.

**Materials and Methods:** Seventeen patients with hypospadias who presented to the Urology Outpatient Clinic of Çanakkale Military Hospital, and 11 healthy individuals of similar age were chosen. The auditory oddball paradigm with ERP from the Cz and Fz head regions were studied. The latency and amplitude of the P300 wave were measured.

**Results:** Both, the study and control groups consisted of young males. Although the study group had a longer P300 latency and lower P300 amplitude when compared to

control group, the results were not statistically significant ( $p$ : 0.059 and 0.346 respectively).

**Conclusion:** Although the results are not statistically significant, our findings indicate that there may be cognitive changes in patients with hypospadias. Further studies of larger sample size and older patient cohorts are needed.

**Keywords:** Hypospadias, Event Related Potentials-P300, Cognition

## 1 Introduction

Hypospadias is a congenital abnormality which affects at least 1 in 300 newborn boys [1]. It is one of the most common urogenital system disorders, and causes several cosmetic and functional problems [1,2]. Male teenagers with hypospadias have behavioral problems, weaker social relationships, and worse academic success when compared to healthy ones [3]. Hypospadias results in similar emotional problems in adult males. Penile deformity is the main cause of emotional stress. As a result of this stress, 40% of patients show differences in social behavior, for example, refraining from the use of public toilets [2,3]. A prior study has shown that 24% of males with hypospadias had problems with erections and 13% of them had difficulty with ejaculation [3].

Event Related Potentials (ERP), occur only when the subject is selectively attentive to the stimulus. Thus, ERPs have gained in popularity in the clinical arena as a tool for assessing cognitive function [4,5]. The most frequently tested ERP responses are the N200 and P300 responses. The anatomic locations of both have not yet been determined, but they are thought to arise from different structures in the brain [6]. In addition, it is thought that the N200 is important for noticing and classifying an impulse [6,7]. Even though a variety of parameters have been recorded, the main discriminating factor in the assessment

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of P300 is the fact that latency increases 2.85 ms per year after age 60 [8]. The P300 test is elicited by infrequent, task-relevant stimuli, which is thought to reflect processes involved in the evaluation and categorization of a stimulus. The presence, magnitude, topography, and timing of this signal is often used as a metric of cognitive function in decision-making processes. A lower P300 amplitude is used to estimate behavioral disorders in young patients, female patients with sexual disorders and to perform a libido assessment in both sexes [9-11].

We think that psycho-sexual problems beginning in childhood in patients with hypospadias could also affect cognitive development. A PubMed-based screening for neurophysiologic studies investigating cognitive development in patients with hypospadias was done, but none were found. With this study, our aim was to investigate whether ERP alterations exist in adults with hypospadias when compared to a normal control group. This would permit the determination of whether there is an effect of hypospadias on cognitive development.

## 2 Materials and methods

Seventeen patients with hypospadias, without other urogenital abnormalities who presented to the Urology Outpatient Clinic of Çanakkale Military Hospital, and 11 healthy males at similar age forming the control group, were studied. Patients who had disorders that could affect cognitive function such as mental disorders, unstable body temperature, the use of medications that could affect ERP responses were removed from the study. Recordings were made while the subject was lying on a bed in an isolated room. Before starting the recording all subjects were clearly informed about the procedure. We used the auditory “oddball 2 tone distinction assignments” method, where low and high frequency tones were given in two second intervals at 80 dB HL with a duration of 50 msc to both ears. All the subjects were asked to count the high frequency (2000 Hz) tones, which were given randomly between 1000 Hz low frequency tones. The ratio of high frequency notes was 20%. The subjects who hadn't managed to determine the target sounds (2000 Hz notes) more than three times were taken to the test again. The ones who couldn't manage to improve their performance were not included to the study.

We used silver disc electrodes for the recordings. Cz and Fz positions were used for the active electrodes and mastoid protuberances were used for the reference electrodes, while the ground was placed on Fpz. Neuropack

MEB-9200 (Nihon Kohden- Japan) was used for the study. We took the average of twenty traces and repeated the test until two similar traces were obtained. After averaging the P300 responses for the infrequent 2000 Hz stimulus, the latencies and the peak to peak amplitudes of the P300 waves were calculated. The Mann-Whitney U test was used for the statistical analyses.

All subjects signed their written informed consent before the study, which was conducted in accordance with the Declaration of Helsinki. The local Medical Ethical Committee of Çanakkale Onsekiz Mart University approved the study in 2009.

## 3 Statistics

The data acquired from the study was analyzed by SPSS® 15.0 statistics program. The median values are shown as minimum and maximum for each group. Mann Whitney-U test was applied for the analysis of the non-parametric variables. All the data are shown in 95% confidence interval by accepting statistically significant p value as 0.05 or below.

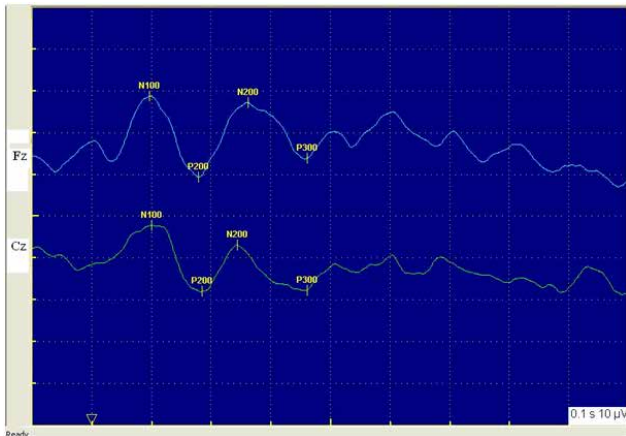
## 4 Results

Age and educational background were similar in both groups ( $p > 0.05$ ). The study group (Figure 1) had a longer P300 latency and lower P300 amplitude when compared with the control group (Figure 2), whereas the results were not statistically significant ( $p$ : 0.059 and 0.346 respectively) (Table 1).

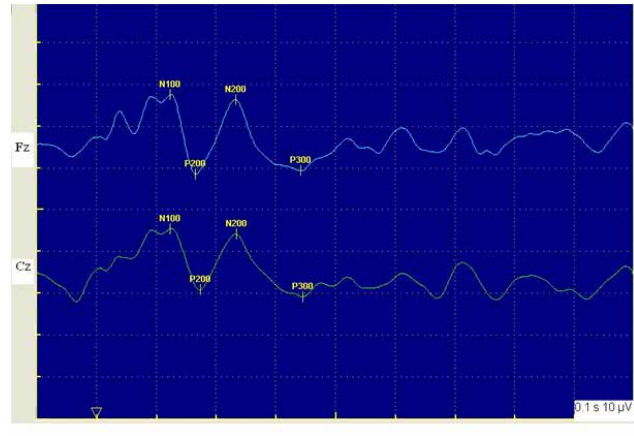
## 5 Discussion

This presented study is the first study on auditory ERP in patients with hypospadias. Although the results were not statistically significant, we found that the study group had a longer P300 latency and lower P300 amplitude when compared with the control group. A small sample size and young patient population may account for the lack of statistical significance. The longer latencies and lower amplitude of P300, suggest that the disease may effect these cognitive processes.

Karademir *et al.*, have shown that psycho-sexual disorders in these patients is not due to the physical



**Figure 1:** P300 response of a patient with a longer latency and a lower amplitude



**Figure 2:** P300 response of a healthy male

**Table 1:** Comparison of demographics and P300 amplitude and latencies in both groups

	Patient n=17	Control n=11	p*
Non-Parametric	Median (min-max)	Median (min-max)	
P300 latency (ms)	321.6 (305.6-332.5)	312.4 (298.3-325.4)	0.059
P300 amplitude (µV)	10.1 (6.1-21.3)	10.8 (8.0-23.6)	0.346
Year in education	8,0 (3,0-15,0)	8,0 (3,0-15,0)	0.723
Age	23.5 (19-28)	24.5 (20-30)	0.465

\* Mann-Whitney U, n = Sample size, min = minimum, max = maximum

deformity, but it is a result of the psychological stress due to that deformity, which may lead to anxiety, aggression and nervous behavior, as well as inability to discuss the emotional issues associated with the disorder [2,3]. In adults, the presence of hypospadias or its correction can cause serious emotional problems. We aimed to detect the effect of hypospadias on cognitive development using ERP, which is now widely being used to investigate these processes.

According to the recent publications, P300 is found to be related with the attention and working memory by the serial and parallel activation of multiple neocortical and limbic regions [12]. Studies have also shown that various neurobehavioral syndromes are related with alterations of ERP [4]. It is suggested that the latency of P300 measures the stimulus evaluation time, which also involves central nervous system, and the amplitude shows the allocation of neural resources, the efficiency of cognitive processing, the certainty of decision-making, and target probability [13].

ERPs have been studied to better understand their role in determining cognitive processing in neurologic, psychiatric and systemic disease processes. Although there are

several studies on evoked potentials in adults with sexual dysfunction, very few studies have been performed on auditory ERP [10,11,14].

Ozcan et al. investigated the cognitive processes in premature ejaculation (PE) by using the auditory ERP [14]. They found that the latencies of the N200 and the P300 in patients with premature ejaculation (PE) were significantly longer than the controls, whereas the comparison of the amplitudes revealed no significant difference. The results can be commented as there is an increased duration of the evaluation and the categorization of sensory stimuli in the central nervous system, but there is no change in the quality of cognitive processing. In our study, we also found that the P300 latency was longer and amplitudes were smaller in the study group.

Vardi et al. reported that ERP is not only useful in the diagnosis of libido and psychological sexual dysfunction, but can also be used to evaluate the treatment progress [10,11].

On the other hand, there are syndromes with hypospadias and agenesis, hypogenesis, hypoplasia of corpus callosum [15-17]. The possible effects of the corpus callosum to ERP have been studied by Polich and Hoffman in 1998

and 1999 [18,19]. Their findings suggest that P300 reflects callosal size and interhemispheric transmission efficacy.

The limitations of our study include young patient population and small sample size. One bias in our study is that we did not investigate patients for any corpus callosum abnormality, and/ or any syndrome with hypospadias and a corpus callosum abnormality. Because of this, the effect of a corpus callosum abnormality on P300 latencies is not known. The ERP components of patients with hypospadias may be affected due to the minimal corpus callosum defects they may have had. The hypothalamus, which is known to have a role in the response to sexual impulses, may play a role in the relationship between hypospadias and cognitive function [20]. Future studies on investigating cases with hypospadias without other urogenital abnormalities with ERP and volumetric examinations of corpus callosum will contribute to an improved evaluation of the cognitive processes accompanying hypospadias.

## 6 Conclusion

Cognitive function is important in the academic and professional success of the people, because of that, it is important to show the effects of frequent abnormalities on cognition, such as hypospadias, to take precautions as early as possible. Even though there is no statistical significance in the results, the longer latency and the lower amplitude of the P300 in the patient group may be an indication of a negative effect of hypospadias on cognitive function. Further studies with a larger sample size, comparison of the P300 values in patients with hypospadias before and after surgical intervention are needed to be done, in order to assess the effect of hypospadias on cognitive function better.

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