



P50 Sensory Gating in Children and Adolescents with Developmental Stuttering

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ÖZET:

Gelişimsel kekemeliği olan çocuk ve ergenlerde P50 duyuşsal kapılama

Amaç: Kekemelik seslerin, hecelerin ve kelimelerin istemsiz tekrarı ve uzatılması ile konuşma akıcılığının bozulduğu, nedeni tam olarak bilinmeyen bir konuşma bozukluğudur. Konuşmanın akıcılığın sağlanmasında psikolojik, sosyal, öğrenme ile ilişkili unsurlar ve sensorimotor değişkenler önemli rol oynar. Beynin gelen uyarıları işlemlenmesinde ve uygun bir davranışsal yanıt oluşturulmasında duyuşsal kapılama gerekli bir işlemdir. Duyuşsal kapılama, sınırlı bilgi işleme kapasitesine sahip olan beyni, sürekli ve yoğun bilgi akışı sırasında gereğinden fazla veya ilişkisiz olan uyarıların filtrelenmesini sağlayarak aşırı yüklenmeden korur. İşitsel uyarıların kapılanamaması, işitsel sinyallerin işlenmesi ve işitsel geribildirim mekanizmasını da bozarak konuşma akıcılığının bozulmasına yol açabilir. Çalışmamızda kekemelikte duyuşsal kapılamanın bozulmuş olabileceği hipotezini test etmek için gelişimsel kekemeliği olan çocuk ve ergenlerde duyuşsal kapılamanın durumunu P50 supresyonu ile değerlendirmeyi amaçladık.

Yöntem: Çalışmaya gelişimsel kekemeliği olan 7-18 yaş aralığında 20 çocuk ve ergen ile, konuşma problemi olmayan yaş ve cinsiyet açısından birebir eşleştirilmiş 20 sağlıklı kontrol alındı. Tüm olgulara bir çocuk psikiyatristi tarafından psikiyatrik değerlendirme yapıldı. Psikiyatrik, nörolojik ve kronik hastalığı olan, santral sinir sistemini etkileyen ilaç kullanımı öyküsü ve ailesinde şizofreni öyküsü olan olgular çalışmaya dışı bırakıldı. Tüm bu değerlendirmelerin ardından P50 supresyon değerlendirmesi elektroensefalogram (EEG) ile kaydedildi. Çalışmanın istatistiksel analizi SPSS paket programı kullanılarak yapıldı. Her iki grubun P50 değerlerini karşılaştırmak için Mann-Whitney U testi kullanıldı ve tüm analizlerde $p < 0.05$ anlamlılık derecesi olarak kabul edildi.

Bulgular: Çalışmada yer alan çocuk ve ergenlerin yaş ortalaması $11,8 \pm 2,7$, kekemelik başlama yaşı $4,6 \pm 1,1$ idi. Çalışmaya katılanların her iki grupta da 16'sı (%80) erkek, 4'ü (%20) kızdı. Her iki grubun P50 amplitütü, latansı, P50 supresyon oranları arasında istatistiksel olarak anlamlı fark saptanmadı.

Sonuç: Bu çalışmanın sonuçları çocuk ve ergenlerde P50 ile kekemelik arasında bir ilişki olmadığını ortaya koymaktadır. Ancak kekemelik çocuk ve ergenlerde duyuşsal kapılama değerlendirildiğinde kullanılan diğer bir test olan prepulse inhibisyonla da, farklı yaş gruplarında ve daha geniş örneklem üzerinde tekrarlanmalıdır.

Anahtar sözcükler: Kekemelik, duyuşsal kapılama, P50

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ABSTRACT:

P50 sensory gating in children and adolescents with developmental stuttering

Objective: Stuttering is a speech disorder, where speech fluency is disturbed by the involuntary repetition and prolongation of words and syllables. Its cause is not fully known. Sensory gating is an essential part of information processing and developing an appropriate behavioral response in the brain. Psychological, social, and learning-related factors together with sensorimotor variables play an important role in ensuring fluent speech. Sensory gating protects the brain from overload by filtering the redundant or potentially irrelevant information from the continuous and intensive stream of information. A lack of sensory gating for auditory stimuli may lead to disturbed auditory signal processing and auditory feedback and result in loss of speech fluency. Our aim in this study was to evaluate the state of sensory gating in children and adolescents with developmental stuttering using P50 suppression to test our hypothesis that sensory gating may be disturbed in stuttering.

Method: A total of 20 stuttering children and adolescents in 7-18 age group and 20 age- and sex-matched healthy controls with no speech problems were included in the study. All children underwent psychiatric evaluation by a pediatric psychiatrist. Patients with psychiatric, neurological or chronic disease, those who had a history of using medication that could affect the central nervous system and children with a family history of schizophrenia were excluded from the study. P50 suppression was then recorded with an electroencephalogram (EEG). Statistical analysis was performed using the SPSS package software program. The Mann-Whitney U test was used to compare the P50 values of the two groups and p value < 0.05 was considered significant for all analyses.

Results: The mean age for the children and adolescents included in the study was 11.8 ± 2.7 years and the age of stuttering started was 4.6 ± 1.1 years. There were 16 males (80%) and 4 females (20%) in both groups. There was no statistically significant difference between the P50 amplitude, latency and P50 suppression ratios of the two groups.

Conclusion: The results of this study have shown no association between P50 and stuttering in children and adolescents. However, this first study evaluating sensory gating in children and adolescents should be repeated with prepulse inhibition, another test used to evaluate sensory gating, on larger samples and in different age groups.

Key words: Stuttering, sensory gating, P50

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INTRODUCTION

Stuttering is a multifactorial speech disorder whose etiology has not been fully elucidated. Genetic,

neurophysiological, and psychological factors are thought to play a role together or in various combinations in the various forms of stuttering (1). The cerebral dominance concept is the first neurophysiological model directed

towards the cause of stuttering and postulates that cerebral dominance does not fully develop for the language function in stutterers (2). Functional neuroimaging studies in the last few decades have demonstrated decreased auditory association cortical activity (3,4,5), increased right frontal and left cerebellar region activity (4), a disturbance of the left hemisphere premotor and primary motor region function timing (6) and increased left putamen, ventral thalamus, and inferior anterior cingulate activity (3) in stutterers. It is still not certain whether the increase in right hemispheric speech region activity shown with functional studies in stutterers is compensatory or a structural difference causing pathology (3,4).

Neuroimaging studies have also shown structural differences in the brains of stutterers compared to controls. Related findings are mostly concentrated in the speech-associated cortical centers (perisylvian frontotemporal region gray matter and planum temporale) and their connections and demonstrate their lateralization differences (7,8). Planum temporale is the auditory association cortex where language-related information is processed at a high level and stutterers have been shown to lack the asymmetry in normal subjects where the left planum temporale is larger than the right. The right temporal gyrus white matter has been demonstrated to be larger in stutterers while the arcuate fascicle connecting the temporal and frontal regions in the left hemisphere is smaller (9). A recent study has reported that many changes listed above and found in adult stutterers show a different structure in children (10). Authors have associated the structural difference between adult and child stutterers with neuroplasticity.

The complexity of the network needed in speech production (auditory, motor, and linguistic systems) makes it difficult to distinguish between causes, and predisposing, precipitating, and perpetuating factors. The fluency of speech can be studied within each of three levels; a processing level (central neural processes), an output level (observable behavior) and a contextual (environment) level. Developmental stuttering may well result from an overall minor disturbance in any one or several of the required modules (11).

The behavior manifested at the output level will provide feedback, through various afferent channels to the central processes. Such afferent signals may, in turn, alter the way these processes function. Examples of this type of

feedback include physical alterations to the articulators, and auditory or proprioceptive feedback. Delayed auditory feedback makes stutterers more fluent but, conversely, disrupts speech production in normally fluent subjects. The neurophysiological basis of the altered auditory feedback (AAF) therapy is based on having the patient listen to altered speech signals. This finding has suggested that auditory signal processing might be fundamentally different in stutterers and fluent speakers and that stuttering may be associated with a sensory gating abnormality (11,12,13). This is supported by the demonstration in stutterers that the basal ganglia also show functional and structural differences in addition to the cortical motor and speech areas (14). One of the important functions of the basal ganglia, which are key structures for motor control and emotional and cognitive functions, is contribution to gating of the sensory input for motor control (15). The current leading psychological interpretation of the sensory gating is that a continuous stream of incoming auditory information is gated or screened – that is, redundant or potentially irrelevant information is filtered out – in order to prevent overloading the limited capacities of higher-order stages of auditory information processing (16,17,18).

Sensory gating is measured using the P50 suppression ratio and the prepulse inhibition. The human startle reflex is typically assessed by using electromyographic (EMG) recordings of the eye-blink component of the startle reflex in response to sudden and powerful multimodal stimuli, most often acoustic stimuli. The magnitude of the eye-blink response is normally reduced when the startling stimulus is preceded by a weak prestimulus (i.e., “prepulse”) (19). The percentage of the reduction in the startle reflex is the operational measure of sensorimotor gating known as “prepulse inhibition.” P50 is another important test used for assessing sensory gating. P50 is the positive component of the event-related potential that occur about 50 msec. after an auditory stimulus. The change in P50 amplitude is typically measured as the response to click pairs separated by 500 msec. (20,21). The percentage of the amplitude reduction of the P50 response from the first to the second click is the dependent variable, P50 suppression.

As far as we are aware, there is a single study on acoustic startle prepulse inhibition (PPI), one of the sensory gating methods in stutterers and this study in the

adult group has demonstrated no relation between stuttering and PPI (22). However, correlational studies (23,24,25,26,19) of the relationship between P50 suppression and prepulse inhibition suggest that they are distinct, complementary measures of sensory and sensorimotor inhibition, respectively. We therefore investigated whether stuttering children and adolescents had a sensory gating disorder with a test (P50) that was different in relation to using different cerebral inhibitory circuits (27) although it is similar regarding gating.

METHOD

This is a case-control study conducted in a total of 20 child and adolescent patients, who had presented at the Department of Child Psychiatry of the Inonu University Medical Hospital during 2006-2007 and received a diagnosis of stuttering according to DSM-IV (Diagnostic and Statistical Manual of Mental Disorders-IV). A control group was created from 20 age- and sex-matched healthy children. All the children and adolescents in the study were right-handed. Local ethic committee approval was obtained before the study.

Stutterers who were aged 7-18 were selected taking into account the age of sensory gating development (28,29). Patients, who had other psychiatric, neurological, or chronic disease accompanying the stuttering or had a history of medication usage, were excluded from the study. Patients with a family history of schizophrenia were also excluded. The consecutively attending stuttering children and adolescents who met the study inclusion criteria and the families were provided information on the study and those who volunteered were included. One child with mental retardation, 3 children with attention deficit hyperactivity disorder and 4 children with anxiety disorder or depression accompanying the stuttering were excluded from the study. An age- and sex-matched control group was created from the children of the hospital staff on a voluntary basis. Patients with psychiatric, neurological or chronic disease, those who had a history of medication use that could affect the central nervous system and children with a family history of schizophrenia were excluded from the study.

Parental consent was obtained for all children. A psychiatric evaluation was performed by a pediatric psychiatrist for all children and adolescents participating

in the study and the structured interview technique of Schedule for Affective Disorders and Schizophrenia for School Aged Children- Present and Lifetime Version (Kiddie-SADS-PL) was administered.

P50 Measurements

The electrophysiological examination was performed only during the morning hours (at the same time of the day for all subjects) at the Laboratory of Clinical Neurophysiology of the Inonu University Department of Neurology. The subjects were seated in a comfortable chair in a sound- and light-attenuated, electrically shielded room. They were instructed to relax with the eyes open and to fixate on a point straight ahead to avoid eye motion artifacts.

The electroencephalogram (EEG) was recorded with a MEM-4200K evoked potential recorder (Nihon Kohden, Japan) system in four channels for recording of evoked responses, integrated with an auditory stimulator. The test stimulus, a click sound of 0.1 sec duration set 60 dB above the auditory threshold with a rarefaction output phase, was presented binaurally through earphones. The auditory threshold of each subject was measured 15 min before recording through the earphones. The interval between the first and second clicks (interstimulus interval = ISI) was 500 ms, and the interval between two pairs of clicks was 10 sec. Electroencephalographic activity was recorded from a disk electrode affixed to the vertex (Cz) and referenced to the left mastoid. The mean signal was registered in two channels, and amplified 20,000 times with a bandpass filter between 1 and 100 Hz. EEG data were collected for 1000 ms. for each paired stimulus presented. Additional channels were used to record the electrooculogram (EOG) between the superior orbita and lateral canthus.

Trials were rejected automatically by the device if they contained artifacts indicated by a response of $\pm 100 \mu V$ over the area of P50 for evoked potentials or the EOG recordings. Thirty non-rejected waves were added together to give an average signal, which was used for analysis. EEG data were collected for 1000 ms. for each paired stimulus presented. The averages of S1 waves and of S2 waves were collected in sequence. The S1 and S2 wave averages were then considered separately for analysis.

The wave peaks were determined visually and the latencies and amplitudes were marked manually. The

most positive peak between 40 and 90 ms after the conditioning stimulus was selected as the P50 final latency and the wave amplitude (S1) was measured from baseline to peak. The second wave (S2= test) was determined using the corresponding peak between S1±10 ms. away from the latency of the first wave form (conditioning) and its amplitude was also measured from baseline to peak.

years for stuttering, 11.8±2.7 (range 7-17) years for controls. The mean age stuttering started was 4.6±1.1 (range 3-8) years. The P50, amplitude, latency, P50 suppression ratio for the two groups and the p values are presented in Table 1. Comparing the stutterers with the normal group did not show any significant difference for conditioning (S1) and test (S2) wave amplitudes, latency and P50 suppression ratio.

Table 1: P50 values of stutterers and normal controls

	Stutterers (n=20) mean±SD (min-max)	Controls (n:20) mean±SD (min-max)	p
P50 response to click 1			
Amplitude (µV) (baseline to peak)	4.5±4.1 (0.2-13.9)	2.3±1.5 (0.8-5.9)	0.06
Latency (ms)	48.3±7.6 (36-63)	50.4±6.5 (38-61)	0.87
P50 response to click 2			
Amplitude (µV) (baseline to peak)	1.4±2.9 (0.01-6.1)	1.4±1.1 (0.07-3.8)	0.37
Latency (ms)	55.1±22.9 (36-43)	50.1±7.8 (37-63)	0.47
The suppression percentage	45.5±35.3 (0-100)	33.3±34.5 (0-96)	0.35

The data were collected by one investigator and analyzed by an independent trained evaluator blind to the state of the subjects. Averages with no discernible conditioning P50 waves were excluded from the analysis and the analysis was repeated in four subjects in this position. The percentage of P50 suppression was calculated by using the following formula: $(1 - [\text{second click amplitude}/\text{first click amplitude}]) \times 100$ (Light 2000).

Statistical Methods

This study was consulted with İnönü University Biostatistics Department. By using "Power Analyses" 20 patients were included in this study. The statistical analyses were performed with the Statistical Program for Social Sciences - SPSS for Windows version 11.0 program. All data were reported as means ± standard deviation (SD) and min-max values. Normality for continued variables in groups was determined by the Shapiro-Wilks test. The variables did not show normal distribution ($p < 0.05$). The Mann-Whitney U test was therefore used for comparison of variables between the studied groups. A p value of < 0.05 was considered significant.

RESULTS

There were 16 males (80%) and 4 females (20%) in both groups with a mean age of 11.7±2.7 (range 7-17)

DISCUSSION

Our study aiming to evaluate sensory gating in children adolescents with P50 did not find an association between stuttering and sensory gating. Ours is the first study evaluating sensory gating in stutterers in this age group. Our results are similar to another study evaluating sensory gating in adolescent stutterers with PPI.

The success obtained with altered auditory feedback therapy in stutterers has directed investigations towards the early periods of auditory information processing period in the physiopathology of stuttering. The sensory gating that falls into the pre-attention early period in information processing is accepted to be an integration of multistep procedures.

PPI is subserved by cortico-striato-pallido-thalamic (CSPT) circuitry that has neural substrates that overlap and interact with P50 generation circuitry, especially in mesial temporal lobe structures (30,31). Both PPI and P50 suppression could involve common forebrain mechanisms that serve to regulate cortical and brainstem responsiveness. The primary neural control of the startle reflex involves brain structures at, or below, the level of the mesencephalon: the auditory nerve, the ventral cochlear nucleus, the dorsal nucleus of the lateral lemniscus, the caudal pontine reticular nucleus, spinal interneurons and spinal motor neurons (32). Modulation of the startle reflex (this includes phenomena such as habituation, sensitization

and fear potentiation apart from the above-mentioned PPI has been suggested to involve a number of brain structures located up to the forebrain (31,33).

Unlike the startle reflex in the PPI paradigm, P50 suppression does not have a substrate that is easily identified across animal species. The temporo-parietal cortex (Brodmann areas 23 and 2) and the prefrontal cortex (Brodmann areas 6 and 25) are thought to have a regulating effect on the early phase of P50 Sensory gating and on the hippocampus in the late phase (27). Although they seem to be related to similar circuits in the brainstem, these two tests have been shown to be different due to the modulatory effects of higher structures. This study with P50 sensory gating in stuttering children showed no difference in the results of the control group and a similar result was previously obtained in the prepulse inhibition

study (22) strongly suggesting that the hypothesis built on sensory gating for stuttering may be invalid. However, our study was on child and adolescent stutterers while the other was on adult stutterers. The results of research on the changes in brain functions and cerebral anatomic structure reveal that there are differences between stuttering children and adults who have developed permanent stuttering (7,8,10). It is also known that there are differences between adult and children stutterers in the success of altered auditory feedback therapy, a treatment that has provided inspiration for sensory gating studies (12). Taking these into account, we believe that the hypothesis of sensory gating disorder in stuttering needs to be retested with both electrophysiological tests in permanent adult stutterers and child stutterer groups with well-defined limits.

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