Original Research

Study on P50 Sensory Gating in Children with Autism Spectrum Disorders in Shanghai

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Unusual reactions to auditory stimuli are often observed in autism and may relate to ineffective inhibitory modulation of sensory (P50 sensory gating). Sensory gating deficit may, however, characterize children with autism spectrum disorders (ASD) reflecting imbalance of neuronal excitation/inhibition in these cohorts. We applied a paired clicks paradigm designed by American Nicolet Bravo Instrument to study P50 sensory gating in children with autism (N=39) and age-matched typically developing children (N=31). The incubation period to auditory stimuli in children with ASD was significantly longer than typically developing children. The data suggests that P50 sensory gating is deficit in children with ASD. The latency of response to the second click was not significantly reduced in children with ASD. The speed of processing auditory stimulation is slower in children with autism than typically developing children. The sensory gating P50 in the autistic children is impairment, and won't improve with the age. The speed of processing sound stimulus in autistic children is much slower than that of control group. The speed of processing sound stimulus in autistic children will increase with the age. The sensory gating P50 in normal control is active and it is improving with the age.

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INTRODUCTION

Autism spectrum disorders (ASD) are common childhood neurodevelopmental disorders with strong genetic liability.[1] Autism spectrum disorders (ASD) are characterized by deficits in social interactions and communication skills, as well as the presence of stereotypic and repetitive behaviors (DMS-V American Psychiatric Association or APA, 2013). Hypersensitivity to sound, or hyperacusis, is also a very common problem in children with ASD, especially in early life[2].The neural origins of such abnormal behavioral responses in children with ASD are poorly understood, and the causal link between these dysfunctions and attention abnormalities is unclear.[3] Several positron emission tomography (PET) and functional magnetic resonance imaging (fMRI) studies have demonstrated decreased left lateralization of activation in autism compared to controls during auditory language processing.[4,5] The role of the P50 component of the auditory event-related potential in early sensory processing has been examined in relation to the gating of irrelevant or repetitive stimulus information ('sensory gating').[6,7] Many psychiatric illnesses with attentional symptoms-including attention deficit-hyperactivity disorder (ADHD), bipolar mood disorder, and schizophrenia are associated with impairment in sensory gating.[8-10] Some studies have confirmed that the abnormal P50 sensory gating may probable lead to mental symptoms. We sought to determine the characteristics of the P50 sensory gating in the children with ASD and to compare those characteristics with those in the typically developing children.

METHODS

The sample consisted of two groups, the children with ASD group and the typically developing children group. Two groups included thirty-nine children with ASD (37 male,2 female) and thirty-one age-matched typically developing children (23 male, 8 female). There're 39 children diagnosed ASD according to DSM-V, 1994 and without other diseases, aged form 23 months to 198 months, the average is 69.44±40.85 months. In another group, there are 31 typically developing children aged 22 to 120 months, an average is 72.77±31.26 months. There is no significance difference between the ages of the two groups. The children with ASD were outpatients from Shanghai Mental Health Centre in 2013 January till 2014 June, and the diagnosis was made by an experienced chief physician based on DSM-V criteria and confirmed by the Childhood Autism Rating Scale.[11] None of the children with ASD had epilepsy or any other known neurological comorbidity. The typically developing children came from the normal school.

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We use the Conditions (S1) - test (S2) auditory stimulus mode. Using the Bravo stimulator, triggered by signal generator to generate 80 db sound intensity in pairs short sound S1 (1) and S2 (2) stimulation. Set S1 to the conditioned stimulus, S2 as test stimulus. S1 and S2 matching time for 500 ms, each composed of 10s' interval of the stimulus. There're 15 pairs of stimulus to each participant to stimulate by headphones. Building up S1 and S2 synchronized by the brain electrical physiological device (Nicolet Instrument Corp, WI, USA). Recording electrodes are Ag/AgCl disk electrode, reference electrodes placed 10/20 international system, at the central region (Cz), parietal region (Pz), frontal zone (Fz), reference electrodes is right earlobe (A2), bonding is forehead (FPz), resistance between the electrode and the skin is less than 5 kΩ, analysis window is 100 ms. P50 wave is a norientake wave appears within 40-80 ms after stimulation. P50 arise out of the S1 stimulate (P50-S1) called the conditioned response, and P50 arise out of the S2 stimulation (P50-S2) known as test reaction. The difference between the latency of P50 wave to S1 and S2 is equal to or less than 10 ms. By measurement of P50 amplitude to various stimuli (P1-S2/S1): also called (S1-S2)/S1 x 100%, the difference between S1-P50 amplitude and S2 - P50 amplitude has been revealed.

Student t-test was used to compare the components of P50 - S1 with that of P50-S2 and using SPSS11.0 for data processing.

Table 1. P50 in the typically developing children ($\bar{x} \pm s$).

Encephalic Region	Case	S1-P50		S2-P50		S2/S1 (%)	S1-S2 (μV)	1-S2/S1 (%)
		Latency (ms)	Amplitude (μV)	Latency (ms)	Amplitude (μV)			
Cz	31	58.55±20.32	5.71±3.75	57.13±18.64	2.71±2.29	53.44±36.99	3.00±3.52	46.56±36.99
Fz	31	59.45±20.19	5.54±3.52	59.48±19.60	2.77±2.25	57.04±39.06	2.77±3.60	42.96±39.06
Pz	31	57.29±20.38	5.75±3.34	61.29±18.82	3.15±2.67	60.09±46.63	2.60±3.70	39.91±46.63
F		0.089	0.030	0.373	0.307	0.203	0.098	0.203
P		0.915	0.971	0.690	0.736	0.816	0.907	0.816

Table 2. P50 in the children with ± ASD ($\bar{x} \pm s$).

Encephalic Region	Case	S1-P50		S2-P50		S2/S1(%)	S1-S2(μV)	1-S2/S1 (%)
		Latency (ms)	Amplitude (μV)	Latency (ms)	Amplitude (μV)			
Cz	39	68.49±16.66	4.09±2.42	65.33±18.28	4.47±3.02	132.55±196.96	-0.38±2.41	-32.5±196.96
Fz	39	68.1±15.4	4.40±2.80	64.85±18.91	4.04±2.88	94.79±35.47	0.36±1.37	5.21±35.47
Pz	39	68.23±16.86	4.26±2.74	64.7±19.77	4.45±3.49	101.20±25.73	-0.18±1.47	-1.2±25.73
F		0.006	0.133	0.012	0.231	1.173	1.743	1.173
P		0.994	0.876	0.988	0.794	0.313	0.180	0.313

Table3. The amplitude of the two stimulus response between the children with ASD and the typically developing children (Cz region).

	Type	Amplitude (μV)	t/Z	P
Typically developing children (31s)	S1-P50	5.71±3.75	4.738	0.000
	S2-P50	2.71±2.29		
Children with ASD (39s)	S1-P50	4.09±2.42	-0.991	0.328
	S2-P50	4.47±3.02		

RESULTS

Comparing P50 in each Encephalic Region between the Two Groups

SG P50 occurred at Cz, Fz, Pz both in the children with autism and typically developing children, and their waveform was similar to each other. There is no significant difference in the latency, amplitude and inhibition occurred in each encephalic region of each group ($P > 0.05$), as shown in **Table 1** and **Table 2**.

Comparing the Latency and Amplitude to the Two Stimulus between the Two Groups

There is no significant difference in the latency and amplitude of SG P50 at different encephalic region each group ($P > 0.05$) In the typically developing children, the amplitude of the response to S2 is significant smaller than that of S1 ($P < 0.05$). However, this difference is not seen in the children with ASD ($P > 0.05$) as shown in **Table 3**.

Comparing SG P50 between the children with ASD and the typically developing children

The difference in S2/S1, S1-S2, 1-S2/S1 between the children with ASD and the typically developing children is significant at Cz, Pz and Fz ($P < 0.05$). The amplitudes of S2-P50 at Cz and Pz is significantly different between the two groups ($P < 0.05$). The latencies of S1-P50 of the children with autism at Pz and Fz are significant different from those of the typically developing children ($P < 0.05$). The amplitude of S1-50 at Pz in the children with autism is significantly different from in the typically developing children ($P < 0.05$) as shown in **Table 4, 5,** and **6**.

Table 4. Compare the latency and amplitude of P50 of the typically developing children with those of children with ASD ($\bar{x} \pm s$) (Cz).

Group	Case	S1-P50		S2-P50		S2/S1 (%)	S1-S2(μV)	1-S2/S1 (%)
		Latency (ms)	Amplitude (μV)	Latency (ms)	Amplitude (μV)			
Typically developing children	31	58.55±20.32	5.71±3.75	57.13±18.64	2.71±2.29	53.4±36.99	3.00±3.52	46.56±36.99
Children with ASD	39	68.49±16.66	4.09±2.42	65.33±18.28	4.47±3.02	132.55±196.96	-0.38±2.41	-32.5±196.96
t/Z		2.249	2.194	1.845	2.68	2.202	4.562	2.202
P		0.028	0.032	0.069	0.009	0.031	0.000	0.031

Table 5. Compare the latency and amplitude of P50 of the typically developing children with those of children with ASD ($\bar{x} \pm s$) (Fz).

Group	Case	S1-P50		S2-P50		S2/S1 (%)	S1-S2 (μV)	1-S2/S1 (%)
		Latency (ms)	Amplitude (μV)	Latency (ms)	Amplitude (μV)			
Typically developing children	31	59.45±20.19	5.54±3.52	59.48±19.60	2.77±2.25	57.04±39.06	2.77±3.60	42.96±39.06
Children with ASD	39	68.10±15.41	4.04±2.88	64.85±18.91	4.04±2.88	94.8±35.47	0.36±1.37	5.21±35.47
t/Z		2.034	1.520	1.160	2.016	4.182	3.539	4.182
P		0.046	0.133	0.250	0.048	0.000	0.001	0.000

Table 6. Compare the latency and amplitude of P50 of the typically developing children with those of children with ASD ($\bar{x} \pm s$) (Pz).

Group	Case	S1-P50		S2-P50		S2/S1 (%)	S1-S2 (μV)	1-S2/S1 (%)
		Latency (ms)	Amplitude (μV)	Latency (ms)	Amplitude (μV)			
Typically developing children	31	57.29±20.38	5.75±3.34	61.29±18.82	3.15±2.67	60.09±46.63	2.60±3.70	39.91±46.63
Children with ASD	39	68.23±16.86	4.26±2.74	64.69±19.77	4.45±3.49	101.20±25.73	-0.18±1.47	-1.20±25.73
t/Z		2.458	2.046	0.730	1.702	4.404	3.946	4.404
P		0.017	0.045	0.468	0.093	0.000	0.000	0.000

DISCUSSION

In the present study, SG P50 occurred at Cz, Fz, Pz both in the children with autism and typically developing children, and their waveform was similar. It is demonstrated that there was filtration to repeat stimulation in whether the children with ASD or typically developing children. There are no difference in the latency and the amplitude of S1-P50 and S2-P50 and P50 sensory gating recorded in Cz, Pz and Fz.Cz has the largest amplitude P50.[12] In order to increase the comparability with previous studies,[13,14] we observed the latency and the amplitude of S1-P50 and S2-P50 and P50 sensory gating at Cz in the research.

Ponton et al proposed that the composition of sensory gating in childhood was observable.[13] Infant P50 sensory gating ratio assessment is feasible,[15] reliable,[16] and stable between infancy and four years of ages.[17] Kisly et al found the function of sensory gating in babies aged 1 to 4 months baby.[15] Studies on auxanology found that the speed of processing the auditory stimulation increased with the age in the typically developing children.[15,18,19] And the latency to the condition stimulus of children aged 10 to 14 years old was significant longer than that of the adult aged 20 to 39 years old.[20] Among 1-65 year - old population, the latency of P50 decreased with the age significantly, but did change significantly in the typically developing children aged 1 to 8 years old.[21] Elena et al found that the speed of processing the conditioned stimulus increased with the age in children with autism, and matured at the age of 5 years old.[22] Also some other studies haven't found the latency of sensory gating P50 changed with the age, and most researches had the consistent results.[6,23,24]

Studies on P50 sensory gating in children with ASD were not frequently reported. In 1982 Kootz et al reported that there were some difficulties in filtering the sensory inputted in children with ASD, and P50 sensory gating in children with ASD might be dysfunction. But no research on this respect has been done until 2002, Kemner et al performed for the first time the research on the P50 sensory gating of the children with autism, and didn't find any difference between the children with high-functioning ASD and the typically developing children aged 7 to 13 years old.[14] After this, Marshall[6] and Brinkman[24] reported that the inhibition of P50 improved with the age in the children with ASD just like the typical developing age cohorts, Seri et al also reported the sensory gating in the young children with ASD might be damaged, and normalized gradually in the process of growth and development.[25] The latency of P50 sensory gating in children with ASD is shorter than in the typically developing children, and the amplitude to the test stimulus (S2) is reduced with age, sensory gating P50 also increased with the age.[22]

In this study, we didn't find significant difference between the latency of the reactive to the conditioned stimuli(S1) and the testing stimulus(S2) in the typically developing children, but the amplitude of the S2-P50 was smaller than that of the S1-P50. However, in the children with ASD, we have found no significant difference in the latency, nor amplitude, between the reactions to the two stimuli. We have found that the amplitude of the S1-P50 in the children with ASD was longer than in the typically developing children, and the amplitude of S1-P50 in children with ASD was smaller than

in the typically developing children. So in the children with ASD, the speed of processing auditory stimulation is slower, suggesting a weaker activation than in the typically developing children. This may be related to the disorder in cerebellar development in ASD, because the autopsy found extensive reduced in the retro-cerebellar neurons and without glial proliferation in the children with ASD. Some children with ASD were not sensitive to noise, "no react to calling", "no react to regard", and made people doubt they were deaf, or that was not sensitive to the auditory organs. The amplitude in P50 sensory gating in children with ASD are obviously bigger than in the typically developing children. We can find that the function of P50 sensory gating in the children with ASD are weaker than in the typically developing children, verified the version proposed in 1982 by Kootze et al, there were some difficulties in filtering the sensory inputted in children with autism, and the P50 sensory gating in children with ASD might be dysfunction. This may be related to the cognition model of children with autism based on preference more local than the whole information processing and they cannot handle the information according to the before and after contact. For the children with autism, the Conditions (S1) - test (S2) auditory stimulus is two separate auditory stimuli, there is no contact between them, so the reaction degree (amplitude) is same. Although the conclusion of this study is different from the Kemner's study,[14] in which he proposed the P50 sensory gating in children with autism was not different from the typical developing children's, it may be due to the objects in Kemner's study are children with high-functional ASD, who were 7-13 years old, but younger for 1.95 to 16.5 years old in this study with an average age of 5.79 years.

We found that the function of sensory gating enhanced with the age in the typically developing children, it is mainly due to the amplitude of the S2- P50 decreased, but that speed of processing auditory stimulation was changed with age. The function of sensory gating in children with ASD didn't change with the age, but only with the speed of processing conditioned stimulus (S1) increased with the age.[26] Marshall et al thought that the enhancement of the P50 sensory gating might be associated with attention deficits.[6] The children with ASD can't follow the instructions well and can't pay their attention completely during the inspection. We therefore failed to find P50 sensory gating potentialize with the age in the children with ASD.

We can predict that the neural development in children with ASD has improved with the age. This result will urge us to think highly of making early diagnosis and early intervention in the children with autism. So it will be helpful to improving the nervous system development and diminishing the difference between the children with ASD and the typically developing peers.

CONFLICT OF INTEREST

None.

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