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MODULATIONS OF VISUAL GAMMA OSCILLATION FREQUENCY AS A BIOMARKER OF ASD[61]

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Abstract. Neuropsychological studies link autism spectrum disorders (ASD) with an imbalance between excitation and inhibition in cortical networks. Brain oscillations in high gamma-band (50 to120 Hz) are sensitive to this imbalance and may be useful biomarkers of certain ASD subtypes. We aimed to explore induced gamma responses to moving annular gratings with changing stimulus velocity in neurotypical children and to look for their possible abnormalities in children with ASD. Our findings suggest that a deficiency in speeded visual processing at the cortical level in individuals with ASD may be an indicator of reduced functionality of inhibitory mechanisms involved in basic visual functions.

Keywords: autism-spectrum disorders, visual gamma oscillations frequency, visual processing

Background

A significant body of evidence (Oblak et al., 2009; Pizzarelli & Cherubini, 2011; Rubenstein & Merzenich, 2003) suggests that alternation of the balance between neural excitation and inhibition (E/I balance) in direction of excitation is an important factor leading to development of autism spectrum disorders (ASD). When present in the visual cortex, the altered E/I balance may account for visual perceptual abnormalities frequently reported in ASD (Simmons et al., 2009). The high-frequency (gamma) oscillations are crucially dependent on functioning of *fast-spiking, parvalbumin*-positive GABAergic inhibitory *interneurons* and may appear valuable correlates of the altered E/I balance (Siegel et al.,2010). In both humans and animals the gamma oscillations are most reliably induced in visual cortex by large high-contrast moving stimuli. The frequency of the visual gamma oscillations reflects kinetics of inhibitory processes in cortical neurons and can be modulated by functional loads, such as velocity of visual motion (Edden et al.,2009). The changes of

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gamma frequency under functional load may provide valuable information about functioning of cortical inhibitory interneurons.

Objectives

We aimed to study whether the modulation of gamma oscillations frequency by velocity of visual motion is altered in children with ASD as compared to the typically developing control children. We also questioned whether such alternations, if present, are related to performance of a visual discrimination task that is particularly sensitive to neural inhibitory function.

Methods

We studied 21 boys with ASD (IQ>60) aged 8–15 years and 26 age- and gender-matched typically developing (TD) boys using whole head magnetoencephalography (MEG). Participants watched annual gratings moving with different speeds while performing a simple detection task. Individual peak frequencies (IPF) of gamma were identified for each participant and for each stimulus velocity at the occipital sensor with the greatest gamma response amplitude. After MEG session the oblique grating orientation discrimination threshold has been measured in 13 ASD and 18 TD participants in a psychophysical experiment.

Table 1. Demographic information

	ASD mean (SD) (N = 21)	NT mean (SD) (N = 26)
AGE (years)	10.4 (2.2)	11.1 (1.7)
Sequential IQ	94.3 (15.4)	100.9 (21.2)
Simultaneous IQ	95.9 (16.2)	120.7 (13.2) *
Mental Processing Composite	93.9 (18.3)	117.6 (12.3) *
Child AQ	87.9 (10.6)	56.3 (15.07)*

Asterisks denote significant difference between ASD and NT group, * $p < .05$

Results

Gamma frequency increased with stimulus velocity in both TD and ASD participants. The relative increase of frequency of gamma oscillations (i.e. gamma dynamic range) was significantly lower in the ASD group ($p < .05$), suggesting worse adaptation of neuronal networks for processing of moving stimuli. Both IPF to the high velocity stimuli and the gamma dynamic range correlated posi-

tively with IQ, but did not correlate with the autism quotient. In the ASD, but not the TD children the wider gamma dynamic range predicted better capacity for discrimination of oblique grating orientation, thus suggesting link between effectiveness of neural inhibition and perceptual processes in ASD.

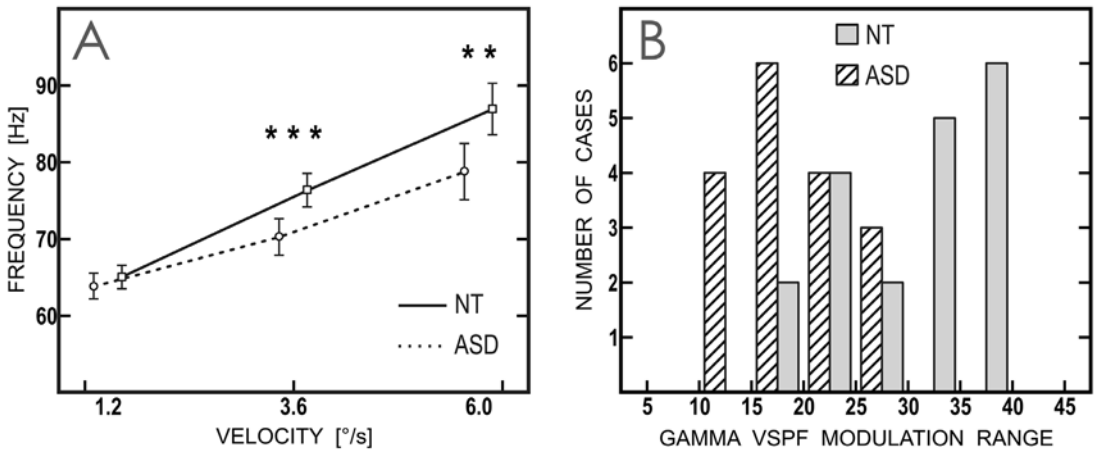

Figure 1. Differences between the NT and ASD group in velocity-related modulation of visual gamma response frequency.

A – ANOVA results for gamma VSPF. Solid line – NT; dashed line – ASD. Asterisks denote significant between-group difference: ** – $p < .005$; *** – $p < .001$. B – Frequency distribution of velocity-specific peak frequency (VSPF) modulation range (i.e. difference in VSPF for the fast and slow stimulus velocities) in NT (white bars) and ASD (striped bars) groups.

Conclusions

The narrow dynamic range of visual gamma oscillations in children with ASD suggest sluggish dynamics of inhibitory processes in visual cortex, which is particularly evident under high functional load. The future studies may help to reveal if similar abnormalities are present in the other sensory and associative cortical areas in people with ASD and other developmental disorders characterized by altered E/I balance.

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Модуляции частоты гамма-осцилляций, вызванных зрительным стимулом, как биомаркер расстройств аутистического спектра

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Аннотация. По данным нейропсихологических исследований, существует связь между аномалиями, присущими расстройствам аутистического спектра (РАС), и дисбалансом процессов возбуждения и торможения нейронных сетей коры головного мозга. В частности, выявлено влияние указанного дисбаланса на корковые осцилляции в верхнем диапазоне гамма-частот (50–120 Гц). Эта особенность может послужить важным биомаркером ряда типов РАС. Мы проанализировали гамма-осцилляции, возникающие при наблюдении за движущимися с переменной скоростью концентрическими зрительными стимулами, у типично развивающихся детей и детей с РАС. Результаты выявили дефицит корковых процессов обработки быстро движущихся стимулов у детей с РАС, который может указывать на недостаточность процессов торможения в корковых нейронных сетях, лежащих в основе зрительной обработки.

Ключевые слова: расстройства аутистического спектра, частота зрительных гамма осцилляций, зрительная обработка