The effect of 5-HTTLPR on EEG reactions among Yakuts and Russians during the recognition of emotionally colored verbal stimuli.

1st Tuyana Ayusheeva
Institute of Cytology and Genetics of SB RAS;
Novosibirsk State University
Novosibirsk, Russia
ayusheeva.ta@gmail.com

2nd Sergey Tamozhnikov
Institute of Physiology and Basic Medicine
Novosibirsk, Russia
s.tam@physiol.ru

3rd Alexandra Karpova
North-Eastern Federal University in Yakutsk
Yakutsk, Russia
karpova74@list.ru

4th Alexander Saprygin
Institute of Physiology and Basic Medicine
Novosibirsk, Russia
saprigyn@mail.ru

5th Natalia Borisova
North-Eastern Federal University in Yakutsk
Yakutsk, Russia
borinat@yandex.ru

6th Alexander Savostyanov
Institute of Cytology and Genetics of SB RAS;
Institute of Physiology and Basic Medicine;
Novosibirsk State University
Novosibirsk, Russia
Alexander.Savostyanov@gmail.com

***Abstract* — The effect of 5-HTTLPR on an emotional speech perception was studied by means of EEG analysis. Two ethnically different groups (Russians and Yakuts) were compared. No significant ethnic effects were found, but significant interaction of the factors "gender" and "genotype" has been revealed for the aggression containing sentences. 5-HTTLPR modulates the perception of aggression, but its effects are opposite for men and women.**

Keywords— 5-HTTLPR, emotion perception, EEG, gender differences.

I. Introduction

The serotonin transporter (5-HTT) is one of the most widely investigated genetic markers of individual variation in serotoninergic function. Its reuptake from a synaptic cleft [2] regulates the strength and duration of serotonin influence on post-synaptic receptors. Human's 5-HTT is coded by SLC6A4 gene, which is localized on the 17-th chromosome [4]. The promoter region of the serotonin transporter gene (5-HTTLPR) contains short (S) and long (L) alleles. The S allele of serotonin transporter gene (5-HTTLPR) has been found to increase the risk of depression and other mental health problems, but some evidence suggests that S-allele carriers outperform subjects with the long allele in an array of cognitive tasks [7].

According to some studies [5; 8; 9; 10], the effect of genetic polymorphism is strongly modulated by personal characteristics of participants, including their sex, age, nationality and social and culture features. The effect of 5-HTTLPR on recognition of emotionally colored Russian sentences in different ethnic (Yakuts and Russians) groups of healthy participants was studied in this research. The EEG reactions in theta and delta ranges were considered as the indicators of brain activity reflecting the involvement of the limbic system in the process of emotion perception.

II. Participants and Methods

A. Participants

125 healthy inhabitants of Novosibirsk, Russia (23,7 ± 3,4 years) and 80 healthy inhabitants of Yakutsk, Sakha (Yakutia) Republic, Russia (22,5± 5,1 years) participated in the experiment. All participants from Novosibirsk were native Russian speakers; the participants from Yakutsk were Russian-Yakut bilinguals.

All applicable subject protection guidelines and regulations were followed in the conduct of the research in accordance with the Declaration of Helsinki. All subjects signed a written informed consent and received a sum equivalent to about 5% of the monthly living wage for participation. The Institutional ethical committee has approved this study.

B. Experimental Procedure and Genotyping

Two hundred sentences in Russian language were selected for the experiment. Half of the sentences (100) contained syntax errors. The task was to find whether the sentence on the screen contains error or not. The experiment also contained a hidden condition: the sentences were grouped by emotional coloring, of which participants were not informed.

There were five groups of sentences:
1) the sentences describing the aggression of the participant;
2) the sentences describing the aggression of other people;
3) the sentences describing the anxiety of the participant;
4) the sentences describing the anxiety of other people;
5) the neutral sentences about inanimate objects.

Buccal cells were taken in each participant for the DNA analysis. The polymerase chain reaction (PCR) was performed with primers: 50-ggcgttgccgctctgaattgc-30 and 50-gagggactg agctggacaacccac-30. Polymorphism of 5-HTTLPR was identified using agarose-gel electrophoresis. The sizes of the S- and L-alleles for 5-HTTLPR were 489 bp and 529 bp, respectively. To determine the LA/LG polymorphism, the products of amplification were digested for 3 hours with MspI endonuclease. The sizes of the products of the digestion of the LA allele were 340, 127, and 62 bp, while those for the LG allele were 174, 166, 127, and 62 bp. The LG allele was included in S alleles group as being functionally similar to the S allele.

C. EEG recording and processing

EEG was recorded during the performance of the task. EEG recording was made with actiChamp amplifier (Brain Products GmbH (Germany)), with 0.1–100 Hz analog bandpass filtering and digitized at 1000 Hz. In Russian group the signal was amplified using 128 active channels; in Yakut group 64 active channels were used. The EEG electrodes were placed according to the extended International 10–10% system using Quik-Cap128 NSL or Quik-Cap64 NSL and

The study was supported by the Russian Science Foundation (RSF) under Grant № 17- 18-01019 and the Russian Foundation of Basic Research (RFBR) under Grant № 18-415-140021.

referred to Cz with ground at FzA. Electrodes impedance was maintained below 5 kΩ. Oculomotor artifacts were rejected using the ICA (independent component analysis) method [3]. Event-related spectral perturbations (ERSPs, [3]) were selected as the indicator of task-related changes in brain activity.

D. Statistical processing

ANOVA with the Greenhouse-Geisser correction was chosen for statistical processing of the data. The variables "task accuracy", "emotional condition", "sagittality" (frontal, medial and occipital), "laterality" (left, middle or right cortical areas) and also "group", "gender" and "genotype (5-HTTLPR)" were used during the statistical processing of ERSP.

III. Results and Discussion

Time-frequency intervals in the theta (4-8 Hz, 500-800 ms after sentence onset) and delta (1-4 Hz, 500-800 ms) ranges were selected as indexes of brain activity associated with the sentences recognition. The theta synchronization is associated with the level of emotional perception, whereas the delta synchronization is associated with the involvement of motivational structures of brain [1; 6; 11]. In this study, the highest amplitude of the theta and delta synchronization was shown for the sentences describing anxiety of other people and aggression of the participant; the lowest amplitude was during the recognition of sentences about inanimate objects (Fig. 1).

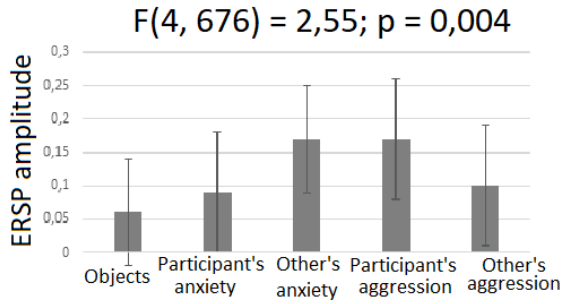

Fig. 1. The main effect of emotional condition in the theta range.

The main effect of ethnicity was statistically highly significant (Fig 2.) The Russian participants demonstrated the reaction of theta synchronization, whereas the Yakut participants demonstrated the reaction of theta desynchronization. This result can be interpreted as greater sensitivity of the Russian group to the emotional coloring of sentences. Perhaps this effect is caused by the better knowledge of Russian language of the Russian group of participants in comparison with the Yakuts.

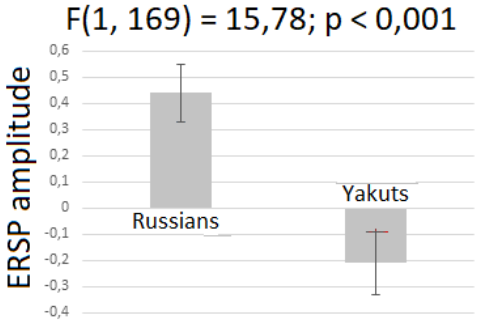

Fig. 2. The main effect of the ethnic group in the theta range.

The theta synchronization in the men with the both genotypes L/- and S/S was not much different (Fig 3). The most difference was during the recognition of the sentences describing participants' aggression (the amplitude of theta synchronization was higher in the men with the S/S genotype than the men with the L/- genotype).

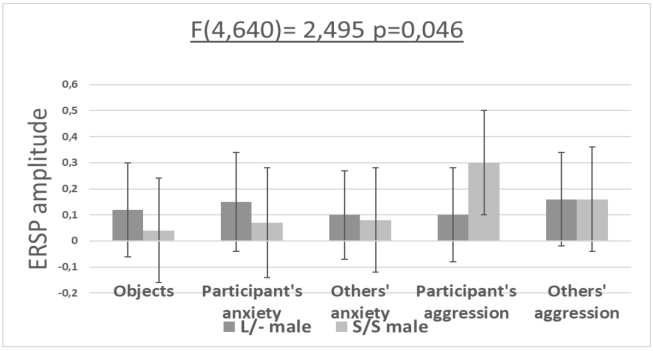

Fig. 3. The interaction of the factors "gender", "genotype (5-HTTLPR)" and "emotional condition" in the theta range (men).

A strong difference between the women with different 5-HTTLPR genotypes was detected. The theta synchronization during the recognition of the all five emotional stimuli was detected only in the women with genotype L/- . The women with S/S genotype demonstrated the theta desynchronization to 4 conditions ("objects", "participant's anxiety", "participant's aggression" and "others' aggression") and theta synchronization (with low altitude) only to the sentences with an anxiety of other people (Fig 4).

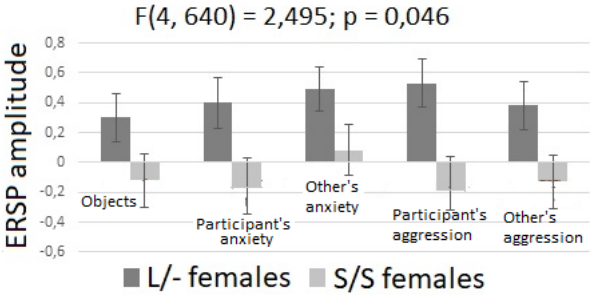

Fig. 4 The interaction of the factors "gender", "genotype (5-HTTLPR)" and "emotional condition" in the theta range (women).

The delta synchronization was also much different in the men and women with the genotypes L/- and S/S during the recognition of the sentences describing the participant's aggression (Fig. 5 and 6). The amplitude of delta synchronization was higher in the men with S/S than the men with L/- whereas the women demonstrated the opposite result (the reaction of delta synchronization in the women with L/- was higher than in the women with S/S).

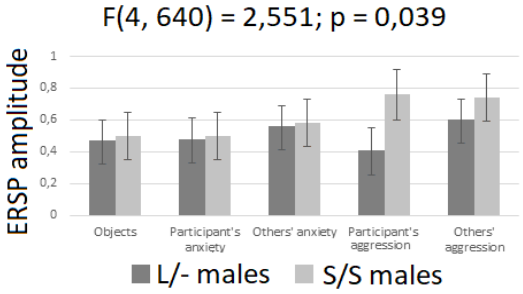

Fig. 5 The interaction of the factors "gender", "genotype (5-HTTLPR)" and "emotional condition" in the delta range (men).

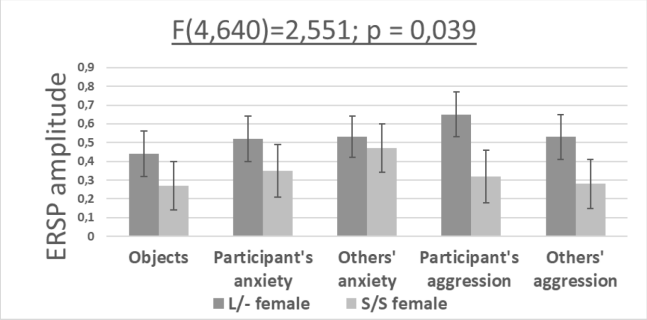

Fig. 6 The interaction of the factors "gender", "genotype (5-HTTLPR)" and "emotional condition" in the delta range (women).

The polymorphism of 5-HTTLPR in men and women has a different effect on the perception of speech emotionality, especially for self- and other-related sentences describing aggression. Russian and Yakut men with S/S genotype demonstrated the higher reaction during the perception of aggressive information than men with L/L and L/S genotypes; the amplitude in Russian and Yakut women with S/S genotype was lower during the recognition of aggressive sentences in comparison with women with other genotypes. The interactions of polymorphism of 5-HTTLPR, gender and ethnicity have not been found during the recognition of sentences describing personal and other's anxiety or non-emotional objects.

IV. Conclusion

The genetic polymorphism of 5-HTTLPR influences recognition of speech information with aggressive emotional coloring, however it is modulated by the gender of participants. The S/S genotype in men is associated with increase of the reaction on aggressive information, whereas women with S/S genotype demonstrated the decrease of the EEG reaction while recognizing the same category of the sentences.

Acknowledgment

The data collection and processing among the Russian participants was supported by the Russian Science Foundation (RSF) under Grant № 17- 18-01019. The data collection and processing among the Yakutian participants was supported by the Russian Foundation of Basic Research (RFBR) under Grant № 18-415-140021.

References

[1] L.I. Aftanas, V.I. Koshkarov, V.L. Pokrovskaja, N.V. Lotova, Y.N. Mordvintsev, "Event-related desynchronization (ERD) patterns to emotion-related feedback stimuli," Int J Neurosci., vol. 87(3-4), pp. 151-173, Nov. 1996.

[2] R.D. Blakely, L.J. Defelice & H.C. Hartzell, "Molecular physiology of norepinephrine and serotonin transporters," J Exp Biol., vol. 196, pp. 263-281, 1994.

[3] A. Delorme, S. Makeig, "EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis," J Neurosci Methods, vol. 134(1), pp. 9-21, Mar 2004.

[4] J. Gelernter, A.J. Pakstis & K.K. Kidd, "Linkage mapping of serotonin transporter protein gene slc6a4 on chromosome-17," Hum Genet., vol. 95, pp.677-680, 1995.

[5] G.G. Knyazev, A.N. Savostyanov, A.V. Bocharov, D.V. Bazovkina, E.A. Proshina, "Resting State Networks Mediate the Effect of Genotype by Environment Interaction on Mental Health," Neuroscience, vol. 369, pp. 139-151, Jan. 2018.

[6] G.G. Knyazev, A.V. Bocharov, E.A. Levin, A.N. Savostyanov, J.Y. Slobodskoj-Plusnin, "Anxiety and oscillatory responses to emotional facial expressions," Brain Res., vol. 1227, pp. 174-188, Aug. 2008.

[7] K.P. Lesch, D. Bengel, A. Heils, S.Z. Sabol, B.D. Greenberg, S. Petri, J. Benjamin, C.R. Muller, D.H. Hamer & D.L. Murphy, "Association of anxiety-related traits with a polymorphism in the serotonin transporter gene regulatory region," Science, vol. 274, pp.1527-1531, 1996.

[8] M. Nomura, M. Kaneko, Y. Okuma, J. Nomura, I. Kusumi, T. Koyama, Y. Nomura, "Involvement of serotonin transporter gene polymorphisms (5-HTT) in impulsive behavior in the japanese population," PLoS One, 2015 Mar 16;10(3):e0119743.

[9] E.A. Proshina, A.N. Savostyanov, A.V. Bocharov, G.G. Knyazev, "Effect of 5-HTTLPR on current source density, connectivity, and topological properties of resting state EEG networks," Brain Res., vol. 1697, pp. 67-75, Oct. 2018.

[10] N.V. Volf, L.V. Belousova, G.G. Knyazev & A.V. Kulikov, "Interactive effect of 5-HTTLPR genotype and age on sources of cortical rhythms in healthy women," International Journal of Psychophysiology, vol. 109, pp. 107-115, 2016.

[11] H.H. Yang, A.N. Savostyanov, A.C. Tsai, M. Liou, "Face recognition in Asperger syndrome: a study on EEG spectral power changes," Neurosci Lett., vol. 492(2), pp. 84-88, Apr. 2011.