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Original Research

The connection between rs6265 polymorphism in the *BDNF* gene and successful mastering of the video-oculographic interface

Yaroslav A. Turovsky[1,2], Artem P. Gureev[3,4,*], Inna Yu. Vitkalova[3,4], Vasily N. Popov[3,4], Alexey A. Vakhtin[5]

[1] *Laboratory of Medical Cybernetics, Voronezh State University, 394018 Voronezh, Russia*

[2] *V. A. Trapeznikov Institute of Control Sciences of Russian Academy of Sciences, 117997 Moscow, Russia*

[3] *Department of Genetics, Cytology and Bioengineering, Voronezh State University, 394018 Voronezh, Russia*

[4] *Laboratory of Metagenomics and Food Biotechnology, Voronezh State University of Engineering Technologies, 394036 Voronezh, Russia*

[5] *Department of Programming and Information Technologies, Voronezh State University, 394018 Voronezh, Russia*

*Correspondence: gureev@bio.vsu.ru (Artem P. Gureev)

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A video-oculographic interface is a system for controlling objects using eye movements. The video-oculographic interface differs from other brain-computer interfaces regarding its improved accuracy, simplicity, and ergonomics. Despite these advantages, all users are not equally successful in mastering these various devices. It has been suggested that the genetic characteristics of the operators may determine the efficiency of video-oculographic interface mastery. We recruited healthy users with rs6313, rs2030324, rs429358, rs10119, rs457062, rs4290270, and rs6265 polymorphisms and analyzed the relationships between these polymorphisms and values of success in video-oculographic interface mastery. We found that carriers of the G/G genotype of the rs6265 polymorphism (*BDNF* gene) demonstrated the best results in video-oculographic interface mastery. In contrast, carriers of the A/A genotype were characterized by large standard deviations in the average amplitude of eye movement and the range of eye movement negatively correlated with goal achievement. This can be explained through the fact that carriers of the A/A genotype demonstrate lower synaptic plasticity due to reduced expression of *BDNF* when compared to carriers of the G/G genotype. These results expand our understanding of the genetic predictors of successful video-oculographic interface management, which will help to optimize device management training for equipment operators and people with disabilities.

Keywords

Video-oculographic interface; Brain-derived neurotrophic factor; rs6265; Eye movement; Working memory

1. Introduction

Scientific and technological signs of progress in computer technology have made a wide range of digital control systems available to users. First, this applies to systems designed for mass use, which have a relatively low cost and do not require significant time for user training. These include input devices, such as keyboards, and non-keyboard input devices, such as mouses, joysticks, touchpads, touchscreens, and trackballs [1]. However, these devices are not always suitable for people with disabilities [2]. Therefore, researchers are actively developing a class of devices based on alternative finger activity mechanisms for generating user commands. An example of this is the so-called "alternative human-computer interfaces", in which the user generates commands through mechanisms such as electrical brain activity (brain-computer interface) [3], electrical muscle activity (myoelectric hand prostheses) [4], changes in the position and activity of body parts (accelerometric interface) [5], or movements of the eyes (video-oculographic interface) [6]. In this respect, video-oculographic interfaces (VOIs) are of the most significant interest due to their high accuracy, simplicity, and ergonomics. First, however, it is crucial to search for correlates associated with compelling performance by users of this class of devices.

Interest has increased in understanding the relationship between users' cognitive state and eye movement features during human-computer interfaces. However, a deeper understanding of this relationship is still required [7]. In addition, there is a significant gap in the genetic determinants of the success of human-computer interfaces operation. This is likely since conducting such research requires integrating specialists in neurophysiology, digital signal processing and molecular genetics. There is some research of relationships between brain-computer interfaces and "genetics", but under the "genetics" term are presented various variants of mathematical algorithms for signal processing [8].

Our preliminary results have demonstrated connections between the number of single nucleotide polymorphisms (SNPs) and values of systemic behavior during device operation (accuracy of achieving goals, characteristics of subjective time scales) [9, 10], as well as characteristics of biomedical signals, such heart rate variability [11]. Previous studies have shown that SNPs in a gene encoding a protein involved in serotonin metabolism are associated with the

mastery of the electromyographic interface [9]. Of particular interest are polymorphism in the brain-derived neurotrophic factor (*BDNF*) gene (such as rs6265 and rs2030324), which is responsible for the regulation of the maturation and differentiation of neurons and forming of working memory [12] and long-term potentiation [13]. In addition, 5-hydroxytryptamine receptor 2A (*HTR2A*) (rs6313 polymorphism) and tryptophan hydroxylase 2 (*TPH2*) (rs4570625 and rs4290270 polymorphisms) genes are involved in the serotonin synthesis and metabolism, which play a critical role in human cognitive performance [14]. The 20 Kb region containing both the translocase of mitochondrial membrane 40 (*TOMM40*) and apolipoprotein E (*APOE*) genes unique thus far in complex human diseases (including cognition impairment such as Alzheimer's disease), which is statistical support [15]. rs10119 and rs429358 polymorphisms were studied from this region. This research focuses on different genetic factors that affect the brain -interfaces technology, in so far as assessing correlations between VOI mastery and SNPs in a gene involved in regulation of serotonin metabolism and cognitive characteristics in humans.

2. Material and methods

2.1 Experimental participants

40 volunteers took part in the experiment, comprising 22 males and 18 females aged between 19 and 23 years; the median age was 20. The volunteers all had no neurological or psychiatric pathologies, did not take drugs affecting their movement coordination or decision times, and had normal or corrected normal vision. Ethics Committee approved the current research of Voronezh State University. All experimental participants gave informed consent for an EEG in accordance with the Helsinki Declaration. Informed written consent for enrollment in the research was obtained from all the participants, who were informed of any subsequent genetic testing conducted using their biological material. The experimental design was presented in Fig. 1.

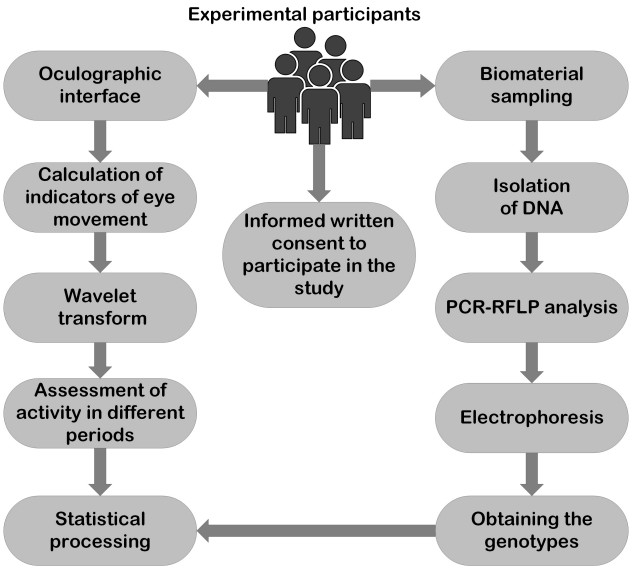

Fig. 1. Experimental design.

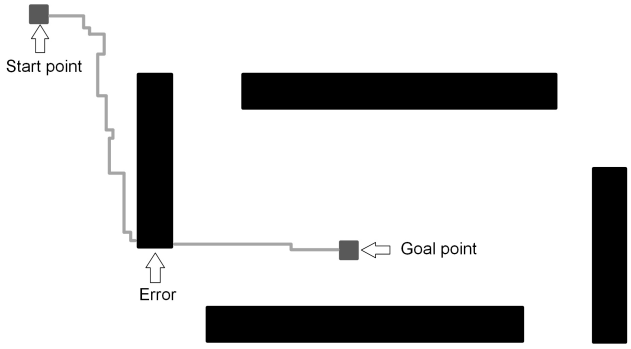

Fig. 2. Example of the virtual marker movement in 2D space during task performance in the VOI. Space included start and goal point and four obstacles (black box). The user's task is to move the virtual marker via eye movements from the start to the goal point bypassing obstacles. The alignment of a marker with an obstacle was regarded as an "error".

2.2 Video-oculographic interface

Software previously developed by the authors [16] was used in these experiments. The software simulates controlling the movement of a virtual marker in 2D space and, thereby, provides training and testing of a user's VOI mastery. The software integrates the hardware of the VOI with a computer, thus allowing the experimenter to set the parameters for video recording of the movement of the virtual marker, calibrate the user's eye movements, and record the user passing through a series of tasks formed by the experimenter. Via eye movements, the user moves the virtual marker across the field from one area to another while bypassing obstacles, the position of which can be changed by the experimenter. Eye position coordinates, marker coordinates, and collisions with obstacles were recorded (Fig. 2).

Users were positioned in front of the monitor screen (22 inches) at a distance they found comfortable. With the VOI, it was possible to obtain a sharper image using a standard video camera with an extracted infrared filter. In addition, a holder was made for the infrared camera that was attached to the head and provided the ability to change camera position. This made it possible to adjust the image coming from the camera, regardless of the head's shape, in order to meet user convenience requirements [6].

After calibration, an experimental field was launched on the monitor screen, including the launch area, rectangular boundaries of several objects, and the target area. The instructions presented to each user were explained to attempt to avoid combining the marker with the obstacles (objects indicated as black rectangles) on the screen. The alignment of a marker with an obstacle was regarded as an "error", which was automatically recorded by the program. The program recorded and recognized movement of the pupil in four directions: "up", "down", "left", and "right". A new command could be generated by the user no more than once per second.

Before each experiment, the necessary device calibration was performed. Each user was given four trials to complete the experiment, each lasting two minutes. The time between trials was from three to five minutes. The first trial was training and not taken into account in statistical analysis. Second, third and fourth trials were measured. The total number of measurements was 120 (three trials for 40 participants).

2.3 Assessment of eye movement parameters

The Haar wavelet discrete transform algorithm was used to assess the parameters of eye movement [17]. First, the entire time series's mean values and standard deviations of the entire time series were calculated for the obtained values and each level of the wavelet transform (Fig. 3). Analysis of the mean values of the coefficients of wavelet transforms—shows the average level of representation in the signal of this wavelet, and standard deviation shows the level of spread of the signal variability. This is important since the eye movement is not constant but salutatory. Therefore, the obtained values are interpreted as the average distance traveled by the users during the experiment. In contrast, the change in distance corresponds to the wavelet transform scale (or level). Accordingly, the standard deviation of the time series data after the wavelet transformation is the average values of the pupil displacements from the average displacement amplitude for the entire time of the test. The obtained values were called approximating sequences (*a*-sequences) and detailing sequences (*b*-sequences) in accordance with the approaches adopted in wavelet analysis. In this case, the wavelet transformation was carried out directly on the data, where the sampling frequency was artificially reduced to 5 Hz. Therefore, the wavelet transform scales had the following periods: 0.4 s, 0.8 s, 1.6 s, 3.2 s, 6.4 s, 12.8 s, which corresponded a1, a2, a3, a4, a5, a6 sequences and b1, b2, b3, b4, b5, b6 sequences.

2.4 Tests for establishing psychological characteristics

The psychological characteristics of the subjects were established using the standard Eysenck test [18], Spielberger test [19], and working memory test. Both Eysenck and Spielberger tests are adapted Russian-language sets of questions, answering which the subjects on specific scales form indicators. The situational and personal anxiety (for the Spielberger test) and indicators of neuroticism and extraversion (for the Eysenck test) are determined. The working memory test is implemented as follows: a 5 $\times$ 5 square matrix was set and, in each trial, a selection of three squares was generated, the sequence of which had to be memorized and correctly determined by the user at the end of each trial; the number of trails was ten.

2.5 DNA extraction

Extraction of total DNA from the buccal mucosa was performed using a genome DNA extraction kit (Dia-M, Russia). The quality and purity of DNA were estimated via gel-electrophoresis using a 2% agarose gel in a TAE buffer.

2.6 PCR-RFLP analysis

Genotyping was performed via polymerase chain reaction and restriction fragment length polymorphism (PCR-RFLP) analysis according to previously described methods [9]. PCR was performed using a Bio-Rad CFX96^{TM} system (Bio-Rad, USA) with HS SYBR qPCR mix (Evrogen, Russia). Initial denaturation was carried out at 95 °C for 3 min, which was followed by 35 cycles of denaturation at 95 °C for 30 s; annealing of primers at 59–71 °C for 30 s, elongation at 72 °C for 30 s. The PCR product was treated by restriction endonucleases (SibEnzyme, Russia) at 37 °C for 2 h, after which deactivation of restriction endonucleases was performed at 65 °C for 20 min. The PCR product was then visualized via gel-electrophoresis using a 2% agarose gel in TAE buffer. The primers sequences, conditions of PCR, and the RFLP analysis are presented in Table 1.

2.7 Statistical analysis

Statistica 10 software (StatSoft, USA) was used for data analysis. The data were represented as the mean $\pm$ standard error mean and Q1; median; Q3. Statistical analysis methods used for descriptive statistics included the Kruskal-Wallace test, Mann-Whitney test, and Friedman tests for paired cases, while the parameter α was taken equal to 5%. To analyze categorical variables, Fisher's exact test and χ^2 test were used. A nonparametric method was used to analyze the relationship between facts—the Spearman's rank correlation coefficient. The effect of multiple comparisons was taken into account. A multivariate analysis of correspondences was used as an experimental method based on the frequencies of specific observations [20].

3. Results

3.1 Relationship between rs6265 polymorphism and VOI performance

Carriers of the A/A genotype were characterized by a significant standard deviation from the mean in the amplitude of eye movement compared to the G/G genotype during performance of tasks using the VOI, which is best seen on *b*-sequences (Table 2). At the same time, the mean amplitude of eye movement was also higher (mean values of *a*-sequences) (Table 3).

The relationship between the rs6265 polymorphism and goal achievement rates was investigated. It was established (df = 2, p = 0.0017, χ^2 criterion = 12.7225) that inferior results (14 experiments with goal achievement, 33 experiments with failure to achieve the goal) were associated with the A/A genotype. The G/G genotype was associated with superior results (15 and 5 experiments for goal achievement and failure, respectively). However, no connection between genotype and the number of errors was found. It is noteworthy that, when the data were divided into two groups (genotypes A/A and A/G versus genotype G/G), there were no differences in the frequency–temporal characteristics of eye movement ($p > 0.05$), however, users in the first group showed significantly higher values of sincerity ($p < 0.05$, H (1, N =

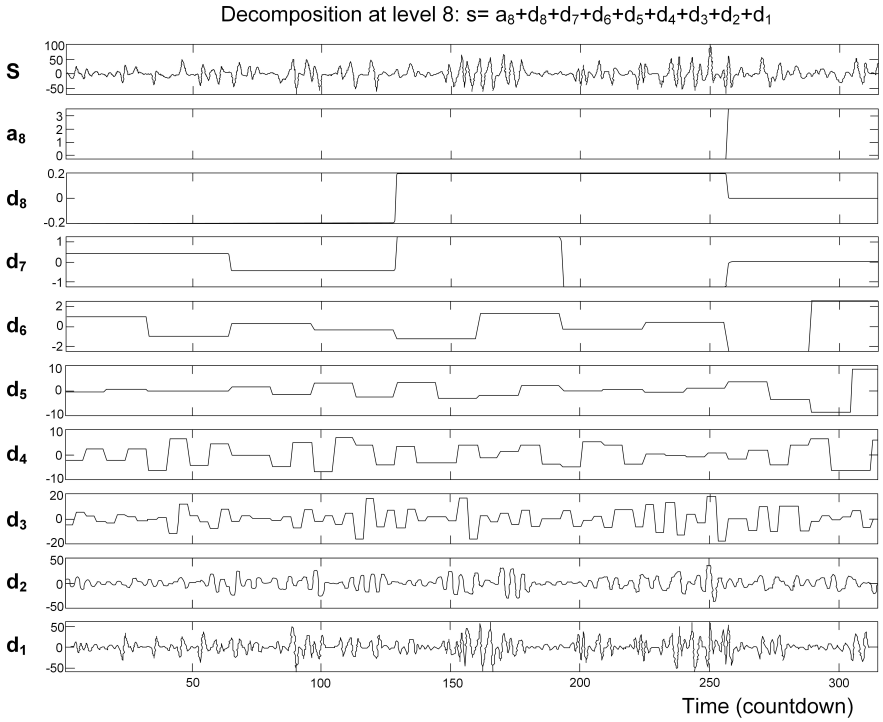

Fig. 3. Example of Haar wavelet. s, initial signal; a, scaling function; d, detailed oscillations for each of the frequencies.

149) = 4.542031) (Fig. 4A) and extraversion ($p < 0.005$, Median Test, Chi-Square = 6.750773 df = 1 $p = 0.0094$) (Fig. 4B).

When the data were divided into two groups according to another principle (genotype A/A versus genotypes A/G and G/G), differences in eye movement parameters were observed. Differences were significant primarily for increases in the range of eye movement of *a*–sequences at all studied periods ($p < 0.001$ for 0.4 s, 0.8 s, 1.6 s, 3.2 s, 6.4 s, 12.8 s) in the first group. For *b*–sequences, which reflect detailed eye movement features, the range of eye movement was significantly higher in the A/A group for all studied periods, as shown in Fig. 5. The A/G and G/G group achieved the goal significantly more often (H (1, N = 149) = 11.39475 $p = 0.0007$). Additionally, this group showed inferior results on working memory tests (H (1, N = 149) = 9.265089 $p = 0.0023$) and lower values of personal anxiety (H (1, N = 149) =8.587107 $p = 0.0034$).

3.2 Relationship between rs2030324 polymorphism and VOI performance

Regarding rs2030324, no differences were found when the SNP was divided into three groups (C/C, T/T, and C/T). However, the sincerity values were significantly higher when the combined genotypes C/C and C/T were compared to the T/T genotype (H (1, N = 149) = 9.185538 $p = 0.0024$) (**Supplementary Tables 1 and 2**). Extraversion and neuroticism were higher for the T/T genotype (H (1, N = 149) = 9.550368 $p = 0.0020$ and H (1, N = 149) = 5.586052 $p = 0.0181$, respectively) on the Eysenck test. A smaller number of goal achievements in the experiment (Median test Chi-Square = 7.143649 df = 1 $p = 0.0075$) corresponded to higher values of extraversion. However, no dependence was found for rs2030324. Comparing the C/T and T/T genotypes to the C/C genotype did not reveal any significant differences.

3.3 Relationships between other polymorphisms and VOI performance

The rs4570625 polymorphism and eye movement relationship were observed for the 0.4 s, 1.6 s, and 3.2 s periods. The differences between T/G and G/G genotypes were expressed in the change in the standard deviation values ($p < 0.01$, $p < 0.01$, $p < 0.05$, respectively), but not the mean value. There were no differences for more extended periods (Tables 4 and 5). There were no associations with achievement or non-achievement of the goal in the experiment.

rs4290270 did not demonstrate a direct relationship with eye movement during VOI performance. However, this SNP positively and negatively influenced various psychological parameters associated with mastering the interfaces (Fig. 6).

The rs429358 SNP showed a connection exclusively with short-periods (0.4–0.8 s) of eye movements. Dividing the data into two groups for this SNP (C/C genotype versus C/T and T/T genotypes) primarily demonstrated differences in the range of eye movement during VOI performance ($p < 0.001$) (Fig. 7).

No associations between the rs6313 polymorphism and eye movement parameters were observed during VOI performance. However, the T/T genotype of this SNP was more likely (Chi-square: 6.01494, df = 1, $p = 0.014187$) not to achieve the experimental task when compared to the combined C/C and C/T genotype group.

Table 1. Condition of restriction fragment length polymorphism analysis.

#	Mutation	Gene	Primers 5′-3′	Annealing t °C	Restriction endonuclease	Product size
			F: AAACATCCGAGGACAAGGTG		HpySE526 I	G/G–207
1	rs6265	*BDNF*	R: CGTGTACAAGTCTGCGTCCTT	59 °C	A↑CGT	A/A–124; 78
					TGC↓A	A/G–78, 207; 124
			F: TCACTCCAAACATCACACAGC		HpySE526 I	T/T–188
2	rs2030324	*BDNF*	R: TGGGCATAAGTTAGAGCTGACA	59 °C	A↑CGT	C/C–134; 54
					TGC↓A	C/T–188; 134; 54
			F: TGAGCTCAACTACGAACTCCCTA		Msp I	T/T–172
3	rs6313	*HTR2A*	R: AGAGACACGACGGTGAGAGG	59 °C	C↑CGG	C/C–99; 72
					GGC↓C	C/T–172; 99; 72
			F: CAGTGGGCCTGGGGTCACGGGAG		Msp I	A/A–155
4	rs10119	*TOMM40*	R: GGAAGCTCCTCTCGCTGCCC	65 °C	C↑CGG	G/G–134; 32
					GGC↓C	A/G–166; 134; 32
			F: CGCCTCGCCTCCCACCTGAGCAAG		HspA I	T/T–72
5	rs429358	*TOMM40*	R: CGCTCGTCGCCCTCGCGGG	71 °C	G↑CGC	C/C–45; 27
					CGC↓G	T/C–72; 45; 27
			F: GGCTAAATTGAACCCTTACCTTT		Psi I	G/G–301
6	rs4570625	*TPH2*	R: GGTAATCAAGATATCCATTGCC	59 °C	TTA↑TAA	T/T–89; 212
					AAT↓ATT	G/T–89; 212; 301
			F: TTTTGTTTTGGGTGCCATTT		FauND I*	T/T–209
7	rs4290270	*TPH2*	R: TGCATGGGAAGGGTATTTTC	59 °C	CA↑TATG	A/A–134; 76
					GTAT↓AC	T/A–209; 134; 76

* 10 mg/mL BSA additionally used.

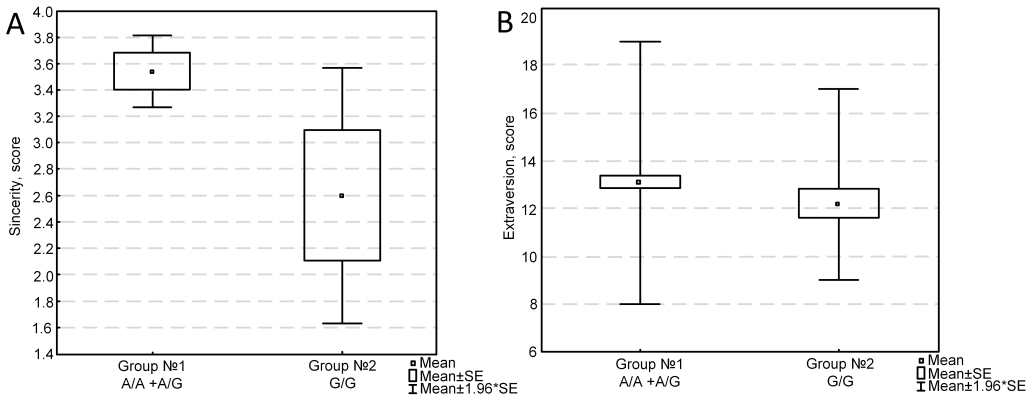

Fig. 4. Psychological tests for the different groups of rs6265 genotypes (genotypes A/A and A/G versus genotype G/G). (A) Values of sincerity according to Eysenck test. Kruskal-Wallace test, $p < 0.05$. (B) Extraversion values on the Eysenck scale. Kruskal-Wallace test, $p < 0.005$.

3.4 Multivariate analysis of correspondences

Large numbers of differences in various values, including those indirectly affecting mastering the VOI, require multivariate statistical approaches. Therefore, as an exploratory method, we used a multivariate analysis of correspondences, which, based on the frequencies of occurrence of specific observations, finds their coordinates in the space of given dimension, in our case amounting to 13 axes (the total number of SNPs and the result of achieving the goal: "achieved" or "not achieved") (Fig. 8).

It is noteworthy that the "achieved" group mainly includes heterozygotes, which are known to have a high adaptive potential due to possessing both allele variants. An exception to this is the rs10119 polymorphism. In contrast, the "not achieved" group generally includes homozygotes, which have a lower adaptive potential than heterozygotes. Again, the rs10119 polymorphism was the exception (Fig. 8).

4. Discussion

rs6265 is the most thoroughly studied SNP in the brain–derived neurotrophic factor (*BDNF*) gene, released in response to synapse activation and plays a crucial role in maintaining synaptic plasticity [21]. The nucleotide substitution from G to A causes a valine (Val) to methionine (Met) substitution at codon 66 [22]. Carriers of the Met allele have decreased *BDNF* secretion activity compared to homozygous carriers of the Val allele, which some researchers associate with the low synaptic plasticity of carriers of the Met allele [21].

Table 2. Values of b-sequences for different scales of discrete wavelet transform (Mean ± S.E.M; Q25; Me; Q75).

Rs6265	A/A	A/G	G/G
	47	82	20
Mean b1 $p = 0.0354$	–0.01 ± 0.10; –0.35; 0.09; 0.40	–0.17 ± 0.06; –0.51; –0.18; 0.15	–0.35 ± 0.16; –0.76; –0.24; 0.03
SD b1 $p = 0.0022$	14.35 ± 0.51; 11.54; 14.32; 16.44	12.16 ± 0.39; 9.88; 11.46; 13.99	13.13 ± 1.08; 8.94; 12.34; 16.81
Mean b2	0.15 ± 0.13; –0.48; 0.17; 0.67	–0.03 ± 0.08; –0.43; –0.06; 0.49	–0.16 ± 0.18; –0.67; –0.15; 0.15
SD b2 $p = 0.0018$	12.46 ± 0.48; 10.33; 12.04; 14.97	10.34 ± 0.39; 7.96; 9.61; 12.31	11.02 ± 0.90; 8.06; 10.04; 13.87
Mean b3	0.12 ± 0.16; –0.47; 0.25; 0.83	–0.18 ± 0.12; –0.71; –0.20; 0.37	0.32 ± 0.22; –0.35; –0.05; 0.69
SD b3 $p = 0.0047$	9.99 ± 0.44; 7.63; 9.55; 12.15	8.21 ± 0.31; 6.35; 7.79; 9.94	9.02 ± 0.80; 6.02; 9.95; 11.73
Mean b4	0.01 ± 0.21; –0.77; –0.34; 1.06	0.00 ± 0.14; –0.47; 0.02; 0.61	–0.02 ± 0.22; –0.44; 0.05; 0.32
SD b4 $p = 0.0000$	7.95 ± 0.25; 6.71; 7.89; 9.28	6.36 ± 0.23; 4.85; 6.26; 7.56	6.82 ± 0.66; 4.42; 6.98; 8.99
Mean b5	0.14 ± 0.21; –0.77; 0.22; 1.15	–0.20 ± 0.11; –0.74; –0.12; 0.53	–0.33 ± 0.27; –1.31; –0.20; 0.27
SD b5 $p = 0.0003$	6.12 ± 0.26; 5.03; 5.85; 7.20	4.97 ± 0.21; 3.69; 4.52; 5.79	4.96 ± 0.50; 3.50; 4.74; 6.66
Mean b6	–0.18 ± 0.24; –1.38; –0.10; 1.22	0.17 ± 0.15; –0.56; 0.04; 0.87	0.24 ± 0.34; –0.77; –0.12; 1.39
SD b6 $p = 0.0013$	4.55 ± 0.23; 3.56; 4.23; 5.23	3.63 ± 0.18; 2.44; 3.38; 4.35	4.03 ± 0.44; 2.45; 3.26; 5.29

p-value is indicated only for cases $p < 0.05$.

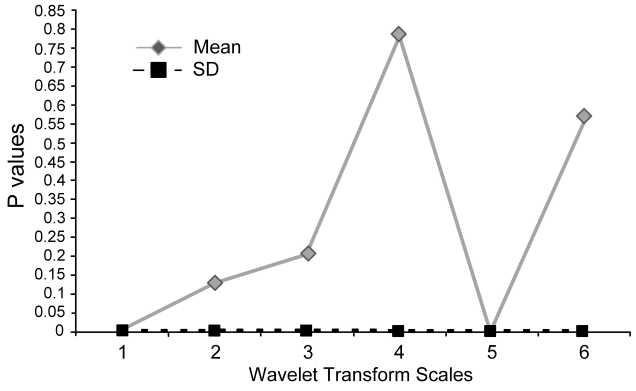

Fig. 5. *p* values for *b*–sequences via comparison group 1 (genotype A/A) versus group 2 (genotypes A/G and G/G). Greyline—*p*- value of differences between the mean of a wavelet transform coefficient. Blackline—*p*-value of differences between the standard deviation of a wavelet transform coefficient.

We have shown that the A/A genotype is associated with a significant standard deviation from the mean in eye movement amplitude. The effects of rs6265 polymorphisms on eye movement patterns have not previously been studied. However, the effects of *BDNF* on global functional connectivity density in the left frontal eye field have been shown [23].

Previous studies using functional magnetic resonance imaging have shown that the A/A genotype of the *BDNF* gene is associated with impaired brain motor function, altered short-term plasticity, and more significant errors in short-term motor learning [24]. In addition, the G/A and A/A genotypes of the rs6265 polymorphism increase the risk of posttraumatic stress disorder [25].

We observed that the T/T genotype of rs6313 did not perform the experimental task significantly more often ($p < 0.05$) than the C/T and C/C genotypes. Earlier results from our group have shown that, on the contrary, carriers of the T allele gave more correct commands. However, these studies involved an electromyographic interface, not VOI [9]. The C allele of the rs6313 polymorphism increases the efficiency of protein translation and concentration of the 5–HT2A receptor, which plays a crucial role in serotonin metabolism [26, 27]. In addition, there is evidence that carriers of the C allele are characterized by increased impulsivity [28, 29]. C allele negatively affects development on the electromyographic interface. However, it helps when performing tasks on the VOI, obviously relating to the different control channels for skeletal muscles and extraocular muscles.

Multivariate analysis of correspondences showed that the "achieved" group mainly includes heterozygotes, which are known to have a high adaptive potential due to possessing both allele variants [30] (Fig. 8). An exception to this is the rs10119 polymorphism, in which the G/G genotype is associated with tremendous success in mastering the VOI. In con-

Table 3. Values of a–sequences for different scales of discrete wavelet transform (Mean ± S.E.M; Q25; Me; Q75).

Rs6265	A/A	A/G	G/G
	47	82	20
Mean a1 $p = 0.0220$	11.02 ± 0.79; 7.48; 9.82; 12.83	8.77 ± 0.36; 6.52; 8.31; 9.75	9.40 ± 1.16; 5.62; 7.12; 11.77
SD a1 $p = 0.0002$	20.62 ± 0.66; 16.94; 19.84; 23.25	16.95 ± 0.57; 13.43; 15.97; 19.63	18.11 ± 1.40; 12.62; 18.62; 22.65
Mean a2 $p = 0.0210$	10.97 ± 0.80; 7.48; 9.82; 12.66	8.69 ± 0.36; 6.50; 8.32; 9.61	9.34 ± 1.17; 5.42; 7.12; 11.77
SD a2 $p = 0.0001$	16.21 ± 0.53; 13.41; 15.28; 19.27	13.12 ± 0.46; 10.30; 12.52; 15.23	14.08 ± 1.13; 9.25; 14.65; 17.96
Mean a3 $p = 0.0253$	10.92 ± 0.80; 7.42; 9.85; 12.66	8.64 ± 0.35; 6.50; 8.29; 9.46	9.29 ± 1.17; 5.22; 7.13; 11.77
SD a3 $p = 0.0001$	12.54 ± 0.40; 10.64; 12.42; 14.03	10.12 ± 0.37; 7.61; 9.65; 11.74	10.49 ± 0.92; 6.96; 10.40; 13.55
Mean a4 $p = 0.0227$	10.85 ± 0.80; 7.42; 9.89; 12.66	8.60 ± 0.36; 6.50; 8.10; 9.48	9.23 ± 1.19; 5.13; 7.12; 11.77
SD a4 $p = 0.0004$	9.54 ± 0.38; 7.72; 9.26; 11.16	7.77 ± 0.30; 5.80; 7.41; 9.01	7.88 ± 0.70; 5.16; 7.13; 10.37
Mean a5 $p = 0.0193$	10.81 ± 0.81; 7.52; 9.83; 12.79	8.52 ± 0.35; 6.33; 7.99; 9.48	9.16 ± 1.18; 5.13; 6.85; 11.60
SD a5 $p = 0.0023$	7.21 ± 0.34; 5.60; 6.46; 8.71	5.88 ± 0.26; 4.20; 5.45; 6.87	6.04 ± 0.55; 4.36; 5.25; 8.01
Mean a6 $p = 0.0307$	10.74 ± 0.80; 7.52; 9.46; 12.79	8.52 ± 0.36; 6.33; 8.04; 9.42	9.18 ± 1.21; 5.13; 6.76; 11.60
SD a6	5.44 ± 0.33; 3.81; 5.15; 7.39	4.63 ± 0.23; 3.24; 4.20; 5.60	4.45 ± 0.36; 3.24; 3.92; 5.47

p value is indicated only for cases $p < 0.05$.

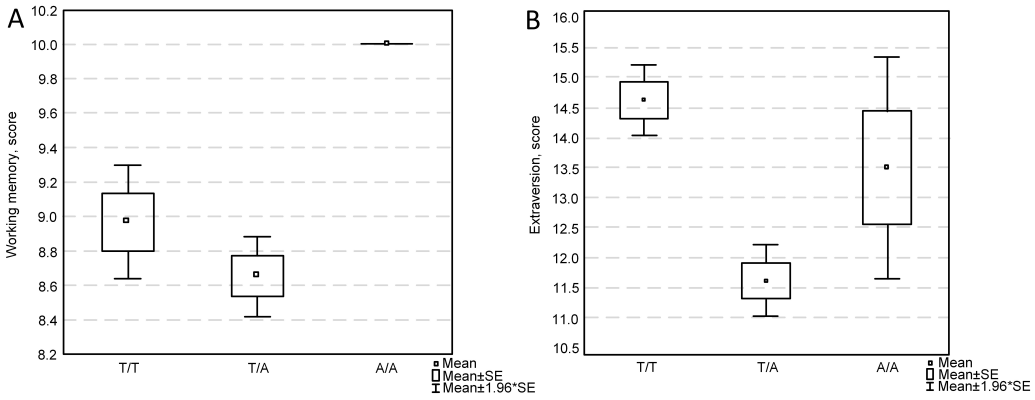

Fig. 6. Results of psychological tests in the different groups of rs4290270 genotypes. (A) Values of working memory. Kruskal-Wallace test, $p < 0.001$. (B) Extraversion values on the Eysenck scale. Kruskal-Wallace test, $p < 0.001$.

trast, the A/A genotype is at risk of developing Alzheimer's disease [31]. In contrast, the "not achieved" group generally includes homozygotes, which have a lower adaptive potential than heterozygotes (Fig. 8). Again, the rs10119 polymorphism was the exception. However, it should note that this mutation is located in the 3'–untranslated (UTR) region of the gene and affects the efficiency, gene transcription, transcript stability and splicing of the *TOMM40* gene [31]. The *TOMM40* gene encodes the TOMM40 protein, whose dimers create pores in the outer mitochondrial membrane through which almost all nuclear–encoded proteins enter the mitochondria. Thus, *TOMM40* is essential for the biogenesis and functioning of mitochondria, and its impairment is fraught with the development of neurodegenerative diseases [15, 32].

The age of the participants is one of the limitations. The success of VOI mastering is probably because the experiment involved participants aged between 19 to 23 years. However, people with disabilities of different ages. Such studies in older people could broaden our understanding of the genetic determinants of VOI success.

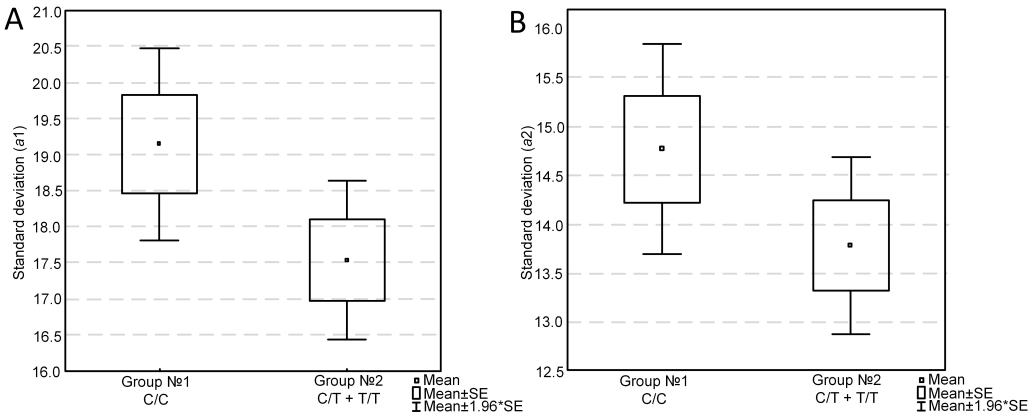

Fig. 7. Differences in the range of eye movement during VOI performance in the different groups for the s429358 genotypes. C/C genotype versus C/T and T/T genotypes. (A) The standard deviation of *a*–sequences for 0.4 s period. Kruskal-Wallace test, $p < 0.01$. (B) Standard deviation.

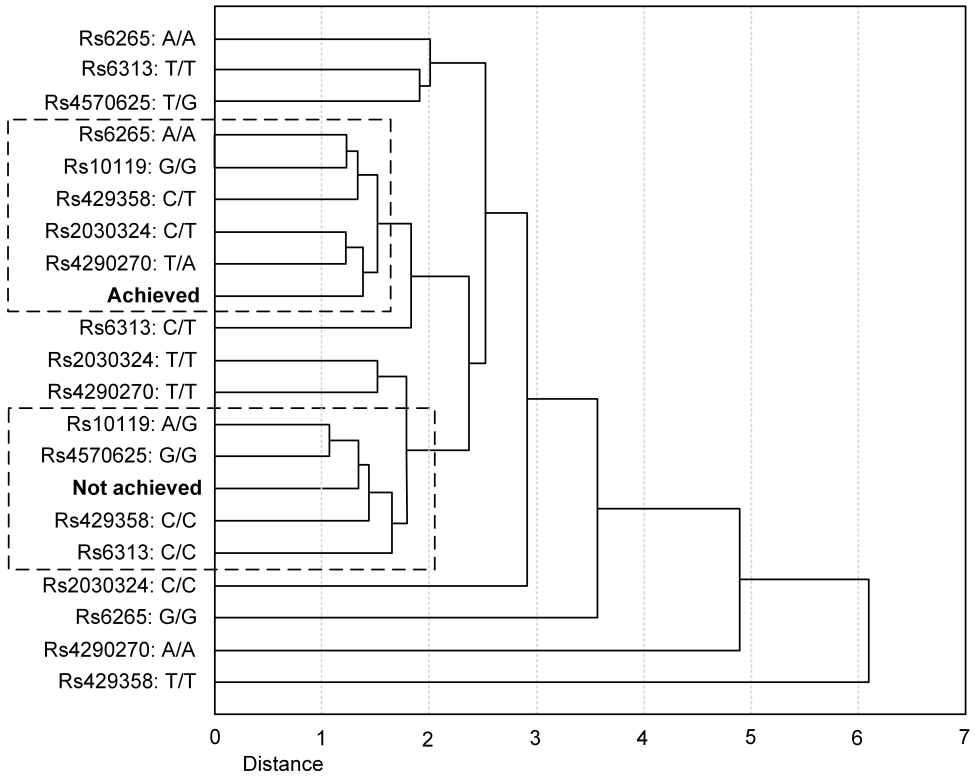

Fig. 8. A multivariate analysis of correspondences based on the frequencies of occurrence of specific observations finds their coordinates in the space of given dimension, in our case amounting to 13 axes (the total number of SNPs and the result of achieving the goal: "achieved" or "not achieved").

5. Conclusions

Thus, we have shown that the success in the VOI is, at least in part, determined by the users' genotype. An essential gene is the *BDNF* gene and the rs6265 polymorphism among the analyzed genes. The product of this gene is significant for working memory and long-term potentiation [33]. The results obtained confirm the assumption that working memory is crucial for developing success in the VOI. These processes are genetically determined to help ensure the optimization of device management training for equipment operators and people with disabilities.

Abbreviations

APOE, apolipoprotein E; *BDNF*, brain-derived neurotrophic factor; DNA, deoxyribonucleic acid; EEG, electroencephalography; HTR2A, 5-hydroxytryptamine receptor 2A; PCR, polymerase chain reaction; PCR-RFLP, polymerase chain reaction-restriction fragment length polymorphism; RFLP analysis, restriction fragment length polymorphism analysis; TAE buffer, Tris-acetate-EDTA buffer;

Table 4. Values of *a*-sequences for different scales of discrete wavelet transform (Mean ± S.E.M; Q25; Me; Q75).

Rs4570625	T/G	G/G
	52	97
Mean *a*1	11.13 ± 0.87; 6.41; 9.03; 15.90	8.72 ± 0.27; 6.76; 8.44; 10.21
SD *a*1 $p = 0.0081$	19.70 ± 0.68; 16.28; 19.21; 22.64	17.49 ± 0.55; 13.43; 16.88; 20.56
Mean *a*2	11.06 ± 0.88; 6.29; 8.88; 15.91	8.66 ± 0.27; 6.71; 8.39; 10.21
SD *a*2 $p = 0.0036$	15.47 ± 0.57; 12.82; 15.16; 17.86	13.55 ± 0.44; 10.35; 12.84; 15.86
Mean *a*3	10.99 ± 0.88; 6.28; 8.50; 15.91	8.62 ± 0.27; 6.74; 8.41; 10.25
SD *a*3 $p = 0.0395$	11.68 ± 0.46; 9.32; 11.55; 13.28	10.53 ± 0.35; 7.53; 10.49; 12.49
Mean *a*4	10.93 ± 0.87; 6.22; 8.22; 15.91	8.57 ± 0.27; 6.68; 8.41; 10.22
SD *a*4	8.79 ± 0.36; 6.74; 8.83; 10.29	8.10 ± 0.30; 5.96; 7.76; 9.39
Mean *a*5	10.88 ± 0.88; 6.18; 8.22; 15.91	8.49 ± 0.27; 6.67; 8.27; 9.95
SD *a*5	6.75 ± 0.34; 4.81; 6.22; 8.21	6.09 ± 0.24; 4.50; 5.84; 7.10
Mean *a*6	10.91 ± 0.87; 6.10; 8.22; 15.85	8.45 ± 0.27; 6.68; 8.22; 9.98
SD *a*6	5.06 ± 0.30; 3.40; 4.41; 6.21	4.76 ± 0.21; 3.35; 4.50; 5.60

p value is indicated only for cases $p < 0.05$.

Table 5. Values of *b*-sequences for different scales of discrete wavelet transform (Mean ± S.E.M; Q25; Me; Q75).

Rs4570625	T/G	G/G
	52	97
Mean *b*1	−0.26 ± 0.11; −0.84; −0.22; 0.24	−0.08 ± 0.05; −0.41; −0.01; 0.19
SD *b*1 $p = 0.0188$	14.16 ± 0.60; 10.80; 13.28; 17.62	12.35 ± 0.34; 10.07; 12.19; 14.73
Mean *b*2	−0.00 ± 0.12; −0.56; 0.00; 0.55	0.02 ± 0.08; −0.42; −0.04; 0.49
SD *b*2	11.80 ± 0.47; 9.55; 11.07; 13.87	10.72 ± 0.37; 7.94; 10.33; 12.85
Mean *b*3	0.04 ± 0.18; −0.75; −0.06; 0.79	−0.05 ± 0.10; −0.59; −0.02; 0.46
SD *b*3 $p = 0.0005$	9.94 ± 0.40; 8.32; 9.97; 11.26	8.31 ± 0.30; 6.20; 7.71; 9.85
Mean *b*4	−0.05 ± 0.23; −0.84; −0.14; 0.98	0.04 ± 0.11; −0.50; −0.08; 0.52
SD *b*4 $p = 0.0207$	7.57 ± 0.32; 6.21; 7.12; 8.51	6.58 ± 0.22; 4.88; 6.71; 8.00
Mean *b*5	−0.41 ± 0.19; −1.50; −0.42; 0.47	0.05 ± 0.11; −0.64; 0.02; 0.93
SD *b*5	5.59 ± 0.24; 4.37; 5.36; 6.50	5.19 ± 0.21; 3.83; 5.03; 6.18
Mean *b*6	−0.08 ± 0.27; −1.32; −0.28; 1.11	0.15 ± 0.12; −0.66; 0.13; 1.09
SD *b*6	4.37 ± 0.25; 3.20; 4.04; 5.46	3.77 ± 0.16; 2.67; 3.56; 4.41

p -value is indicated only for cases $p < 0.05$.

TOMM40, translocase Of Outer Mitochondrial Membrane 40; TPH2, tryptophan hydroxylase 2; SNP, single nucleotide polymorphism; UTR, untranslated; VOI, video-oculographic interface.

Author contributions

These should be presented as follows: YAT, VNP and AAV designed the research. YAT and AAV performed the research using a video-oculographic interface. AAP and IYV performed genetic research. YAT analyzed the data. YAT, AAP, IYV wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The Ethics Committee approved the current research of Voronezh State University (Protocol No. 42-03 dated February 13, 2017). All experimental participants gave informed consent for an EEG in accordance with the Helsinki Declaration. Furthermore, informed written consent for enrollment in the research was obtained from all the participants, who were informed of any subsequent genetic testing conducted using their biological material.

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Conflict of interest

Given his role as the Review Board Member of JIN, Dr. Artem P. Gureev had no involvement in the peer-review of this article and has no access to information regarding its peer-review.

Supplementary material

Supplementary material associated with this article can be found, in the online version, at https://jin.imrpress.com/EN/10.31083/j.jin2002028.

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