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Startle Modification and P50 Gating in Schizophrenia Patients and Controls: Russian Population

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Abstract. Prepulse modification of the acoustic startle response (ASR) and P50 gating are potential neurophysiological endophenotypes of schizophrenia and may be used in the construction of valid clinical biomarkers. Such approach requires a large amount of data obtained in the representative samples from different gender, socio-typological and ethnic groups, replicating studies using the similar protocols and meta-analyses. This is a replication study of ASR and the first study of P50 suppression in Russian patients with schizophrenia (n = 28) and healthy controls (n = 25). ASR and P50 were estimated according to standard protocols. Patients exhibited increased baseline ASR latency (d = 0.35, p = .026) and reduced prepulse inhibition (PPI) at 60 ms interval (d = 0.39, p = .003) and 120 ms interval (d = 0.37, p = .005) relative to controls. In the P50 test patients displayed greater S2 response amplitude (d = 0.24, p = .036) and deficit of P50 suppression (d = 0.43, p = .001). No correlations of PPI and P50 suppression were found in both groups. Only in controls prepulse ASR facilitation (at 2500 ms interval) positively correlated with P50 suppression (r = –.514, p = .013). In patients PPI displayed significant correlations with Difficulty in abstract thinking (N5: r = –.49, p = .005) and Hallucination (P3: r = .40, p = .036) PANSS scales. Logistic regression showed that the combination of PPI and P50 suppression could serve as a diagnostic predictor. Obtained results demonstrated that both PPI and P50 could be regarded as potential schizophrenia biomarkers in Russian population.

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Deficits in early information processing potentially leading to sensory overload have been considered a central feature of schizophrenia. Sensory-motor and sensory gating are measured by prepulse inhibition (PPI) of the acoustic startle response (ASR) and P50 suppression of the auditory event-related potential respectively.

PPI normally occurs when a weak prestimulus precedes a strong "startling" stimulus by 50–300 ms. This weak prestimulus inhibits the response to startling stimulus measured by m. orbicularis oculi EMG, i.e. motor response. Other startle parameters, such as habituation, baseline amplitude and latency also may be useful measures of information processing. PPI is deficient in schizophrenia patients and unaffected relatives (Kumari, Das, Zachariah, Ettinger & Sharma, 2005; Wynn et al., 2004).

The P50 is an early positive component of the auditory averaged response with latency about 50 ms. When using a paired click paradigm with a 500-ms interval, a reduced P50 response after the second click (S2, or test stimulus) compared with P50 response after the first click (S1, or conditioning stimulus) is observed in healthy subjects. P50 suppression is thought to be related to auditory sensory gating (Freedman, Waldo, Bickford-Wimer, & Nagamoto, 1991), because the dependent measure is an event related potential (ERP) rather than a motor response. P50 suppression deficits in schizophrenia patients are persistent and found in both acutely ill and more stable schizophrenic outpatients as well as in their unaffected relatives (Thaker, 2008; Turetsky et al., 2007).

Being the putative measures of early information gating P50 and PPI generally are not associated and "diverge" in normal subjects (Brenner, Edwards, Carroll, Kieffaber, & Hetrick, 2004; Schwarzkopf, Lamberti & Smith, 1993) and in schizophrenia patients (Braff, Light, & Swerdlow, 2007; Hong et al., 2007).

The lack of association between P50 suppression and PPI is not surprising because of different stimulus parameters (usually clicks vs. noises), different responses (cortical vs. muscular) and different optimal lead intervals (500 ms vs. 60–120 ms). Even being elicited by the same stimuli and the same lead intervals PPI and P50 suppression don't display significant relation (Oranje, Geyer, Bocker, Kenemans, & Verbaten, 2006).

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PPI is subserved by various forebrain structures including hippocampus and cortico-striato-pallido-thalamic circuitry. The existing data suggest that P50 suppression is regulated by wide-ranging neural circuitry, involving hippocampal structures, temporo-parietal and prefrontal cortical regions (Adler et al., 1998; Arciniegas et al., 2001; Grunwald et al., 2003; Turetsky et al., 2007). Thus, P50 generation circuitry has neural substrates interacting and overlapping with those of PPI, especially in mesial temporal lobe structures (Li, Du, Li, Wu, & Wu, 2009; Swerdlow, Geyer, & Braff, 2001) and frontal cortex (Oranje et al., 2006). Both common and distinct neurochemical mechanisms were also revealed for PPI and P50 suppression (Leonard et al., 2002; Mann et al., 2008).

PPI and P50 suppression are promising as neurophysiological probes in psychiatric researches and as biomarkers in clinical trials (Kumari et al., 2012). These measures are also viewed as valid candidates to endophenotypes of schizophrenia, i.e., quantitative traits in the putative pathophysiologic pathway from the genotype to the phenotype (Turetsky et al., 2007).

The absence of close association between these biomarkers seems to be advantageous for their concurrent use for elaboration of complex strategy in the neurophysiological and genetic subtyping of the disorder. According to opinion of leading investigators in this field (Swerdlow, Weber, Qu, Ligh, & Braff, 2008; Turetsky et al., 2007) the development of such complex strategy needs combination of multiple measures, in particular, PPI, P50 suppression and antisaccades.

At the same time, constructing of valid clinical biomarkers and endophenotypes needs closer examination of the traits using representative samples from different gender and ethnic groups, replicating studies using the similar protocols and several biomarkers, and meta-analyses (Calkins et al., 2007). The most possible ethnic variability of experimental cohort is of great advantage in the study of any psychophysiological tests especially those, which may be promising as disease hallmarks.

The aim of the present study was the concurrent estimation of PPI and P50 suppression in Russian population of schizophrenia patients and healthy participants. We also intended preliminary estimation of these measures and their combination validity as possible tools for differentiation of healthy participants and schizophrenia patients.

Materials and method

Participants

53 male subjects (aged 19–54 years) participated in the study: 28 schizophrenia patients (SCH group) and 25 healthy volunteers (CON group).

The patients (mean age 35.3 ± 2.5 years) were admitted to Serbsky National Centre for Social and Forensic Psychiatry to undergo examination: 25 patients were criminal offenders, and 3 persons were examined within the framework of civil litigation. Most of patients (23 subjects) were classified as paranoid (F20.06), one patient had undifferentiated schizophrenia (F20.3), another one had residual schizophrenia (F20.5) and three patients had simple schizophrenia (F20.6) according to ICD-10. Patients' current symptomatology was assessed with Positive and Negative Symptom Scale (PANSS). Mean sum of PANSS scales was 86.83 ± 2.34.

All of the patients were free from medication for the period exceeding one month before the investigation.

Healthy participants (25 subjects, mean age 26.4 ± 1.3 years) were ethnic Russians recruited from the central part of European Russia; 4 subjects were criminal offenders.

The subjects of the control group were evaluated by a psychiatrist to exclude any psychiatric diagnosis. Subjects with a history of neurological disorder, head trauma with loss of consciousness, substance abuse, or other medical condition that might affect brain functioning were excluded from participation in the study.

Written informed consent for the investigation was obtained from all subjects.

Each subject participated in two experimental sessions: (1) acoustic startle response (ASR) recording, and (2) P50 recording. Sessions (1) and (2) were carried out separately in two days. The sequence of sessions was counterbalanced.

Participants were asked to refrain from smoking for 1 hour prior to the testing.

Procedure

The testing took place in a quiet, lighted, and electrically shielded room. During the experimental session, participants were seated comfortably in a reclining chair and instructed to look straight ahead at a neutral picture and keep their eyes open.

Acoustic Startle Measurement

Experimental design

The procedure was developed on the basis of Consortium on Genetics of Schizophrenia recommendations (Calkins et al., 2007).

ASR was evoked using 110 dB, 40-ms bursts of white noise. The prepulse stimuli were 85 dB, 20-ms bursts of white noise presented with leading interval (LI) of 60, 120 and 2500 ms prior to the startle stimulus. The stimuli were delivered binaurally from a computer sound card via earphones.

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The startle session began with a 60 second acclimation period consisting of 70 dB white noise, which continued as the background noise throughout the session. The session included 4 experimental blocks. First block was a habituation series of 5 pulse alone stimuli (HAB1). HAB1 was followed by two PPI-BLOCKS. Each PPI-BLOCK consisted of 8 pulse alone trials and 8 prepulse trials (prepulse plus pulse) at each of the three designated prepulse intervals (60, 120 and 2500 ms), for a total of 32 startle stimuli presented in a pseudorandom order. Finally, a second habituation block (HAB2) of five pulse alone stimuli was presented at the end of the session. Inter-trial intervals were 8–22 s (M = 15 s).

Signal Recording

Two Skintact 10 mm Ag/AgCl electrodes (Leonard Lang GMBH, Austria) were positioned below and lateral to each eye over m. orbicularis oculi, with a ground electrode on the middle of forehead. Electrode impedance was kept below 10 kΩ. The eye-blink component of the acoustic startle response was measured using a 4-channel NeuroMyograph-01 (MBN, Russia). Sampling rate was 1000 Hz, band-pass filters 0.5–200 Hz. Recorded EMG activity was analyzed visually to remove artifact trials. Trials containing marked muscle activity from 20 ms before to 20 ms after the main stimulus delivery were discarded.

Integrated EMG traces were obtained by digital high-pass filtration with a cut-off frequency of 10 Hz (to remove low-frequency components), followed by rectification and smoothing with a moving average filter. Amplitude and latency of the maximum deviation from the baseline were determined automatically at 20–200 ms after the main stimulus presentation in integrated EMG traces.

Definition of Variables

Baseline startle magnitude was calculated as a mean for 5 pulse alone trials during the 1st (habituation) block. Percent habituation was calculated using the first and last five pulse alone blocks ([(mean amplitude HAB1-mean amplitude HAB2)/mean amplitude HAB1] ×100).

PPI was calculated for each of the three leading intervals: LI = 60ms, LI = 120ms and LI = 2500 ms as:

100 × (1 – [(mean magnitude on prepulse trials) / (mean magnitude on PPI-BLOCK pulse alone trials)]).

PPI calculation was performed separately for 2nd and 3rd blocks as well as total for whole experiment.

P50 suppression

Experimental design

Auditory stimuli (85 dB, 1 ms) were delivered using Stim2 software (Compumedics NeuroScan) through earphones. The subjects were presented with pairs of auditory clicks (S1, conditioning click, S2, testing click) with a 500 ms inter-click interval. Inter-trial intervals were randomized between 8 and 15 s. Two runs, each consisting of 50 identical pairs of clicks (100 total trials) were recorded.

Signal Recording

Electroencephalographic (EEG) recordings were made with 19 Ag/AgCl electrodes mounted according to the international 10–20 system and left and right earlobes. All active electrodes were referred to the left mastoid. Electrode impedance was kept below 5 kΩ. Prior to further analysis, all channels were recalibrated (off-line) with respect to linked (averaged) earlobes.

EEG was amplified and monitored with Synamp2 (Compumedics NeuroScan) amplifier. Data were collected at a sampling rate of 1000 Hz with an analog band-pass filter of 1–100 Hz.

EEG records were filtered with high-pass filter 10Hz, 6-dB slope. The trials then were visually examined to reject muscle, EOG and other apparent artifacts.

Time-locked evoked potentials were obtained by averaging all artifact-free epochs. The vertex channel Cz was used for P50 data analysis (Nagamoto, Adler, Waldo, Griffith, & Freedman, 1991).

Definition of Variables

For S1, P50 was defined as the most positive deflection from 40 ms to 90 ms after stimulus presentation. For S2, P50 was selected within a window of the S1 latency ± 10 ms for each subject. P50 amplitude was defined as the absolute difference between the P50 peak and the preceding negative trough. P50 suppression was defined as percent of P50 amplitudes ratio [(S1 amplitude – S2 amplitude)/ S1 amplitude x 100].

Subjects were not included in analyses if they had unacceptably small initial P50 amplitude (i.e., < 1.0 μV) or were P50 "nonresponders". Therefore eight subjects had to be excluded from analysis and the data of 20 control subjects and 25 schizophrenia patients were analyzed in the P50 suppression paradigm.

Statistical analysis

Non-parametric Mann-Whitney test was applied for between-group difference estimation. Spearmen Rank Order Correlations were calculated to assess association of PPI and P50 suppression rates.

Logit analysis was applied for preliminary study of probable validity of PPI, P50 suppression rate, and their combination for differentiation of participants groups.

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STATISTICA 6.0 software was used in all analytical procedures.

Results

Baseline parameters and habituation of ASR

No significant between-group difference in baseline startle amplitude was seen. SCH group displayed significantly longer baseline latency of response recorded from the right eye and a trend to increase of response latency at the left eye (Table 1).

Prepulse inhibition of ASR

In SCH group PPI deficit relative to control level was observed at LI 60 ms and 120 ms. At the left eye PPI impairment was significant during 2nd and 3rd blocks, and in whole experiment. At the right eye PPI decrease in SCH group relative to healthy participants was significant during 2nd block and in whole experiment whereas data obtained during 3rd block displayed between-group differences of borderline significance.

No PPI was found at LI 2500 ms in either group (Table 2). Sixty-seven and fifty-five of participants in CON and SCH groups respectively displayed prepulse facilitation at this LI so that response to prepulse + pulse trials was increased relative to response to pulse alone ones. No between-group difference in prepulse modulation at LI 2500ms was revealed by Mann-Whitney test.

P50 suppression

The data of 20 control subjects and 25 schizophrenia patients were analyzed.

Comparison of P50 amplitudes to conditioning S1 click revealed no significant between-group difference (Table 3). At the same time, P50 amplitudes to S2 click were significantly higher in SCH compared to CON group. This suppression difference was reflected in P50 rate that was significantly lower in patients than in healthy subjects.

The effect of age

Age was differentially distributed across groups; the SCH group was older than the CON group (35.3 ± 2.5 vs. 26.4 ± 1.3 years, $p = .0022$). Correlation analysis revealed no significant effects of age on P50, ASR and PPI measures in either of groups, as well as in total cohort of participants ($R < 0.26$, $p > .209$ in CON group, and $R < 0.19$ $p > .162$ in Sch group). At that, the pattern of between-group differences in ASR and P50 measures remained unchanged after exclusion of the youngest 20% of healthy controls and the oldest 20% of patients (mean age SCH vs. CON = 30.4±6,0 y vs. 27,8±5,3 y, $p = .18$).

Comparison of the mean values of PPI at the right and left eyes in groups adjusted for age (Table 4) by Wilcoxon matched pairs test for dependent variables revealed in SCH group significantly higher level of PPI (LI = 60 ms) at the right than at the left eye ($n = 22$, $T = 65$, $p = .045$). In CON group the difference between PPI levels obtained at the left and right eye was not significant. The between-group difference of PPI at LI 120 ms was significant at the left eye and was at the level of trend at the right eye.

Correlations of ASR and P50 measures

Analysis was performed in 20 control subjects and 25 schizophrenia patients. Baseline ASR amplitude, habituation rate, PPI at LI 60 ms and 120 ms didn't display any significant correlations with S1 and S2 amplitudes or P50 suppression in either group. In CON but not in SCH group baseline ASR latency at the right eye displayed moderate negative correlation with P50 suppression ($r = –0.514$, $p = .013$).

Only in CON but not in SCH group PPI at LI 2500 ms recorded at the right eye during the 2nd block positively correlated with S2 amplitude of P50 ($r = 0.62$, $p = .0029$) and negatively with P50 suppression rate ($r = –0.57$, $p = .0073$).

Correlations with PANSS scales

Baseline ASR amplitude displayed significant positive correlation with scale O2 – Anxiety and O4 - Tension.

Table 1. *Baseline parameters and habituation of ASR in CON and SCH groups*

	CON group ($n = 25$)			SCH group ($n = 28$)				
	M	*SD*	*Mdn*	*M*	*SD*	*Mdn*	*p*	*Effect size*
ASR magnitude. right eye (μV)	66.0	112.8	22.2	46.4	65.9	24.5	.696	–
ASR magnitude. left eye (μV)	71.3	128.3	28.3	40.4	63.3	19.0	.133	–
ASR latency. right eye (ms)	61.9	10.6	61.2	70.6	13.3	67.6	.026	.35
ASR latency. left eye (ms)	62.2	8.6	60.2	66.8	10.3	69.2	.058	.21
ASR habituation. right eye (%)	47.9	45.5	35.6	30.0	41.4	35.6	.121	–
ASR habituation. left eye (%)	43.1	42.3	40.8	27.7	44.8	40.8	.195	–

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Table 2. *PPI at different lead intervals in CON and SCH groups (%%)*

			CON group (n = 25)			SCH group (n = 28)				
Lead Interval	Eye	Block	*M*	*SD*	*Mdn*	*M*	*SD*	*Mdn*	*p*	*Effect size*
60 ms	Right	2	67.0	29.7	80.9	49.5	32.2	61.2	.023	.21
		3	56.2	44.0	66.1	45.7	31.7	53.5	.056	.14
		2 + 3	66.7	26.2	75.3	48.2	30.9	60.6	.013	.20
	Left	2	68.8	25.8	74.0	49.2	29.9	47.8	.007	.36
		3	64.5	24.3	70.2	42.4	36.2	43.7	.023	.24
		2 + 3	67.8	24.4	71.4	46.8	30.0	46.0	.003	.39
120 ms	Right	2	68.0	27.5	77.7	51.0	29.7	52.7	.023	.21
		3	52.7	47.4	68.0	38.1	37.5	36.8	.092	.19
		2 + 3	64.7	29	77.5	45.9	31.7	44.7	.024	.22
	Left	2	65.2	40.7	74.3	48.6	29.0	51.3	.005	.31
		3	61.3	32.5	72.5	41.9	36.8	48.9	.016	.30
		2 + 3	64.8	30.8	72.7	46.3	28.1	44.6	.005	.37
2500 ms	Right	2	–0.4	30.1	–4.2	–9.3	26.8	–3.2	>.1	–
		3	–8.9	59.5	7.2	–7.3	43.2	–2.0	>.1	–
		2 + 3	0.5	32.1	1.2	–6.9	27.5	–1.9	>.1	–
	Left	2	–9.5	22.0	–14.7	–7.4	28.9	–5.3	>.1	–
		3	–3.7	51.5	–6.2	–3.2	36.0	–0.1	>.1	–
		2 + 3	–6.7	6.6	–2.4	–3.4	25.9	–4.9	>.1	–

Table 3. *Comparison of Group Means (Mann-Whitney test) for P50 suppression measures in healthy subjects and schizophrenia patients*

	CON group (n = 20)			SCH group (n = 25)				
	M	*SD*	*Mdn*	*M*	*SD*	*Mdn*	*p*	*Effect size*
S1 response amplitude (μV)	1.915	.875	1.800	1.590	.673	1.470	.3310	–
S2 response amplitude (μV)	.821	.634	.660	1.298	1.033	.955	.0355	.24
P50 suppression (%)	58.93	22.38	59.2	17.92	47.98	38.01	.001	.43

Table 4. *PPI and P50 measures in CON and SCH groups adjusted for age*

	CON group (n = 20)			SCH group (n = 22)				
	M	*SD*	*Mdn*	*M*	*SD*	*Mdn*	*p*	*Effect size*
PPI at LI 60 ms. left eye (%)	67.1	24.8	75.4	28.2	24.8	36.3	.001	.39
PPI at LI 60 ms. right eye (%)	65.7	23.3	68.4	41.4	24.1	45.3	.007	.30
PPI at LI 120 ms. left eye (%)	66.2	22.8	61.4	23.8	33.1	42.4	.004	.36
PPI at LI 120ms. right eye (%)	59.5	34.0	64.3	38.2	39.4	43.6	.066	.24
ASR latency, left eye (ms)	60.6	10.3	62.0	66.7	5.1	67.4	.031	.29
ASR latency right eye (ms)	60.5	5.5	63.1	66.8	7.2	68.3	.024	.31
S1 response amplitude (μv)	2.04	.91	1.88	1.45	.56	1.52	.18	–
S2 response amplitude (μv)	.83	.57	.91	1.03	.48	.93	.22	–
P50 suppression (%)	58.9	21.8	57.2	16.8	31.9	25.7	.014	.39

ASR habituation rate positively correlated with N3 scale - Poor rapport, O11 scale – Poor attention and P6 scale - Suspiciousness /persecution.

Surprising positive correlation was revealed between PPI level and P3 scale - Hallucinations. At the same time PPI displayed negative correlation with N5

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scale – Difficulty in abstract thinking (Table 5). Correlation between N5 and P3 scales was not significant ($r = –0.20$, $p = .28$).

No correlations between P50 gating and PANSS scales were detected.

Predictive logit-models

Results in the previous sections show that SCH patients differed significantly from controls on P50 suppression rate and on PPI level, and these two measures were not associated in either group. We tried then to examine whether P50 suppression rate and PPI or their combination could serve as a predictor for groups differentiation, using binary logistic regression, where P50 suppression rates and PPI (measured from the left eye, whole experiment) were taken as independent variables, and group (y = 0 for CON and y = 1 for SCH) as the dependent variable.

Three equations had been generated by STATISTICA 6.0 (Table. 6) where ***y*** was a probability of tested person attribution to SCH group and three sets of predictors (PPI, P50, P50+PPI) were used as arguments.

Thus, relative high level of specificity (attribution of healthy subjects to CONl group) – about 85–90% - was observed for all three models (Table 6). At the same time sensitivities (attribution of patients to SCH group) of models developed with P50 gating only or with PPI only as predictors were quite low (35.71 and 57.41% respectively). The combination of these measures increased sensitivity of model up to 71.43%. It can be concluded that complex use of P50 suppression rate and PPI improves the model quality and predictive validity.

Discussion

This article presents the results of replication study of acoustic startle prepulse modification and P50 suppression in Russian schizophrenia patients' and healthy subjects population.

We didn't observe any difference in baseline ASR amplitude and habituation rate between patients and healthy persons. These results are in agreement with those obtained by some (Hasenkamp et al., 2010; Quednow et al., 2008; Wynn et al., 2004) but not all (Braff, Grillon, & Geyer, 1992; Geyer, Swerdlow, Mansbach, & Braff, 1990; Ludewig, Geyer, & Vollenweider, 2003; Quednow et al., 2006) authors. ASR habituation is regarded as a kind of information gating measures (Blumental, 1997), but its impairment isn't seen in schizophrenics as stable as PPI deficit and this problem is to be solved.

Differences between schizophrenics and healthy participants in ASR latency have been reported previously (Braff, Swerdlow, & Geyer, 1999; Geyer & Braff, 1982; Swerdlow et al., 2006), but not in all studies (Braff et al., 1992; Parwani et al., 2000). High level of heritability of ASR latency was displayed by Hasenkamp et al. (2010) and significant effect of ethnicity was proved for this measure (Hasenkamp et al., 2008; Swerdlow et al., 2007). In the present study, longer ASR latency was shown to be inherent for Russian patients with schizophrenia. In our previous study (16 healthy and 16 patients with schizophrenia) between-group difference in ASR latency was at the level of a trend (59.4 ± 2.3 ms compared to 65.0 ± 2.4, $p = .076$) (Storozheva et al., 2012).

In agreement with our previous results (Storozheva et al., 2012) this replication study revealed deficit of PPI in SCH group at LI 60 and 120 ms, which was more prominent at the left eye. Our results contradict the data obtained by other authors who found mainly right-sided PPI impairment in schizophrenia (Braff, Grillon, & Geyer 1992; Filion, Dawson, & Schell, 1993; Hasenkamp et al., 2010; Parwani et al., 2000). This discrepancy may be due to ethnic peculiarity of our participants or be specific for personality of our participants who were mainly criminal offenders. The difference in PPI between offenders and non-offenders suffering from schizophrenia as well as the possible influence of eye dominance have to be studied in larger cohort of participants.

Data about association of PPI and psychotic symptom severity in schizophrenia are controversial (Hasenkamp et al., 2011; Swerdlow et al., 2006). We found negative correlations between Difficulty in abstract thinking scale and PPI. In our previous investigation the correlations of PPI parameters with P3 and N5 PANSS scales reached the level of a trend ($.07 < p < .1$) only in cohort without experience of psychoactive substances (16 persons). This somewhat corresponds to data obtained by Perry & Braff (1994) who showed association of PPI decrease and Ego Impairment Index. Positive correlations between PPI and Hallucinations scale revealed in our study may reflect compensatory mechanisms. It was proposed by Cadenhead (2011) who showed that greater PPI in prodromal state associated with higher probability of further psychosis development. Ambiguous associations between PPI and psychotic symptoms were shown in experiments with dopamine agonists and NMDA antagonists, which evoked psychotic-like state in healthy humans and at the same time might increase PPI in some individuals depending on substances' doses (Abel, Allin, Hemsley, & Geyer, 2003; Duncan et al., 2001; Swerdlow et al., 2009; Talledo, Sutherland Owens, Schortinghuis, & Swerdlow, 2009; It's worth to note that hallucinations are viewed by some investigators as reflection of compensatory mechanisms in diseased brain (Sperling, Bleich, Maihöfner, & Reulbach, 2009).

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Table 5. *Correlations of ASR measures with PANSS scales in SCH group*

Measure	O2 Anxiety	O4 Tension	N3 Poor rapport	O11 Poor Attention	P6 Suspiciousnes/persecution	P3 Halluci-nations	N5 Difficulty in abstract thinking
ASR amplitude. left eye	R = .49. p = .02	R = .45 p = .037	ns	ns	Ns	ns	ns
ASR amplitude. right eye	R = .56. p = .007	R = .62 p = .002	ns	ns	Ns	ns	ns
ASR habituation. right eye	ns	ns	R = .67. p = .003	R = .567. p = .0099	R = .563. p = .0063	ns	ns
PPI at LI 60 ms. left eye	ns	ns	ns	ns	Ns	R = .40 p = .036	R = –.49 p = .005
PPI at LI 60 ms. right eye	ns	ns	ns	ns	Ns	R = .40 p = .034	R = –.55 p = .003
PPI at LI 120 ms. left eye	ns	ns	ns	ns	Ns	R = .47 p = .011	R = –.45 p = .009
PPI at LI 120ms. right eye	ns	ns	ns	ns	Ns	R = .44 p = .018	R = –.47 p = .008

Note: R – Spearmen rank-order correlation, *ns* – non-significant R.

Table 6. *Results of logit analysis of PPI and P50 suppression as predictors for differentiation of CON and SCH groups*

Parameter	Equation	Model quality	Specificity (%)	Sensitivity (%)	Percent correct total	Odds ratio
P50 suppression only (x_1)	$y = exp(1.588178 – 0.043852^* x_1)/ [1+exp(1.588178 – 0.043852 ^* x_1)]$	χ^2 = 9.97 df = 1 p = .0016	85 (17 of 20)	36 (9 of 25)	57.8	3.21
PPI from left eye only (x_2)	$y = exp(1.651011+ 0.03438^* x_2)/ [1+ exp(1.651011+ 0.03438^* x_2)]$	χ^2 = 9.71 df = 1 p = .0018	84 (21 of 25)	57 (16 of 28)	69.8	7.9
P50 suppression (x_1) and PPI from left eye (x_2)	$y = exp(3.20669–0.044833^* x_1+0.956157^* x_2)/ [1+ exp(3.20669–0.044833^* x_1+0.956157^* x_2)]$	χ^2= 14.22 df = 2 p = .0010	90 (18 of 20)	76 (19 of 25)	82.2	23.6

Another kind of information gating, i.e. P50 suppression, also was studied for the first time in Russian population. In the P50 paradigm, we didn't observe any between-group difference in S1 response amplitude. At the same time, S2 response amplitude was significantly greater and P50 suppression was impaired in patients group. These results are in agreement with data presented by many authors (Adler et al., 1982; Adler et al., 1998; Braff et al., 2007; Freedman et al., 1996; Hall, Taylor, Salisbury, & Levy, 2011; Nagamoto et al., 1991; Oranje et al., 2006,). We didn't reveal any correlations of P50 suppression and PANSS scales, which also corresponds to results of the most of studies (Braff et al., 2007; Brenner et al., 2007; Hong et al., 2007; Potter, Summerfelt, Gold, & Buchanan, 2006; Schwarzkopf et al., 1993).

We have found no correlations between PPI and P50 suppression in either group. Some authors (Braff et al., 2007; Hong et al., 2007) pointed out that an absence of association between P50 suppression and PPI is at least partially due to the difference in the length of stimuli onset asynchrony. In this study, we have revealed correlation between long-lead prepulse facilitation of ASR (at LI 2500 ms) and P50 suppression. Similar correlation was found by Hong et al. (2007) for LI 500 ms (i.e. the equal to the length of S1-S2 interval in P50 suppression test). ASR facilitation by discrete prepulse at long-lead interval was shown to be purely human phenomenon, and it wasn't observed in animals (Hoffman & Wible, 1969, Putnam & Vanman, 1999).). It is thought to be a measure of sustained attention to irrelevant stimuli, especially at the beginning of stimuli delivery when prepulse hadn't acquired conditional signal quality yet (Filion et al., 1993, Filion, Dawson, & Schell, 1994). In such way correlations between ASR prepulse facilitation and P50 suppression may reflect the existence of common brain mechanisms for sensory (but not sensory-motor) gating and sustained attention to irrelevant signals.

Negative correlation of ASR baseline latency and P50 suppression needs further study and can be regarded as an evidence of significance of information processing velocity for sensory gating. It should be noted that associations of P50 and ASR measures were observed only in healthy participants but not in schizophrenia patients. This difference of correlation pattern may reflect a change in interaction of brain structures involved in information processing which occurs in patients.

Preliminary analysis showed that neither P50 suppression nor PPI could serve alone as valid diagnostic tool. PPI impairment is observed in several other neuropsychiatric disorders including obsessive-compulsive disorder, comorbid attention-deficit hyperactivity disorder and tic disorder, and Huntington's Disease (Carroll, Vohs,O'donnell, Shekhar, & Hetrick, 2007; Conzelmann et al., 2010; Giakoumaki et al., 2007; Swerdlow et al., 1995). P50 suppression deficit has been found after traumatic brain injury (Arciniegas et al, 2001), and in bipolar illness (Olincy & Martin, 2005; Schulze et al., 2007). But according to supposition of Swerdlow et al. (2008) we have shown that concurrent use of PPI and P50 paradigms significantly increased the quality of diagnostic model. It can be concluded that complex study of multiple measures of forebrain inhibitory functions may help to identify patterns of normal vs. deficient functions.

In Russian population increased baseline startle latency at the right eye, impaired PPI (more prominent at the left eye), increased P50 amplitude to S2 click, and decreased level of P50 suppression were found in schizophrenia patients (most of patients were criminal offenders) compared to healthy subjects. P50 suppression level didn't correlate with PPI in any group, but in healthy control it displayed negative correlation with baseline ASR latency and positive correlation with long-lead prepulse facilitation of ASR. P50 suppression and PPI level could be regarded as potential disease biomarkers that are promising for the development of additional psychophysiological methods of diagnosis and examination in studied ethnic and socio-typological population.

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