

Response preparation and intra-individual reaction time variability in schizophrenia

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Background. It is important to prepare response in advance to increase the efficiency of its execution. The process of response preparation is usually studied using the precueing paradigm. In this paradigm subjects have to employ the preceding information about further imperative stimulus to perform proper response preparation, which shortens the reaction time of subsequent response execution. Previous studies detected the impairment of response preparation in schizophrenia only with the help of electroencephalographic parameters, but not with the assessing of reaction time. Therefore, in this study we attempted to find a behavioural parameter that could detect impairment in response preparation of schizophrenia patients. It was recently found that appropriate response preparation not only shortens the reaction time but also increases its stability, which is measured with the intra-individual reaction time variability. It was also revealed that response stability could better find cognitive dysfunction in some studies of schizophrenia disorder than classical behavioural parameters. Hence, the main goal of this study was to verify if intra-individual reaction time variability could detect the impairment of response preparation in schizophrenia patients.

Materials and methods. In order to achieve the main purpose, we carried out a study with 14 schizophrenia patients and 14 control group subjects. We used precueing paradigm in our research, in which participants had to employ information about stimulus probability for the proper response preparation.

Results. Our main result showed that despite the responses of schizophrenia patients were faster to the high-probability stimulus than to the low-probability one ($F(1, 13) = 30.9, p < 0.001$), intra-individual reaction time variability did not differ in this group between the responses to more and less probable stimuli ($F(1, 13) = 0.64, p = 0.44$).

Conclusions. Results of the study suggest that people with schizophrenia were able to use precueing probabilistic information only to shorten their reaction time, but not to increase response stability. Therefore, it was found that intra-individual reaction time variability parameter could detect response preparation impairment in schizophrenia, and could be used in clinical purposes.

Keywords: response preparation, response stability, intra-individual reaction time variability, schizophrenia

INTRODUCTION

It is well known that in order to increase efficiency of response execution it is important to prepare it in advance (1). The process of response preparation is usually studied using the precueing paradigm (e. g. 2–5, 1). This paradigm relies on two types of stimuli: precue and imperative one. The precue stimulus provides advance information about the subsequent imperative stimulus, and the former requires a certain response. It was found that the reaction time (RT) decreases with the increasing amount of information provided by the precue. This particular reduction of response time (a precueing effect) is related to the response preparation processes occurring in the foreperiod interval – a timescale between precue and imperative stimuli (for review, see 1).

The precue stimulus can provide different types of precedent information regarding the imperative signal. For instance, it may define its location or time of occurrence (4, 5). However, employing of probabilistic information about the upcoming imperative stimulus has a particular advantage in such studies. Prediction of future situation is not always exact in everyday life. Rather, our brain makes probabilistic predictions of different future events and prepares adequate responses. Therefore, using information about upcoming stimulus probability in the precueing paradigm makes the experiment closer to real life conditions (6–8).

It was found that the higher the probability of imperative stimulus is, the faster the subjects respond to it (e. g. 9–13). For example, in Miller's (1998) experiment the probability of one imperative stimulus was 75%, while the probability of another one was accordingly 25%. The RT result showed that subjects were more prepared to react to the higher probability imperative stimulus. This was confirmed by occurrence of the Lateralized Readiness Potential (LRP) during the foreperiod showing that response time reduction to more probable stimulus is related to the process of response preparation. LRP is defined as the difference between potentials at contra- and ipsilateral central electrodes processing before the movement of a certain hand. This parameter serves as an index of lateralized motor preparation and it appears in case participants prepare movement of one hand more than another (e. g. 14).

Previous studies showed that different brain processes linked to future events such as foresight (15), anticipation (16–18) and planning (19–22) are impaired in schizophrenia patients. However, it was revealed that people with schizophrenia are able to employ different precue information (including a probabilistic one) to produce faster reaction time. This evidence suggested that response preparation is not impaired in the case of this disorder (4, 23–25). Nevertheless, electroencephalographic studies detected that response preparation is reduced in people with schizophrenia when assessed with the LRP parameter, although not all researches found the significant reduction (26–28, 25).

While the attempts to discover the impairment of response preparation in the case of schizophrenia disorder with the help of RT measuring failed, we tried in our study to find the behavioural parameter, which could detect this impairment. The previous electroencephalographic study suggested that response preparation not only speeds up the reaction, but it also increases its stability (13). Response stability is measured with intra-individual reaction time variability (IIV). This latter parameter is based on the reaction time standard deviation and it provides useful predictive information about cognitive functioning (29–31). Numerous studies of IIV have been published during the last decades, particularly in the field of psychiatric and neurological disorders. For instance, response stability reductions were found in the case of frontal lobe lesions (32, 33), schizophrenia (34–36, 30, 31), dementia (37, 38), attention deficit hyperactivity disorder (ADHD) (39, 40) and Parkinson's disease (41). In addition, exploring of IIV is also used in gerontology studies (37).

The previous studies found that employing of IIV parameter has some advantage as compared with classic response measurements, because it can detect more subtle differences between cognitive functioning in healthy persons and in potential patients (42–44, 33, 31). Bearing in mind all previous information, we provided a hypothesis that assessing of response stability could detect the impairment of response preparation in schizophrenia patients. Therefore, the main purpose of our study was to analyze if people with schizophrenia are able to use probabilistic information in response preparation to increase not

only the speed of reaction but also its stability. The result of such analysis would not only help to investigate the subtle characteristic of response preparation in the case of schizophrenia disorder but also can be employed in clinical purposes.

MATERIALS AND METHODS

Participants

Fourteen schizophrenia inpatients (5 males and 9 females) were recruited from the Republican Vilnius Psychiatric Hospital for this study. Diagnosis of schizophrenia was made by clinicians, according to the International Classification of Diseases criteria (ICD-10; 45). The mean age of patients was 36.5 years ($SD = 14.2$). The control group comprised 14 healthy volunteers (7 males and 7 females), the mean age was 41.4 years ($SD = 13.4$). All individuals of both groups were right-handed and had normal or corrected-to-normal vision. This study was approved by the local Medical Ethic Committee.

Procedure

The study was carried out in the Electrophysiology Research Department of Republican Vilnius Psychiatric Hospital in a specially equipped laboratory room that eliminates extraneous visual and audible disturbances. Participants were seated at a comfortable distance in front of a computer monitor. They had to use the right hand in response to the stimuli. Before the beginning of the study, the participants were instructed to place the middle finger on the right button and the index finger on the left button of a response device.

The method of our study was based on Miller's (1998) research. The experimental task was developed and performed using the E-Prime 2.0 software (Psychology Software Tools, Inc.). At the beginning of each trial, a precue stimulus showing a picture of an outstretched left hand (mirroring the participant right hand) holding fingers in a prepared position appeared in the center of the screen. After a foreperiod of 1 s one of two possible imperative stimuli ('0' symbol or 'X' letter) followed the precue signal. The stimuli were shown one at a time in a light colour on the black background. Participants were asked to respond with the middle finger to the '0' stimulus and with the index finger to the 'X' one.

The probability of the '0' imperative stimulus was 75%, while the 'X' stimulus appeared with 25% probability. The participants were not informed about the probabilities of stimuli during the study. They had from 150 ms until 2000 ms to perform the response and were instructed to react as fast and as accurately as possible.

After the response was performed, short feedback signaling if the response was correct or wrong appeared in the center of the screen. The study consisted of six series of 32 trials occurring in a random order. The first series was considered as a practice and was not counted in the final analysis.

RESULTS

Data analysis

We eliminated all trials with wrong key responses. All remaining trials, which had reaction times 2.5 SD slower or faster than the mean for each participant, were considered to be outliers and were also eliminated from the result analysis. 2.54% of trials were eliminated in the schizophrenia group and 2.45% of trials were eliminated in healthy subjects. Reaction times, intra-individual reaction time variability and response accuracy were counted for all remaining trials considered as accurate. Following Elvevåg et al. (2000), who had also investigated response performance to different target probabilities in schizophrenia, we provided empirical log odds transformation of response accuracy data. The results with the statistical values are presented in the Figure and the Table. The results of response accuracy in the Figure and the Table represent the untransformed data.

Response execution

At first, we investigated the ability to execute responses in schizophrenia patients when compared with healthy subjects. In order to achieve this purpose, we investigated three different response parameters in both groups. The RT, IIV and response accuracy were analyzed separately for the responses to the high- and low-probability stimuli (Figure). The one-way ANOVA analysis revealed that schizophrenia patients had significantly slower reaction time than the control group, responding to the high-probability stimulus ($F(1, 26) = 15.4, p = 0.001$) and to the low-probability one ($F(1, 26) = 15.3, p = 0.001$) (Figure, A). It has also been found that the clinical group had reliably

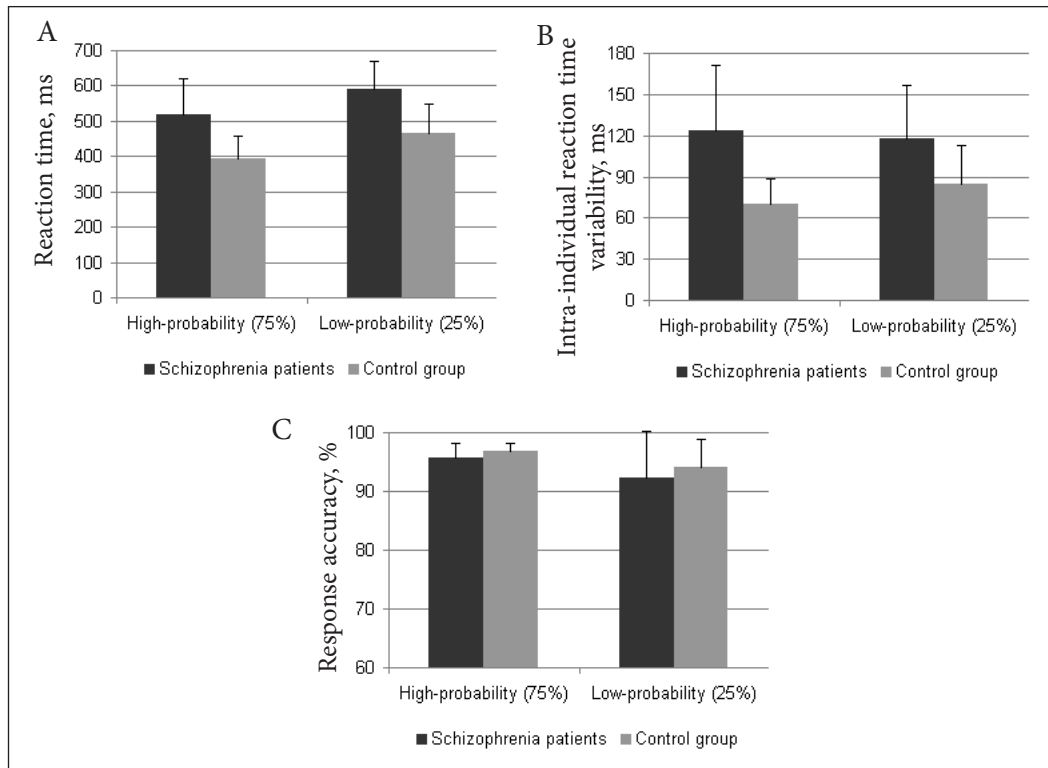


Figure. Comparison of reaction time, intra-individual reaction time variability and response accuracy between schizophrenia patients and control group subjects

higher IIV than healthy subjects when they responded to both the more probable stimulus ($F(1, 26) = 16.1, p < 0.001$) and the less probable one ($F(1, 26) = 6.7, p < 0.05$) (Figure, B). Nevertheless, the analysis of response accuracy did not reveal any difference between schizophrenia patients and the control group in the cases of both types of responses: to the high-probability stimulus ($F(1, 26) = 2, p = 0.17$) and the low-probability one ($F(1, 26) = 0.1, p = 0.76$) (Figure, C).

Response preparation

Secondly, we investigated the main goal of our study – exploring behavioural parameters of response preparation in people with schizophrenia. In order to achieve this purpose, we compared the reaction time, IIV and response accuracy between the responses to high- and low-probability stimuli separately in both groups (Table). The presence of a statistically significant difference between the latter parameters was an indicator of the ability

Table. Comparison of reaction time, intra-individual reaction time variability and response accuracy to high- and low-probability stimuli

	High-probability stimulus (75%)	Low-probability stimulus (25%)	Statistic	
			F (1, 13)	<i>p</i>
Schizophrenia patients				
Reaction time, ms (SD)	519 (101)	589 (82)	30.9	<0.001
Intra-individual reaction time variability, ms (SD)	124 (47)	118 (39)	0.64	0.44
Response accuracy, % (SD)	95.6 (2.6)	92.3 (7.8)	3.3	0.09
Control group				
Reaction time, ms (SD)	394 (64)	467 (83)	52.4	<0.001
Intra-individual reaction time variability, ms (SD)	70 (19)	85 (28)	15.8	<0.01
Response accuracy, % (SD)	96.7 (1.5)	94.1 (4.8)	7.5	<0.05

of using the probabilistic precueing information to the appropriate response preparation. According to the one-way repeated measure ANOVA analysis, both groups were reliably faster responding to the more probable stimuli than to the less probable ones. Nevertheless, IIV was significantly lower in responses to the high-probability stimuli than to the low-probability ones only in the control group subjects. The response accuracy was higher in reactions to the high-probability stimuli. However, the difference was significant only in the subjects of the control group.

DISCUSSION

This study was carried out to examine subtle behavioural properties of response preparation in the case of schizophrenia disorder. Despite a relatively small number of participants that could essentially affect the results, the obtained statistical p values have a high significance level. The former evidence suggests that the results of the study were reliable enough. The results of this study would not only expand our understanding about the process of response preparation but also can be used in clinical purposes. At first, we have analyzed behavioural parameters of response execution which revealed that schizophrenia patients were slower than healthy subjects responding to both high- and low probability stimuli. Such data coincides with the results of previous studies (24, 25). The previous studies also found that response stability of schizophrenia patients is lower than the response stability of healthy subjects (34–36, 30, 31). The results of our study have supplemented this evidence with finding that this data is also valid in case when stimuli have different probabilities. In this case, schizophrenia patients are less stable than healthy subjects responding to both high- and low-probability stimuli.

Investigating the response preparation process, we have revealed that people with schizophrenia are able to prepare response enough to react faster to high-probability stimuli than to low-probability ones. Similar findings were obtained in previous researches, in which schizophrenia patients also had to employ preceding probabilistic information (24, 25). However, the most important analysis of our study was assessing response preparation with the IIV parameter. It was found that responses to high-probability stimuli are more stable than to low-probability

ones only in the group of healthy subjects. This result coincides with the previous finding (13). Nevertheless, we did not detect any difference between the stability of responses to more and less probable stimuli in the schizophrenia group. This finding showed that response preparation in schizophrenia patients was not intact enough to provide a more stable response to the more probable stimulus. Therefore, our study revealed that the impairment of response preparation in schizophrenia could be detected only by assessing the IIV parameter. In general, this evidence coincides with the findings of previous studies, which revealed that this parameter could detect the impairment in the nervous system disorder in cases when classical behavioural test results could not find it (33, 31).

Previous electroencephalographic studies detected impairment of response preparation in people with schizophrenia only with LRP measuring. Hence, additionally to the electroencephalographic parameter we have found a behavioural one, which was also able to assess reduction of response preparation in the case of schizophrenia disorder. Behavioural parameters have some advantages as compared with electroencephalographic ones in the clinical practice. For instance, they do not need any special EEG equipment, are faster and easier to obtain. Finding of a new behavioural parameter specific to schizophrenia disorder can help in diagnostic purposes and in assessing of the efficiency of the medical treatment.

The mechanism of subtle impairment of response preparation in schizophrenia can be related to the pathology of frontal cortex neurons in these patients. Previous studies found the impairment in response preparation after the damage of the frontal cortex (46–48). However, it is well known that the activity of neurons in the frontal cortex is also disturbed in the case of schizophrenia (e. g. 49–52). The former evidence determines the similarities of cognitive impairment in frontal lobe lesion and schizophrenia patients (e. g. 53–56). Nevertheless, in the case of schizophrenia, disturbance of the frontal cortex neurons is not as severe as after frontal lobe damage. This evidence could be a reason why impairment of response preparation cannot be detected in schizophrenia patients with a help of reaction time measuring as it takes place in the case of frontal cortex damage. We suggest that impairment of response preparation in the case of schizophrenia is more subtle than after lesion of the frontal cortex, and it can be detected only with assessing of response stability.

CONCLUSIONS

Our study revealed that schizophrenia patients were able to use precueing probabilistic information in response preparation only speeding up the reaction time but not increasing its stability. Therefore, it was revealed that in the case of schizophrenia disorder intra-individual reaction time variability could detect impairment of response preparation (contrary to the parameter of reaction time). This finding showed the new advantages of employing response stability measurements in scientific and clinical studies.

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ATSAKO PARUOŠIMAS IR ASMENINIS REAKCIJOS LAIKO KINTAMUMAS ŠIZOFRENIJOS ATVEJU

Santrauka

Ižanga. Norint padidinti atsako atlikimo efektyvumą, svarbu paruošti jį iš anksto. Dažniausiai atsako paruošimo tyrimuose taikoma įspėjančio stimulo paradigma. Šioje paradigmoje tiriamieji turi pasinaudoti išankstine informacija apie artėjančią stimulą, kad galėtų tinkamai paruošti atsaką, o tai sutrumpintų atsako atlikimo laiką. Ankstesnieji tyrimai aptiko atsako paruošimo sutrikimą šizofrenijos atveju tik taikant elektroencefalografinius parametrus. Tačiau matuojant dažniausiai taikomą elgseninį parametrą – reakcijos laiką, rasti šio sutrikimo nepavyko. Tyrimo metu buvo bandoma nustatyti tokį elgseninį rodiklį, kuris galėtų aptikti atsako paruošimo sutrikimą sergantiems šizofrenija pacientams. Neseniai nustatyta, kad tinkamas atsako paruošimas ne tik sutrumpina reakcijos laiką, bet ir padidina atsako stabilumą, kuris vertinamas asmeninio reakcijos laiko kintamumo matavimu. Taip pat išsiaiškinta, kad atsako stabilumo parametras gali geriau nustatyti kai kurių kognityvinių funkcijų sutrikimus šizofrenijos atveju negu klasikiniai elgseniniai parametrai. Pagrindinis šio tyrimo tikslas – patikrinti, ar asmeninis reakcijos laiko kintamumas gali parodyti atsako paruošimo sutrikimą sergantiems šizofrenija.

Metodika. Ištyrėme 14 sergančiųjų šizofrenija pacientų ir 14 kontrolinės grupės sveikų tiriamųjų. Tyrime taikyta įspėjančio stimulo paradigma, kai dalyviai tinkamam atsako paruošimui turėjo pasinaudoti informacija apie artėjančių stimulų tikimybę.

Rezultatai. Pagrindiniai tyrimo rezultatai parodė, kad nežiūrint į tai, jog sergantys šizofrenija pacientai greičiau reagavo į didesnės tikimybės stimulą ($F(1, 13) = 30,9$, $p < 0,001$), jų asmeninio reakcijos laiko kintamumas reaguojant į abu stimulus buvo vienodas ($F(1, 13) = 0,64$, $p = 0,44$).

Išvados. Tyrimas patvirtino, kad sergantieji šizofrenija galėjo pasinaudoti išankstine tikimybine informacija, tačiau tai tik sutrumpino reakcijos laiką, bet nepadidino atsakų stabilumo. Nustatyta, kad asmeninis reakcijos laiko kintamumo parametras gali aptikti atsako paruošimo sutrikimą šizofrenijos atveju.

Raktažodžiai: atsako paruošimas, atsako stabilumas, asmeninis reakcijos laiko kintamumas, šizofrenija