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Intra-individual reaction time variability and response preparation: an EEG study

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To behave more efficiently the human brain must anticipate future events with different probabilities and prepare appropriate responses. Previous studies demonstrated that participants react faster to more probable stimuli. It has been shown that this effect in reaction time reduction is related to the response preparation process. However it is still unknown what the minimum difference in stimulus probabilities is that is sufficient to elicit response preparation as measured with the EEG.
Intra-individual reaction time variability indicates the stability of an individual's response performance and provides useful information about cognitive functioning. It's use has become prevalent in recent clinical studies. In order to extend understanding of cognitive and neural mechanisms of response stability we hypothesized that intra-individual reaction time variability relates to the response preparation process. Specifically, we hypothesized that response preparation to more probable stimuli would result in not only faster reaction time but also in a reduction of response variability. To verify this hypothesis, we tested 14 healthy subjects using reaction time and EEG as dependent measures. Two different stimuli with probabilities of 33.3% and 66.6% were assigned to two counterbalanced responses.
The results of our study showed that stimulus probabilities of 66.6% and 33.3% were sufficient to elicit response preparation. Our data also revealed that response preparation to more probable stimuli speeds RT and reduces RT variability.

Key words: response preparation, intra-individual reaction time variability, stimulus probability, response stability

The human central nervous system predicts future events and prepares appropriate responses. Responses to stimuli are more effective if they are prepared in advance (Volz et al. 2003, Hawkins and Blakeslee 2004, Leuthold et al. 2004, Feigenberg 2008, Bruhn 2013). Many studies have revealed that reaction times are faster when subjects respond to high-probability stimuli (e.g. Hyman 1953, Laming 1968, Heuer 1982, Miller 1998, Scheibe et al. 2009). For instance in Miller's (1998) study there were two types of stimuli, S_1 and S_2, which required two responses, R_1 and R_2. The probability of one stimulus was 75% while the probability of the other was 25%. Participants responded about 90 ms faster to the more probable stimulus (Miller 1998, Katzner and Miller 2012). This reduction in reaction time is related to the response preparation process. Participants have better prepared responses to the more probable stimulus. This results in faster reaction times (Miller 1998). Response preparation to the more probable stimulus was indicated by the Lateralized Readiness Potential (LRP) (Miller 1998). The LRP is the average amount of EEG activity above the contralateral motor cortex during the foreperiod. This parameter serves as an index of lateralized motor preparation, and it appears only when participants prepare movement of one hand more than the other (Miller 1998).

In contrast to Miller (1998), Scheibe et al. (2009) obtained different results. These authors carried out a more complex experiment using three different precues. Each precue signaled which of three different stimulus probability ratios would occur, specifically 50:50, 75:25 and 100:0. However, contrary to Miller's (1998) results, they did not find any significant LRP effect in the case of the 75:25 stimulus probability ratio. Scheibe et al. suggested that the stimulus with a probability of 75% was too weak to elicit response preparation. This finding raises an important question:

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what is the minimum stimulus probability ratio needed to elicit response preparation measured with the LRP? In order to investigate this question we carried out a study based on Miller's (1998) experimental paradigm. Katzner and Miller (2012) suggested that response preparation was absent in the Scheibe and others (2009) study because of the complexities of their experimental task. Therefore, we decided to replicate Miller's study using a less contrasting ratio of stimulus probabilities, specifically 66.6:33.3 rather than 75:25. Data from previous reaction time studies revealed that responses to stimuli with a probability of 66.6% are faster than to those with a 33.3% probability (LaBerge et al. 1969).

The execution of responses can be studied not only by measuring reaction time (RT) itself, but by measuring within-person fluctuations in RT as well. This latter parameter is the standard deviation of an individual's reaction time and is called intra-individual RT variability (IIV). This measure reflects the stability of response performance and provides useful predictive information about cognitive functioning (MacDonald et al. 2006, Roalf et al. 2013, Shin et al. 2013). Intra-individual RT variability has been widely

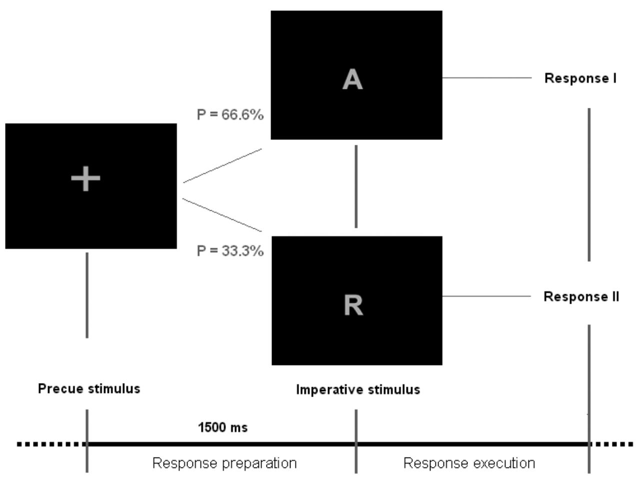

Fig. 1. Study design. Experiment started with precue stimulus – a symbol '+' exposed for 1500 ms during response preparation foreperiod. Afterwards one of two possible imperative stimuli, the letters 'A' or 'R', appeared with different probabilities 33.3% and 66.6% respectively. The response required pressing the '1, 3 and 2' keys by the right hand and the 'c, z and x' keys by the left hand. Half of participants had to perform the left hand response to the 'R' and right hand response to the 'A'. The other half had to make reverse responses.

used in several recent studies, particularly in studies of psychiatric and neurological disorders. Reductions of response stability were found after frontal lobe lesions (Stuss et al. 2003, Picton et al. 2007), in schizophrenia (Winterer et al. 2004, Kaiser et al. 2008, Cole et al. 2011, Roalf et al. 2013, Shin et al. 2013), dementia (Hultsch et al. 2002, Tales et al. 2012), attention deficit hyperactivity disorder (ADHD) (Westerberg et al. 2004, Rubia et al. 2007, Henríquez-Henríquez et al. 2015, van Belle et al. 2015) and Parkinson's disease (Camicioli et al. 2008). In addition, IIV is used in gerontology studies (Hultsch et al. 2002). Previous investigators found that intra-individual RT variability can detect more subtle differences between cognitive functioning in healthy persons and in patients when compared with classic response execution measurements (Collins and Long 1996, Hultsch et al. 2000, Klein et al. 2006, Picton et al. 2007, Rentrop et al. 2010, Shin et al. 2013).

Previous studies of IIV demonstrated that this variable is related to such cognitive functions as top-down attention control, executive function and monitoring (Stuss et al. 2003, Bellgrove et al. 2004, Simmonds et al. 2007, Picton et al. 2007, Ramchurn et al. 2014). In order to extend our understanding of IIV cognitive and neural mechanisms, we tested a new hypothesis that response stability is related to the response preparation process. In light of the previous results, we hypothesize that response preparation to the more probable stimulus results not only in lower RT, but also in lower IIV. Therefore, response preparation makes responses not only faster, but also more stable. Examination of this hypothesis is the main goal of our study.

Fourteen healthy right-handed volunteer subjects participated in the study, six males and eight females. The mean age of participants was 23.6 years (SD=3.1, range 19–30 years). All subjects had normal or corrected to normal vision. The study was carried out in the Electrophysiology Research Department of the Republican Vilnius Psychiatric Hospital. The study was approved by local Medical Ethics Committee. All participants gave written informed consent to participate in the study.

Our study was based on Miller's (1998) method. In line with previous studies (e.g. Orenstein 1970, Miller 1998), we used uppercase letters as stimuli in our study. The visual angle of each letter was about 1.6° for both height and width. All letters were presented in the center of computer screen (with diagonal of 19'') in a

Table I

RT, IIV and Errors for different stimulus probabilities

	High-probability stimulus (66.6%)	Low-probability stimulus (33.3%)	F (1,13)	P
RT (SD), ms	409 (52)	450 (40)	17.66	0.001
Response errors (SD), log	−4.51 (0.89)	−3.62 (0.99)	7.65	0.016
IIV(SD)	64.9 (19.3)	78.1 (23.5)	32.69	<0.001

RT – reaction time, IIV – intra-individual reaction time variability, SD – standard deviation

light silver color on the black background. Participants sat in a comfortable chair in an electrophysiology laboratory specially equipped to minimize distracting factors such as noise. In the study, participants had to provide two types of different responses. These responses were sequences of three key stokes on a standard computer keyboard using the index, ring and middle fingers in that order. Responding with the right hand participants had to press the combination of keys '1, 3 and 2', while the left hand response required presses of keys 'c, z and x'.

Each trial began with a precue (a light silver color '+' symbol on the black background) shown in the center of screen followed after 1500 ms by an imperative stimulus. The imperative stimulus required one of two possible responses depending on the stimulus type. The response had to be performed as fast and as accurately as possible. After each response, feedback showing the correctness of response appeared for 1200 ms. The next trial started in 500–800 ms with a mean of 650 ms. This period was not constant in order to desynchronize successive trials. There were seven blocks of 30 trials with breaks of 1–2 min, if participants wanted, after each block.

Participants were not informed about the probabilities of the stimuli during the study. There were two types of stimuli: the letter 'R' was presented with a 66% probability and the letter 'A' shown with a probability of 33%. Half of the subjects had to perform a left hand response to the 'R' letter and a right hand response to the 'A' letter stimulus, while the other half had to make reverse responses (Fig. 1).

Electroencephalographic data were continuously recorded with a 'Galileo Mizar Sirius' computerized EEG system (EBNeuro, Italy). 20 Ag/AgCl electrodes, irrigated with 0.9% NaCl solution and attached to the scalp according to the international electrode placement 10–20 system. The ground electrode was attached to the frontal scalp area at the place of Fpz electrode. Two reference electrodes were attached to the earlobes. The first two blocks were considered practice and were not counted in the final analysis. We also eliminated all trials with wrong key responses and trials deviating more than 4.5 SD from the mean RT calculated for each participant. The number of excluded trials was approximately 2%. For all remaining trials reaction time, inter-individual RT variation and response errors were calculated for each stimulus probability. The results and the statistical test outcomes are shown in Table I. Following Elvevåg and others (2000), who had also investigated response performance to different target probabilities, we provide empirical log odds transformation of response error data because of potential floor effects. F and p values are given in the text only if they are not provided in the table. In the electroencephalographic data analysis, trials with different artifacts caused by horizontal eye movements, eye blinks, muscular activity of the scalp or other reasons were removed manually. Approximately 15% of trials was thus eliminated. The continuous EEG was segmented into epochs. An epoch started 200 ms before the precue stimulus. This 200 ms time period was used for baseline counting. The epoch then lasted for an additional 1500 ms to allow for response preparation from precue until the imperative stimulus was presented. An epoch ended 500 ms after the response. Impedances of electrodes were kept below 10 kΘ and bandpass filters of 0.3–70 Hz were used. All electroencephalographic signals were digitized at 512 Hz.

The LRP was computed from averaged evoked potentials at C3 and C4 electrodes according to the standard formula (e.g. Eimer 1998):

$$\frac{(C4'-C3')\ \text{left hand} + (C3'-C4')\ \text{right hand}}{2}$$

The LRP amplitude in foreperiod between the precue and the imperative stimulus was computed as the average voltage over baseline.

We first compared RT and response errors to different stimulus probabilities using one-way repeated measure ANOVA (Table I). The analysis revealed that responses to the more probable stimuli were significantly faster. Such result coincided with previous reports (e.g. Hyman 1953, Laming 1968, Heuer 1982, Miller 1998). We also found that responding to the high-probability stimuli resulted in fewer errors.

Secondly, we compared IIV of responses to the high- and low-probability stimuli (Table I). According to the one-way repeated measure ANOVA, response variability was reliably lower to the more probable stimulus. To explore if this trend in IIV was related to response preparation, we computed the LRP and compared its amplitude to zero using t-tests (Fig. 2). This statistical analysis showed that the LRP average amplitude was −0.65 μV (SD=0.35), which was significantly different from zero (t_{13}=6.88, P<0.001). In Miller's (1998) study stimulus probabilities of 75% and 25% were used. Using a similar LRP analysis Miller found that response preparation to more probable stimuli results in a reduction in reaction time. Therefore our LRP data not only coincided with Miller's (1998) result, but also revealed evidence that a probability ratio of 66.6:33.3 is sufficient to elicit response preparation based on the LRP data. This data raises the possibility that even less contrasting ratios of stimulus probabilities (e.g. 60:40 or even 55:45) might elicit response preparation measured with the LRP.

According to MacDonald and colleagues (2006) measurements of only mean RT in neuropsychological studies have largely overshadowed research on intra-individual variability. These authors argue that this is a serious theoretical and practical oversight because IIV indicators confer unique predictive information about cognitive functioning over and above mean performance. IIV has been found to render differences between populations more apparent (MacDonald et al. 2006). A number of previous studies has revealed that during performance of certain tasks IIV showed better discriminative abilities than RT between patients with CNS disorders and healthy subjects (Collins and Long 1996, Hultsch et al. 2000, Klein et al. 2006). Moreover in some cases patients differed from healthy subjects only in IIV but not in RT results (Picton et al. 2007, Rentrop et al. 2010, Shin et al.

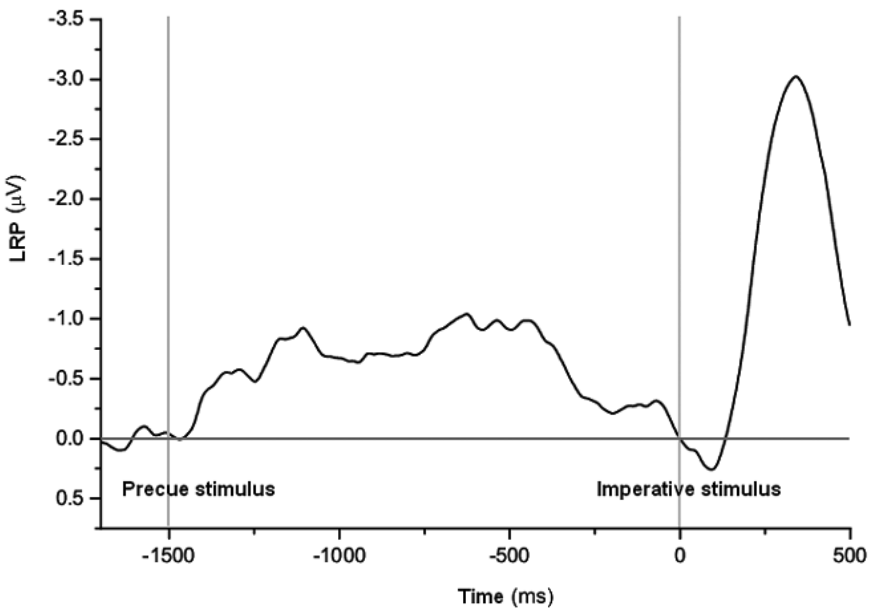

Fig. 2. Lateralized Readiness Potential (LRP) during the foreperiod of 1500 ms between precue and imperative stimuli. LRP elicit above zero baseline indicates hand specific response preparation process to more probable stimulus.

2013). This evidence shows an important advantage of IIV measurements because they might detect more subtle cognitive impairments than standard measures of task performance and might be helpful in differentiating between patients and controls (Kaiser et al. 2008).

Previous studies have also found special neuroanatomical correlates of IIV. Picton and others (2007) showed that after damage to the right ventrolateral prefrontal cortex only an IIV increase was obtained, while RT results were normal. With the help of fMRI Bellgrove and others (2004) found functional neuroanatomical correlates of response variability in frontal and parietal cortices and did not observe any relationship between mean reaction time and intra-individual variability. In summary, it has been shown that IIV is an important measure of cognitive functioning that is not directly related to RT.

Hints about the neural and cognitive mechanisms of IIV have been suggested by previous studies. Damage to the superior and lateral prefrontal cortex suggested that IIV is related to top–down control of attention (Stuss et al. 2003). Results of right anterior cingulate cortical lesion studies have shown that IIV is associated with sustaining of stimulus-response mappings. At the same time, right ventrolateral PFC damage data suggested a relation of IIV to monitoring cognitive function (Picton et al. 2007). ERP and fMRI studies suggested that IIV is associated with executive functions (Bellgrove et al. 2004, Simmonds et al. 2007, Ramchurn et al. 2014). Extending our understanding of the neural and cognitive mechanisms of IIV we have found that the response preparation process results not only in faster responses to the more probable stimulus but also in higher response stability. As was mentioned above, use of the IIV measures is becoming common in current neurological and psychiatric studies. Therefore, our results show that IIV can be used in clinical studies exploring response preparation in different brain disorders and provide more information than using only RT, as has been widely done previously (e.g. Verfaellie and Heilman 1987, Carnahan et al. 1994, Turken and Swick 1999, Triviño et al. 2010).

CONCLUSION

The results of our study revealed that stimulus probabilities of 66.6% and 33.3% are different enough to elicit response preparation, which can be indicated by an LRP during a foreperiod. Our results also showed that the response preparation process makes reacting to a stimulus with higher probability not only faster but also more stable. This finding contributes to the understanding of the cognitive and neural mechanisms of intra-individual reaction time variability. It also shows that this method can be used in clinical studies of central nervous system disorders.

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