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Commentary

Looking at Change: Examining Meaningful Variability in Psychophysiological Measurements

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Variation in event-related potentials (ERPs) has long been a topic of discussion, but primarily as an inconvenient byproduct of noisy physiological measurement. Most ERP research uses the signal averaging approach to remove variability assumed to be noise by averaging the raw ERP response across repeated trials. This process removes trial-to-trial variation and maintains what is thought to be signal specific to the event (stimulus or response), producing averaged waveforms for each experimental condition within each participant. Researchers have developed strategies for assessing the quality of averaged waveforms (1,2) and guidelines for how many trials should be included in an averaged waveform (3) and have addressed other psychometric concerns within the signal-averaging approach (4). Importantly, the signal-averaging approach assumes that the underlying stimulus or response-locked signal is constant across trials and represents some essential unvarying psychological process. However, it is extremely unlikely that any psychological process of interest is elicited in exactly the same way across trials because of varying properties of the stimulus or response, learning or habituation, fatigue over the course of a long experimental task, or random fluctuations in engagement. Thus, examining meaningful variability in ERPs can be an extremely useful tool in understanding how psychophysiological processes of interest vary.

Several approaches have been developed to examine meaningful variation in single- trial ERPs, including multilevel modeling approaches (5,6). Multilevel modeling has become an increasingly popular statistical technique in ERP research, especially when examining single-trial ERPs, because of its flexibility and power. Multilevel models can account for different sources of variance in ERPs, including participants, electrodes, or items, by including these sources in the model as random factors. Variance in the outcome accounted for by random factors is estimated along with the fixed effects of any predictors included in the model. When applied to single-trial ERPs, partitioning of random and fixed effects isolates signal from noise as the signal-averaging approach does, bypassing the need to first average across trials before any analysis is done. In addition, multilevel models are able to 1) accommodate unbalanced data, which is common when different numbers of trials are rejected or accepted for different participants during the cleaning process, 2) include trial-level predictors, and 3) include both continuous and categorical predictors (7).

Although traditional multilevel models explicitly estimate variance in ERP responses as a function of random factors (e.g., quantifying the amount of between-person variance) along with the fixed effects, they are unable to examine how specific predictors or covariates contribute to variation in ERPs across trials. In the current issue of *Biological Psychiatry: Cognitive Neuroscience and Neuroimaging*, Clayson *et al.* (8) address this problem and propose a novel application of location-scale multilevel models that extend traditional multilevel models in a key way. Traditional models, which can be thought of as location-only models, provide estimates of the fixed and random effects on the conditional or marginal means of the outcome. The fixed effects examine differences in the model-estimated means across different levels of the predictors. Using the error-related negativity (ERN) component as an example, this might be the fixed effect of response type on ERN amplitude, such that the conditional mean for ERN amplitude across the sample is higher after error responses relative to correct responses. Traditional multilevel models also provide estimates of the random effects for the conditional means, which describe the variance in conditional means across levels of a random factor. For example, if participants are used as a random factor, the model would estimate how much each participant's average ERN (adjusted by the model) varies across participants. These fixed and random effects constitute a location-only multilevel model.

Location-scale models extend location-only models by additionally estimating fixed and random effects for the residual variance, which constitute the scale portion of the model. In other words, location-scale models estimate how the residual variance surrounding the conditional means varies as a function of other variables (fixed and random). Using the previous example of the ERN, the fixed effect of response type in the location portion of the model estimates the difference in the conditional means of the ERN across correct and error responses, whereas the fixed effect of response type in the scale portion of the model estimates how residual variance around the conditional mean (i.e., how much the ERN varies from trial to trial) differs between correct and error responses. By modeling effects of fixed effects on residual variance, we might see that there is more variability in error responses than correct responses or vice versa. In addition to expanding the fixed effects, location-scale models also estimate random effects on residual variance, such as how variability in ERN responses varies across levels of a random factor (e.g., how variability in the ERN differs across participants if participant is included as a random factor). Because of the explicit modeling of fixed and random effects on the variance around the conditional means in this way, location-scale models provide a powerful tool to examine how different factors influence variance in ERP responses.

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Using these models, Clayson *et al.* (8) make a significant contribution to our understanding of how the ERN varies from trial to trial and how this variation may be meaningful (or not) for clinical groups. Specifically, they compare variability in the ERN across three psychopathology groups (major depressive disorder, generalized anxiety disorder, and obsessive-compulsive disorder) along with healthy control subjects. Previous research has examined how individuals' mean ERN amplitude differs according to clinical diagnoses with mixed results. By using location-scale models, Clayson *et al.* (8) extend previous research by examining how within-person variability in ERN amplitude may differ as a function of clinical diagnosis. The authors use a procedure of model selection to compare location-only models with their corresponding location-scale models to determine the benefit of modeling variability in ERN responses in addition to conditional means of ERN responses. They compare several pairs of location-only and location-scale models that include different predictors to determine the relative contribution of response type, clinical diagnosis, and measured psychiatric symptoms in predicting both conditional means (i.e., location) and variance around the mean (i.e., scale).

Through model comparison, the authors find evidence of important intraindividual differences in variability in the ERN (i.e., that variance in ERN amplitude differs from person to person) and evidence that this variability also differs as a function of response type (correct and error responses). Specifically, ERNs elicited in error trials varied more than responses elicited in correct trials, suggesting that conflict processing is more variable when participants make mistakes in the flanker task relative to successful task performance. Interestingly, variability in an individual's ERN amplitude was not predicted by clinical diagnosis or group, suggesting that individuals with major depressive disorder, generalized anxiety disorder, or obsessive-compulsive disorder do not differ from healthy control subjects in how much their ERN varies from trial to trial. Despite the null result, Clayson *et al.* (8) highlight the importance of estimating and examining intraindividual variability to understand what factors meaningfully predict (or do not predict) variability. Although clinical diagnosis or psychiatric symptoms do not seem to predict individual variation in ERN responses, other important factors may, which is important for understanding processes related to conflict monitoring across people.

Application of this approach can positively contribute to understanding variability in other areas of cognition, with and without clinical implications. For example, researchers could examine how specific attributes of faces contribute to trial-to-trial variability in processing those faces (one possibility is that processing of outgroup faces is more variable than processing of ingroup faces or vice versa), or how variation in language-specific processing differs across dominant and nondominant languages among bilingual subjects owing to differences in reading automatization. Although the statistical expertise needed to appropriately fit and interpret these models is not trivial, I hope these approaches become more widely used. Examining meaningful variation in ERPs from trial to trial is essential in understanding how psychological processes that underlie physiological signal vary, what that variation may depend on, and what it predicts.

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