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Spotlight

The cardiac cycle
modulates
learning-related
interoceptionMiriam S. Nokia ^{1,2,*,@},
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Behavior is guided by the compatibility of expectations based on past experience and the outcome. In a recent study, Fouragnan and colleagues report that absolute prediction error (PE)-related heart-evoked potentials (HEPs) differ according to the cardiac cycle phase at outcome, and that the magnitude of this effect positively correlates with reward learning in healthy adults.

According to a dominant perspective on brain function, the brain is constantly predicting what will happen next [1]. When these predictions fail, certain brain regions respond to the error. Interestingly, these same brain regions are also involved in detecting bodily states, which suggests that the tendency to change one's behavior might be sensitive to visceral sensations [2]. Indeed, ample research now suggests that brain activity, cognition, and behavior are modulated by bodily rhythms, including the cardiac cycle. In one line of this broader research program, research suggests that sensory accuracy and speed vary between the systole and diastole phases of the cardiac cycle [3]. For example, in the context of classical conditioning, presenting an auditory warning signal at the diastole phase (during expiration) rather than the systole phase (during inspiration) enhances the probability that the signal will evoke a learned defensive reflex [4].

The effects of cardiac cycle phase on cognition and behavior could be related to

interoception, the conscious or subconscious sense of the internal state of one's body. Interoception is often quantified as the magnitude of the HEP (reviewed in [5]) of the electroencephalogram (EEG). HEP is assumed to reflect processing of cardiac activity in the neocortex, which is dependent on the insula especially [6]. It has been suggested that the brain responds differently to external and internal signals during the diastole and systole phases. Specifically, exteroceptive signals may be more heavily weighted during the diastole phase and interoceptive signals more heavily weighted during the systole phase. Interestingly, PEs are associated with slowing of the heartbeat (reviewed in [7]). External feedback from the error may be combined with interoceptive signals in the brain, which, again, could shape predictions and behavior to minimize errors in the future. A study in skilled musicians [8] reported that behavioral adaptations following an error were smaller if the mistake took place during systole rather than diastole, despite larger error-related event-related potentials at systole compared with diastole. This suggests that the cardiac cycle influences how information about PEs is used to modify behavior. However, it is still unclear which aspects of error processing are affected by the cardiac cycle phase, on what timescale, whether there are individual differences, and how all of this connects to learning.

To examine the effects of cardiac cycle phase on internal representations during learning, Fouragnan *et al.* trained healthy young adults in a reward-learning paradigm using visual stimuli [9]. During each trial, two cues (face or house) were presented in sequence (four possible combinations) after which the participant predicted what the outcome (blue or orange circle) would be. The task was divided into four types of block, each repeated twice, in which: (i) neither cue predicted the outcome; (ii) one cue predicted the outcome while the other did not; (iii) both cues predicted

different outcomes; or (iv) both cues predicted the same outcome. After the participant had made their prediction, the outcome was presented visually (correct/incorrect) and HEP magnitude was measured following outcome onset. Participants were incentivized with a monetary reward that was partially dependent on task performance.

Fouragnan and colleagues [9] analyzed their data using both simple measures of behavior (correct versus incorrect predictions, or rewards collected) and computational modeling. Out of the four options tested, a simple cue model appeared to explain the behavioral choices of the participants best and, thus, this model was used for estimating outcome-related signals from the neural data. The authors found that the HEP amplitudes were modulated by both learning outcome valence (correct versus incorrect) and two computationally derived learning signals: signed PEs and absolute PEs using traditional event-related potential (ERP) analysis. Converging evidence was found between trial-by-trial variation in the absolute PE (i.e., how surprising the outcome is) and HEP using multivariate pattern analyses. Interestingly, the HEP around 100–300 ms specifically after the first heartbeat following the outcome feedback was found to be most strongly linked with the absolute PE. This suggests an effective time window of ~1 s during which the brain is more responsive to interoceptive signals after error detection. This HEP component (denoted as absPE-HEP) was found to be stronger if the outcome was presented at diastole than at systole. Cardiac cycle phase at feedback did not affect (stay versus switch) behavior directly but interacted with the absolute PE. Finally, the degree of difference in the absPE-HEP between diastole and systole was positively associated with measures of learning. To summarize, cardiac cycle phase at outcome affected absolute PE-related (interoceptive) processing in the brain immediately after the feedback, and

individuals with greater effect of cardiac cycle phase learned better.

Some issues in the data analyses by Fouragnan *et al.* [9] should be noted: the HEPs elicited following feedback presentation at diastole versus systole phases were not temporally aligned; that is, they occurred at different delays from the visual feedback. Therefore, the responses could be confounded by other feedback-related neural processes with varying timelines. Additionally, both the event-related potential and multi-voxel pattern analyses were conducted at the sensor level; thus, the underlying brain sources of the absPE-HEP component remain unclear.

An important point that the current work by Fouragnan and colleagues brings up is the interindividual variation in how bodily state affects information processing in the brain to produce behavior change. Taken to the extreme, some people might be relatively unaffected (or immersed) by their internal signals, which might hinder their ability to match the external and internal

world to obtain a comfortable level of homeostasis. Recent evidence suggests that HEPs are stronger in adolescents with high rather than low levels of self-reported inattention and hyperactivity [10] but more studies are needed. The interindividual variation might explain some of the discrepancies in findings in this field of study (see [3]). Given that voluntary control of breathing is a powerful way to also modulate heart rate, it would be interesting to see how these two bodily signals together affect error-related processing in the brain and, thus, influence adaptation of behavior.

Declaration of interests

None declared by authors.

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