This Week in The Journal

"Event Files" Guide, but May Impede, Future Behaviors

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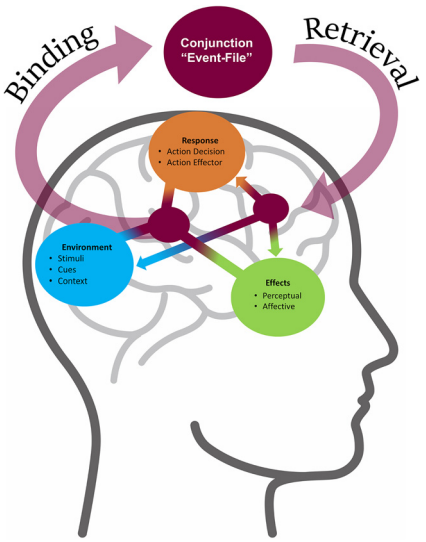
(see pages 282–292)

As we interact with the world, our brains form a representation of the features of a task such as its associated context, stimuli, actions, and outcomes—called an event file. These event files may be recalled to help us achieve the same task in the future. But rules to complete a task may change over time, requiring different actions. Could previously formed event files actually impede the completion of future tasks? Rangel et al. set out to answer that question by measuring brain activity using electroencephalography (EEG) in 35 adult participants as they completed a complex task-switching paradigm that entailed moving a digital target according to coded directions. Using a previously developed technique, the authors confirmed that they could decode the strength of the event file from EEG data. Importantly, response times were improved when the elements of the event file representing the cue, target, and response were stronger, indicating that a more strongly encoded event file aided participants in successive task completion. However, as predicted, when the rules of the task changed, participants' accuracy and response times suffered. The researchers then examined the link between the strength of the event file formed with the initial instruction and the extent to which performance declined when the task switched. As they hypothesized, a stronger initially formed event file led to longer response times on the new task, suggesting that event files can be detrimental to the completion of future tasks when the rules change. The study provides further support for the Theory of Event-Coding, which postulates that event files are formed during task completion and can be automatically retrieved to guide future behaviors. But the work also suggests that event file formation can interfere with the formation of updated event files for subsequent tasks. This work extends researchers' understanding of human adaptive and flexible behavior.



Proposed network underlying construction of "event files."

Neural Plasticity Varies with Opioid Exposure Pattern

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(see pages 308–318)

Opioid addiction stems from a vicious cycle of euphoric reward brought on by the drug and the dysphoria of withdrawal from it, which can be alleviated by taking more drug. Addiction behaviors are driven by adaptations in overlapping yet distinct neural networks, but the timing of opioid delivery and withdrawal have variable effects on neuronal function and behavior. This week, researchers investigate in mice how the pattern of continuous opioid delivery punctuated by periodic withdrawal affected synaptic plasticity in the nucleus accumbens (NAc), a major hub for reward signaling. The NAc contains GABAergic medium spiny neurons (MSNs) containing either D_1- or D_2-type receptors, and these two populations are thought to promote and dampen reward, respectively. Mice were implanted with minipumps to continuously deliver morphine or saline and were injected twice daily with either saline or naloxone, the opioid receptor antagonist, to interrupt continuous opioid exposure. When placed in an open field, mice receiving continuous morphine displayed increased psychomotor activity and developed psychomotor tolerance, meaning they decreased their distance traveled from day 1 to day 6. But in mice that received naloxone interruptions of morphine exposure, that tolerance was reversed. The authors then made electrophysiological measurements from *ex vivo* slices containing NAc MSNs. The intrinsic excitability of MSNs was not changed by morphine exposure, but when the researchers measured spontaneous EPSCs (sEPSCs) from D_1 MSNs, they saw significantly higher-amplitude sEPSCs in neurons from mice that received morphine with intermittent naloxone compared to mice with continuous morphine. Experiments using paired-pulse ratios indicated an elevated glutamate release probability onto D_1 but not D_2 MSNs in all mice exposed to morphine. Measurement of spontaneous IPSCs (sIPSCs) suggested that continuous morphine augmented inhibitory signaling at D_1 MSNs, whereas interrupted morphine dampened inhibitory signals to D_2 MSNs. Remarkably, the results also showed sex-specific forms of inhibitory plasticity at D_1 MSNs with continuous morphine exposure that were absent in mice that received naloxone-mediated withdrawal. Together, the data reveal complex, sex-dependent neural adaptations in the mesolimbic system in response to varied patterns of opioid exposure. The authors conclude that maintaining continuous exposure to opioids without withdrawal could reduce vulnerability to opioid use disorder.

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