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SPECIAL ISSUE/PRECLINICAL ASSAYS

Pictures at an exhibition: A commentary on Benn & Robinson (2024)

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At its broadest level, attention is the ability to focus on and respond appropriately to specific features of the environment. Abnormalities in attention accompany and can even be cardinal features of numerous neuropsychiatric conditions, including attention-deficit/hyperactivity disorder, schizophrenia, depression, Lewy body dementias, and Alzheimer's disease. It has long been recognized that attention is not a unitary construct, but rather a collection of cognitive operations that can be dissociated in both the laboratory and the clinic. For example, attention requires perception (the ability to detect a stimulus), discriminative accuracy (the ability to discriminate among target and nontarget stimuli), inhibitory control (the ability to withhold responses to nontarget stimuli), and vigilance (the capacity to sustain all of these abilities over a defined period of time), which can be assessed and differentiated to varying degrees in humans using assays such as continuous performance and rapid serial visual presentation (RSVP) tasks (Kahn et al., 2012; Peters et al., 2012). Analogous tasks have been developed for rodents, such as the 5-choice serial reaction time task (5-CSRTT) and other analogues of continuous performance tasks (Robbins, 2002). These rodent tasks have been valuable for revealing neural mechanisms of attentional processes, as well as for testing novel pharmacotherapies for modulating attention. Each suffers from limitations, however, in that it can be challenging to differentiate between effects of pharmacological or other manipulations on the various components of attention.

In the current CABN Special Issue, Benn & Robinson (2024) describe a novel task for rodents—the rat-Rapid Serial Visual Presentation (rat-RSVP) task, which helps to address some of the limitations of previous tasks. This task models RSVP tasks used in humans, in which a sequence of images is presented rapidly on a video screen, and subjects must identify target images among numerous distractor images (Peters et al., 2012). On each trial in the rat-RSVP task, rats are presented with a sequence of six visual stimuli on a touch-sensitive video screen (each visible for 2–3 s), one of which is a target and the others are nontarget distractors. A touch on the target stimulus earns a food reward, whereas touches on nontarget stimuli are considered incorrect and result in a timeout period. Importantly, the order in which the images are presented in the sequence is randomized across the trials in each session, such that rats cannot predict when in a sequence the target image will appear. As such, sustained attention to the visual stimuli over the course of each trial is required for accurate performance. Under baseline conditions, rats performed well on the task, responding to the target stimulus on roughly 60% of the trials in each session. These correct responses varied considerably, however, depending on the ordinal position of the target stimulus. Performance was nearly perfect when the target was in the first or second position in the sequence, but it declined substantially when presented later in the sequence, which the authors suggest could reflect a decline in vigilance or sustained attention across the trial.

A distinct advantage of the use of touchscreens over traditional operant chambers for assessing rodent cognition is the near-limitless range of visual stimuli that can be employed. Benn & Robinson took full advantage of this feature in a variation of the rat-RSVP task in which they replaced one of the nontarget distractor stimuli (all of which were very distinct from the target stimulus) with a "false-alarm" stimulus, which shared

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some features with the target stimulus. Unsurprisingly, addition of the false-alarm stimulus reduced overall accuracy (due to an increase in the proportion of responses to the false alarm) but provides a measure of discriminative accuracy, which can be differentiated from other components of attention.

To determine the extent to which rat-RSVP performance is comparable to performance in other rodent attentional tests (as well as in human subjects), the authors evaluated effects of acute administration of several drugs known to affect attention in other tasks. Amphetamine produced an overall dose-dependent decrease in accuracy, with this reduction being most pronounced when the target stimulus was later in the sequence. Interestingly, there was also a small but significant amphetamine-induced increase in accuracy when the target was in the first position in the sequence, as well as a reduction in trial omissions (trials on which rats failed to respond to any of the stimuli). Although such improvements could reflect a selective enhancement in attention and/or vigilance, they were accompanied by greater overall propensity to respond to images earlier in the sequence (as reflected in shorter response latencies), suggesting that amphetamine's effects are better characterized by deficits in response inhibition (i.e., motor impulsivity). In contrast, acute administration of atomoxetine had effects that were nearly opposite those of amphetamine. These included an overall increase in accuracy (although this was accompanied by reduced accuracy when the target was in the first position in the sequence), an increase in omissions, and an increase in both correct response and overall response latencies. Atomoxetine also reduced the proportion of false-alarm responses, suggesting an improvement in discriminative accuracy.

The distinct effects of amphetamine and atomoxetine on different components of rat-RSVP performance are comparable to findings from previous work in other tasks (e.g., Baarendse & Vanderschuren, 2012) but extend this work in several important ways. Varying the ordinal position of the target in the rat-RSVP image sequence creates a wide parametric space in which both increases and decreases in response accuracy can be detected simultaneously and distinctly from other aspects of task performance (e.g., response latencies). In addition, the use of touchscreens enables assessment of discriminative accuracy in a manner that is at least partly dissociable from perception or target detection. As the authors acknowledge, however, their initial description of the rat-RSVP task leaves a number of unanswered questions. For example, it was unclear why methylphenidate did not affect rat-RSVP performance in their hands, as it has effects similar to amphetamine in other rodent attentional tasks. In addition, only male rats were used in the present study, and only a single stimulus set was evaluated. Finally, it may be useful in future work to compare directly the performance in the same animals in the rat-RSVP and other, more widely-used tasks such as the 5-CSRTT, to determine the extent to which the same constructs are being measured across tasks.

As described above, attentional dysfunction is prevalent across multiple neuropsychiatric disorders, and therapeutic options are limited and not appropriate for all patient populations. Translational behavioral assays are critical for the development of these needed therapies. Thus, it will be important in future work to determine whether the rat-RSVP task is sensitive to attentional impairments in rodent models of neuropsychiatric disorders. In addition, it will be important to determine whether attentional impairments in these models can be remediated by existing therapeutics (particularly nonstimulant medications used in conditions in which stimulants are counterindicated), as well as whether the efficacy of novel therapeutics can be accurately predicted. With the rat-RSVP task, Benn & Robison have provided a useful tool for future research focused on therapeutic development, which of course can also be leveraged to address fundamental questions concerning the neurobehavioral mechanisms of attention.

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