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A rodent model of the human psychomotor vigilance test: Performance comparisons

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HIGHLIGHTS

- Analogous to the human PVT, the rPVT is an effective task for preclinical studies.
- Describes the design and empirical validation of a novel PVT for use with rats.
- Results demonstrate effectiveness of the rodent PVT (rPVT) for assessing attention.
- Amphetamine increases while zolpidem decreases rPVT performances in rats.
- The rPVT is sensitive to radiation-induced deficits in attention.

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ABSTRACT

Background: The human Psychomotor Vigilance Test (PVT) is commonly utilized as an objective risk assessment tool to quantify fatigue and sustained attention in laboratory, clinical, and operational settings.
New method: Recent studies have employed a rodent version of the PVT (rPVT) to measure various aspects of attention (lapses in attention, reaction times) under varying experimental conditions.
Results: Data are presented here to evaluate the short- and long-term utility of the rPVT adapted for laboratory rats designed to track the same types of performance variables as the human PVT—i.e., motor speed, inhibitory control ("impulsivity"), and attention/inattention. Results indicate that the rPVT is readily learned by rats and requires less than two weeks of training to acquire the basic procedure. Additional data are also presented on the effects of radiation exposure on these performance measures that indicate the utility of the procedure for assessing changes in neurobehavioral function in rodents across their lifespans.
Comparison with existing method(s): Once stable performances are obtained, rats evidence a high degree of similarity to human performance measures, and include similarities in terms of lapses and reaction times, in addition to percent correct and premature responding. Similar to humans, rats display both a vigilance decrement across time on task and a response-stimulus interval effect.
Conclusions: The rPVT is a useful tool in the investigation of the effects of a wide range of variables on vigilance performance that compares favorably to the human PVT and for developing potential prophylactics, countermeasures, and treatments for neurobehavioral dysfunctions.

1. Introduction

The human psychomotor vigilance test (PVT) is a widely validated and broadly applied assay of vigilant attention and basic neurocognitive function. It is partly rooted in the simple reaction time (SRT) procedure that has a long history in human psychology, starting back in the German laboratory of Wilhelm Wundt in late 19th century, and continuing on into the early 20th century at the Columbia laboratory of Cattell (1947). The human PVT as originally developed by Dinges et al. (1987), Dinges and Powell (1985), Kribbs et al. (1993), however, differs substantially from typical SRT procedures in terms of its procedural emphasis on assessing reaction time stability as well as general performance stability

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(e.g., errors of commission and omission) across time within individual sessions. The modern PVT has been greatly refined over the years by Basner and Dinges (2011), Basner et al. (2011), Dinges et al. (1997), Drummond et al. (2005), Jewett et al. (1999), Lim and Dinges (2008a), Van Dongen and Dinges (2005), Van Dongen et al. (2001) as a human cognitive neurobehavioral assay for tracking temporally dynamic changes in sustained attention, and has been shown to be sensitive to sleep deprivation, fatigue, drug use, and age (Blatter et al., 2006; Lim and Dinges, 2008b). The PVT is a deceptively simple procedure that requires a subject to touch a screen when a stimulus (typically an LED counter) appears after 2–10 s, with the counter being incremented in milliseconds and stopped when the subject touches the screen, thus displaying to the subject his/her reaction time (RT) to the stimulus onset. The PVT reliably tracks fatigue-related decrements in vigilant attention as shown by a slowing in reaction time, an increase in "lapses" (errors of omission, typically defined as RTs > 500 ms), and an increase in errors of commission ("false starts", or premature responses prior to the stimulus onset); however, other additional measures, including the fastest 10% of RTs (Q-10), the slowest 10% of RTs (Q-90), median RTs (Q-50), and mean RTs, can be acquired with the PVT and have been used to investigate various parameters such as gender and age differences (for a review, see Basner and Dinges, 2011). Further, the PVT has been used in human risk assessment in a range of operational environments (e.g., the military, the aviation and railway industries, first responders) and also employed in extreme environments such as NASA's Extreme Environment Missions Operations (NEEMO), the international Mars500 Project (Basner et al., 2013), and on the International Space Station (ISS) where it is referred to as the "Reaction Self-Test" and provides astronauts with individualized performance feedback.

While SRT procedures have been used for decades in animal research to examine a variety of sensory and motor functions (see Moody, 1970), animal versions of the human PVT have only recently begun to appear. One of the earliest uses of a human SRT procedure adapted for animals was provided by Skinner (1946), who trained pigeons with a "ready" or alerting signal to indicate the subsequent occurrence of a "reaction time" stimulus. Short-latency responses to the reaction time stimulus were additionally differentially reinforced. With this procedure he was able to obtain latencies in the range of 200–300 ms (see Moody, 1970). Since that time, numerous versions of the SRT procedure have been used in a wide range of animal research which in general may be subdivided into "signaled" (containing an alerting or "ready" signal) and "unsignaled" (i.e., no alerting signal) RT procedures, with the latter types being in essence analogs of the human PVT. SRT's in rats, for example, typically consist of training rats to respond on a manipulandum (e.g., pressing a response lever with a paw, poking a lighted key with the nose, breaking a photo beam with the head) when a cue light is randomly illuminated, and to refrain from responding in the absence of the cue light (Baunez et al., 2001; Brown and Robbins, 1991; Domenger and Schwarting, 2006; Eckart et al., 2012; Li et al., 2010; Mayfield et al., 1993; Muir et al., 1996; Phillips and Brown, 1999; Pirch, 1980; Smith et al., 2010; Ward et al., 1998).

Despite the human PVT's decades of demonstrated utility and popularity, a direct rodent counterpart was first reported in the literature by Christie and colleagues who developed a version for rats and demonstrated that it tracks the same types of performance variables as the human PVT – e.g., general motor function and speed, premature responding and lapses in attention – and that it also is sensitive to decreased vigilance following sleep deprivation (Christie et al., 2008a, 2008b; for more recent versions of the rPVT, see also Deurveilher et al., 2015; Loomis et al., 2015; Oonk et al., 2015). While these reports have demonstrated the utility of the rPVT procedure in assessing the effects of sleep deprivation on sustained attention, the rats in many of these studies emitted large numbers of premature responses that frequently made up more than 40% of the total number of responses, which is quite unlike any typical human PVT performance. This difference may be due to the specific parameters employed in the human vs. the rodent PVT; for example, the Christie et al. version of the rPVT used a variable 3–7 s foreperiod, compared to a human PVT that typically uses a 2–10 s foreperiod (although there is a 3-min version of the human PVT that uses a 1–4 s foreperiod; see Basner et al., 2011). Such relatively short variable foreperiod values may have promoted the increased numbers of premature responses reported in many of these rodent rPVT studies.

The version of the rPVT described in the current study improves upon the previously-published rPVT by training rats to a greater level of behavioral control by (1) the use of variable foreperiod values between 3 and 10 s that more closely mimic the values used in the human PVT (i.e., 2–10 s); (2) the use of a short response window following stimulus onset (referred to below as the limited hold; 1.5 s in the present study compared to 3.0 s in the previous studies); (3) the demonstration of predictable changes in performance metrics that parallel those seen in humans when examining the vigilance decrement (Lim et al., 2010); (4) demonstration of changes similar to the variable response-stimulus interval (RSI) effect seen in the human PVT (Tucker et al., 2009) within the 3–10 variable foreperiod; and (5) the dissociation of these latter two metrics as previously reported for the human PVT (Tucker et al., 2009). As an additional step in validating the rPVT as a rodent model for assessing neurobehavioral function, the present study provides normative animal performance data using the rPVT as well as further demonstrations of the sensitivity of the rPVT to the long-term effects of radiation exposure on the CNS, to the effects of acute drug injections, and to circadian disruptions.

2. Methods

2.1. Subjects and apparatus

Over the last six years, approximately 500 rats have been trained on the rPVT procedure in the laboratory. For the present report, data are presented for 122 male Long-Evans rats exposed to an automated training program that gradually shaped each rat's behavior until the final rPVT performance was established. Data are also reported for 5 previously trained female Long-Evans rats for general performance comparisons between males and females. All rats were acquired at approximately 12 weeks of age, and were housed individually under a 12:12 h light/dark cycle (lights on at 0600 h) with continuous access to water and with food freely available. Animals were allowed to free-feed until their weights approximated the 340 to 350 g range (235–250 g for females) at which body weights were maintained for the following behavioral studies (Ator, 1991). Under the rPVT procedure, rats earned food (45-mg Noyes Precision rat pellets) during the experimental sessions, and were supplemented with commercial laboratory rat chow after the sessions to maintain their weight. When sessions were not conducted, the rats were fed 10–20 g of the rat chow, which resulted in weight stability or weight gain on the day the rats were next weighed. Extra food was also provided on weekends, or when no experimental sessions occurred. All rats were run at the same time of day by use of identically constructed experimental chambers (Med Associates®). The front wall of each chamber contained 1 back-illuminated nose-poke response key on the left, an overhead house light, and a food cup on the center for delivery of food pellets. All chambers were enclosed in sound-attenuating chambers equipped with an exhaust fan. Experimental contingencies were controlled by MedPC behavioral control programs running on PCs; the programs recorded all data on a trial-by-trial basis to provide for a wide range of subsequent analyses.