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Animal models relevant to digital technology-based disorders

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COMMENTARY

ABSTRACT

Animal models utilizing Pavlovian and instrumental conditioning paradigms have advanced our understanding of the mechanisms underlying drug addiction and certain behavioral addiction such as gambling disorder, but so far there is no animal model for digital technology-based disorders such as (Internet) gaming disorder, which is an emerging issue in our digital society. Casile et al. (2025) introduced a rat touchscreen paradigm recapitulating several key phenotypes relevant to gaming disorder, including preoccupation with the touchscreen and behavioral persistence despite non-reinforcement. However, the paradigm's reliance on food reinforcers limits translational relevance. We suggest integrating Casile et al. touchscreen paradigm with *non*-food operant paradigms (e.g., light self-administration), to dissociate any intrinsic reinforcing effects of touchscreen interaction and response-contingent sensory feedback from hedonic values of food. Potential differences in sensory habituation between rats and mice highlight the need for cross-species comparisons, to distinguish species-specific responses from general behavioral mechanisms in non-human animals and humans. While animal models cannot fully capture the multifaceted nature of digital technology-based disorders, they provide simplified models to examine how behavioral persistence can be shaped and maintained by non-food, non-drug reinforcement contingencies without the influence of cultural and social factors.

KEYWORDS

gaming disorder, digital devices, light, instrumental conditioning, rats, mice

INTRODUCTION

In recent years, the widespread use of digital technologies such as online games, social media, and streaming platforms has raised growing concerns about their possible negative effects on mental health, especially when their use becomes excessive or resembles addictive behavior. While the addictive nature of excessive and problematic use in the domain of digital technologies remains debated, (Internet) gaming disorder has been included into the manuals for psychiatric disorders in the *DSM-5* (included as "condition requiring further study"; American Psychiatric Association, 2022) and *ICD-11* (World Health Organization, 2021). Some of the diagnostic criteria for gaming disorder, including impaired control over gaming, preoccupation with gaming, and continuation and escalation of gaming despite negative consequences, overlap with the criteria for substance-related addictive disorders (Brand et al., 2025; Darvesh et al., 2020). The etiology of gaming disorder is multifaceted, reflecting the contributions of environmental factors, game features, and individual vulnerabilities including comorbid psychiatric conditions (Brand et al., 2025; Király, Koncz, Griffiths, & Demetrovics, 2023).

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Over the past decades, substance addictions (or substance use disorders) have been reconceptualized as chronic disorders of the brain (Koob & Volkow, 2016). This shift in understanding was largely driven by findings from animal models and translational neuroimaging studies, showing that the progression from voluntary substance use to compulsive addiction involves neuroplastic adaptations brain circuits responsible for motivation, reward, and habit formation (Everitt & Robbins, 2016; Zhou et al., 2019). A plethora of preclinical studies, primarily in laboratory rodents, investigated the mechanisms of addictive behavior related to drug use utilizing Pavlovian (classical) and instrumental (operant) conditioning paradigms (Everitt & Robbins, 2016; Kuhn, Kalivas, & Bobadilla, 2019; Müller, 2018; Spanagel, 2017). Unlike for drug addiction, however, animal models for digital technology-based disorders are lacking (Marraudino, Bonaldo, Vitiello, Bergui, & Panzica, 2022), leading to continuing debates about the neurobiological commonalities and differences between substance addiction and digital technology-based disorders (Montag, Marciano, Schulz, & Becker, 2023).

Experimental models with clearly defined (primary or conditioned) reinforcers and reinforcement schedules are needed to understand the general mechanisms underlying different types of behavioral addiction (James & Tunney, 2017; Tunney & James, 2017). Various food-based operant paradigms have been developed in rats (Kim, Cho, Kwak, & Kim, 2017; Rivalan, Ahmed, & Dellu-Hagedorn, 2009; Setlow, Blaes, Burns, Dragone, & Orsini, 2020; Zeeb, Robbins, & Winstanley, 2009) and pigeons (Zentall, 2023), to model suboptimal (impulsive) behavioral choice related to gambling disorder. But so far there is no established animal model for digital technology-based disorders including gaming disorder, which represents an impasse in the field (Marraudino et al., 2022; Montag & Becker, 2023). Although it is often suggested that digital environments function as virtual Skinner boxes delivering (excessive) variable-scheduled rewards to users (Lembke, 2021; Lindström, 2021; Young et al., 2026), animal operant conditioning models related to digital technology-based disorders remain largely unexplored (apart from Augusti Lignier's *Selfie Rats* 2021; Anthes, 2024). This is partly because virtual rewards in digital environments, such as gratification of entertainment (Montag, Yang, & Elhai, 2021) and social validation (Lindström et al., 2021), cannot be easily operationalized in animal operant studies (see Tam, Stryjska, Gu, & Becker, 2025, Tam, Xiao, Cheng, Kwok, & Becker, 2026 for a discussion on the limited range of non-food, non-drug reinforcers in rodents). Although animal models cannot fully capture the complexity of digital technology-based disorders (Brand et al., 2025; Király et al., 2023), they provide experimental paradigms to examine how behavioral persistence can be shaped and maintained by environmental contingencies (Ferster & Skinner, 1957) without the influence of cultural and social factors (Zentall, 2023). In this regard, the timely study by Casile et al. (2025) represents one of the first detailed investigations in which rats were trained to interact with a touchscreen device in an operant chamber, showing behavioral phenotypes potentially relevant to gaming disorder (see also Casile, 2025; Casile et al., 2024, 2026).

Here we describe the touchscreen paradigm developed by Casile et al. (2025). We then summarize the key phenotypes reported in their study and discuss a potential alternative mechanism underlying persistent touchscreen responding in rats, before considering the major limitation of their paradigm. Finally, we suggest how this food-based touchscreen paradigm can be integrated with non-food operant paradigms (Tam et al. 2025, 2026) to improve translational relevance to gaming disorder.

1. CASILE ET AL. (2025) TOUCHSCREEN PARADIGM

In Casile et al. (2025), a touchscreen (screen brightness not specified) was used as the operandum in the chamber, and the task involved interacting with a white circle presented on a black background on the touchscreen. Touching the white circle triggered delivery of a drop of strawberry yogurt. Rats were *not* food- or water-restricted in the study, so that responding was not primarily driven by caloric hunger or thirst but could be due to the palatability of the food reinforcer (see section 4. **A Major Limitation of the Touchscreen Paradigm** below). In the "gaming disorder" (GD) groups, rats of both sexes were trained for 5 weeks under fixed-ratio schedules (FR1, FR2, and FR3) and random-ratio schedules (RR not specified) in the touchscreen chamber, whereas control groups were *not* given any training. The training phase was followed by a series of short probe trials (each lasted for 10 min), in which GD and control rats were given a concurrent choice between the touchscreen *versus* another stimulus (**Test 2:** *a running wheel*; **Test 3:** *an opposite-sex conspecific*; and **Test 4:** *a same-sex conspecific*). These other stimuli could be accessed *via* a small opening located on the opposite wall (their **Figures 2B** and **2D**; Casile et al., 2025). On probe trials, touchscreen responding was reinforced under RR. As anticipated, GD rats explored and interacted with the touchscreen (i.e. engaged with "the game") more than control rats, confirming the acquisition of instrumental contingency between touching the white circle on the screen and delivery of the food reinforcer.

2. PHENOTYPES POTENTIALLY RELEVANT TO GAMING DISORDER

Various aspects of their study are relevant to the understanding of the general mechanisms underlying gaming disorder; here we highlight three key findings from their study:

(a) *Preoccupation with the touchscreen.* The first key behavioral finding is based on probe sessions **Tests 3** and **4**, where animals were given a concurrent choice

between the touchscreen *versus* a conspecific of the opposite sex. On these probe trials, control rats spent all their exploration time interacting with the conspecific, showing no interest in the touchscreen. In contrast to the behavior of control rats, GD female rats exhibited a preference for (i.e. spending more than half of the exploration time with) the touchscreen over the conspecific, as indicated by the dark blue bar *versus* orange bar in their **Figures 5F** and **6E** (Casile et al., 2025). GD females exhibited a stronger preference for the touchscreen over the opposite-sex conspecific than GD males (Casile et al., 2025); this could be partly due to the limited reinforcing value of male conspecifics in female mice (Matthews, Abdelbaky, & Pfaff, 2005). In a follow-up study reported elsewhere (Casile, 2025; Casile et al., 2024), GD male rats' preference for the touchscreen over the conspecific was attenuated by systemic administration of selective serotonin reuptake inhibitor fluoxetine (at doses of 2.5 and 5 mg/kg)—an antidepressant that can reduce compulsive behavior in certain clinical populations (e.g., Issari, Jakubovski, Bartley, Pittenger, & Bloch, 2016; Kotapati et al., 2019; Reddihough et al., 2019). Together, in Casile et al. touchscreen paradigm GD rats' behavioral choice resembles a key phenotype in gaming disorder, namely preoccupation with the touchscreen over other concurrent choices (e.g., Darvesh et al., 2020). This may mirror the symptoms of preoccupation with gaming and increasing priority of gaming over other activities that are at the core of the diagnosis of the human condition (American Psychiatric Association, 2022; World Health Organization, 2021).

(b) *Continuation or escalation of responding despite the lack of positive consequences.* Another key behavioral finding from Casile et al. (2025) comes from their final probe session (**Test 5**), in which the white circle was presented on the touchscreen but responding was not rewarded; no concurrent choice was presented in the chamber. In the extinction session, GD rats of both sexes showed persistent and heightened operant responding to the white circle on the touchscreen relative to responding in the reinforced session (their **Figure 7F**; Casile et al., 2025). The persistence of touchscreen responding after cessation of reinforcement corresponds to another key behavioral phenotype in gaming disorder (e.g., Darvesh et al., 2020) and may mirror the transition toward compulsive behavior (Robbins, Banca, & Belin, 2024).

(c) *Brain regions involved in the touchscreen task.* To examine brain activity patterns after task engagement, Casile et al. (2025) examined cFos levels (a commonly used molecular marker of neuronal activity) in different brain regions (their **Figure 8** and **Supplementary Table 3**). In GD male and female rats, cFos levels were consistently upregulated in the orbitofrontal cortex (OFC), prelimbic cortex (PrL), central nucleus of the amygdala (CeA), and basolateral amygdala (BLA); whereas cFos was consistently downregulated in the ventral tegmental area (VTA). These brain regions contribute to reward-related processing, and neuroplastic changes in these circuits have been associated with the development and maintenance of substance addiction (Koob & Volkow, 2016). In other brain regions that are also involved in these processes, such as the nucleus accumbens (NAc), dorsal striatum, bed nucleus of the stria terminalis (BNST), and ventral hippocampus, neuronal activity showed sexually dimorphic patterns after task engagement**:** cFos levels were upregulated in GD male rats but downregulated in GD female rats. Although it is not straightforward to relate the sex difference in brain cFos patterns (GD ♂ > GD ♀) directly to response levels (GD ♂ < GD ♀), the paradigm may nonetheless provide a promising approach for exploring sexually dimorphic brain responses during interaction with touchscreen devices.

3. A POTENTIAL ALTERNATIVE MECHANISM UNDERLYING PERSISTENT RESPONDING

The increase in touchscreen responding during the 10-min extinction test in Casile et al. (2025) could be partly driven by *frustrative non-reward* (FNR; Amsel, 1958; Papini et al., 2024)—a general response to any mismatch between the animal's reward expectation and the actual outcome delivered. In standard extinction procedures, when food reward expectation is violated during initial non-reinforcement, rodents begin to emit longer lever presses interspersed with the typical shorter presses; these longer presses dissipate rapidly once the reward is reintroduced. This behavioral pattern can be revealed by examining within-session changes in response-duration (i.e. holding) variability (Papini et al., 2024). FNR is well documented in food-based operant tasks in laboratory rodents (see Amsel, 1958; Papini et al., 2024, for historical and recent reviews, respectively). A similar response has also been reported in a touchscreen task in macaques, where pictorial stimuli and short movie clips served as sensory reinforcers (Blatter & Schultz, 2006). In this study, after animals acquired the contingency between touchscreen responding and visual cue delivery, shortening of visual cue duration (16, 8, or 4 s) led to an increase rather than a decrease in touchscreen responding (Blatter & Schultz, 2006). This FNR-*like* effect could be due to a negative contrast between the animal's expectation and the actual sensory reinforcer delivered (cf. Papini et al., 2024). Therefore, FNR may have contributed to the increase in touchscreen responding during the brief extinction session in Casile et al. (2025), although it remains to be determined how long such an effect would persist under prolonged non-reinforcement.

4. A MAJOR LIMITATION OF THE TOUCHSCREEN PARADIGM

Although rats in Casile et al. (2025) exhibited phenotypes relevant to gaming disorder, the major factor limiting the

paradigm's translational relevance is the reliance on food reinforcement. Rats in Casile et al. (2025) were fed *ad libitum*; however, touchscreen responding may have been maintained by the palatability of the food reinforcer (e.g., the sweetness of the strawberry yogurt), even in the absence of hunger or thirst (cf. Berridge, 1991). Accordingly, responding may be driven by the following factor(s):

(a) the hedonic value of the food reward, whereby the white circle (signaling the occasion for food delivery) acquires incentive salience and promotes sign-tracking behavior (Robinson, Robinson, & Berridge, 2013; Robinson & Flagel, 2009);
(b) the intrinsic rewarding effects of touchscreen interaction and associated sensory feedback (e.g., disappearance of the white circle; activation of the liquid dispenser pump), which may function as reinforcers (see Egelkamp & Ross, 2019, pp. 228–229, for a review on the reinforcing value of touchscreen in non-human primates).

Regarding (***b***), Casile et al. (2025) included control rats that did not receive any training with food; however, these animals had *less* exposure to the chamber than GD rats, meaning that experience with the touchscreen device was not equated between groups before the test phase. Without further evidence to confirm (***b***), available evidence can only suggest that the touchscreen paradigm in Casile et al. (2024, 2025) is *not* fundamentally different from other established (and procedurally more complex) food-based operant paradigms (some of which are used for studying neuropsychiatric disorders other than addiction). This includes the Bussey–Saksida touchscreen paradigm, in which animals are maintained at ≥85% of their free-feeding weight and visual discrimination on the touchscreen is motivated by food palatability in addition to caloric hunger (Bussey et al., 2012; Horner et al., 2013; Palmer et al., 2021; Piantadosi et al., 2025). In fact, the touchscreen paradigm described in Casile et al. (2025) is procedurally similar to the pretraining phase of the Bussey–Saksida touchscreen paradigm (see e.g., Horner et al., 2013, p. 1967). This highlights the need to integrate touchscreen paradigms with other operant paradigms that utilize *non*-food reinforcers.

5. INTEGRATING THE TOUCHSCREEN PARADIGM WITH NON-FOOD PARADIGMS

In line with the effort by Casile et al. (2025), we have recently proposed the light self-administration paradigm as a translational model for digital technology-based disorders involving LED displays (such as gaming disorder), as (colored) light possesses reinforcing values in humans (Holte, Giesen, & Ferraro, 2023; Holte & Ferraro, 2020) and rodents (Tam et al., 2025). In our recent study (Tam et al., 2026), we have confirmed that a response-contingent (green) light cue delivered under FR, but not non-contingent light delivery, can establish persistent responding in mice. Among high-responding mice, light preexposure produces only a modest response reduction, indicating that light seeking cannot be easily "satiated" despite preexposure equivalent to hundreds of light-cue presentations. In contrast to the mouse *operant sensation seeking* paradigm where sensory reinforcement comprises a compound cue with sound and light of *varying* duration, flickering frequency, and spatial position (Olsen & Winder, 2009), light self-administration is not driven by novelty, uncertainty, or other non-specific cues (Tam et al., 2026). This is because the light stimulus remains invariant across trials, with both the timing and duration of the stimulus strictly controlled by the experimenter.

To dissociate the potential reinforcing value of touchscreen interaction and response-contingent sensory feedback from the hedonic value of food in Casile et al. (2025) paradigm, we suggest incorporating at least two *non*-food conditions into the experimental design; these are summarized in Fig. 1. First, a *no*-reinforcer condition can be

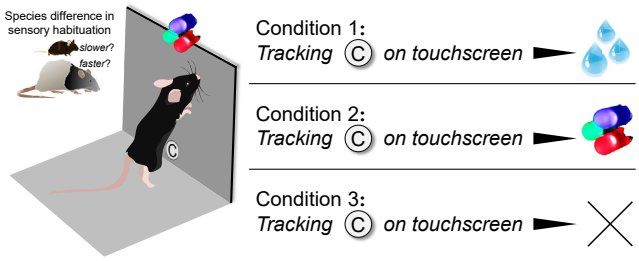

Fig. 1. Integrating rodent paradigms relevant to gaming disorder: An example

Condition 1 represents the training procedure in the GD ("gaming disorder") group in Castile et al. (2025), where tracking the visual cue (C) on the touchscreen is reinforced by a food reward (e.g., strawberry yoghurt) under fixed-ratio (FR) and random-ratio (RR) schedules. Although their GD rats were fed *ad libitum* in home cages, touchscreen responding could be motivated by food palatability (even when animals were not hungry or thirsty). To dissociate the contribution of food-motivated responding, two *non*-food conditions can be incorporated into their experimental design. In **Condition 2**, touchscreen interaction is reinforced by light reinforcers, based on our empirical results that response-contingent green light can be an effective primary reinforcer, just like food, to establish and potentiate persistent responding in mice (Tam et al., 2026). A *no*-reinforcer condition (**Condition 3**) can also be included, as touchscreen interaction and associated sensory feedback may be intrinsically rewarding (cf. Egelkamp & Ross, 2019). Note that **Condition 3** is not the same as the control groups in Castile et al. (2025): their control rats did not receive any training in the touchscreen chamber before the test phase, whereas their GD rats received five weeks of training in the touchscreen chamber. Future studies may also benefit from species comparisons using equivalent procedures, as available findings suggest that rats and mice habituate to sensory reinforcers at different rates (Glow & Russell, 1973; Lloyd et al., 2014; Tam et al., 2026). Illustrations of rodents (*left*) and reward water drops (*top right*) are obtained and adapted from SciDraw repository: doi.org/10.5281/zenodo.10940481; doi.org/10.5281/zenodo.3925935; doi.org/10.5281/zenodo.3925993; and doi.org/10.5281/zenodo.3926077

included to examine whether non-reinforced touchscreen training is sufficient to establish persistent responding (see Egelkamp & Ross, 2019, pp. 228–229, for a review on the reinforcing value of touchscreen devices in non-human primates). Second, a *light*-reinforcer condition can be added, based on our findings that response-contingent light delivered under fixed-interval schedules (FI) and FR can establish persistent responding (Tam, 2024; Tam et al., 2026). This allows us to examine whether touchscreen interaction (which may be intrinsically rewarding) can be potentiated by a sensory reinforcer. Comparing these *non*-food conditions to the existing food-reinforcer condition in Casile et al. (2025) can clarify the contribution of food-motivated responding in the touchscreen paradigm.

6. CONSIDERING SPECIES DIFFERENCES

Future studies may also benefit from cross-species comparisons (Fig. 1), as available evidence suggests potential differences in how rats (e.g., Wistar, Sprague–Dawley) and mice (e.g., C57BL/6) respond to sensory reinforcers. When response-contingent light is used, rats show a rapid within-session decline in operant responding (Lloyd, Medina, Hawk, Fosco, & Richards, 2014) and no improvement across training sessions (Glow & Russell, 1973)—a pattern that has been interpreted as reflecting rapid habituation to light under FR1 (Lloyd et al., 2014). By contrast, mice exhibit a gradual increase in responding across FR1 training sessions (Tam et al., 2026), suggesting that the rate of habituation to sensory reinforcers may differ between rats and mice. Although these findings come from separate studies, they nonetheless suggest potential species differences in sensory habituation processes that may influence the strength and persistence of the acquired behavior. A cross-species approach is therefore needed to validate the integrated non-food paradigms in non-human animals and human subjects. This is important for distinguishing species-specific responses (cf. Bolles & McGillis, 1968) from general behavioral mechanisms across species.

SUMMARY AND CONCLUSIONS

The touchscreen paradigm (section 1) developed by Casile et al. (2025) represents an important step in revealing behavioral phenotypes in rats that are relevant to gaming disorder (section 2), but the reliance on food reinforcers limits translational relevance (section 4). By incorporating *non*-food conditions into the touchscreen paradigm, future work can dissociate potential reinforcing values of touchscreen interaction and response-contingent sensory feedback from the hedonic value of food in rats and mice (section 5), which may show differences in sensory reinforcer habituation (section 6). In addition to the commonly used response rate measure in operant studies, response durations (i.e. holding times) and their variability can be examined to reveal behavioral persistence (e.g., FNR-*like* effects) in the touchscreen paradigm (section 3). While animal models cannot fully capture the multifaceted nature of digital technology-based disorders (Brand et al., 2025; Király et al., 2023), they provide simplified models to examine how brain reward circuits and behavioral persistence can be shaped by non-food, non-drug reinforcement contingencies without the influence of cultural and social factors (Zentall, 2023). Finally, the effectiveness of novel pharmacological agents (e.g., Soler-Cedeno et al., 2025) and non-pharmacological interventions to alleviate symptoms of (behavioral) addiction (e.g., Li et al., 2026) can be evaluated in animal models before being translated into human studies.

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