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Research paper

The subjective value of probabilistic outcomes: Impact of reward magnitude on choice with uncertain rewards in rats

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HIGHLIGHTS

- We assessed gambling proneness in rats using the "Probabilistic Delivery Task" (PDT).
- We investigated the role of rewards magnitude (threefold vs fivefold ratio).
- We found increased gambling-like behaviour with increasing size ratio.
- A five-folded ratio was not only more attractive but also less frustrating.
- A gambling profile is more effectively induced by marked contrast between rewards.

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ABSTRACT

Interest is rising for animal modelling of Gambling disorder (GD), which is rapidly emerging as a mental health concern. In the present study, we assessed gambling proneness in male Wistar-Han rats using the "Probabilistic Delivery Task" (PDT). This operant protocol is based on choice between either certain, small amounts of food (SS) or larger amounts of food (LLL) delivered (or not) depending on a given (and progressively decreasing) probability. Here, we manipulated the ratio between large and small reward size to assess the impact of different magnitudes on rats' performance. Specifically, we drew a comparison between threefold (2 *vs* 6 pellets) and fivefold (1 *vs* 5 pellets) sizes. As a consequence, the "indifferent point" (IP, at which either choice is mathematically equivalent in terms of total foraging) was at 33% and 20% probability of delivery, respectively. Animals tested with the sharper contrast (*i.e.* fivefold ratio) exhibited sustained preference for LLL far beyond the IP, despite high uncertainty and low payoff, which rendered LLL a sub-optimal option. By contrast, animals facing a slighter contrast (*i.e.* threefold ratio) were increasingly disturbed by progressive rarefaction of rewards, as expressed by enhanced inadequate nose-poking: this was in accordance with their prompt shift in preference to SS, already shown around the IP. In conclusion, a five-folded LLL-to-SS ratio was not only more attractive, but also less frustrating than a three-folded one. Thus, a profile of gambling proneness in the PDT is more effectively induced by marked contrast between alternative options.

1. Introduction

In view of the growing prevalence of gambling disorder (GD), its serious mental and social consequences, and the still preliminary nature of its treatment, it is urgent to employ diverse approaches and methods to further deepen our comprehension of the neuronal and psychological underpinnings of this behavioural disorder. Interest is therefore rising for animal modelling of GD, as evidence derived from non-human subjects can inform the research on human (pathological) gambling in several ways (for a review, see Ref. [25]).

In animal models, many operant paradigms have been developed to study tolerance to uncertainty and/or gambling proneness, such as the "Iowa Gambling Task" (IGT; *e.g.* [35]), the "Probabilistic Delivery Task" (PDT; [4]), the "Risky Decision-Making Task" (RDT; [33]), and the "rodent Slot Machine Task" (rSMT; [36]). Gambling-prone subjects are detected by suboptimal preferences and poor decisions taken under conditions of uncertainty.

In the PDT, rats initially learn to discriminate and consequently to prefer nose-poking for a large over a small food reward. Subsequently, the probability of occurrence of large reward-delivery decreases progressively to very low levels ([23]). Final sessions

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with very high uncertainty levels (in which choice for large reward is mathematically suboptimal) represent the real "gambling" part of the experiment ([6]). Thus, to maximize their payoff, subjects should be flexible enough to refrain from their previously developed large-reward preference. Optimal performance is consequently expressed by a choice-shift towards a small reward; this requires a self-control effort in order to overcome the "innate drive" that is justified by the attractiveness of a large, yet probabilistic reward. By contrast, a sustained preference for a highly uncertain reward, in spite of this one becoming a suboptimal, disadvantageous option (in terms of total foraging) denotes temptation to gamble ([2,3,5,19]).

Obviously, when performed on animals, these paradigms involve real, ethologically relevant rewards (like food). To be effective, the contrast between alternative rewards (*i.e.* amount of food delivered with the large *vs* the small option) cannot be as marked as it would be desired to mimic thousandfold prizes common in human gambling behaviour. In fact, when these tasks are performed on animals, the large reward's magnitude shall be accurately calibrated, in order to enable them to discriminate between rewards and to prevent them from eating to satiety during the task. Nevertheless, in the framework of probability discounting, the rewards' magnitude still remains a relevant, though often disregarded, issue that can potentially affect the profile of gambling proneness ([34]). On the contrary, the issue of amount-dependent temporal discounting (the so called "magnitude effect") has been extensively investigated in both humans and animals ([1,13,15,16,24,27]).

In a previous study, we have already shown that the session length, which in turn affects and limits the maximum number of trials each subject can perform within a single session, is a crucial temporal constraint in the PDT, whose duration should be carefully evaluated, with a full awareness of its influence on subjects' performances ([37]). Specifically, we found that, by providing a lower number of gambling opportunities, it was possible to induce in rats a more marked profile of gambling proneness.

Given the above considerations, we specifically test and discuss in the present work the impact of reward magnitude differences, to ascertain if rats' gambling proneness in the PDT was affected. As for the different magnitudes, we drew a comparison between a threefold and a fivefold reward size. Our expectations were based on the notion that the mesolimbic dopamine system is more strongly activated under condition of uncertainty when differences between rewards are large than when they are small ([14]), thus weakening the influence of the cognitive control system ([22]). Therefore, we predicted that, in the "gambling" part of the PDT, rats would choose more likely from the large, uncertain hole as the contrast between the two alternative rewards become sharper (*i.e.* from threefold to fivefold).

2. Materials and methods

Twenty-four adult (mean bodyweight 320.61 g) Wistar-Han male rats (Charles River, France) were used in total for this study. For housing conditions, see Supplementary Data. All experimental procedures were approved by Institutional Animal Survey Board on behalf of the Italian Ministry of Health (licence to GL). Procedures were in close agreement with the European Communities Council Directive (2010/63/EU).

2.1. Experimental procedure and protocol

The testing apparatus consisted of operant walls from PRS Italia placed in polycarbonate cages (same size as the home-cage) with sawdust bedding. These experimental cages were placed in the animal facility room, close to subjects' home-cages. For additional information on the apparatus, see Supplementary data.

After 10 days of habituation to the housing conditions and handling by the experimenters, rats were daily tested, seven days a week, during the dark phase of their light-dark cycle (between 10.00 a.m. and 16.00 p.m.), with sessions always starting at the same hour. Five subjects were tested at the same time for a total of five runs. After each daily 25-min session, rats were returned to their home-cage. For details on food-restriction schedule, see Supplementary data.

2.1.1. Training

During the training phase (6 days), nose-poking in one of the two holes resulted in the delivery of the "Small & Sure" reward (SS: 1 or 2 pellets, depending on the configuration), whereas nose-poking in the other hole resulted in the delivery of the "Large & Luck-Linked" reward (LLL: 5 or 6 pellets, depending on the configuration). For half of the animals (N = 12), contrast between the two rewards was relatively slight (*i.e.* threefold; "2 *vs* 6" pellets configuration). For the other half (N = 12), contrast between rewards was sharper (*i.e.* fivefold; "1 *vs* 5" pellets configuration). Within each housing pair, rats were randomly assigned to either configuration.

2.1.2. Testing

The training sessions allowed most subjects to reach a significant preference for the large reward. During the testing phase (13 days), a probabilistic dimension was associated with the delivery of the large reward, which was randomly omitted ("unlucky event"), according to a given level of probability ("p" = percentage of lucky events: actual food delivery over total LLL demands). The probability level was kept fixed for each daily session, and was decreased progressively over days to very low levels. The small-reward delivery was always unchanged ("p" = 100%).

A landmark in the PDT protocol is the "indifferent point" (IP), that is, the specific level of uncertainty at which the animals can choose either option with no effect on the overall economic convenience. Since the ratio between large and small reward size was either threefold or fivefold, the IP was at "p" = 33% for the "2 *vs* 6" pellets configuration and at "p" = 20% for the "1 *vs* 5" pellets configuration. We initially imposed a range of "p" values before the IP (100%, 84%, 66%, 50%) when LLL was always the optimal choice. Rats were then tested far beyond the IP (17%, 14%, 11%, 9%; *i.e.* the final "gambling" part) when LLL became a sub-optimal option and the economic benefit was attained unequivocally by choosing repeatedly the SS option.

2.2. Analysis of behavioural data

As a measure of gambling proneness, the dependent variables were (i) the choice preference (%) for the LLL reward over total choices expressed and (ii) the steepness of the corresponding curve. As a general measure of motor impulsivity ([30,31,38]), the dependent variable was the total number (towards either the SS or the LLL hole) of inadequate nose-pokes per trial (*i.e.* nose-pokes performed during the 15-s timeout interval, TO, which were recorded but were without any scheduled consequence).

2.2.1. Experienced "odds"

Odds are defined as the mean number of omitted large-reward deliveries ("unlucky" events) before a successful delivery. The relation between "p" level and odds value is mathematical: $\mathbf{odds = (1/p) - 1}$ or $\mathbf{p = 1/(odds + 1)}$. The protocol employed a fully probabilistic generation of reward delivery *vs* omission, thus resulting in a totally random sequence of "lucky" *vs* "unlucky" trials. Therefore, a discrepancy likely appears (due to the stochastic fluctuations)