The free-exploratory paradigm as a model of trait anxiety in rats: Test–retest reliability

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ABSTRACT

The free exploratory paradigm has been proposed as a model of trait anxiety. By definition, trait anxiety does not vary from moment to moment, therefore any model used to evaluate it needs to give the same results in sequential trials. With this in mind, the test–retest reliability of the free-exploratory paradigm in rats was evaluated. The behaviour of drug-naive, adult, male, Wistar rats was measured in the free-exploratory apparatus on two occasions, either one week apart (Experiment I) or four weeks apart (Experiment II). The following parameters were evaluated: percentage of time spent in the novel compartment of the free exploratory box; percentage of novel compartment units visited; percentage of time rearing in the novel compartment; and attempts to enter the novel compartment. Subsequently, the intraclass correlation coefficient (ICC) and the kappa index (κ) were calculated for each of these parameters. The "percentage of time spent in the novel compartment" was found to be stable over time. Analysis of this parameter in Experiment I showed high values of ICC (0.805) and κ (0.716), indicating good reliability with a one-week inter-trial interval. In Experiment II, although the same parameter's kappa index (0.255) failed to show a reasonable test/retest concordance, the ICC value (0.760) still demonstrated a good test/retest correlation, suggesting that with a four-week inter-trial interval, the reliability may diminish, but still exists. Therefore, our results bring further support to the free-exploratory paradigm as an animal model of trait anxiety.

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1. Introduction

In the field of anxiety research, animal models have mainly been used for two purposes: 1) for the pre-clinical evaluation of new drugs with a potential anxiolytic effect, and; 2) for the study of mechanisms underlying emotional behaviour [1–3]. There are currently a number of animal models of anxiety [4], however they may not all measure the same psychophysiological state, as anxiety is not a unitary phenomenon [5], something evidenced by the heterogeneity of anxiety disorders (DSM-IV-R). There is also an important distinction to be made between trait and state anxiety. State anxiety is the anxiety a subject experiences at a particular moment in time, it is transitory and may be influenced by external stimuli; whereas trait anxiety is considered to be an enduring feature of an individual and is relatively stable over time [4,6].

Most animal models of anxiety confront the animals with an anxiety provoking situation, either through anxiogenic chemicals (β-carbolines, yohimbine, caffeine), conflict tests (Geller and Seifter box, light/dark chamber, elevated plus-maze) or exposure to aversive stimuli (defensive burying; [3], thus modelling state anxiety. While this approach is practical and convenient, it must be remembered that a drug that is effective in these animal models, and which may therefore reduce state

anxiety in humans in threatening situations, might not be effective in reducing long-term anxiety in chronically anxious patients. Furthermore, the underlying biological mechanisms of state and trait anxiety may not be the same [4].

Recently, the free exploratory paradigm has been proposed as a model of trait anxiety [7]. In this situation, animals are given the opportunity to move around freely within an environment containing both familiar and novel parts. This approach allows the evaluation of neophobic responses. As the animals have a choice between novelty and familiarity, it is expected that individuals with low trait anxiety would exhibit a preference for novelty, whereas high trait anxiety subjects would prefer familiarity. This free choice paradigm was first described by Hughes [8,9], who observed that Wistar rats actually preferred the novel environment, spending more time in it. Subsequently, Griebel and collaborators [7], comparing two strains of mice, BALB/c and C57BL/6, known respectively as "emotional" and "non-emotional", observed that BALB/c mice presented a marked preference for the familiar environment, while C57BL/6 mice exhibited a preference for novelty. This result suggests that the free-exploratory paradigm can differentiate traits of anxiety. There is also some evidence showing that there is no change in state anxiety during this test situation. Misslin and colleagues [10,11] observed that Swiss mice did not present physiological signs of fear unless they were forced into the novel environment, while Belzung and Le Pape [5], using a principal component analysis, demonstrated that variables measured

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