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Trait and state anxiety in animal models: Is there correlation?

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ABSTRACT

It is believed that subjects with high trait anxiety levels tend to present state anxiety reactions with greater intensity than individuals with low trait anxiety levels. In order to verify if this premise is valid for animal models of anxiety, the present work investigated the possible correlation between two behavioral tests: the elevated plus-maze, a classic model of state-anxiety, and the free-exploratory paradigm, which has been proposed as a model of trait anxiety. The behavior of 46 drug-naive, adult, Wistar, male rats was measured in these two models on two occasions, 1 week apart. Subsequently, the intraclass correlation coefficient (ICC) was calculated for the parameters "percentage of time in the novel side" (%TNS; free-exploratory paradigm), "percentage of time in the open arms" (%TOA; elevated plus-maze) and "percentage of entries into the open arms" (%EOA; elevated plus-maze). These parameters were also used to classify the animals into groups presenting high, medium or low levels of anxiety in both tests, so that the concordance between the models could be evaluated through the kappa test. The analysis resulted in low ICC (%TNS × %TOA: −0.127; %TNS × %EOA: 0.040) and low kappa index (%TNS × %TOA: −0.017; %TNS × %EOA: −0.044), suggesting a poor correspondence between the free-exploratory paradigm and the elevated plus-maze. In conclusion, the data presented here indicate that the premise of correlation between trait and state anxiety is not necessarily true for animal models of anxiety and, therefore, care must be exercised when using state anxiety models in order to determine animals' anxiety profile.

Among psychiatric disorders, anxiety is the most prevalent disease in general population [1]. Nowadays, various groups of drugs are being used for the relief of anxiety symptoms, including benzodiazepines, tricyclic antidepressants, monoamine oxidase inhibitors, serotonin selective reuptake inhibitors and β-adrenergic antagonists. However, these drugs can present important side effects, such as sedation, cognitive deficit, ataxia, aggression, sexual dysfunction, tolerance and dependence [11,14]. Furthermore, not all patients benefit from the available treatments, and only a few of them have a response near to complete recovery [4]. These facts have justified a considerable number of recent studies to develop new drugs for the control of anxiety disorders.

For the experimental evaluation of new drugs with a potential anxiolytic effect there are a number of animal models that can predict clinical activity, such as the plus-maze, the open-field and the light–dark paradigm [5,18,24]. These models confront the animals with an anxiety provoking situation, modeling the so-called state anxiety, which is the anxiety a subject experiences at a particular moment in time, when facing threat. However, there is another concept of anxiety, which is trait anxiety, considered to be an enduring feature of an individual, relatively stable over time [25], and particularly important in anxiety patients, as they tend to present greater anxious trait in comparison to healthy subjects [17].

To the best of our knowledge, the only test that has been proposed as an animal model of trait anxiety is the free-exploratory paradigm [13]. In this situation, animals are given the opportunity to freely move around 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 [15,16], who observed that Wistar rats actually preferred the novel environment, spending more time in it. Subsequently, Griebel et al. [13], 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. Also, some evidence shows that there is no change in state anxiety during this test situation. For example, Misslin et al. [20,19] observed that Swiss mice did not present physiological signs of fear, unless they

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