

Compulsive checking behavior of quinpirole-sensitized rats as an animal model of Obsessive-Compulsive Disorder(OCD): form and control

ABSTRACT

Checking behavior induced by quinpirole is not irrepressible but can be suspended. Results strengthen the quinpirole preparation as an animal model of OCD compulsive checking.

INTRODUCTION

Background Obsessive-compulsive disorder (OCD) is a psychiatric illness, more prevalent than schizophrenia or panic disorder. The most frequent symptom of OCD is compulsive checking, shown by 63% of the patients. Compulsive checking interferes with normal everyday functioning because of the many hours of time spent in the performance of checking rituals, a preoccupation that in extreme cases may even prevent the OCD sufferer from leaving home [1, p. 86]. Like normal behavior, OCD checking involves the performance of actions supposedly related to security, orderliness or accuracy, but is characterized by the repeated and excessive re-doing of such rituals. These repetitions do not reflect a problem with memory recall but rather an impediment in achieving a sense of task completion. In a recent publication we propose that behavior induced by chronic treatment with the D2/D3 dopamine agonist, quinpirole, may constitute an animal model of OCD checking. This proposal is based on three lines of evidence. First, the behavior of quinpirole-treated rats looks like OCD checking in that it meets formal ethological criteria of OCD compulsive checking identified by the investigators: a) a preoccupation with and an exaggerated hesitancy to leave the item(s) of interest; b) a ritual-like motor activity pattern; and, c) dependence of checking behavior on environmental context. Second, the behavior of quinpirole-treated rats is directed at a likely stimulus for checking activity - the home base, and is thus an exaggerated form of normal checking in the rat, similar to the human condition where OCD compulsive checking is an exaggerated form of normal checking regarding one's well-being and security. Finally, the checking behavior of quinpirole rats is partially attenuated by clomipramine, a drug used in the treatment of OCD. In the present report, we investigate whether the checking behavior of quinpirole rats is subject to interruption, which is another attribute characteristic of OCD compulsions. Despite the urge to perform them, OCD patients may resist engagement in rituals for varying amounts of time depending on situational circumstances. In fact, one of the most effective psychotherapies for OCD - exposure and ritual prevention (ERP) therapy - relies on this property. Patients are persuaded by the therapist to expose themselves daily to the ritual-provoking cues and to stay in contact with them without ritualizing for at least one hour or until any discomfort slowly subsides. This form of therapy has a success rate that may be higher and longer-lasting than anti-compulsive medication, and produces brain changes in OCD patients similar to those found with drug therapy (reviewed in). Here, we asked whether like OCD patients, quinpirole rats can desist from compulsive checking in the presence of checking-evoking cues. As a potential non-trivial manipulation that could interrupt the incessant checking activity of quinpirole rats, we placed a cage in the open field environment and examined the effect of two factors on checking behavior: familiarity with the cage introduced into the open field, and the time at which the cage was introduced into the open field. With regard to the first factor, the cage was either the rat's home-cage (very familiar) or one that the rat has never seen before (completely unfamiliar). With regard to the time factor, the cage was introduced into the open field either at the

start of the open field test (i.e., immediately after injection of quinpirole) or 60 min after start of the test (i.e., after the rat has been engaged in checking behavior for an hour). These factors were aimed to constitute a gradient making the suppression of quinpirole-induced checking more or less difficult, akin to the variable success that OCD patients have in resisting obsessions. Thus, it was expected that the familiar cage introduced at the start of testing would yield the maximum suppression and the unfamiliar cage introduced 60 min after drug injection would yield the least suppression of checking activity.

CONCLUSION

Conclusions Like the compulsive behavior of OCD patients, so, too, the compulsive checking behavior induced by quinpirole is not irrepressible but can be suspended in the presence of appropriate stimuli. However, when checking-evoking cues remain, the suspension of checking behavior is not sustained and after a period of time rats resume their checking behavior, akin to the failed resistance that OCD patients show in refraining from performance of their compulsive rituals. These findings strengthen the quinpirole preparation as an animal model of OCD.