Drug Screening Animal Model for Anti-compulsive Activity (Ramot)

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We have developed the signal attenuation rat model of obsessive-compulsive disorder (OCD). This model is based on the theoretical proposition that compulsive behaviors result from a deficit in the feedback, which is associated with the performance of normal goal-directed responses.
In our model, the goal-directed behavior is lever-pressing for food. The feedback associated with making a response is manipulated as follows: Rats are first trained to lever-press for food, whose delivery is accompanied by a stimulus which was previously paired with food. Thus, the stimulus is established as a feedback cue, which signals that the lever-press response was effective in supplying food. The “signaling” property of the stimulus is then attenuated by repeatedly presenting the stimulus without food. Finally, the effects of Signal Attenuation on lever-press responding are assessed under extinction conditions (i.e., pressing the lever results in the presentation of the stimulus but no food is delivered).
In order to differentiate between the effects of signal attenuation and of extinction per se, the behavior of rats undergoing an extinction test preceded by a signal attenuation stage is compared to that of rats in an extinction session that is not preceded by signal attenuation (a procedure referred to as ‘regular extinction’). An anti-compulsive effect in the model is evidenced in a decrease in the number of excessive lever-presses that are not followed by magazine entry (ELP-U) in rats that underwent signal attenuation but not in rats that underwent regular extinction.
This model can be used for testing compounds or drugs that are targeted towards OCD. It has been validated by testing two SSRIs (paroxetine and fluvoxamine), which were found to exert an ‘anti-compulsive’ effect in this model, whereas on the other hand, a tricyclic antidepressant (desipramine), an anxiolytic (diazepam) and an antipsychotic (haloperidol) drug, did not exert this effect.

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