

Animals exposed to stress are considered to be models for depression. In humans, stress is thought to initiate or exacerbate a number of psychiatric disorders such as post-traumatic stress syndrome or major depression. To improve our knowledge of the causal mechanisms of stress-related disorders, and to bridge the gap between experimental models and the situation in humans, we need naturalistic animal models with psychological types of stressors. The psychosocial stress model in male tree shrews (*Tupaia belangeri*) represents a promising paradigm. In their natural habitat, adult male tree shrews display an intense territoriality [3] that can be used to establish a naturally occurring challenge situation under experimental control. In the laboratory, coexistence of two males in visual and olfactory contact leads to a stable dominant-subordinate relationship, with subordinates showing distinct stress-induced behavioral, physiological and central nervous alterations. These reactions to stress resemble depressive-like symptoms in humans. We investigated the effect of several psychotropic drugs on behavioral and endocrinological parameters [2, 4, 5].



Experimental Groups	Experimental time periods		
	Control	No stress	No stress
Control + Treatment	No stress	No stress	No stress + treatment
Stress	No stress	Stress	Stress
Stress + Treatment	No Stress	Stress	Stress + Treatment
	10 days	10-14 days	7-32 days

*Figure 1. Experimental schedule. No-stress: time period without any treatment. Stress: period of daily exposures to a dominant male. Treatment: period of drug treatment. In the antidepressant experiments, the stress period lasted 10 days and the treatment period 28-32 days. In the diazepam experiment, the stress period lasted 14 days and the treatment period 7 days.*

**EXPERIMENTAL PROCEDURE**

In our experiments, we tested the effects of different antidepressants (clomipramine, fluvoxamine) and an anxiolytic (diazepam). Treatment started after the stress-induced depressive-like symptoms were established. In figure 1 the experimental schedule is visualized. We measured the behavior before and during the stress/treatment period.

**MONITORING AND ANALYSIS OF BEHAVIOR**

Quantitative behavioral analysis showed that chronically stressed tree shrews tend to withdraw from the field of the dominant, reduce their locomotor activity, and cease auto-grooming behavior. It is impossible to observe the behavior of the animals in front of their cages, since 1) they are easily disturbed, 2) the animals are too fast, and 3) animals are singly housed, which makes it impossible to observe different animals at the same time. Therefore, we needed a video analysis system, which is easy to handle and able to record and analyze behavioral sequences. The

Observer Video-Pro, which combines video and time code hardware and The Observer software, proved to be very useful. Using a behavior sampling procedure, behavior (marking, grooming, eating and drinking) was quantified from the tapes during a 15-minute period. With The Observer Video-Pro it is possible to start the behavioral analysis for every animal at the same time. Fast behaviors can be analyzed by slow-motion replay and non-activity periods can be fast-forwarded. With the software it is very easy to assign certain behaviors to a key on the computer keyboard. Playing the videotape on the computer, one just pushes the keys to which the behavior is assigned. Subsequently, it is possible to calculate different characteristics of the behavior (frequency, duration, latency etc.), selecting the different options that the analysis module of The Observer offers.

## RESULTS AND CONCLUSIONS

We conducted several experiments to assess the validity of the psychosocial stress paradigm in tree shrews as a model for depression and to investigate the role of the HPA-axis and serotonergic system in the effects of antidepressant treatment. Stress-induced changes in behavioral and endocrine parameters, e.g. a reduction in locomotor activity, increased urinary free cortisol levels and a decrease in body weight resemble symptoms observed in depressed patients. We thus conclude that the model possesses strong face validity for depression. The predictive validity was assessed by investigating the effects of antidepressants in stressed tree shrews. We expected that antidepressants would diminish the stress-induced changes. Clomipramine antagonized stress-induced behavioral and endocrine changes [1]. We further validated the model by treating the animals with an antidepressant specifically acting on the serotonergic system, fluvoxamine. This led to a reduction of the stress-induced decrease in marking behavior and the stress-induced increase in urinary free cortisol [2]. In contrast, treating stressed animals with the anxiolytic diazepam did not normalize the depressive-like symptoms, suggesting that the chronic stress paradigm in tree shrews is not a valid model for anxiety [4]. From these results it can be concluded that the psychosocial stress model in tree shrews is useful for studying the effects of stress on behavioral symptoms and to investigate the effects of antidepressant treatment on these depressive-like symptoms.

## REFERENCES

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