Factors influencing isolation distress vocalization in mouse pups

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Rodent pups emit ultrasonic distress vocalizations (USVs) when separated from their mother and littermates. [1,2] This emotional response can be used to detect anxiolytic properties of drugs. Anxiolytic compounds reduce the duration and number of calls [3]. The ultrasonic distress vocalization test has good predictive validity in rats. With the increasing use of transgenic and knock-out mice in brain research, the ultrasonic distress vocalization test is now also more frequently performed in mice to detect differences in anxiety behavior between genotypes [4]. Here we report on factors that influence ultrasonic distress vocalization in mice. We studied differences between background strains (129Sv, Swiss Webster, C57Bl6/J) and gender, as well as the influence of weight, age and temperature of the test environment. Additionally, we measured USV in mice overexpressing corticotropin releasing factor (CRF transgenics) and studied the effect of the anxiolytic diazepam in wildtype mice and CRF transgenics. CRF is an important neuropeptide, which is released in various brain regions at times of stress. CRF integrates the behavioral and autonomic response to stress. There are indications that too much CRF may contribute to the development of anxiety disorders[5].

To conduct the test, mouse pups were put on a metal plate, which was kept at 19 or 30 °C. On top of the test plate, a chamber was mounted with a batdetector, set on 80 kHz (S-25, Ultra Sound Advice, UK) . Audio data ran through a filter to a computer running Ultravox 2.0 (Noldus Inc., Wageningen, The Netherlands). Animals remained on the plate for 5 minutes while vocalisations were registered.

An important finding of our studies was that weight is a better selection criterion to achieve optimal vocalization than age. Furthermore, we found that 129Sv emitted most USVs, followed by Swiss Webster and then C57Bl6J. This finding can be used when choosing an optimal background strain for genetic modification. CRF transgenics (C57bl6J background) vocalized significantly more than wild type mice, indicating that CRF excess in the brain enhances the anxiety response. Diazepam reduced USVs in both genotypes. Interestingly, CRF transgenics were far more sensitive to the anxiolytic effect of diazepam than there littermates, suggesting that elevated CRF levels may result in hypersensitivity of the GABA benzodiazepine receptor complex.

In conclusion, when optimizing the conditions to measure USVs in mice, this test can be used to detect genotype differences as well as differences in pharmacological sensitivity between genotypes.

References

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