Neuroscience 2003 Abstract

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Abstract Title:	The CRF antagonist R121919 increases dominant behaviors of swim-high and swim-low rats.
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By using selective breeding, we have developed two lines of Sprague-Dawley rats that show high activity (SwHi) and low activity (SwLo) in a swim test. Although these two lines show markedly different behavior in the swim test, results from other tests (open field, 24-hour ambulatory activity) show no gross differences in general activity in the two lines. Further characterization of these lines revealed that chronic (but not acute) antidepressant drug administration increased struggling behavior in the swim test in SwLo rats; antidepressant drug administration had much less effect on struggling in SwHi animals.
CRF receptor antagonists have been postulated to have novel anxiolytic and/or antidepressant actions. In this study, we investigated how the selective CRF1 receptor antagonist R121919 would affect activity of SwHi, SwLo, and nonselected (SwNs, used as a control group) rats. Male and female rats of these strains were injected subcutaneously with 10.0 mg/kg of R121919 or vehicle, and spontaneous ambulatory activity and swim test behavior were measured. R121919 did not affect spontaneous ambulatory activity in any strain. In SwHi rats, which normally show much struggling in the swim test, R121919 significantly elevated struggling even further (by ~40%) without affecting floating. In SwLo animals, which normally show much floating (i.e., immobility) in the swim test, R121919 increased floating even further (also by ~40%) without affecting struggling. In contrast, in SwNs rats R121919 did not significantly affect either struggling or floating behavior. In summary, R121919 given to SwHi and SwLo rats accentuated their dominant behavior, resulting in increased struggling of SwHi rats and increased floating of SwLo rats. These results suggest that, in two rat strains that show strong behavioral propensities, CRF acts to modulate their behavior, exerting an influence to reduce the dominant behavioral propensity of the animal.

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