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an animal model of anxiety or depression in mice is provided along with evidence that defeat has profound effects on D1/D2 dopamine receptors as well as indicators of serotonergic activity. A model is also used to illustrate (using immunocytochemical techniques) the chronic adaptations in opioidergic and aminergic neurons to defeat.

The Importance of Social Housing in Social Defeat Induced Changes in Behavior and HPA Regulation

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Several studies using chronic recording techniques indicate that social stress in male rats has long-term physiological and behavioral consequences. A single social defeat appears to induce a reduction in the circadian variation in body temperature, growth, sexual interest, open field exploration and changes food preference from carbohydrate to fat intake. Some of these changes may last about ten days after the social stress. There are several reasons to assume that the single social defeat induces a state like depression. First of all, many of these long-term changes can be considered as part of the symptomatology of human depression. Secondly, the behavioral changes induced by the social defeat can be antagonized by standard antidepressive treatments. The change in regulation of the hypothalamic-pituitary-adrenocortical (HPA) axis is highly characteristic for depression in human beings. The majority of depressed patients show a hyperactivity of the HPA axis manifested by increased basal plasma cortisol concentration and a blunted adrenocorticotrophic hormone (ACTH) response to exogenously administered Corticotrophin Releasing Hormone (CRH). In the male rat, a single social defeat induces initially a hyper reactivity of ACTH and corticosterone to a CRH challenge, which normalizes after three weeks. At the same time however a gradual reduction of the corticosterone feedback develops, as reflected in a significant reduction of GR/MR binding and an enhanced ACTH and corticosterone response in the combined dexamethasone CRH challenge test at week three. These data show a gradually developing change in HPA axis regulation at various levels of organization. Recent studies indicate that this dynamic change in HPA axis regulation depends on the social housing conditions after the defeat. There appears to be a complex interaction between defeat and social isolation. This, in combination with behavioral data, suggests that the absence of some form of social support after the experience of social defeat is essential for the development of depression-like symptoms in the male rat.

The Impact of Social Defeat on Cardiac Activity in Rats

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Social defeat by a coespecific male is one of the most robust of the various stimuli used to induce physiological stress responses in the rat, particularly with respect to the magnitude of plasma catecholamine and corticosterone responses. This social aversive context produces not only strong neuroendocrine responses, but also significant heart rate, blood pressure, and temperature changes. Therefore, it may represent a useful experimental model in studying sympatho-vagal interactions and susceptibility to cardiac arrhythmias under challenging conditions. This paper summarizes the results of a series of experiments aimed at quantifying the impact of this experimental paradigm on the rat ECG, in comparison to other commonly used non-social stressful stimuli. ECG signals were obtained in wild-type rats using a telemetry system which does not interfere with the animal behavior,
and were continuously recorded from each rat in baseline, test, and recovery conditions. The 15-min test period consisted of one of the following stress situations: social defeat (resident-intruder test), restraint (confinement in a plexiglass cylinder), shock prod test (presentation of an electrified probe) and swimming. The influence of each stressor on the balance between the two branches of the autonomic nervous system was measured via quantification of the variability of heart rate and the occurrence of different kinds of cardiac arrhythmias. Defeated animals showed a much higher heart rate acceleration and a much lower variability of heart rate (indicating a marked shift of the autonomic balance towards sympathetic dominance), together with a much larger incidence of cardiac arrhythmias (mostly ventricular extrasystoles). Ventricular arrhythmias were mainly observed in the periods immediately following attacks, periods which were also characterized by peaks of heart rate and further reduction of heart rate variability. These data indicate that, by inducing a strong shift of autonomic balance towards the sympathetic branch, social aversive contexts can be far more detrimental to cardiac electrical stability than other non-social aversive stimuli.

**Adaptation in Patterns of C-fos Expression in the Brain of Male Rats by Repeated Exposure to Social Defeat**

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Defeat resulting from an intraspecific confrontation between male rats represents a biologically relevant form of social stress. C-fos expression was used to map the pattern of neural activation following either a single or repeated exposure of an intruder male to a larger male in the latter’s home cage. Sixty minutes after a single defeat, there was intense c-fos expression (quantified using image analysis) in restricted areas of the basal forebrain (including lateral septum, bed nucleus of stria terminalis, lateral preoptic area, lateral hypothalamic area, paraventricular nucleus, medial and central amygdala) as well as in the autonomic and monoaminergic nuclei of the brainstem (central grey, dorsal and median raphe, locus coeruleus and nucleus of the solitary tract). After the tenth defeat, this pattern was modified despite persistently high levels of aggression. Some areas in the forebrain (bed nucleus of stria terminalis, paraventricular nucleus and medial amygdala) continued to express increased c-fos; others (the septum, lateral hypothalamus, lateral preoptic area and central amygdala) no longer expressed c-fos. The brainstem response was equally varied: the central grey and the raphe nuclei continued to respond after repeated defeat, whereas the solitary nucleus and locus coeruleus did not. This study shows the pattern of adaptation at a cellular level in the basal forebrain and brainstem to repeated defeat. In a posterior study the role of serotonergic system in this process of adaptation was assessed by depleting 5-HT by bilateral icv infusion of 5,7-dihydroxytryptamine. The induction of c-fos expression was not affect by depletion of 5-HT. Another study is being conducted in which animals are exposed to 1, 2, 5, 10 or 20 consecutive defeats, being the pattern of c-fos expression currently analysed. Supported by the DG CYT (PR95-030); University of Valencia (2212); Acciones Integradas (160B); BBV Foundation; Cambridge Commonwealth and Overseas Trust, and Oversea Research Studentship of UK.