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Biological Bases of Aggressiveness Studies on the Rats

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One the first important problem to consider when the biological bases of aggressiveness are studied in the rats, is the applicability on the man of the results obtained from the mouse pattern. In fact, the motor sequences, as well as the targets, are different in mouse and rat on the one hand, and in man on the other hand; for instance, the male rat does not generally attack the female, whilst the woman is often an object of violence by the man. However, in spite of these differences, the mouse pattern is considered valid, because the main molecular mechanisms on the basis of aggressive behaviours are the same in mice, in rats and in man [1].
In rats, the intermediate hypothalamic area and the ventrolateral pole are considered the centres organising the aggressive responses. Such areas receive afferences by the prefrontal cortex, the medial amygdala and the lateral septum, and they send efferences to the lateral septum, the medio-dorsal thalamus and the dorsal part of the periaqueductal grey substance [2].
Other involved nervous centres are the dorsal and medial raphe, the accumbens nucleus and the olfactory bulbs. In particular, the bilateral extirpation of these ones induces a mouse-killing behaviour (that is the behaviour of an isolated rat towards an anaesthetized mouse placed in its cage) in the 100% of the rats.
Although during the last years the number of molecules involved in the aggressive behaviour have considerably increased, serotonin (5-HT) remains the neurotransmitter mainly involved in this kind of behaviour; the other molecules regulate its cerebral levels, regulate the affinity of its several receptors or modulate its postreceptorial effects.
In our laboratories we used the mouse-killing behaviour as experimental pattern for the study of interspecific aggressiveness in the rat; some rats spontaneously kill the mouse (natural killer), other do not show any kind of aggressiveness.
This behaviour is affected by the 5-HT in the Central Nervous System (CNS); in fact, it is promoted by a tryptophan lacking diet, which is an essential amino acid and a 5-HT precursor: almost the 2/3 of not mouse-killer rats subjected to a tryptophan lacking diet become mouse-killer after 3 days of diet, or at least show a definite increase of their aggressiveness [3].
An inverse relation exists between strong aggressiveness and low liquoral levels of 5-HT and of 5-hydroxindoleacetic acid, its main catabolite; furthermore, drugs increasing cerebral levels of 5-HT (reuptake inhibitors) or 5-HT1A and 5-HT1B receptor agonists reduce aggressiveness.
The aggressive behaviour is also affected by sexual hormones. In fact, it is well known that the aggressive behaviours (intra and interspecific) are clearly more frequent amongst the male rats.
We have shown that the mouse-killing behaviour is affected by the presence of testosterone, both in neonatal and in adult age. In fact, the castration at birth of male rats reduces the percentage of mouse-killer animals, whilst the neonatal androgenization of female rats increases it. Moreover, during the adult age, the administration of testosterone propionate in non-killer animals leads to the mouse-killing behaviour above all in the castrated at birth males (whose brain has always been exposed to the low sexual hormones levels); the administration of ciproterone acetate (an antiandrogen) to the killer animals, induces the disappearence of the mouse-killing behaviour above all in the androgenised at birth females and the control males (i.e. animals whose brain has been exposed to androgens in perinatal period), but not in castrated at birth males [4].
Testosterone organizes CNS in a "male" way, not only for the neuroendocrine function, but also for the behavioural one.
The action mechanism of testosterone is related to its aromatization into estrogens, as it has been shown using male mice with targeted disruption of the gene encoding ?-receptor of estrogen (?-ERKO mouse) [5].

Key words

Aggressive behaviour, serotonin, testosterone, tryptophan

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