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Strain differences of dopamine receptor levels and dopamine related behaviors in rats

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Abstract

Here we have investigated whether differences in levels of dopamine D1-like, D2-like receptors, dopamine D3 receptors, and dopamine transporter could be related to behaviors such as immobility response and locomotion between Wistar rats and Sprague-Dawley rats. The levels of the dopamine receptors and transporter were measured by autoradiographic study at the level of basal ganglia and the limbic subregion. The behavioral study was done by open-field and immobility response tests. The Wistar rats exhibited a higher level of D1 receptor binding in the basal ganglia subregions than Sprague-Dawley rats. The Wistar rats have higher levels of dopamine D2 receptor binding and dopamine transporter binding in the dorsolateral part of the caudate-putamen. In addition, the dopamine transporter binding were also higher in the Wistar rats than in Sprague-Dawley rats in the ventral part of the caudate-putamen and nucleus accumbens core. However, there were no differences in the level of D3 receptor binding in the limbic or basal ganglia subregions between these two strains. In Wistar rats, the duration of the immobility responses was longer and with less locomotor activity after these immobility responses compared with Sprague-Dawley rats. These data suggest that the differences in dopamine receptors in these two rat strains may in part relate to the behavioral differences reported in these two strains.

Keywords: Wistar rat; Sprague-Dawley rat; Locomotor activity; Immobility response; Dopamine receptor; Dopamine transporter

1. Introduction

The dopaminergic systems have been the focus of much research, mainly because several neuropsychiatric disorders and conditions such as schizophrenia, Parkinson's disease, substance abuse, and Huntington's disease are widely accepted to have a basis in a dysregulation of dopaminergic transmission. In general, dopamine (DA) receptors are classified into two broad families, namely the D1-like (D1 and D5) and D2-like (D2, D3, and D4) receptors (for review, see [40]). Both the D1 and the D2 receptors are abundantly expressed and widely distributed throughout striatal and limbic dopamine fields, including the nucleus accumbens and the olfactory tubercle [3,4,57]. Stimulation of the D1-like receptors increases stereotypical oral behavior in the animals [41]. Activation of either D1- or D2-like receptors results in increase of locomotion [14,25,49,54,56]. Furthermore, stimulation of both D1 and D2 receptors is essential to produce maximum locomotor activation [13,25]. On the contrary, D3-prefering agonists inhibit locomotor activity [8,50]. The D3 receptor has a specific distribution to limbic areas such as the shell of the nucleus accumbens, the olfactory tubercle, and the islands of Calleja of both Sprague-Dawley (SD) [3,4,35] and Wistar (W) [47] rats. These limbic areas of the brain are associated with emotional and endocrine functions, and seem to mediate some of the effects of antipsychotic

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drugs and drugs used against Parkinson's disease, which were previously thought to interact only with D2 receptors [16].

The most used strains of rats in research are the W and SD. Some studies have shown differences between these two strains in neurobiological functions [1,2,28,46,58]. Differences in the prepulse inhibition–disruptive effects of apomorphine have been reported between W and SD rats [30,52,53], and several studies indicated that mesolimbic and nigrostriatal DA transmission may, in part, regulate the prepulse inhibition (PPI) [10,51,59]. DA plays an important role in the control of many neurobiological functions, including locomotion, emotional behavior, cognition, positive reinforcement, and neuroendocrine regulation.

The immobility response (IR) is regulated by emotions such as fear, and by dopaminergic drugs such as haloperidol (DA antagonist). The IR is considered a temporary state of profound motor inhibition and relative unresponsiveness caused experimentally by some types of stimulation and restraint. The manipulations used in the laboratory to induce IR are an attempt to simulate the physical restraints that can result in the immobility of a prey when caught or carried by a predator. In nature, this behavior is part of antipredatory behavior and the last resource used by prey to reduce the probability of continued attack by the predator [31,42]. This immobility can be produced experimentally in a variety of species [21]. In rats, the immobility induced by clamping the neck (ICN) is caused by clamping the skin of the nape and placing the animal on its back [11]. Another kind of immobility, the dorsal immobility (DI), also can be triggered in the rat by grasping the animal by the skin of the dorsal surface of the neck and lifting it off its feet [45]. Many brainstem and basal forebrain regions have been implicated in the IR. One part of the neural mechanism may include descending motor inhibition, known to arise from the medial reticular formation (MRF). Modulating influences on the MRF come from other parts of the brain, most notably the limbic system (fear potentiates IR), the neocortex, which inhibits IR, and the basal ganglia (dopaminergic blockade in the striatum promotes IR) [33]. Fear-provoking stimuli, such noise and electric shock, potentiate IR, whereas those stimuli that are fear-reducing, such a handling, taming, and repeated testing, cause the response to wane [7,19,21]. In lizards, lesions of the homologous mammalian central amygdale reduce the duration of IR [9].

In our study, we investigated some DA-mediated behaviors and the regional distribution and levels of DA receptor subtypes (D1-like, D2-like, and D3) and DA transporters in the basal ganglia and limbic subregions of W and SD rats using quantitative autoradiography. In behavioral experiments, open-field activity and immobility responses were measured in both W and SD rats. The differences observed between these strains for DA receptors and DA transporter, together with DA-related behaviors, are discussed.

2. Material and methods

2.1. Animals and housing

Male Wistar and Sprague-Dawley rats (14 weeks old, $n = 10$ per group), from our animal care facilities were used (Harlan Laboratories was the original source). Rats were housed in groups of four in a Plexiglas cage with a stainless steel cover in a light- (00:70–19:00 lights on) and temperature- (20–22 °C) controlled room. Food and water were always available. The rats were allowed to acclimatize to the colony-room conditions for at least 2 weeks before the start of the experiments. Behavioral testing was done between 09:00 and 13:00. All experimental procedures described in this study are in accordance with the guidelines of the Laws and Codes of Mexico in The Seventh Title of the Regulations of the General Law of Health Regarding Health Research. Every effort was made to alleviate any pain or distress that might be experienced by the animals during this experiment. We used the minimum number of animals required to attain the goals of this study.

2.2. Behavioral testing

Six W and six SD rats were used in the behavioral tests, which were recorded on videotape using a VHS video camera (NV-N3000PN, Panasonic) for later examination.

2.2.1. The open-field test

This test has been regularly used to assess emotionality in rodents [26]. The animal was transferred to the testing room and immediately placed on the middle of the open-field (black-painted wooden square 60 cm per side and 50 cm above the floor). The light conditions were comparable to the light intensity in the housing room; two 39 W overhead fluorescent bulbs were suspended 180 cm above the center of the field and provided 210 lux at floor level. Because of rodents' unconditioned aversion to heights and open spaces [15], and to increase the emotionality of rats in a novel environment, the open-field used here had no walls and was 50 cm above the floor. The spontaneous locomotor activity in unfamiliar environment was measured using a video image analyzer (Videomex-V, Columbus Instruments). It keeps track of the distance the animal travels (DT), the amount of time spent travelling (TA), the amount of time spent in a non-ambulatory activity (TNA), and the amount of time resting (TR). It also displays the path tracings during the session.

2.2.2. Immobility responses

The immobility induced by clamping the neck (ICN) was made by applying a clamp (a 5 cm alligator clip with its tips covered with masking tape to avoid any injury to the rat's skin) between the base of the skull and the back of ears with the pressure being sufficient to lift the whole animal by the clamp. A second clamp was applied to the ventral part of the neck to increase the pressure in this area. The animal was then