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Chronic stress in pregnant rats: effects on growth rate, anxiety and memory capabilities of the offspring

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Abstract

Female rats were repeatedly stressed for 10 periods of 15 min by the presence of a cat, at the 10th (S10) or the 19th (S19) gestational day. The litter from stressed females often contained a majority of males or a majority of females, especially in the S19 group. The death of pups was dramatically high in the S19 group and, compared with controls, growth of the surviving animals was slower. When adult, their long-term memory was altered and they exhibited an aversive behavior relative to wide areas. Moreover, cognitive alterations were revealed by the low level of exploration and the inability to rapidly process the relevant environmental cues. These deficits resemble those of psychiatric patients who had been submitted to pre-natal stress.

Keywords: Chronic stress; Growth, Anxiety; Memory; Cognitive functions; Rat

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1. Introduction

Many studies have investigated the harmful effects of stress during pregnancy on offspring. Indeed, it has been shown to prevent pregnancy and provoke abortion (Runner, 1959; Weir and De Fries, 1963; De Catanzaro, 1988), to reduce the number of litters or the litter size (Zondek and Tamari, 1967; Euker and Riegle, 1973; Wildt et al., 1975), to produce a high mortality of neonates or small-for-date animals (Pollard, 1984; Guo et al., 1993) and lowered birthweight of offspring (Calhoun, 1962; Christian et al., 1965; Johnson et al., 1976; Salgado et al., 1977; Pollard, 1984). Stress during pregnancy also provokes physiological alterations in the offspring, such as hypoxia, arterial hypotension and bradycardia (Myers, 1975; Morishima et al., 1978) or an increase in heart rate (Sontag, 1941) as well as abnormal adrenal gland response (Pollard, 1984). In women, epidemiological observations have shown that stress during pregnancy is likely to produce abortion or hard delivery, infants have lower birthweights and the percentage of premature infants and of neonatal pathologies is increased (David and Devault, 1962; Shaw et al., 1970; Blomberg, 1980; Homer et al., 1990; Richard, 1990). Besides these physiological alterations in pre-natally stressed animals and humans, hyperactivity (Sontag, 1965), increased emotionality (Thompson, 1957), cognitive defects (Stott et al., 1957) and neurological and behavioral abnormalities (Stott, 1973), such as infanticide (Lamp, 1967) have also been observed.

Few studies have investigated the effects of stress during pregnancy on the learning capabilities of the offspring. It is known that the offspring of rats stressed during pregnancy have a lowered ability in water maze learning (Thompson and Sontag, 1956) and in discrimination learning (Smith et al., 1981) compared with controls. In these studies, stresses were given chronically for several days during the first or the second half of pregnancy. We have previously investigated the effects of an acute stress given to pregnant rats at the 10th or the 19th gestational day on growth rate, learning and memory capabilities of the offspring (Lordi et al., 1997). The aim of the present study was to look for the effects of stresses given repeatedly to rats at the 10th or the 19th gestational day on growth rate, anxiety and memory capabilities of the offspring with the hypothesis that repeated stresses at short intervals would elicit much more alterations in the offspring than an acute stress.

2. Materials and methods

2.1. Animals

The animals were DA/HAN strain rats (pigmented rats), born in the laboratory and housed in standard conditions: 12 h light (08.00–20.00 h)/12 h dark (20.00–8.00 h), 20–22°C, food and water available ad libitum. They were studied early in the morning and late in the evening, i.e. during the active phase of their cycle.

2.2. Experimental protocol

Fifteen primiparous rats, 3–4 months old, were submitted to a repeated stress either at the 10th gestational day (G10; $n = 4$), when the neural tube was being formed, or at the 19th gestational day (G19; $n = 11$), i.e. 2 or 3 days before delivery, once fetuses have already developed sensory capacities and their central nervous system has acquired enough expanded maturity (Witschi, 1956). Three females and two males were put together in a cage in the evening and the following day, in the morning, the vaginal smear was examined. The presence in the smear of both vaginal cells typical of the estrous stage and spermatozoids indicated day 1 of pregnancy. For both groups, G10 and G19, stress was elicited by the presence of a cat close to the rat. The cat and the pregnant rat were put in a wooden box ($60 \times 60 \times 40$ cm) for 10 periods of 15 min, two successive periods being separated by a 15-min interval. The cat was generally very cool and, in most cases, ignored the presence of the rat; however, the experimenter carefully looked at the rat to prevent any possible aggression. Although the rats could avoid close contact with the cat, they exhibited motor and