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## Maternal separation induces anhedonia in female heterozygous serotonin transporter knockout rats

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### Abstract

The serotonin transporter (SERT) gene has been linked to depression, especially the short allele of the serotonin transporter linked polymorphic region (5-HTTLPR). When short allele carriers are exposed to stressful life events, their risk for developing depression is increased. The neurochemical properties of the short allele of the 5-HTTLPR in humans can be mimicked in heterozygous serotonin transporter knockout (SERT<sup>+/-</sup>) rats. These animals have a similar reduction in SERT expression as humans with a 5-HTTLPR short allele. Several stress protocols have been used in SERT<sup>+/-</sup> animals but behavioural outcomes were mixed. Many studies used males to examine the behavioural effects of stress in SERT<sup>+/-</sup> rats, ignoring possible effects in females. However, women are depressed twice as often compared to men, therefore it is of great importance to study the effects of stress in females as well. Because early postnatal adversity can contribute to the psychopathology of depression, especially in vulnerable individuals, our aim was to investigate the effects of early-life stress in female SERT<sup>+/-</sup> rats and determine whether female SERT<sup>+/-</sup> rats could model the human short allele 5HTTLPR carriers.

To this end, SERT<sup>+/-</sup> rats were maternally separated for six hours a day from postnatal day 2-15. Control rats were handled for 15 minutes from PND2-15 to control for litter disturbances. In adulthood, female rats were assessed for affective, social and coping behaviour. In addition, nerve growth factor (NGF) gene expression in the basolateral amygdala (BLA) and paraventricular nucleus of the hypothalamus (PVN) and basal plasma corticosterone levels were measured.

Results show that maternal separation lowered sucrose preference in female SERT<sup>+/-</sup> rats compared to control SERT<sup>+/-</sup> rats, reflecting anhedonic behaviour. In addition, compared to control SERT<sup>+/-</sup> rats, maternal separation significantly lowered NGF gene expression in SERT<sup>+/-</sup> rats in both BLA and PVN, but did not affect

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