Neuropeptide S reduces mouse aggressiveness in the resident/intruder test through selective activation of the neuropeptide S receptor

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Neuropeptide S (NPS) regulates various biological functions by selectively activating the NPS receptor (NPSR). In particular NPS evokes robust anxiolytic-like effects in rodents together with a stimulant and arousal promoting action. The aim of the present study was to investigate the effects of NPS on the aggressiveness of mice subjected to the resident/intruder test. Moreover the putative role played by the endogenous NPS/NPSR system in regulating mice aggressiveness was investigating using mice lacking the NPSR receptor (NPSR(-/-)) and the NPSR selective antagonists [^{t}Bu-D-Gly^{5}]NPS and SHA 68. NPS (0.01 – 1 nmol, i.c.v.) reduced, in a dose dependent manner, both the time that resident mice spent attacking the intruder mouse and their number of attacks, producing pharmacological effects similar to those elicited by the standard anti-aggressive drug valproate (300 mg/kg, i.p.). This NPS effect was evident in NPSR wild type (NPSR(+/+)) mice but completely disappeared in NPSR(-/-) mice. Moreover, NPSR(-/-) mice displayed a significantly higher time spent attacking than NPSR(+/+) mice. Of note, the pharmacological block of the receptor obtained with [^{t}Bu-D-Gly^{5}]NPS (10 nmol, i.c.v.) and SHA 68 (50 mg/kg, i.p.) did not change the behavior of mice in the resident/intruder test. In conclusion, the present study demonstrated that NPS produces anti-aggressive effects in mice and that the endogenous NPS/NPSR system can exert a role in the control of aggressiveness levels under the present experimental conditions.