Opposite Effects of Central Amygdaloid Vasopressin and Oxytocin on the Regulation of Conditioned Stress Responses in Male Rats

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The central nucleus of the amygdala (CEA) seems to be selectively involved in the passive component of the behavioral (immobility) and the accompanying parasympathetic response (bradycardia) during conditioned environmental challenges,[1] leaving conditioned sympathetic, adreno-medullary, and adreno-cortical responses unaffected (Roozendaal *et al.*, in preparation). Robust monosynaptic, peptidergic connections to the vagal complex and periaqueductal gray may be mediating these effects.

Intracerebroventricularly administered arginine-8-vasopressin (AVP) potentiates these stress-induced bradycardiac and immobility responses.[2] AVP may exert these effects via AVP and/or oxytocin (OT) receptive systems in the CEA.[3] Microinfusion of AVP (dissolved in 1 μl artificial CSF) into the CEA of conscious male Wistar rats under resting conditions, leads to a dose-dependent change in heart rate and behavior: A high dose of AVP (2 ng), but not lower ones (20 and 200 pg), causes a transient increase in heart rate and behavioral activity.[4] Moreover, in a part of the animals, the low dose of AVP even causes an opposite effect, that is, bradycardia. OT administration (2 ng) induces responses similar to those induced with the high dose of AVP. Neither plasma norepinephrine nor epinephrine is influenced after AVP infusion, suggesting that the tachycardia is due to reduced parasympathetic control, rather than a stimulation of the sympathetic outflow. The effects of AVP and OT during conditioned stress were studied in male Roman high-avoidance (RHA) and Roman low-avoidance (RLA) rats, selected genetically for shuttle-box acquisition behavior. In RLA rats the cardiac and behavioral responses to the emotional stressor are bradycardia and immobility,

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suggesting an important role of the CEA in these rats. The RHA rats, however, fail to show any change in heart rate or immobility in response to a conditioned stress situation. The low dose of AVP in the CEA of conscious RLA rats causes an enhancement of the stress-induced bradycardiac and immobility response. However, the high dose of AVP (2 ng) and OT (200 pg) attenuate the bradycardiac and immobility response in the RLA rats. As expected, infusion of AVP and OT in the RHA rats fails to induce any change in heart rate or immobility. Binding studies revealed that in contrast to the selective and highly potent AVP receptor, the OT receptor recognizes AVP and OT with similar affinity.[5] This suggests that the behavioral and autonomic responses of the high dose of AVP may be caused by OT receptor activation.

In conclusion, central amygdaloid vasopressinergic and oxytocinergic receptor-mediated mechanisms seem to exert opposite effects on the regulation of stress-induced autonomic and behavioral responses. AVP enhances the passive components of the conditioned stress response. The oxytocinergic system attenuates the CEA output. The stimulating role of AVP in passive coping may be general and has also been reported in other brain regions. The differences between RLA and RHA males suggest that these peptidergic mechanisms are only active in rats that preferentially adopt a passive coping strategy.[2]

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