

Title: Estrus cycle stage modulation of conditioned contextual fear may involve differential neuronal activation within subnuclei of the bed nucleus of the stria terminalis of female rats

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Abstract: It is well established that gonadal hormones and their metabolites modulate learned fear in both humans and rodents. We recently demonstrated in naturally cycling female rats that inhibiting the synthesis or action of allopregnanolone (ALLO), a progesterone metabolite and GABA_A receptor modulator, through infusions targeting the bed nucleus of the stria terminalis (BNST), increased contextual fear as evidenced by freezing behavior, but had no effect on fear to the auditory conditioned stimulus (CS). The BNST is a site of hormonal modulation in the brain and ALLO levels fluctuate in a similar manner to progesterone during the rat estrous cycle. The potential effects of ALLO on the acquisition and expression of learned fear and its relation to neuronal activation in the BNST can therefore be examined. To this end, we are using the naturalistic model of gonadally intact, cycling female rats in high (late proestrus, P) or low (late diestrus, D2) progesterone states. Animals were trained with 5 CS (2 kHz, 10 s, 80 dB)-footshock (2 s, 1 mA) pairings and subsequently tested for contextual fear for 10 min in the conditioning chamber. Training and testing was timed such that rats were in one of the following combinations of estrus cycle stages: P-P, D2-D2, P-D2, or D2-P. Subjects trained in high progesterone states and tested in low progesterone states appear to have impaired contextual fear recall. Immunoreactivity for the immediate early gene protein, c-fos, was quantified in specific subnuclei of the BNST after context testing to assess neuronal activation following the expression of contextual fear. Preliminary results suggest differential activation of neurons across BNST subnuclei during P and D2 stages. These findings indicate that differences in conditioned contextual fear during high and low progesterone estrus cycle stages may be due to differential neuronal activity within subnuclei of the BNST.