

## STEREOLOGICAL ANALYSIS OF NORADRENERGIC AND HYPOCRETINERGIC CELL GROUPS AFTER DEPRIVATION OF RAPID EYE MOVEMENT SLEEP

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In neonates, suppression of rapid eye movement sleep (REMSD) with antidepressants and through instrumental methods leads to permanent changes in brain development, sleep patterns and other adult depression-like behaviors. In adults, however, REMSD is therapeutic for major depressive disorder. The mechanisms at work leading to the depressogenic effect of REMSD in neonates and the opposite therapeutic effect in adults are unknown. This study was designed to examine age-related changes induced by REMSD in the hypothalamic hypocretinergic system in rats. Hypocretin (Hcrt, also known as orexin) is a hypothalamic neuropeptide linked to narcolepsy, a disorder characterized by profound disturbances in sleep pattern. Major targets of Hcrt-containing fibers include a dense innervation of the locus coeruleus (LC), an area whose suppressed functionality is a leading candidate hypothesis for major depression. Results are presented for adult, Wistar (WIS) and Wistar-Kyoto (WKY) rats with depressive characteristics. Immunocytochemistry and stereological analysis furnished unbiased estimates of total number and sizes of Hcrt-positive (Hcrt-ir) cells of the hypothalamus. WKY rats, whose number and size of Hcrt immunoreactive cells were 18% and 15% significantly lower, respectively, than those of WIS rats, showed a 20% increase in the number of Hcrt-ir neurons after REMSD. Large platform control (LPC)-WKY rats showed an even larger 30% increase in hypocretin-positive neurons compared with cage controls (CC). These alterations in the Hcrt system after REMSD and LPC groups suggest that Hcrt neurons have increased activity possibly due to stress-responses and that REMSD may result in decreased transmitter expression in the Hcrt cells of the hypothalamus. Future experiments will be conducted to compare these adult findings to the effect of REMSD on Hcrt hypothalamic neurons in young rats as well as possible changes in aged rats that might explain age-related changes in sleep patterns.