

MRTG-2/15/2009-Bajic (Dusica)

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"Age Differences of Brain Circuits Mediating Morphine Effect and Development of Morphine Tolerance"

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Summary: Accumulating evidence suggests that opioid tolerance rapidly develops in neonates and infants. The ventrolateral periaqueductal gray (vlPAG) is a key component of supraspinal pain-modulatory pathways, and plasticity in this area is strongly implicated in analgesic tolerance. This proposal focuses on understanding how adaptations in the vlPAG that occur with tolerance may differ between young, intermediate-aged and adult rats. Neurons associated with tolerance will be identified by the presence of the immediate early gene product Fos, as well as the neuronal isoform of nitric oxide synthase (nNOS). The proposed studies would represent the *first step* in our understanding of neurochemical changes in the vlPAG associated with tolerance in developing brain. *This is an important new area of research that may provide novel insights into molecular mechanisms of opioid tolerance that will lead to novel clinical therapies that differ with age.*