Social Neuropeptides Oxytocin and Vasopressin are Dysregulated in Williams Syndrome

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ABSTRACT

Introduction: The social neuropeptides, oxytocin (OT) and vasopressin (AVP) are involved in the control of social and reproductive behaviors broadly in mammals but whether they play a role in the internal circuitry regulating human behavior is unknown. Williams Syndrome is a neurobehavioral disorder that is caused by a ~1.5 Mb deletion of 7q11.23 and is uniquely associated with a gregarious personality, a strong drive to approach strangers and an attraction to music. Williams Syndrome provides an unprecedented opportunity to link genetics, neurobiology, and behavior.

Methods: We hypothesized that alterations in oxytocin and vasopressin might in part underlie the increased social behavior and response to music in WS. To test this, we established levels of oxytocin and vasopressin at two baseline points and at eight points after stimulation with music (a self-defined positive stimulus), followed by a mild stressor (cold pressor). Samples were collected beginning 30 mins after placement of an indwelling catheter and analyzed using enzyme immunoassays.

Results: The data from thirteen subjects with Williams Syndrome and eight age, gender, and ethnicity matched controls revealed altered regulation of OT and AVP in subjects with Williams Syndrome. Williams Syndrome subjects showed five-fold higher mean basal oxytocin ($p<0.001$) and three-fold higher vasopressin ($p=0.15$) levels vs. controls. Longitudinal changes in oxytocin (expressed as % Δ vs. baseline in the peak response during and immediately following the stimulus) exhibited both greater variability ($p=0.025$ with music; $p=0.007$ with cold) and greater average increases in WS subjects vs. controls (30% vs. 9% geometric mean increase, $p = 0.21$, with music; 21% increase vs. 2% decrease, $p= 0.01$, with cold). Longitudinal changes in vasopressin exhibited similar but weaker trends, which did not reach statistical significance, for greater variability and greater average increases in Williams Syndrome subjects vs. controls.

Conclusion: The results indicate that Williams Syndrome subjects exhibited amplified peak releases of oxytocin, and possibly vasopressin, in response to music and cold compared to controls. This is the first direct evidence in humans showing that endogenous circuitry involving oxytocin and vasopressin might regulate the response to social-emotional stimuli. Furthermore, the genetic circuits that regulate oxytocin and vasopressin are largely unknown and the data implicate one or a cluster of specific genes in the Williams Syndrome region. Williams Syndrome thus provides a unique genetic model for understanding the neurobiology of human sociality and emotion.