Title: Associations among pain neuropeptides and inflammatory cytokines/chemokines in plasma from children with and without self-injurious behavior

Authors: Adele F. Dimian & Frank J. Symons

Introduction: It is well established scientifically and clinically that environmental factors, mediated through operant (and likely respondent) conditioning mechanisms, contribute significantly to self- injurious behavior (SIB) among individuals with intellectual and developmental disability (IDD). The physiological mechanisms related to SIB remain less clear. Our previous work investigating nociceptive ('pain') and inflammatory relevant peripheral biomarkers showed differences in epidermal nerve fiber density values and mast cell activation between individuals with SIB and those without (Symons et al., 2008). Altered cytokine profiles have also been found to be linked to repetitive behavior and stereotypy among individuals with autism (Ashwood et al., 2011). The purpose of this study was to investigate the relation between nociceptive/ inflammatory relevant molecules and SIB among a clinical sample of children with IDD.

Method: Blood (~ 10 ml) samples were collected from a cross-sectional convenience sample of children with IDD (n=19; 95% male; mean age= 5.5 years; range= 2-13 years). From plasma, we assayed molecules relevant to nociception and inflammation including Substance P (SP), Beta-endorphin (BE), met-enkephalin (Met), Dynorphin A (Dyn), monocyte chemotactic protein-1(MCP-1), tumor necrosis factor alpha (TNF-a) and interleukin-6 (IL-6), and interleukin-10 (IL-10). Profiling of multiple cytokines/chemokines was performed through the Cytokine Reference Laboratory using a commercially available 22-plex Human Cytokine Array Panel (LUH000, R&D Systems, Minneapolis, MN). The Repetitive Behavior Scale-Revised (RBS-R) and the Child Development Inventory (CDI) were used to characterize SIB and adaptive behavior. Descriptive analyses, Independent sample T-tests, nonparametric Spearman -rank order correlations, and Fisher's Z-tests were conducted to examine the relation of the biochemicals assayed within and between SIB (n=12) and no SIB cases (n=7).

Results: There were no statistically significant differences between the SIB and No SIB groups in terms of age, overall repetitive behavior score, and CDI general development score. Over half of the children with SIB exhibited 4 or more SIB topographies. Within group correlations indicated statistically significant relations within the SIB group for the following molecules: SP and BE (r=0.83, p=.001), SP and TNF-a (r= -0.75, p= .01, BE and IL-6 (r= -0.82, p= .001), and BE and IL-8 (r= -0.62, p= .03). The associations between SP and BE (r= 0.86, p= .01) and Dyn and Met (r= 0.86, p= .01) were also significant for the No SIB group. Fisher's Z-tests showed statistically significant differences between correlations for Dyn and Met (Z= 2.04, p= .04) and Dyn and BE (Z=2.15, p= .03) between the SIB and No SIB groups.

Discussion: In this preliminary sample, there were significant differences in associations among a number of opioid peptides between the SIB and no SIB groups, consistent with differences in nociceptive function; there were also strong negative correlations within the SIB group between BE and IL6 and IL8 implicating possible differences in inflammatory signaling and endogenous opioid 'cross-talk' within the SIB group. Larger sample sizes are necessary to test further the reproducibility of our observations. We have a general working hypothesis that enhanced nociceptive and inflammatory signaling may be part of a pathophysiological set of mechanisms relevant to understanding SIB in IDD. If we could identify reliable pattern differences in pain-relevant biochemistry between SIB and no SIB cases, there may be the possibility of testing the patterns as biomarkers predictive of SIB risk or identifying new medication treatment targets.

References:

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[1] University of Minnesota