

Neuroscience in Anesthesiology and Perioperative Medicine - Alterations in Amygdala Functional Connectivity in Juvenile Non-Human Primates 2 Years after Anesthesia Exposure during Infancy.

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Introduction: The latest clinical studies with prospective assessments indicate that early-in-life anesthesia exposure causes behavioral alterations later in life, but does not affect general intelligence. Preclinical studies, including those in non-human primates (NHPs), report functional alterations after early-in-life anesthesia exposure. Recently, we found that juvenile NHPs display decreased close social behaviors 2 years after early-in-life isoflurane exposure, but similar to clinical findings, the juveniles showed no cognitive impairments. Histopathological analysis of the juvenile NHP brains revealed increased gliosis in the amygdala, a brain region important for processing of social behaviors. Resting state functional connectivity MRI (rs-fcMRI) noninvasively allows the detection of alterations in functional connectivity (fc) of specific areas of the brain. However, whether early-in-life anesthesia exposure causes changes in fc of brain areas associated with social behavior remains unknown. We hypothesized that early-in-life isoflurane exposure of NHPs causes alterations in fc of the amygdala of the juvenile animals two years after the exposure.

Methods: Rs-fcMRI was performed in 2-year-old NHPs under light anesthesia, after early-in-life exposure to 5 hours of isoflurane, either one (1X), or three times (3X), or to room air only. The NHP brain was segmented into 82 regions of interest (ROIs). Based on blood-oxygen-level dependent (BOLD) contrast imaging data, amygdala-ROI fcs were determined. To identify differences in fc between the

three groups we used ANOVA and Bonferroni correction for multiple comparison.

Results: We found significant differences in fc among groups for the left and right amygdala with the primary auditory cortex (A1). Specifically, the fc between the left amygdala and the right A1 was significantly different among the three groups, and post hoc analysis revealed significantly decreased fc in the 3X group compared to both, the control, and the 1X group. For the right amygdala, we found a significant difference in its fc with the left A1 among the three groups. Post-hoc testing revealed that the 3X group showed a significant increase in fc with the left A1 as compared to the 1X group, however this increase was not significant when compared to the control group.

Conclusions: Early-in-life anesthesia exposure of NHPs causes changes in the fc of their amygdala evident at the age of 2 years. Since the amygdala is critical for processing of social behaviors, alterations in its connectivities may contribute to impairments in social functioning.

References: None.