

Altered cortisol regulation and reactivity in pre-school aged children who had surgery early in life for congenital heart disease.

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Introduction: Early life stress is associated with alterations in the physiological stress response system, and poorer neurodevelopmental and psychosocial outcomes. The Hypothalamic Pituitary Adrenal (HPA) axis, which regulates cortisol secretion, undergoes critical development during the first months of life and may be reprogrammed through excessive stress. Cardiac surgery causes significant stress. In this study we compared cortisol diurnal circadian rhythm and cortisol response to a stressor in preschoolers with congenital heart disease (CHD) who had early surgery (before 6 months of age) with those who had no or later surgery.

Methods: Twenty eight preschoolers with CHD (Early surgery =14, Control = 14) were enrolled. Diurnal cortisol regulation was measured in saliva samples collected from the children at prescribed intervals (30 minutes after waking, 11am, 3pm and bedtime) over two weekend days. Cortisol response to a stressor was measured in saliva samples collected at commencement of, and 30 and 60 minutes after, routine review echocardiogram. Multilevel analysis (hierarchical linear modelling) was employed to analyse the data.

Results: Diurnal cortisol levels and those in response to a stressor differed between groups. The early surgery group had lower cortisol concentrations throughout the day ($p=0.03$) and a different slope ($p=0.002$) compared to the control group. T tests demonstrate that the early surgery group had significantly lower mean waking cortisol levels than controls ($M = 2\text{ng/mL}$, $SD= 0.99$ vs $M=4.35$, $SD= 1.79$, $p=0.001$) but similar mean bed time values ($M=0.97$, $SD= 0.7669$ vs $M=1.192$, $SD= 0.885$, $p=0.49$) indicating a flatter decline throughout the day. The early surgery group demonstrate a different response to the echocardiogram when compared to controls (group x time interaction, $p=0.007$). Cortisol levels of the early surgery group increased 30 and 60 minutes post echocardiogram vs. controls who demonstrated the normal recovery pattern of declining levels.

Conclusions: This study provides preliminary evidence that the experience of cardiac surgery in the first 6 months may alter HPA axis, and therefore stress, regulation. Given the importance of stress regulation in neurodevelopmental and psychosocial outcomes, further study may be warranted.