

Concept Paper Addendum

Paper Title: Midlife Structural Neural Correlates of Adverse Childhood Experiences

(Long-term neural embedding of adverse childhood experiences in a population-representative birth cohort followed for five decades)

Proposing Author: Maria Gehred

Author's Email: maria.gehred@duke.edu

P.I. Sponsor: Terrie Moffitt, Ahmad Hariri, & Avshalom Caspi

Today's Date: June 17th, 2020

Changes to study:

Three changes were made to the analysis plan in the period from when the concept paper was first submitted to when the paper was prepared for submission. These changes are described below.

Change 1: Dropped two outcome measures from the study

First, we dropped total brain volume as an outcome measure from the current paper. Total brain volume, a composite of cortical surface area, cortical thickness, and cortical gyrification, is highly correlated with total cortical surface area ($r = .92$). Therefore, total brain volume was rendered redundant, and we chose not to include the measure in the final paper. Instead, we chose to focus on two structural features of the cortex—cortical thickness and surface area—that reflect distinct genetic, developmental, and structural factors (Raznahan et al., 2011; Wierenga et al., 2014). Many previous studies have investigated cortical grey matter volume differences associated with childhood adversity, but relatively few studies have investigated whether these differences encompass both surface area and cortical thickness. Including both of these structural features of the cortex as outcome measures allowed us to do so.

Second, we dropped total white matter hyperintensity volume from the current paper. This measure will instead be included in a follow-up paper that focuses more specifically on ACE associations with age-related brain outcome measures. This change was made to reduce the scope of the current paper and to ensure that the paper conformed to word limits.

Change 2: Did not use adult stressful life events covariate

Adult stressful life events were not included in the current paper. This adult stress variable was not developed by the time analyses for this project were underway. Therefore, we used the Perceived Stress Scale (Cohen et al., 1994) to account for adult stress.

Change 3: Included 10 regions in regional analyses of subcortical GMV

Our concept paper was not clear as to the subcortical regions we would include in our analysis. We detailed that we were interested in investigating “associations between prospective and retrospective ACEs and grey matter volume (GMV) of the hippocampus and amygdala, which may be especially sensitive to the effects of childhood maltreatment and adversity”, but also mentioned that our regional analyses would broadly include “GMV values of...subcortical parcels for parcel-wise analyses”. We would like to clarify that we have not restricted our analyses to only the hippocampus and amygdala but have included 10 subcortical structures in our analyses: accumbens, amygdala, brainstem, cerebellum, caudate, hippocampus, pallidum, putamen, thalamus, and ventral diencephalon (freesurfer aseg parcellation, bilateral).