Appendix Section B(2): CONCEPT PAPER TEMPLATE

DUNEDIN MULTIDISCIPLINARY HEALTH AND DEVELOPMENT STUDY

(The Dunedin Study)

CONCEPT PAPER TEMPLATE

(July 2024)

DUNEDIN STUDY CONCEPT PAPER

Provisional Paper Title: Childhood adversity and midlife decline in structural brain integrity.

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Today's Date: 1/21/2025

Please describe your proposal in 2-3 pages with sufficient detail for helpful review by addressing all areas outlined below.

Objective of the study:

Childhood adversity is associated with poor long-term physical and mental health outcomes (Felitti et al., 1998). The Adverse Childhood Experience (ACE) model, developed by the Centers for Disease Control (CDC), has become widely applied to research and policy initiatives seeking to better understand the nature of these associations. Of particular interest for mental health, we have used the ACE model in the Dunedin Study to demonstrate that the experience of childhood adversity is associated with lower structural brain integrity decades later in life (Gehred et al., 2021). Because these findings were identified through cross-sectional analyses, they could reflect either long-term, stable differences between individuals or a pattern of accelerated decline over time following adversity. Understanding the relative contributions of these two pathways can help inform efforts to mitigate the impact of childhood adversity on later health.

Here we propose to again use the ACE model to explore associations between childhood adversity and longitudinal *decline* in midlife structural brain integrity using MRI data collected from Study members at ages 45 and 52. This will allow us to test whether childhood adversity predisposes people for more rapid decline of the brain decades later, potentially increasing their risk for neurodegenerative diseases. Given the critical importance of measurement reliability for individual differences research (Elliott, Knodt, et al., 2020), our analyses will focus on MRI-based measures of structural decline that exhibit good or better test-retest reliability. This not only increases our confidence in any observed associations but also the likelihood for replication in independent datasets thereby contributing to a cumulative science better positioned to inform interventions.

Data analysis methods[1]:

[1] A key concern for the Dunedin Study is superficial analyses of data that simply identify differences or deficits between ethnic groups or other communities where inequities exist (e.g. persons with disabilities, Pasifika peoples, members of migrant and SOGIESC (Sexual Orientation, Gender Identify and Expression and Sexual Characteristics)

This study will use the Dunedin Study dataset, a population-representative cohort of individuals born in New Zealand in 1972 and 1973. Specifically, we will utilize prospective measures of childhood adversity and MRI data collected at ages 45 and 52. Using linear modeling, we will assess if childhood adversity broadly (i.e., prospective ACE–Total scores) is associated with accelerated structural brain decline from 45 to 52. We will also explore if there are differences according to type of childhood adversity using the prospective ACE–Deprivation (poverty, hunger, homelessness, etc.) and prospective ACE-Threat (abuse, natural disaster, etc.) subscores, respectively. Finally, we will compare whether retrospective measures of childhood adversity show similar or different associations with brain decline.

Variables needed at which ages:

Primary Independent Variables

RetroACEs ACEs retrospective_1June2015
RetroACEs_trunc ACEs retrospective, 4+ = 4, 1June 2015
ProACEs Prospective ACEs scale
ProACEs_trunc Prospective ACES, 4 or more = 4, 20 April 2015

Primary Dependent Variables

Change scores for all T1 weighted metrics that have ICC of 0.5 or greater

Covariates

Perinatal Complications

There is evidence that perinatal complications result in increased biomarkers of aging at mid-life (Shalev et al., 2014), and complications related to pre-term births (included in the perinatal complication measure) are also related to grey matter alterations (Bauml et al., 2015; Meng et al., 2016). Thus, we will conduct sensitivity analyses while including this variable as a covariate.

Age 3 Brain Health

Age 3 brain health has also been demonstrated to be a predictor of poor adult outcomes (Caspi et al., 2016), and is significantly positively correlated with average cortical thickness, total surface area, and total brain volume at age 45. Thus, we will conduct sensitivity analyses while including this variable as a covariate.

Adult Stress

Used as a covariate to isolate the effects of ACEs from current or recent stressors.

Significance of the Study (for theory, research methods or clinical practice):

The proposed study, through its analyses of longitudinal data, will address unanswered questions regarding the nature of previously reported associations between childhood adversity and midlife structural brain integrity. Finding that childhood adversity is associated with greater brain decline in midlife would suggest that accelerated aging could be a mechanism through which early

communities). The cumulative effect of these types of studies is stigmatising and not of benefit. Any research that identifies differences must (a) incorporate information on the broader context (e.g. historical or political factors); (b) where possible undertake additional analyses to examine the source of the difference/s, and (c) include policy recommendations for its resolution.

adversity may impact later health.

How the paper will contribute to Māori health advancement and/or equitable health outcomes[2]

This study will not include separate analysis of specific ethnic groups, but the results are expected to be generalizable to the Māori community. Childhood adversity is disproportionately present in socio-economically disadvantaged communities and an improved understanding of their impact on the brain will provide meaningful insight to support those most affected.

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[2] Helpful information can be found here: https://www.hrc.govt.nz/sites/default/files/2020-01/NZ%20Prioritisation-Framework-FA-web_0.pdf