Concept Paper Template

Provisional Paper Title: White Matter Lesions in Middle Age Are Associated with Diverse Measures of Intelligence

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P.I. Sponsor: Ahmad Hariri & Avshalom Caspi
(if the proposing author is a student or colleague of an original PI)

Today's Date:
June 4, 2018

Please describe your proposal in 2-3 pages with sufficient detail for helpful review.

Objective of the study:

Aging takes a toll on the brain and body. As people get older they show increased risk for heart disease, diabetes, and marked declines in many cognitive functions (Anstey & Smith, 1999; Unverzagt et al., 2001). In addition, the brain begins to accrue damage and deteriorate. One form of damage is white matter lesions, which accumulate as adulthood progresses (Au et al., 2006; Habes et al., 2016; Hedden et al., 2012; Tuladhar et al., 2015). While white-matter hyperintensity load has been linked to cognition, to our knowledge this has only been shown in samples with a broad range of age (Au et al., 2006; Habes et al., 2016). In addition, previous studies have failed to address the fact that chronological age is confounded with the effects of interest, due to the fact that aging is related to both declines in health and cognition as well as the accrual of white matter lesions (Anstey & Smith, 1999.; Habes et al., 2016). Here we propose investigating the links between white matter lesions and cognition in a longitudinal birth cohort of 1000 individuals all aged 45. An important advantage of the Dunedin dataset is that cognitive ability has been measured in both childhood and adulthood. We will leverage this data to address whether childhood cognitive ability leads to white matter lesions or whether white matter lesions drive cognitive decline.

Data analysis methods:

To generate measures of white matter lesion prevalence, we used the UBO pipline (https://cheba.unsw.edu.au/group/neuroimaging-pipeline), which was trained using vascular cohorts and demonstrates reliable identification of white matter lesions in out of sample images (Jiang et al., 2018).
The statistical software R (v. 3.4.4) will be used to run linear regression to test for predictive relationships. All code will be made available.

Variables needed at which ages:

UBO White matter lesion outputs
Brain Integrity, Age 3

Childhood WISC IQ (7-11)
Performance IQ (7-11)
Verbal IQ (7-11)
WAIS IQ (Age 45) plus the four index scores:
WMI (45)
PRI (45)
VRI (45)
PSI (45)
Trail making test (13 and 45)
Rey Auditory-Verbal Learning Test (age 13 and 45)
Grooved Pegboard Test (age 13 and 45)
Self-reported Mild Cognitive Impairment at 45
Informants report of Mild cognitive impairment at 45
Educational GWAS polygenic score (EA3)

Significance of the Study (for theory, research methods or clinical practice):
To further expand our knowledge of how white matter lesions in middle aged adults are associated with IQ and cognition, at different timepoints of life. White matter lesions may represent an early sign of problematic aging that could be a surrogate biomarker for early aging trials and intervention.

References cited:

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Data Security Agreement

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Proposing Author	Tracy d'Arbeloff & Max Elliott
Today's Date	6/04/2018

Please keep one copy for your records and return one to the PI Sponsor

Please initial your agreement

X	I am current on Human Subjects Training (CITI (www.citiprogram.org) or equivalent)
X	My project is covered by Duke or Otago ethics committee OR I have /will obtain ethical approval from my home institution.
X	I will treat all data as "restricted" and store in a secure fashion. My computer or laptop is: a) encrypted (recommended programs are FileVault2 for Macs, and Bitlocker for Windows machines) b) password-protected c) configured to lock-out after 15 minutes of inactivity AND d) has an antivirus client installed as well as being patched regularly.
X	I will not "sync" the data to a mobile device.
X	In the event that my laptop with data on it is lost, stolen or hacked, I will immediately contact Professor Moffitt or Caspi. (919-684-6758, tem11@duke.edu, ac115@duke.edu)
X	I will not share the data with anyone, including my students or other collaborators not specifically listed on this concept paper.
X	I will not post data online or submit the data file to a journal for them to post. *Some journals are now requesting the data file as part of the manuscript submission process. The Dunedin Study Members have not given informed consent for unrestricted open access, so we have a managed-access process. Speak to Terrie or Avshalom for strategies for achieving compliance with data-sharing policies of journals.*
X	I will delete all data files from my computer after the project is complete. Collaborators and trainees may not take a data file away from the office. The data remains the property of the Study and cannot be used for further analyses without an approved concept paper for new analyses.

Signature: _____Tracy C. d'Arbeloff_____