

Concept Paper Template 2018

Provisional Paper Title: The effect of lifetime alcohol trajectories on reward-related processing in the ventral striatum and related circuitry

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

Today's Date: 30 April 2018

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

Objective of the study:

Prior neuroimaging studies have reported widespread associations between alcohol dependence and the structure, function, and connectivity of the human brain¹⁻³. There is further evidence that such associations are magnified in older individuals⁴⁻⁶, suggesting that prolonged alcohol dependence and/or initiation of heavy drinking later in life is more problematic for brain health. Despite their relative abundance, existing research is based predominantly on cross-sectional data in small numbers of individuals resulting in weak power to reliably detect almost certainly small effects.

Here, we propose to address these limitations by examining associations between alcohol dependence and the structure, function, and connectivity of the brain in the Dunedin Multidisciplinary Health and Development Study. The neuroimaging portion of the "Dunedin Study" examines 4 neural hubs each coordinating information processing through a distributed circuitry supporting 4 behavioral capacities. For this Concept Paper, we will focus on reward-related processing through the ventral striatum (VS) hub. Alterations in VS structure⁷, VS function⁸⁻¹², and functional connectivity^{13,14} have been previously reported in individuals with alcohol dependence. We seek to leverage the unique nature of the "Dunedin Study" to further explore how different lifetime trajectories of alcohol dependence map onto midlife VS-dependent reward-processing.

Data analysis methods:

A series of analyses will be conducted comparing different alcohol trajectories (i.e., developmentally limited, adult onset, persistent) in:

1. Reward-related VS function as measured with BOLD fMRI during the Monetary Incentive Delay Task.
2. If significant differences between trajectories are observed in VS function we will examine differences in VS gray matter volume using high-resolution structural MRI data.
3. If significant differences between trajectories are observed in VS function we will also examine differences in functional connectivity between the VS and distributed circuit nodes (e.g., prefrontal cortex).
4. If significant differences between trajectories are observed in VS functional connectivity, we will next examine differences in microstructural integrity of pathways linking the VS with distributed circuit nodes using diffusion weighted MRI data.

At each of these steps we will also contrast alcohol trajectory results with results in the full sample examining lifetime booze years. This will provide evidence as to whether any finding is unique to a specific trajectory of drinking or rather a result of varying exposure to heavy alcohol use.

Finally, if well powered to do so, we will test for sex differences.

Variables needed at which ages:

Booze years @ age 45

Child brain integrity factor @ age 3?

Psych diagnoses – comorbid and lifetime

Alcohol trajectory variable @ age 45

Neuroimaging variables (in house)

SES

Education level

Lifetime stress/adversity, childhood trauma?

Measures of impulsivity – ideally at age 45 – not sure what is available

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

As described above previous research examining the effect of alcohol dependence on brain outcomes has been limited by the confounding of alcohol dependence diagnosis and age. These previous studies have often lacked a reliable assessment of alcohol dependence across the lifespan and therefore could not tease apart the effects of alcohol dependence and aging. Therefore, the current study takes a novel approach to assessing the effect of alcohol dependence on brain outcomes, namely reward-related VS processing, by examining the effect of alcohol dependence trajectories above and beyond lifetime alcohol consumption.

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Data Security Agreement

Provisional Paper Title	The effect of lifetime alcohol trajectories on reward-related processing in the ventral striatum and related circuitry
Proposing Author	Megan Cooke
Today's Date	4/30/2018

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

Please initial your agreement

MC	I am current on Human Subjects Training (CITI (www.citiprogram.org) or equivalent)
MC	My project is covered by Duke or Otago ethics committee OR I have /will obtain ethical approval from my home institution.
MC	I will treat all data as "restricted" and store in a secure fashion. My computer or laptop is: <ul style="list-style-type: none"> 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.
MC	I will not "sync" the data to a mobile device.
MC	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)
MC	I will not share the data with anyone, including my students or other collaborators not specifically listed on this concept paper.
MC	I will not post data online or submit the data file to a journal for them to post. <i>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.</i>
MC	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: _____ **Megan Cooke** _____

CONCEPT PAPER RESPONSE FORM

A

Provisional Paper Title	The effect of lifetime alcohol trajectories on reward related processing in the ventral striatum and related circuitry
Proposing Author	Megan Cooke
Other Contributors	Ahmad Hariri, Terrie Moffitt, Avshalom Caspi, HonaLee Harrington, Richie Poulton, Sandhya Ramrakha, David Ireland, Tracy Melzer, Ross Keenan, Annchen Knodt
Potential Journals	Biological Psychiatry, Alcoholism: Clinical and Experimental Research
Today's Date	4/30/2018
Intended Submission Date	At the end of Dunedin neuroimaging and Phase 45 data collection

Please keep one copy for your records and return one to the proposing author

B. To be completed by potential co-authors:

<input type="checkbox"/>	Approved
<input type="checkbox"/>	Not Approved
<input type="checkbox"/>	Let's discuss, I have concerns

Comments:

Please check your contribution(s) for authorship:

<input type="checkbox"/>	Conceptualizing and designing the longitudinal study
<input type="checkbox"/>	Conceptualizing and collecting one or more variables
<input type="checkbox"/>	Data collection
<input type="checkbox"/>	Conceptualizing and designing this specific paper project
<input type="checkbox"/>	Statistical analyses
<input type="checkbox"/>	Writing
<input type="checkbox"/>	Reviewing manuscript drafts
<input type="checkbox"/>	Final approval before submission for publication
<input type="checkbox"/>	Acknowledgment only, I will not be a co-author

Signature:
