Concept Paper Template

Provisional Paper Title: Assessing the Developmental Taxonomy: functional neural correlates of life-course persistent vs. adolescence-limited antisocial behaviour in a longitudinal birth cohort

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P.I. Sponsor: Ahmad Hariri & Terrie Moffitt, with Essi Viding
(if the proposing author is a student or colleague of an original PI)

Today's Date: 8th August, 2018

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

Objective of the study:

Conduct disorder (CD) is characterized by persistent and pervasive antisocial behaviour which typically emerges early in life, usually during childhood or adolescence. Developmental Taxonomic Theory[1] suggests that there are two pathways by which antisocial behaviour arises, persists and desists, each linked to different hypothesized aetiological profiles. 'Life-course persistent' (LCP) antisocial behaviour characterizes a relatively small group of individuals who exhibit antisocial behaviour beginning in childhood which persists through adolescence and into adulthood. It is thought that LCP antisocial behaviour is neurodevelopmental in origin, characterized by neuropsychological impairment in executive functions and emotional reactivity. On the other hand, 'adolescence-limited' (AL) antisocial behaviour describes a comparatively larger group of individuals exhibiting such behaviour beginning in adolescence and primarily limited to this developmental window[2]. AL antisocial behaviour is thought to be developmentally normative in most cases, influenced by a gap in maturity between biological and social factors during adolescence[3,4]. In line with the Developmental Taxonomy[1], studies comparing these subtypes on neuropsychological function have shown that cognitive abnormalities are more pronounced in the LCP subtype[5,6]. Neuroimaging research into the Developmental Taxonomy is currently sparse, restricted to studies from a single research group focusing on a small sample of cognitively able adolescents from relatively high socioeconomic backgrounds. The neuroimaging findings (both functional and structural) from this sample regarding the Developmental Taxonomy have been mixed, with some analyses differentiating the LCP and AL groups, whilst others have not differentiated these individuals by age of onset[7,8]. These results are difficult to interpret given the demographic differences between the neuroimaging sample from these studies, and those derived empirically from longitudinal epidemiological cohorts.

Here, we propose to compare brain function of individuals with a history of LCP or AL antisocial behaviour from the Dunedin Multidisciplinary Heath and Development Study. The functional neuroimaging phase of this study focuses on 4 neural 'hubs', each coordinating information processing through distributed brain circuitry supporting 4 behavioral capacities: (1) the ventral striatum (VS) and reward, (2) the amygdala and emotion/threat, (3) the dorsolateral prefrontal cortex (dlPFC) and executive control and (4) the hippocampus and episodic memory. Dysfunction involving these processes has been proposed in individuals with a history of antisocial behavior and CD[9,10]. We aim to leverage the unique nature of this cohort to investigate whether dysfunction in the underlying neural circuitry supporting these functions is seen across subtypes or whether such neuropsychological abnormalities are specific to or more pronounced in LCP individuals.

Data analysis methods:

Analysis of fMRI data will be conducted in accordance with existing preprocessing pipelines set up by Prof Hariri and colleagues (Annchen Knodt and Max Elliot). Analyses outlined below will be conducted comparing groups of LCP or AL individuals as determined by longitudinal reports of antisocial behaviour. A series of whole brain and region of interest analyses will be conducted comparing trajectories of brain function in adulthood on:

1. Reward-related VS activity as measured with BOLD fMRI during the Monetary Incentive Delay task
2. Threat-related amygdala activity during an facial emotion processing task[11]
3. Executive control-related dlPFC activity during a colour-word Stroop task
4. Episodic memory-related hippocampal function during a memory encoding/retrieval task[12]

In addition to group comparisons, whole-sample reliability analyses will be conducted to ensure the fMRI tasks elicited activation in expected brain regions.

We will also conduct secondary analyses including covariates (SES, IQ, head injury, substance use, and schizophrenia) to test for confounding effects of these factors which may relate to an antisocial lifestyle or might have brought about brain changes after childhood.

In line with previous work and the trajectories of antisocial behaviour in males vs. females, this study will focus on males only[13].

Variables needed at which ages:

- Antisocial conduct problems trajectory variable (LCP, AO, low)[14,15]
- fMRI data and task performance data from amygdala, VS, dlPFC and hippocampus tasks (age 45) – in house

Due to the fact that fMRI scans were collected at a later time point (age 45) compared to indices of antisocial behaviour (assessed at ages 7-26), it may be beneficial to conduct post-hoc analyses investigating the potential confounding impact of the following variables on neurocognitive findings:

- Childhood SES - SES115 (birth to age 15)
- Adult/concurrent SES - age 38
- WISC-RIQ7911
- WAIS-IQ38
- Alcohol abuse history: N of Study phases diagnosed with alcohol dependence
- History of Traumatic Brain Injury variable
- Schizophrenia group 1 diagnosis up to age 38[16]

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

It is unclear based on prior research to what degree the neurocognitive profile differs between LCP and AL groups. Existing studies lack a reliable assessment of antisocial behaviour and associated neurocognitive deficits across the lifespan. This is due in part to the nature of the sample that is used in existing studies, which is not representative of LCP and AL groups as derived from epidemiological samples. The Dunedin Study presents a unique opportunity to combine rich multi-source observational measures of behaviour with neuroimaging data to investigate the association between CD subtypes and neurocognitive trajectories.

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Data Security Agreement

Provisional Paper Title	Assessing the Developmental Taxonomy: functional neural correlates of life-course persistent vs. adolescence-limited antisocial behaviour in a longitudinal birth cohort
Proposing Author	Christina Carlisi
Today's Date	10/08/2018

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

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CC	I am current on Human Subjects Training (CITI (www.citiprogram.org) or equivalent)
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CC	I will not "sync" the data to a mobile device.
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CC	I will not share the data with anyone, including my students or other collaborators not specifically listed on this concept paper.
CC	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.*
CC	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: __  _____

CONCEPT PAPER RESPONSE FORM

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Provisional Paper Title	Assessing the Developmental Taxonomy: functional neural correlates of life-course persistent vs. adolescence-limited antisocial behaviour in a longitudinal birth cohort
Proposing Author	Christina Carlisi
Other Contributors	Essi Viding, Ahmad Hariri, Annchen Knodt, Terrie Moffitt, Avshalom Caspi, From Dunedin: Richie Poulton, Sandhya Ramrakha,
Potential Journals	
Today's Date	10th August, 2018
Intended Submission Date	December 2018

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B. To be completed by potential co-authors:

	Approved
	Not Approved
	Let's discuss, I have concerns

Comments:

Please check your contribution(s) for authorship:

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

Signature: