Concept Paper Template 2019

Provisional Paper Title: Is physical health and the pace of ageing, worse for adults with high autistic traits? Physical health and ageing correlates of the AQ-10 at 45 years in the Dunedin Study.

Proposing Author: Francesca Happé

Co Authors: Temi Moffitt, Avshalom Caspi, Dunedin team, David Mason (PhD student), Angelica Ronald, Richie Poulton, Sandhya Ramrakha, Renate Houts, Jasmin Wertz.

Author's Email: Francesca.happe@kcl.ac.uk

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

Today's Date: November 19th 2019

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

Objective of the study:

Background and gaps in the literature

An autism diagnosis is based on several domains of functional impairment: social interaction, communication, and restricted interests/repetitive behaviours. Recent research measuring these traits in the general population supports a dimensional approach. For instance, the same genetic influences appear to operate on individual differences in subclinical autistic traits and on diagnosed autism. Moreover, behaviourally these traits form a smooth distribution through the general population to those diagnosed with autism. In addition, behavioural genetic studies suggest largely independent genetic influences operating on the social and nonsocial domains of autistic traits; indeed, in the general population many participants will show impairment in just one domain (e.g. social communication; see the 'fractionated triad' account, Happe et al, 2006). Research with general population samples, taking a (multi)dimensional approach, is thus increasingly seen as a tractable route to discovering more about autism.

Recent research suggests that autistic adults have significantly higher rates of almost all physical health conditions (Croens et al, 2015). These data, from

medical insurance records, report greatly elevated odds ratios (OR) for many physical health conditions: e.g., diabetes (OR=2.18), thyroid disease (OR=2.46), constipation (OR=3.11). Moreover, population register data from Sweden indicate an elevated risk of premature mortality for autistic people compared to the general population, with average mortality occurring 17 years earlier in the autistic sample (Hirvikoski et al 2016).

It is as yet unknown whether high autistic traits also predispose to elevated rates of physical health conditions, as seen in diagnosed autism. Establishing this, and future studies with polygenic scores, may help unpick whether high rates of physical health conditions in autism are due to genetic (e.g. a common etiology for autism and physical illness), phenotypic(e.g. poorer communication leading to reduced help seeking), or societal factors (e.g., victimization, reduced access to health care). Moreover, the nature of the association may be different for different specific health conditions. Longitudinal data would help address causal paths to ill health in autism.

Many of the conditions found at greatly raised levels in previous studies of autistic adults (Croen et al, 2015) are age-related: e.g., dementia (OR=4.40), cardiovascular disease (OR=2.54), hearing impairment (OR=2.35), and low vision/blindness (OR=7.85). No longitudinal studies of physical health and ageing in autism exist. Cross-sectional studies (e.g., Fortuna et al., 2016) suggest some conditions are significantly more prevalent in older than younger autistic adults. Cross-sectional differences, however, may be explained by cohort effects. Therefore, a longitudinal examination of physical health and pace of ageing in adults high in autistic traits, would make a significant contribution to the field.

Aims and objectives:
The aim of this study is to examine the association between autistic traits and physical health and the pace of ageing in midlife.

Objectives
   A. Cross-sectional analysis at age 45:
   1. To report on the proportion of Dunedin participants scoring high for autistic traits (social-communicative and nonsocial subscores, on the AQ-10) at age 45, and those scoring below the cutoff (see methods below; hereafter 'low scorers').
   2. To report the physical health status of high scorers compared to low scorers (e.g. compare rates of health conditions and compare to existing studies; Croen et al, 2015). The McClintock scale is a good place to start as it summarises health conditions at age 45.
   3. To report the correlation between autistic traits dimensionally and physical health and pace of ageing from Phase 26 to 45.

Data analysis methods:

Data from the AQ-10 will be used to identify those with high autism traits. The usual cut-off of 6/10 would identify just 27 participants [to be confirmed using ARC/NICE coding], but the full range of scores would also be informative, taking a dimensional approach. We would also follow the 'fractionated triad' idea and look at items by underlying construct (social-communication versus nonsocial traits), to identify individuals scoring high in one domain.

As well as group comparisons (high and low traits compared with e.g. ANOVA or Krushkal-Wallis), correlational and regression analyses would be conducted to identify whether higher autism traits are related to worse physical health and more rapid Pace of Ageing.

All distributions will be checked, and where necessary, variables may be transformed to approximate normality.

Variables needed at which ages:

AQ-10, age 45

Outcome measures of health and aging:

Physical health outcome measures, age45: McClintock Scale in first instance (if significantly associated with AQ scores, may request more detailed physical health measures)

Pace of Aging, age 26-45.

Self-perceived ageing

informant reports of vitality

Facial age at 45

Other measures:

Gender

SES, childhood and at age 45

Cognitive functioning, age 11 and age 45 (WAIS IQ)

DSM diagnoses of Anxiety, Depression, ADHD, at 45 (to control for possible confounding effects and establish specificity of AQ's relationship with ageing variables)

Temperament measures from age 3 (Researchers' observational notes from age 3 and any clinical notes from childhood) to support AQ-10 status developmentally

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

To establish the relevance of autistic traits for healthy ageing; if negatively related, these traits may be relevant to assess in primary care in order to identify a vulnerable group needing preventative health care.

To establish whether high autism traits are associated with increased rates of physical health conditions seen in autism. This information will be important in beginning to untangle if associated health problems are genetically linked to autism, or phenotypic (due to living with autism).

Possible patterns of specific association between autistic traits and physical conditions may be important for specific etiological theories of autism (e.g. inflammation, autoimmune accounts).

Pace of ageing has never been explored in autistic adults or in relation to autism traits, but alterations in maturational trajectories (e.g. head and brain 'overgrowth' in the first 4 years of life) have been considered important clues to the fundamental biology of autism. If associations with autistic traits are found, this would lay the groundwork for studies in diagnosed autism samples, as well as further work to untangle the causal chain from socio-communicative and/or rigid and repetitive difficulties to faster ageing.

Data Security Agreement

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Proposing	Francesca Happé, David Mason, Angelica Ronald, Temi Moffit, Avshalom Caspi
Today's	November 2019

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

Please initial your agreement: (customize as necessary)

FH	I am current on/will refresh my Human Subjects Training [CITI www.citigrogram.org] or equivalent.
FH	My project is covered by the Dunedin Study's ethics approval OR I have /will obtain ethical approval from my home institution (please specify).

FH	I will treat all data as "restricted" and store in a secure fashion. My computer or laptop is: • encrypted (recommended programs are FileVault2 for Macs, and Bitlocker for Windows machines) • password-protected • configured to lock-out after 15 minutes of inactivity AND • has an antivirus client installed as well as being patched regularly.
FH	I will not "sync" the data to a mobile device.
FH	In the event that my laptop with data on it is lost, stolen or hacked, I will immediately contact my PI Sponsor or Study Director
FH	I will not share the data with anyone, including my students or other collaborators not specifically listed on this concept paper.
FH	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 your PI Sponsor or Richie Poulton for strategies for achieving compliance with data-sharing policies of journals.*
FH	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:

F. Happé.