

CONCEPT PAPER FORM

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Proposed co-authors: Avshalom Caspi, Dan Belsky, Richie Poulton, Sandhya Ramrakha, Reut Avinun, Bob Hancox, Judith Sligo

Provisional Paper Title: Can polygenic scores for educational attainment help identify targets for environmental intervention? The case of parenting.

Date: 03/01/2017

Objective of the study:

Recent genome-wide association studies have uncovered genetic variants associated with educational attainment (Rietveld et al., 2013; Okbay et al., 2016). The results of these studies can be used to compute a polygenic score for educational attainment, i.e. a combination of multiple genetic markers into a single score for an individual person. In previous research, we followed-up GWAS discoveries for educational attainment using the polygenic score method (Belsky et al., 2016; Wertz et al., in prep). A key finding from these studies is that genetics discovered in GWAS of educational attainment are related not only to education but also to life-course social success and adversity more generally. Our developmental analyses further revealed two pathways through which these associations came about. One pathway was genetic influence on early-emerging individual differences in cognitive and non-cognitive skills. This finding bolsters arguments for early intervention to promote development of these skills as an effective strategy to support socioeconomic achievement later in life. A second pathway was suggested by our finding of a gene-environment correlation: children who carried more education-associated alleles tended to grow up in more socially advantaged family environments. A portion of genetic associations with life-course socioeconomic success was explained by the early "head start" created by these environments. Further research is needed to understand the family processes that mediate this head start. Socially advantaged family environments are thought to promote positive development because they structure successful family dynamics, including warm, sensitive parenting and stimulating home environment. We propose to test if genetics associated with achieving socioeconomic success are also associated with cultivating a warm, sensitive, and stimulating environment for one's children. A better understanding of how genetics shape family processes can inform environmental interventions to promote successful family dynamics and positive development in children.

We propose to test our hypothesis of a genetic association with warm, sensitive parenting and stimulating home environment using data on Dunedin participants' parenting of their offspring, collected when their children were 3 years old. Specifically, the questions we propose to address in this study are:

1) How are genetics discovered in GWAS of educational attainment related to the parenting and caregiving environment Dunedin participants provide to their own children?

We will examine associations between Dunedin participants' polygenic scores for educational attainment and two sources of data that capture Dunedin participants' parenting: videotaped observations of participants interacting with their 3-year olds as well as systematic assessments of the home environment participants create. Our main objective will be to examine associations with overall factors of parenting, generated using factor-analyses of single parenting scales. For example, the video observations of

participants' parenting were coded on scales that reflect aspects of parenting such as warmth or cognitive stimulation, and a previously computed factor analysis of all scales revealed a main factor of "warm, sensitive, stimulating parenting" (Belsky, Jaffee, Sligo, Woodward, & Silva, 2005). We will also examine associations with single scales, to test whether genetic associations are similar across these.

2) What developmental and behavioral pathways that are amenable to intervention connect polygenic scores with parenting?

If polygenic scores are associated with parenting, we will test (non-mutually exclusive) explanations for why this is the case. First, it is possible that participants with higher polygenic scores have a personality profile that is associated with more warm, sensitive, stimulating parenting; e.g. they may have greater cognitive ability and display less antisocial behavior (Jaffee et al., 2006; van Bakel & Riksen-Walraven, 2002). Second, participants with higher polygenic scores may have better resources that affect their parenting, e.g. they may have attained a higher socioeconomic status, or be in a higher-quality relationships with their partners (Grych, 2002). We will test whether these explanations can account for associations between polygenic scores and parenting.

3) How are genetics discovered in GWAS educational attainment associated with "upward mobility" of parenting, i.e. the transition from receiving harsh parenting as a child to becoming a warm, sensitive caregiver to one's own children? This is often called "breaking the cycle."

One factor that predicts individuals' parenting is the quality of parenting they themselves received (Belsky et al., 2005). Based on this finding, we will take an intergenerational perspective to test whether higher polygenic scores can help participants overcome the experience of being poorly parented, and become more warm, sensitive, stimulating parents themselves.

Statistical analyses:

For Aim 1) How are genetics discovered in GWAS of educational attainment related to the parenting and caregiving environment Dunedin participants provide to their own children?

To test this aim we will use regression models, with the polygenic score as the independent variable and parenting as the outcome. We will use regression models appropriate for the scale and distribution of our parenting variables. We will first run models without any adjustment, and then test whether associations remain once we adjust for a) age of parent when they had their first child, and b) sex of parent.

For Aim 2) What developmental and behavioral pathways connect polygenic scores with parenting?

We will use the same regression models as in Aim 1, but add variables that we hypothesized could explain associations between the polygenic score and parenting. We will observe whether the association reduces significantly once we add these variables to the model, i.e. whether they mediate parts or all of the association.

For Aim 3) How are genetics discovered in GWAS educational attainment associated with "upward mobility" of parenting, i.e. the transition from receiving harsh parenting as a child to becoming a warm, sensitive caregiver to one's own children?

We would run the same models as in Aim 1, but run them within groups of participants who experienced poor, average, or high-quality parenting as children. We would test whether the associations between polygenic scores and parenting are similar across these three groups.

Variables Needed at Which Ages (names and labels):

Study: Dunedin (all participants)

Note: Please include the most recent complete set of variables

- Participants' polygenic scores, residualised, non-clumped
- Whether they are a parent or not
- From the parent interview
 - o Parents' age at birth of first child
 - o Gender of parent
 - o Who is currently living with X and yourself
 - o Marital status currently
 - o Marital status with biological parent
 - o Finances
 - o Planned/unplanned pregnancy
- Parenting variables from the video recordings
 - o vidratp3_sensitive_2016 Video Rating parent sensitivity
 - o vidratp3_intrusive_2016 Video Rating parent intrusiveness
 - o vidratp3_detach_2016 Video Rating parent detachment
 - o vidratp3_cogstim_2016 Video Rating parent cog stimulation
 - o vidratp3_posreg_2016 Video Rating parent positive regard
 - o vidratp3_negreg_2016 Video Rating parent negative regard
 - o vidratc3_posmood_2016 Video Rating child positive mood
 - o vidratc3_negmood_2016 Video Rating child negative mood
 - o vidratc3_activitylvl_2016 Video Rating child activity level
 - o vidratc3_persistence_2016 Video Rating child persistence/sustained attn
 - o kidposv3_2016 Video rating child positivity, hi = high positive
 - o kidnegv3_2016 Video rating child negativity, hi = high negative
 - o parposv3_2016 Video rating parent positivity, hi = high positive
- HOME variables
 - o HOMEresp3_2016 Responsiveness, SM as parent of 3 yo, HOME InfantToddler_Bradley, RW impression
 - o HOMEhrsh3_2016 Harsh parenting, SM as parent of 3 yo, HOME InfantToddler_Bradley, RW impression
 - o HOMEopa3_2016 Opportunity for Productive Activity, HOME InfantToddler_Bradley, RW impression
 - o HOMELrn3_2016 Learning Materials, SM as parent of 3 yo, HOME InfantToddler_Bradley, RW impression
 - o HOMEstim3_2016 Stimulation, SM as parent of 3 yo, HOME InfantToddler_Bradley, RW impression
- Composite variables of parenting that Dunedin participants received
 - o posparec positive parenting (early childhood)
 - o posparmc positive parenting (mid childhood)
 - o posparea positive parenting (early adolescence)
 - o negparec negative parenting (early childhood)
 - o negparmc negative parenting (mid childhood)
 - o negparea negative parenting (early adolescence)
 - o cogstiec cognitive stimulation (early childhood)
 - o cogstimc cognitive stimulation (middle childhood)

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

In general, this proposed project is intended to uncover what behavioral and contextual processes mediate genetic effects on parenting styles, because doing so affords targets of intervention—just as it does in research on the genetics of other outcomes. Research in the Dunedin cohort has illustrated this approach previously, for outcomes such as obesity and educational attainment (Belsky et al, 2012; Belsky et al., 2016). For example, knowing about ‘when’ polygenic influences on obesity manifest as traits and behavior points to windows of opportunity for obesity prevention; knowing that polygenic influences predict educational attainment by affecting how rapidly children learn to read points to a window of opportunity for education promotion. And, even polygenic effects on parenting that are not mediated by parents’ SES and education must still be mediated by something, so if these obvious first-line mediators do not entirely explain genetic associations with parenting, this finding would highlight the need for other researchers to pursue such “known unknowns”.

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Data Security Agreement

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Proposing Author	Jasmin Wertz
Today's Date	02.17.2017

Please keep one copy for your records

(Please initial your agreement)

 JW_ I am current on Human Subjects Training (CITI (www.citiprogram.org) or training in human subject protection through my post or courses.

 JW_ My project is covered by Duke or King's IRB OR I have /will obtain IRB approval from my home institution.

 JW_ I will treat all data as "restricted" and store in a secure fashion.

 JW_ I will not share the data with anyone, including students or other collaborators not specifically listed on this concept paper.

 JW_ 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 E-Risk Study cannot be shared because the Study Members have not given informed consent for unrestricted open access. Speak to Terrie or Avshalom for strategies for dealing with data sharing requests from Journals.

 JW_ Before submitting my paper to a journal, I will submit my draft manuscript and scripts for data checking, and my draft manuscript for co-author mock review, allowing three weeks.

 JW_ I will submit analysis scripts and new variable documentation to project data manager after manuscript gets accepted for publication.

 JW_ I will return all data files to the Data Manager after the project is complete. Collaborators and graduates of DPPP may not take a data file away from the DPPP office. The data remains the property of the Study and cannot be used for further analyses without express, written permission.

 JW_ I will ensure geographical location information, including postcodes or geographical coordinates for the E-Risk study member's homes or schools, is never combined or stored with any other E-Risk data (family or twin-level data)

Signature:J. Wertz.....

CONCEPT PAPER RESPONSE FORM

A. To be completed by the proposing author

Proposing Author:

I have read the data-sharing policy guidelines and agree to follow them

Provisional Paper Title: Can polygenic scores for educational attainment help identify targets for environmental intervention? The case of parenting.

Potential co-authors: Terrie Moffitt, Avshalom Caspi, Dan Belsky, Jay Belsky, Richie Poulton, Sandhya Ramrakha, Reut Avinun

Potential Journals:

Intended Submission Date (month/year):

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

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: