BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: CASPI, AVSHALOM

eRA COMMONS USER NAME (credential, e.g., agency login): ACASPI

POSITION TITLE: Edward M Arnett Professor of Psychology and Neuroscience

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of California, Santa Cruz	BA	05/81	Psychology
Cornell University, Ithaca, NY	MA	05/83	Developmental Psychology
Cornell University, Ithaca, NY	PhD	06/86	Developmental Psychology

A. Personal Statement

My research spans the fields of psychology, epidemiology, and genetics. My work is concerned with three broad questions. (1) How do childhood experiences shape aging trajectories? (2) How do genetic differences between people shape the way they respond to their environments? (3) What are the best ways to assess and measure personality and mental health across the life course, from childhood to old age? To address these questions, I conduct longitudinal research. Longitudinal research is an inherently horizon-scanning enterprise, and I relish forward-planning, anticipating new trends, and asking new questions. My team has a good track record as first adopters of new research technologies; for example we were among the first cohorts to collect DNA, in 1996; among the first to use retinal imaging, in 2009; and among the first to integrate nationwide administrative data with clinical-level cohort data, in 2014. My work is about as inter-disciplinary as it gets; my team generates the most innovative discoveries when we make surprising dataset combinations across previously unconnected disciplines. I am a developmental psychologist, but I have a published record of collaboration with economists, geneticists, epidemiologists, sociologists, demographers, neuroscientists, and medical scientists, even ophthalmologists and dentists. The resulting products make an impact, as illustrated by my H-index (>170; https://scholar.google.com/citations?user=7iOXJVoAAAAJ&hl=en), one of the highest in psychology/psychiatry. I bring to projects expertise in longitudinal methods, developmental theory, personality assessment, life-course epidemiology, and genomics in behavioral science. In my research and in training students, I draw expertise from centers where I am a faculty affiliate, including the UNC Center for Developmental Science; Duke's Center for Genomic and Computational Biology; and King's College London Institute of Psychiatry Centre for Social, Genetic, and Developmental Psychiatry. As a participant in the P2C Duke Population Research Center (DPRC), I am involved in hosting guest speakers, presenting and attending lectures, seminars, and student presentations, reviewing pilot projects, and participating in collaborations with faculty at Duke and elsewhere in conjunction with the grant. For my effort on funded projects I typically conceptualize hypotheses, design data-collection protocols, monitor quality control during data collection, supervise data and biobank managers, conduct statistical analyses of data, write reports for publication, and deliver lectures at scientific meetings. I have a clear track record of bringing in large-scale research projects on-time and on-budget. I share data from these projects with investigators all over the world; over the past decade, I have provided data to over 3 dozen investigators on 5 continents. I also have an appetite for

mentoring young scientists, and I am good at identifying young people with talent. I provide them with high-quality data on which they can train, and with which they can develop new, independent ideas. I meet for 2 hours weekly with each Ph.D. student or postdoc involved in my projects. I have trained 29 young scientists from all over the world; have placed them in top-flight and influential positions; and they have won more than 40 prestigious early-career awards and fellowships. I have 30 years experience in mentoring undergraduate students at Harvard University, University of Wisconsin, undergraduate medical students at King's College London, and Duke University. Undergraduate students are involved in our research by conducting laboratory work, data coding work, and data analysis work. They participate in laboratory meetings, and are provided with one-on-one mentorship in all steps of the scientific enterprise, and also collaborate on papers.

Web Page: www.moffittcaspi.com.

B. Positions and Honors

Positions and Employment

1986 - 1989 Assistant Professor of Psychology, Harvard University
1989 - 2007 Assistant, Associate (1991), Full (1995) Professor of Psychology, U of Wisconsin, Madison
1997 - Professor of Personality Development, MRC Social, Genetic and Developmental Psychiatry Research Centre, Institute of Psychiatry, King's College London, England
2007 - Edward M Arnett Professor of Psychology and Neuroscience, Duke University

Other Experience and Professional Memberships

Honors

1995 Distinguished Scientific Award for Early Career Contribution, American Psychological Association
1995 Robert L. Fantz Award, American Psychological Foundation
2002 Elected Fellow, Academy of Medical Sciences (UK)
2005 Maccoby Book Award in Developmental Psychology, American Psychological Association
2006 Wolfson Research Merit Award,The Royal Society
2007 Mortimer D. Sackler MD Prize for Distinguished Achievement in Developmental Psychobiology, by the faculties of the Sackler Institutes of Developmental Psychobiology at Columbia University Medical Center and at Weill Cornell Medical College of Cornell University
2008 Rema Lapouse Award for Significant Contributions to the Scientific Understanding of Epidemiology and Control of Mental Disorders, American Public Health Association
2008 Distinguished Scientific Contribution Award, International Society for the Study of Behavioral Development (ISSBD)
2010 Klaus J. Jacobs Research Prize for Productive Youth Development, Jacobs Foundation
2010 Ruane Prize for Outstanding Achievement in Childhood Psychiatric Disorders, NARSAD (National Alliance for Research on Schizophrenia and Depression)
2013 Honorary Doctorate, Tilburg University,The Netherlands
2014- Highly Cited Researcher (top 100 in Psychology/Psychiatry), Thomson Reuters
2016 Distinguished Scientific Contribution Award, American Psychological Association
2018 Paul Hoch Award, American Psychopathological Association

C. Contributions to Science

1. Gene-environment interaction (GxE). Genetic endowment contributes to psychiatric disorders by shaping how people respond to environmental pathogens. Of course, this idea was around for many years, but it remained an abstract statistical concept in psychiatry until 2002/2003 when we provided the first empirical evidence of GxE interactions, in conduct disorder and depression. The work has not been uncontroversial (although oft-replicated), but lost in the debate over the use of candidate genes is the transformative nature of our discoveries. First, geneticists can leverage information about environmental exposures to identify genetic effects. Second, neuroscientists who are looking for gene-to-brain connections can uncover these connections by experimentally manipulating participants' exposure to relevant environmental stimuli. Our GxE interaction papers also proved influential in the public's understanding of genetic science. These reports vividly contradicted the public's pervasive belief in genetic determinism, by showing how genetic effects on health and behavior often depend on lifestyle factors under human control. This work launched a new era in the study of

how gene-environment interplay causes human behavior, and was recognized with prestigious prizes from NARSAD, the Sackler Foundation, and the Jacobs Foundation.

a. Caspi A, McClay J, Moffitt TE, Mill J, Martin J, et al. Role of genotype in the cycle of violence in maltreated children. Science. 2002 Aug 2; 297 (5582):851-4. PubMed PMID: 12161658.
b. Caspi A, Sugden K, Moffitt TE, Taylor A, Craig IW, et al. Influence of life stress on depression: moderation by a polymorphism in the 5-HTT gene. Science. 2003 Jul 18; 301 (5631):386-9. PubMed PMID: 12869766.
c. Caspi A, Moffitt TE. Gene-environment interactions in psychiatry: joining forces with neuroscience. Nat Rev Neurosci. 2006 Jul;7(7):583-90. PubMed PMID: 16791147.
d. Caspi A, Hariri AR, Holmes A, Uher R, Moffitt TE. Genetic sensitivity to the environment: the case of the serotonin transporter gene and its implications for studying complex diseases and traits. Am J Psychiatry. 2010 May;167(5):509-27. PubMed PMID: 20231323; PubMed Central PMCID: PMC2943341.

2. Our team is ushering in the post-GWAS era by documenting how GWAS-discovered genetic risks shape the development of illness and well-being. GWAS are turning up “hits” for many diseases and traits, and the next step is to uncover how these genetic variants work. One way to move from discovering a variant to understanding when and how it manifests to cause disease is to work from the bottom up, by tracing the path from variation in the DNA sequence to differences in RNA transcription and onwards up through disease pathogenesis, in order to identify a molecule that can be targeted for intervention. Our complementary approach works from the top down in order to inform interventions that can mitigate genetic risk. We do this by using data from our longitudinal birth cohort studies to test how genetic differences shape development and experience. For example, we found that genes detected in GWAS of BMI influenced adult obesity by shaping rapid infant growth; that genes detected in GWAS of adult smokers are unrelated to smoking initiation, but they influence rapid progression from first cigarette to addiction; that genes related to educational attainment shape social and economic success because they are linked to accelerated cognitive development and better self-control skills. Our team is integrating molecular genetic discoveries into the social and behavioral sciences to fashion models of gene-environment interplay than can be used to better explain, predict, and change behavior.

a. Belsky DW, Moffitt TE, Houts R, Bennett GG, Biddle AK, et al. Polygenic risk, rapid childhood growth, and the development of obesity: evidence from a 4-decade longitudinal study. Arch Pediatr Adolesc Med. 2012 Jun 1;166(6):515-21. PubMed PMID: 22665028; PubMed Central PMCID: PMC3534740.
b. Belsky DW, Domingue BW, Wedow R, Arseneault L, Boardman JD, Caspi A, Conley D, Fletcher J, Freese J, Heard P, Moffitt TE, Poulton R, Sicinski K, Wertz J, Harris KM. Genetic analysis of social-class mobility: Evidence from five longitudinal studies. PNAS. 2018 115: E7275-E7284. PubMed PMID: 29987013: Pub Med Central PMCID: PMC6077729
c. Belsky DW, Moffitt TE, Corcoran DL, Domingue D, Harrington HL, Hogan S, Houts R, Ramrakha S, Sugden K, Williams B, Poulton R, Caspi A The Genetics of Success: How Single-Nucleotide Polymorphisms Associated With Educational Attainment Relate to Life-Course Development. *Psychological Science. 2016 July; 27: 957-972.* PubMed PMID: 27251486: PubMed Central PMCID: PMC4946990
d. Wertz J, Caspi A, Belsky DW, Beckley AL, Arseneault L, Barnes JC, Corcoran DL, Hogan S, Houts RM, Morgan N, Odgers CL, Prinz J, Sugden K, Williams BS, Poulton R, Moffitt TE. Genetics and crime: Integrating new genomic discoveries into psychological research about antisocial behavior. Psychological Science. 2018 1-13. PubMed PMID: 29513605: PubMed Central PMCID: PMC5945301

3. Life-long legacy of temperament and personality. We have identified how early-emerging temperament differences between young children shape their subsequent development. This line of research has shown how to reliably measure personality differences between children as young as age three; provided evidence that personality rivals social class and intelligence in shaping the course of life; plus identified multiple testable hypotheses—and spawned new research programs—into the mechanisms by which personality shapes life outcomes. As examples of impact, our work on toddlers' under-control is used to argue that preschool education promoting self-control could have remarkable economic benefits and our longitudinal studies tracking continuity and change in personality provided the empirical base for today’s emphasis on personality in healthy aging. It is often forgotten that when we began this work there was widespread doubt about the existence of early-emerging personality differences and skepticism about their influence on people’s lives. Today this is taken as fact, and our research on personality development has 'entered the vernacular.'

a. Caspi A, Moffitt TE, Newman DL, Silva PA. Behavioral observations at age 3 years predict adult psychiatric disorders. Longitudinal evidence from a birth cohort. Arch Gen Psychiatry. 1996 Nov; 53(11):1033-9. PubMed PMID: 8911226.
b. Caspi A, Roberts BW, Shiner RL. Personality development: stability and change. Annu Rev Psychol. 2005; 56:453-84. PubMed PMID: 15709943.
c. Roberts BW, Kuncel NR, Shiner R, Caspi A, Goldberg LR. The power of personality: The comparative validity of personality traits, socioeconomic status, and cognitive ability for predicting important life outcomes. Perspectives on Psychological Science. 2007; 2(4):313-345. PMCID: 4499872
d. Moffitt TE, Arseneault L, Belsky D, Dickson N, Hancox RJ, et al. A gradient of childhood self-control predicts health, wealth, and public safety. Proc Natl Acad Sci U S A. 2011 Feb 15; 108(7):2693-8. PubMed PMID: 21262822; PubMed Central PMCID: PMC3041102.

4. The effects of early-life adversity on lifelong health. Victimized young people are at risk for a variety of poor health outcomes. But are these effects specific to some psychological functions? Are they causal? And how do they emerge? Answers to these questions are fundamental to basic research about stress and to intervention research. We have used genetically-informed longitudinal studies to answer these questions about the link between childhood adversity and adult mental health, brain health, and physical health. For example, we have established that victimization has causal (but non-specific) effects on psychiatric disorders, whereas associations with compromised cognitive development are most likely non-causal. Our team has also contributed knowledge about how early-life psychosocial stress is converted to physiological abnormalities in biomarkers, thus leading to poor health and accelerated aging. For example, our research has pointed to the importance of chronic inflammation in adult victims of child abuse. Collectively, this body of work has accelerated knowledge about the enduring effects of stress, put a nail in the coffin of unproductive hypotheses, and opened up new avenues of research.

a. Danese A, Pariante CM, Caspi A, Taylor A, Poulton R. Childhood maltreatment predicts adult inflammation in a life-course study. Proc Natl Acad Sci U S A. 2007 Jan 23; 104(4):1319-24. PubMed PMID: 17229839; PubMed Central PMCID: PMC1783123.
b. Moffitt TE. Childhood exposure to violence and lifelong health: clinical intervention science and stress-biology research join forces. Dev Psychopathol. 2013 Nov; 25(4 Pt 2):1619-34. PubMed PMID: 24342859; PubMed Central PMCID: PMC3869039.
c. Danese A, Moffitt TE, Arseneault L, Bleiberg B, Dinardo P, Gandleman S, Houts R, Ambler A, Fisher H, Poulton R, Caspi A The origins of cognitive deficits in victimized children: Implications for neuroscientists and clinicians. American Journal of Psychiatry. 2016. 174: 349-361. PubMed PMID: 27794691; PubMed Central PMCID: PMC5378606
d. Marzi SJ, Sugden K, Arseneault L, Belsky DW, Burrage J, Corcoran DL, Danese A, Fisher HL, Hannon E, Moffitt TE, Odgers CL, Pariante C, Poulton R, Williams BS, Wong C, Mill J, Caspi A. Analysis of DNA methylation in young people reveals limited evidence for an association between victimization stress and epigenetic variation in blood. American Journal of Psychiatry 2018. 1-13.

5. Psychiatric epidemiology. Our research has yielded three novel findings about the developmental epidemiology of mental illness. First, over half of adult patients with psychiatric disorders have their first diagnosable disorder before 15 years of age, suggesting that most of the burden of adult mental disorder could be prevented by effective screening and treatment for young people. Second, if people are followed long enough, while being assessed frequently for mental disorders, almost everyone will experience diagnosable anxiety, depression, or substance dependence. Less than 20% of a birth cohort makes it to midlife without ever experiencing any mental disorder. This surprising finding has been replicated by several longitudinal studies. Third, rather than distinct, categorical conditions, common psychiatric disorders in adulthood may be characterized by three underlying core psychopathological processes: an internalizing dimension, indicating liability to experience mood and anxiety disorders; an externalizing dimension, indicating liability to experience substance disorders and antisocial disorders; and a psychotic experience dimension. Our continuing work on the structure of psychopathology suggests that all psychiatric symptoms a person ever experiences can fit onto one single dimensional scale of severity (the “p factor”), with symptoms of thought disorder at its extreme end. As a result of these studies, researchers are asking why so many people experience mental disorder and what

this means for the way we define mental health, design research, deliver psychiatric services, and count the economic burden of mental illness. At the least, the finding that most people will experience disorder if they live long enough should reduce stigma against mental illness.

a. Krueger RF, Caspi A, Moffitt TE, Silva PA.The structure and stability of common mental disorders (DSM-III-R): A longitudinal-epidemiological study. Journal of Abnormal Psychology. 1998 May;107(2):216-27. PubMed PMID: 9604551

b. Kim-Cohen J, Caspi A, Moffitt TE, Harrington H, Milne BJ, Poulton R. Prior juvenile diagnoses in adults with mental disorder: Developmental follow-back of a prospective-longitudinal cohort. Archives of General Psychiatry. 2003 Jul;60(7):709-17. PubMed PMID: 12860775
c. Schaefer JD, Caspi A, Belsky DW, Harrington HL, Houts R, Horwood J, Hussong A, Ramrakha S, Poulton R, Moffitt TE. Enduring mental health: Prevalence and prediction. Journal of Abnormal Psychology. 2017 126: 212-224; PubMed PMID: 27929304, PubMed Central PMCID: PMC5304549
d. Caspi A, Moffitt TE. All for one and one for all: Mental disorders in one dimension. American Journal of Psychiatry. 2018 PubMed PMID: 29621902

D. Additional Information: Research Support and/or Scholastic Performance
Ongoing Research Support

2009/03/01-2020/03/31
RO1 AG032282, National Institute on Aging (NA)
MOFFITT, TERRIE E (PI)
Aging in 1000 healthy young adults
Aims to track biological aging in young to midlife adulthood, and study its social and genomic correlates.
Role: CPI

2017/01/01-2021/12/31
P005918, UK Medical Research Council
MOFFITT, TERRIE EDITH (PI)
Midlife Pace of Aging in the Dunedin Study, 2017-2021
This project supports data collection in the Dunedin longitudinal study.

2015/07/15-2020/02/29
1RO1 AG049789, National Institute on Aging (NIA)
MOFFITT, TERRIE Edith (PI) and HARIRI, AHMAD (Co-PIs)
Neural signatures of health and unhealthy aging: The Dunedin Study
Aims to collect and study brain imaging data in the Dunedin cohort
Role: Co-Investigator