BIOGRAPHICAL SKETCH 2023

NAME: CASPI, AVSHALOM

eRA COMMONS USER NAME (agency login): ACASPI

POSITION TITLE: Edward M. Arnett Professor (Duke), Professor of Personality Development (King's College London)

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
University of California, Santa Cruz	BA	05/1981	Psychology
Cornell University, Ithaca, NY	MA	05/1983	Developmental Psychology
Cornell University, Ithaca, NY	PHD	05/1986	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 mental health problems unfold across and shape the life course? (3) What are the best ways to assess and measure accelerated aging? I am a psychologist, but I have a published record of collaboration with economists, geneticists, epidemiologists, sociologists, demographers, neuroscientists, and medical scientists. The resulting products make an impact, as illustrated by my H-index (>200), one of the highest in psychology/psychiatry in the world and ranked 207th among all scientists in the world. I bring to projects expertise in longitudinal methods, developmental theory, life-course epidemiology, and genomics in behavioral science. I maintain active collaborations with colleagues in North America, South America, Europe, Asia, Australia, and New Zealand**.** I am also committed to mentoring young scientists. I meet for 2 hours weekly with each Ph.D. student or postdoc involved in my projects. I have trained scientists from all over the world and have placed them in top-flight and influential positions.

Ongoing and recently completed projects that I would like to highlight include:

NIA R01AG073207-01A1 Validating a 3rd-generation methylation measure of accelerated aging: DunedinPACE. 2022-2026. Joint Principal Investigator (with TE Moffitt)

NIA R01AG069939 Comprehensive portrait of long-term cannabis users: Are they ready for old age? 2020-2024. Co-Investigator (PI TE Moffitt)

NIA R01AG032282 Aging in 1000 healthy young adults: Phase 52 of the Dunedin Study. 2009-2027. Joint Principal Investigator (with TE Moffitt)

NIA R01AG049789 Quantifying individual differences in midlife structural brain integrity associated with later AD/ADRD risk. 2015-2027. Co-Investigator (with joint PIs TE Moffitt & A Hariri)

UK MRC MR/P005918 Midlife pace of aging in the Dunedin study: Cognition. 2017-2027. Joint Principal Investigator (with TE Moffitt)

Rockwool Foundation - Inequality in service uptake: A comparative study. 2020-2023. Co-Investigator (PI S Andersen)

B. POSITIONS AND HONORS

Positions and Employment

2020 – Research Professor, University of Oslo, Norway
2007 – Edward M Arnett Professor of Psychology and Neuroscience, Duke University

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

Selected Honors

2024 Ranked 8th of scientists in psychology in the world, https://research.com/scientists-rankings/psychology
2022 Elected Fellow, American Academy of Arts and Sciences
2022 Rutherford Medal, Royal Society of New Zealand (with Moffitt, Poulton, Thomson)
2019 Outstanding Postdoctoral Mentor, Duke University Graduate School
2019. Listed among the elite (or .01 percent) scientists worldwide. PloS Biology, 2019
2018 Paul Hoch Award, American Psychopathological Association
2016 The Prime Minister's (New Zealand) Science Prize | Te Puiaki Pūtaiao Matua a Te Pirimia (awarded to the Dunedin Study investigators)
2016 Distinguished Scientific Contribution Award, American Psychological Association
2014 – Highly Cited Researcher (top 100 in Psychology/Psychiatry), Thomson Reuters/Clarivate (continuous since 2014)
2013 Honorary Doctorate, Tilburg University, The Netherlands
2010 Ruane Prize for Outstanding Achievement in Child and Adolescent Psychiatry, Brain & Behavior Foundation (formerly NARSAD)
2010 Klaus J. Jacobs Research Prize for Productive Youth Development, Jacobs Foundation
2008 Distinguished Scientific Contribution Award, International Society for the Study of Behavioral Development (ISSBD)
2008 Rema Lapouse Award for Significant Contributions to the Scientific Understanding of Epidemiology and Control of Mental Disorders, American Public Health Association
2007 Mortimer D. Sackler MD Prize for Distinguished Achievement in Developmental Psychobiology
2006 Wolfson Research Merit Award, The Royal Society
2005 Maccoby Book Award in Developmental Psychology, American Psychological Association
2002 Elected Fellow, Academy of Medical Sciences (UK)
1995 Robert L. Fantz Award, American Psychological Foundation
1995 Distinguished Scientific Award for Early Career Contribution to Psychology, American Psychological Association

C. CONTRIBUTIONS TO SCIENCE

1. **Integrating GWAS discoveries into life-course epidemiology**. 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 in life-course epidemiology works from the top down in order to inform interventions that can mitigate genetic risk. We do this by using data from 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, & change behavior.

a. Belsky DW, Moffitt, TE.....Caspi, A. Polygenic risk, rapid childhood growth and the development of obesity: Evidence from a 4-decade longitudinal study. JAMA Pediatrics. 2012.
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. PMID: 29987013; PMCID: PMC6077729
c. Belsky, DW, Caspi, A., Corcoran D, Domingue B, Harris KM, Arseneault L, Houts R, Mill J, Moffitt TE, Prinz J, Sugden K, Wertz J, Williams BS, Odgers CL. Genes and the geography of health, behavior, and attainment. Nature Human Behaviour. 2019 PubMed Central PMCID: PMC6565482
d. Wertz J, Moffitt TE, Arseneault L, Barnes JC, Boivin B, Corcoran DL, Danese A, Hancox R, Harrington HL, House RM, Langevin S, Liu H, Poulton R, Sugden K, Tanksley PT, Williams BS, Caspi A. Genetic associations with parental investment from conception to wealth inheritance in six cohorts 2023. Nature Human Behavior.

2. **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, and identified multiple testable hypotheses—and spawned new research programs—about 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. PMID: 8911226
b. 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. PMID: 26151971 PMCID: PMC4499872
c. Moffitt TE, Arseneault L, Belsky D, Dickson N, Hancox RJ, ...Caspi A. 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. PMID: 21262822; PMCID: PMC3041102
d. Belsky J, Moffitt TE, Poulton R, **Caspi A**. *The Origins of You: How Childhood Shapes Later Life.* 2020. Harvard University Press

3. 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. PNAS. 2007. Jan 23; 104(4):1319-24. PubMed PMID: 17229839; PubMed Central PMCID: PMC1783123
b. 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
c. Rasmussen LJH, Moffitt TE, Arseneault L, Danese A, Eugen-Olsen J, Fisher HL, Harrington HL, Houts, RM, Matthews T, Sugden K, Williams BS, **Caspi A**. Association of adverse experiences and exposure to violence in childhood and adolescence with inflammatory burden in young people. JAMA Pediatrics 2019. PubMed Central: PMID: PMC6830440
d. Gehred MZ, Knodt AR, Ambler A, Bourassa KJ, Danese A, Elliott ML, Hogan S, Ireland D, Poulton R, Ramrakha S, Reuben A, Sison M, Moffitt TE, Hariri AR, **Caspi A**. Long-term neural embedding of childhood adversity in a population-representative birth cohort followed for five decades. Biological Psychiatry. 2021. doi.org/10.1016/j.biopsych.2021.02.971

4. **Mental health across the life course**. Our longitudinal research is yielding four new insights about the developmental epidemiology of mental illness. First, mental disorders are very common, eventually affecting the majority of people in the population. 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 past midlife without ever experiencing any mental disorder. This surprising finding has been replicated by several longitudinal studies. Some disorders are brief (like the flu, low back pain, or a broken leg) and others chronic (like COPD, arthritis, or diabetes) lasting to old age. But all are debilitating. Just because something is common does not make it inconsequential. It is our hope that increased public recognition of ubiquitous mental-health problems in the population can reduce stigma, promote earlier and increased treatment uptake, and facilitate prevention. Second, few people actually retain just one disorder over their lives. Rather, the more typical pattern is for people to shift between different disorders. This novel insight is important because it helps to account for one of the more interesting findings that has emerged in genetics and in neuroscience: Many different psychiatric disorders share the same risk factors. Our new data suggest that it is not a surprise that different conditions have the same causes because the same people have different conditions, when studied over time. This also implies that we need to rethink how we evaluate and roll out treatments. It may be that the same treatments may work for many different conditions. There is increasing appreciation that this is exactly what is happening, e.g., with novel anti-inflammatory treatments for psychiatric disorders. Third, over half of adult patients with psychiatric disorders have their first diagnosable disorder before 15 years of age. Early-onset disorders – disorders that onset in the first two decades of life – tend to last longer and to be more pervasive, morphing into increasingly more complex and comorbid conditions, suggesting that most of the burden of adult mental disorder could be prevented by effective screening and treatment for young people.

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. 107(2):216-27. 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. 60 (7):709-17. PMID: 12860775
c. **Caspi A**, Moffitt TE. All for one and one for all: Mental disorders in one dimension. American Journal of Psychiatry. 2018. PMID: 29621902 PMCID: PMC6120790
d. **Caspi A**, Houts RM, Ambler A, Danese A, Elliott ML, Hariri A, Harrington HL, Poulton R, Ramrakha S, Rasmussen LJH, Reuben A, Richmond-Rakerd L, Sugden K, Wertz J, Williams BS, Moffitt TE. Longitudinal assessment of mental health disorders and comorbidities across 4 decades among participants in the Dunedin birth cohort study. JAMA Network Open. 2020. 3(4). PMID:32315069 PMCID: PMC7175086

5. **Early-life psychiatric disorder is a precursor to late-life physical diseases.** Threats to early-life mental health are also threats to later-life physical health. Using longitudinal cohort studies, we have shown that a history of psychiatric illness is a risk factor for accelerated aging. Using nationwide administrative records, we

are tracking people for several decades and finding that mental disorders are not just a cause of premature mortality due to death from unnatural causes (e.g., suicide), but are also associated with increased risk for a wide variety of physical health problems in late life, with number of hospitalizations, length-of-stay, and healthcare costs. The same people who experience mental health problems when they are young go on to experience physical health problems when they are older adults, suggesting that psychiatry and psychology have an opportunity to prevent the rising burden of age-related disease.

a. Moffitt TE, **Caspi A**. Psychiatry's opportunity to prevent the rising burden of age-related disease. JAMA-Psychiatry. 2019. PMID: 30916735 DOI: 10.1001/jamapsychiatry.2019.0037
b. Richmond-Rakerd LS, D'Souza S, Milne BJ, **Caspi A,** and Moffitt TE. Longitudinal associations of mental disorders with physical diseases and mortality among 2.3 million New Zealand Citizens. JAMA Network Open. 2021. PMID: 33439264 PMCID: PMC7807295 DOI: 10.1001/jamanetworkopen.2020.33448
c. Wertz J, **Caspi A**, Moffitt TE, et al. History of psychiatric illness as a risk factor for accelerated aging: Evidence from a population-representative longitudinal cohort study. JAMA Psychiatry. 2021.
d. Richmond-Rakerd LS, D'Souza, S, Milne BJ, **Caspi A**, and Moffitt TE. Longitudinal associations of mental disorders with dementia: 30-year analysis of 1.7 million citizens. JAMA Psychiatry. 2022

6. Measuring accelerated aging. Biological aging is the gradual, progressive decline in system integrity that occurs with advancing chronological age, causing morbidity and disability. The geroscience hypothesis states that biological aging causes the exponential rise in morbidity across the second half of the lifespan by driving deterioration across all organ systems. The implication is that by slowing biological aging directly, instead of managing each disease separately, risk for all chronic age-related diseases could be simultaneously reduced. However, to achieve maximal prevention of age-related diseases, interventions to slow biological aging will need to target individuals in midlife before decades of subclinical organ decline have accumulated. It is thus vital to develop tools to measure meaningful variation in biological aging among younger adults. We are tackling this problem. We study the pace of biological aging by tracking change across multiple organ systems (e.g., pulmonary, periodontal, cardiovascular, renal, hepatic, and immune function, for 4 data waves across 20 years), and we developed an index, called the Pace of Aging, to capture aging-related decline. We have shown that already by midlife the Pace of Aging is associated with established signs of functional deterioration that herald chronic diseases in older adults. We have further developed a DNA-methylation predictor of the Pace of Aging (called PoAm), which provides a way to assess the Pace of Aging using a single-time-point measure in a blood sample. This new tool is opening the door for us to further interrogate the antecedents and consequences of accelerated aging.

a. Belsky DW, **Caspi A, ...**Moffitt TE.. Quantification of biological aging in young adults. PNAS. 2015. 77:601-617. PMID: 26150497 PMCID: PMC4522793 DOI: 10.1073/pnas.1506264112
b. Elliott ML, **Caspi A**, ...Moffitt. Disparities in the pace of biological aging among midlife adults of the same chronological age: Implications for future frailty risk and policy. Nature Aging. 2021. NIHMS1672843
c. Belsky DW, **Caspi, A**.....Moffitt TE. DunedinPACE: A DNA methylation biomarker of the Pace of Aging. eLIFE 2022.
d. Sugden, K, **Caspi, A**.....Moffitt TE. Association of Pace of Aging measured by blood-based DNA methylation with age-related cognitive impairment and dementia. Neurology. 2022.

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/1lkghO6DJPY9X3/bibliography/public/