

NAME OF PRESENTING AUTHOR: Jessie Baldwin

EMAIL ADDRESS OF PRESENTING AUTHOR: j.baldwin@ucl.ac.uk

Adverse childhood experiences and mental health: A genetically informed study

Jessie R. Baldwin^{1,2}, Hannah M. Sallis^{3,4,5,6}, Tabea Schoeler¹, Mark J. Taylor⁷, Alex S. F. Kwong^{3,8}, Laura D. Howe³, Andrea Danese^{2,9,10}, Eamon McCrory^{1,11}, Fruhling Rijdsdijk², Jorim J. Tielbeek¹², Wikus Barkhuizen¹, Henrik Larsson^{7,13}, Sebastian Lundström^{14,15}, Robert Karlsson⁷, Paul Lichtenstein⁷, Marcus Munafò^{3,4,5}, & Jean-Baptiste Pingault^{1,2}

¹Department of Clinical, Educational and Health Psychology, Division of Psychology and Language Sciences, University College London, London, UK

²Social, Genetic and Developmental Psychiatry Centre, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK

³MRC Integrative Epidemiology Unit at the University of Bristol, Bristol Medical School, University of Bristol, Bristol, UK

⁴School of Psychological Science, University of Bristol, Bristol, UK

⁵NIHR Biomedical Research Centre, University Hospitals Bristol NHS Foundation Trust and University of Bristol, Bristol, UK

⁶Centre for Academic Mental Health, Population Health Sciences, Bristol Medical School, University of Bristol, Bristol, UK

⁷Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Nobels väg 12A, 171 77 Stockholm, Sweden

⁸Division of Psychiatry, Edinburgh Medical School, University of Edinburgh, Edinburgh, EH10 5HF, UK

⁹Department of Child & Adolescent Psychiatry, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London SE5 8AF, United Kingdom

¹⁰National and Specialist CAMHS Trauma, Anxiety, and Depression Clinic, South London and Maudsley NHS Foundation Trust, London, UK

¹¹Anna Freud National Centre for Children and Families, London, UK

¹²CNCR, Amsterdam Neuroscience Campus, VU University, Amsterdam, The Netherlands

¹³School of Medical Sciences, Örebro University, Örebro, Sweden

¹⁴Gillberg Neuropsychiatry Centre, Institute of Neuroscience and Physiology, University of Gothenburg, Gothenburg, Sweden

¹⁵Centre for Ethics, Law and Mental Health (CELAM), Institute of Neuroscience and Physiology, University of Gothenburg, Gothenburg, Sweden

KEYWORDS: Childhood adversity; mental health; gene-environment correlation; genetic confounding; polygenic scores

ABSTRACT:

Children exposed to adverse childhood experiences (ACEs) have an elevated risk of mental health problems, but it is unclear whether these associations reflect genetic confounding. We tested (1) whether children with genetic liability to psychopathology are more likely to experience ACEs, and (2) the extent to which the associations between ACEs and mental health are genetically confounded. Participants were 6,411 children from the Avon Longitudinal Study of Parents and

Children (ALSPAC). ACEs (including maltreatment, domestic violence, and parental psychopathology, substance abuse, criminality, and separation) were prospectively measured through parent reports at multiple assessments between birth and age 9. Internalizing and externalizing problems at age 9 were assessed through parent reports on the Development and Wellbeing Assessment. We derived polygenic scores for a range of psychiatric disorders. Children with greater genetic liability to psychopathology had a small elevation in risk of ACEs (pooled odds ratio=1.05, 95% CI=1.01-1.09). Measured polygenic scores accounted for a very small proportion of the associations between ACEs with internalizing problems (pooled average across ACEs=3.6%) and externalizing problems (pooled average=4.8%). However, latent polygenic scores capturing SNP heritability in mental health outcomes explained a larger proportion of the associations between ACEs with internalizing problems (pooled average=63%) and externalizing problems (pooled average=17%). Risk of mental health problems in children exposed to ACEs is partly, but not completely driven by pre-existing genetic liability to psychopathology. Assuming the absence of nongenetic confounding, these findings are consistent with a partly causal effect of ACEs on mental health.

GRANT SUPPORT: Wellcome Trust grant 215917/Z/19/Z.