NAME OF PRESENTING AUTHOR: Kai Xiang Lim

EMAIL ADDRESS OF PRESENTING AUTHOR: kai.lim@kcl.ac.uk

Investigating the etiology of self-harm by integrating Mendelian randomization within twin modelling

Kai Xiang Lim[1], Olakunle Oggini[1], Kaili Rimfeld[1], Jean-Baptiste Pingault[1,2], Fruhling Rijsdijk[1].

[1] Social, Genetic and Developmental Psychiatry Centre, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK.

[2]Department of Clinical, Educational and Health Psychology, Division of Psychology and Language Sciences, University College London, London, UK.

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ABSTRACT:

Self-harm can be further delineated into suicidal self-harm (SSH) and non-suicidal self-harm (NSSH). By fitting Mendelian Randomization - Direction of Causation (MR-DoC) models, we investigated if there is any etiological difference between NSSH and SSH in terms of their causal relationships with mental health conditions. We used data from 9,373 twins (62.3% females, mean age = 22.3 years) in the Twins Early Development Study (TEDS). In each MR-DoC model, the exposure was either a parent- or child-rated mental health measure collected at age 16 years. The instrumental variable was a polygenic score (PS) for the exposure chosen, whereas the outcome was either NSSH or SSH. MR-DoC models were fitted using raw maximum likelihood estimation. We found significant causal effects flowing from child-rated depressive symptoms to both NSSH (g1 = 0.194, 95% CI: 0.131, 0.257) and SSH (g1 = 0.210, 95% CI: 0.125, 0.295). A similar pattern was observed for causal effects flowing from parent-rated depressive symptoms to NSSH (g1 = 0.092, 95% CI: 0.004, 0.181) and SSH (g1 = 0.165, 95% CI: 0.051, 0.281). All pleiotropic pathways in models with depressive symptoms were significant. There was no significant causal effect flowing from parent-rated ADHD symptoms to NSSH and SSH, but the pleiotropic pathway was significant in the ADHD-SSH model (b2 = 0.079, 95% CI: 0.027,0.131), and not significant in the ADHD-NSSH model. In terms of causal effects in MR-DoC models, we found no evidence of etiological difference between NSSH and SSH, suggesting they are on the same continuum.

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