



Nederlands Tweelingen Register

Tweeling- en familieonderzoek



BIONIC

BIObanks Netherlands Internet Collective

A Novel Way of Homogeneous Phenotyping

Floris Huider, Iryna Fedko, Mariska Bot, Brenda Penninx, and Dorret Boomsma
Dept Biological Psychology, Dept Psychiatry, VU Amsterdam, Amsterdam, the Netherlands



Introduction

The goal of the BIONIC project is to gain insight into the biological processes associated with mood and health, with a focus on Major Depressive Disorder (MDD) -> Insight into biological mechanisms and genetic architecture of MDD:

- Genetically complex heterogeneous phenotype
- $H^2 \sim .40$, but difficulty finding sign. SNPs
- Minimal phenotyping not ideal (Cai et al. 2018)
- Wray et al. 2018: 44 risk variants
- Howard et al. 2019: 102 risk variants
- BUT... SNP- h^2 remains the same $\sim 8.7\%$



Nederlands Tweelingen Register

Twin- and familyresearch



44%

People that experience periods in which they feel down, empty or depressed, or lose their interest, often suffer from other symptoms as well. During this period of at least two weeks in which you felt down, empty or depressed, or lost your interest in things:

... did you experience a lack of energy or did you feel tired, more so than usual?

- Yes
- No

... did you have a lower appetite than usual, almost on a daily basis?

- Yes
- No

... did you lose weight without trying, at least one kilogram per week for several subsequent weeks?

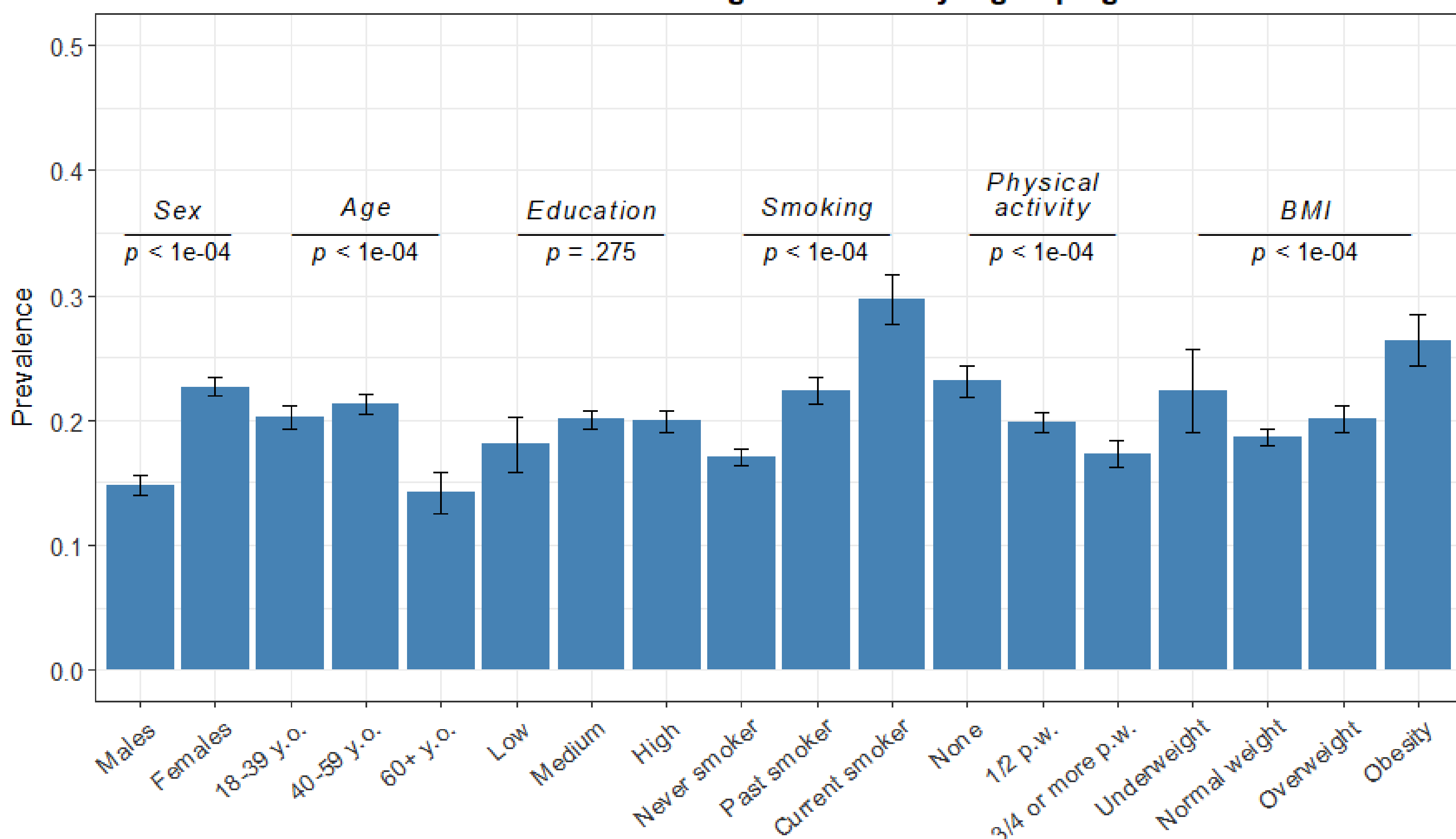
- Yes
- No

PREVIOUS

NEXT

44%

Lifetime Prevalence of MDD Conditional on biological and lifestyle grouping



LIDAS

Lifetime Depression Assessment Self-report
Newly developed online MDD-questionnaire based on the widely used Composite International Diagnostic Interview (CIDI) that assesses lifetime MDD diagnosis according to DSM-V criteria. Validity assessment (Bot et al. 2016):

- Sensitivity and specificity analyses
 - Cases = 177, controls = 87
 - Sensitivity: 85%
 - Specificity: 80%
- Feasibility analysis $n = 245$
 - Prevalence of 20.8%

A promising tool for rapid determination of lifetime MDD status in large samples, as is needed in genomics studies.

Methods and Prelim. Results

MDD prevalence in the Dutch population was determined based on the official DSM-V criteria in $n = 19.919$. Biological and lifestyle variables were measured to determine and compare prevalence between several demographic groups using chi-squared analyses. Heritability was estimated using the Netherlands Twin Register pedigree, $n = 267.683$ (Boomsma et al. 2018).

Prevalence and heritability meta-analysis

- Lifetime prevalence = 19.89%
- $H^2 \sim .29$
- PRS = 1.46% (Fedko, 2019)

Acknowledgements:

BBMRI-NL Rainbow project Phenomics 2.0 - proof of principle for major depressive disorder (RP-12)

Future Steps

The next steps in the BIONIC project involve:

- Investigating whether this form of phenotyping leads to increased power
- Performing a GWA-meta analysis in the BIONIC cohorts
- Estimating the SNP- h^2

- Boomsma, D. I., Helmer, Q., Nieuwboer, H. A., Hottenga, J. J., de Moor, M. H., van Den Berg, S. M., ... & Willemsen, G. (2018). An extended twin-pedigree study of neuroticism in the Netherlands Twin Register. *Behavior Genetics*, 48(1), 1-11.
- Bot, M., Middeldorp, C. M., de Geus, E. J. C., Lau, H. M., Sinke, M., van Nieuwenhuizen, B., ... & Penninx, B. W. J. H. (2017). Validity of LIDAS (Lifetime Depression Assessment Self-report): a self-report online assessment of lifetime major depressive disorder. *Psychological Medicine*, 47(2), 279-289.
- Cai, N., Kendler, K., & Flint, J. (2018). Minimal phenotyping yields GWAS hits of low specificity for major depression. *bioRxiv*, 440735.
- Fedko, I. O., Hottenga, J. J., Helmer, Q., Mbarek, H., Smit, J. H., de Geus, E. J. C., Penninx, B. W. J. H., Boomsma, D. I., & Bot, M. (2019). Measuring lifetime depression in the Netherlands and the genetic architecture of the phenotype as assessed by LIDAS (Lifetime Depression Assessment Self-report). *Unpublished manuscript*.
- Howard, D. M., Adams, M. J., Clarke, T., Hafferty, J. D., Gibson, J., Shirali, M., ... & McIntosh, A. M. (2019). Genome-wide meta-analysis of depression identifies 102 independent variants and highlights the importance of the prefrontal brain regions. *bioRxiv*, 433367.
- Wray, N. R., Ripke, S., Mattheisen, M., Trzaskowski, M., Byrne, E. M., Abdellaoui, A., ... & Bacanu, S. A. (2018). Genome-wide association analyses identify 44 risk variants and refine the genetic architecture of major depression. *Nature Genetics*, 50(5), 668.