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TITLE: Patterns of item nonresponse to questionnaires are systematic and have a genetic basis.

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ABSTRACT:

Item nonresponse occurs when no substantive answer is recorded for a study participant on a given item. This nonresponse is interesting both as a behavioural choice and as a statistical concern from the resulting missing data. The current study aims to evaluate the contribution of genetics in item nonresponse between individuals. We examined this behaviour in 109 items from the initial survey of UK Biobank (N=360,628), focusing on the options “Prefer not to answer” (PNA) and “I don’t know” (IDK).

GWAS of the two nonresponding behaviours identified 39 genome-wide significant loci and significant SNP-heritability for both PNA ( $h^2=2.04\%$ ,  $P=3\times 10^{-16}$ ) and IDK ( $h^2=6.75\%$ ,  $P=4\times 10^{-112}$ ). PNA and IDK are highly genetically correlated with each other ( $r_g=0.73$ , [0.70,0.76]) and with socioeconomic factors. Genomic SEM allowed to ‘subtract’ the genetic effect of IDK from PNA and vice-versa. IDK-adjusted PNA maintained a significant association with lower EA and income ( $r_g=-0.37$ , [-0.31,-0.43], for both) and poorer general health ( $r_g=0.26$  [0.21,0.31]). IDK-adjusted PNA became associated with bipolarism ( $r_g=0.25$ , [0.13,0.37]) and schizophrenia ( $r_g=0.30$ , [0.23,0.37]). The genetic variance unique of PNA and IDK after subtracting the SES effect was 1.33% ( $P=2\times 10^{-16}$ ) and 5.09% ( $P=9\times 10^{-78}$ ), respectively.

Both PNA and IDK capture a similar socioeconomic background among nonresponders; although, while IDK reflects a more random nonresponding behaviour, PNA-specific genetic signal was positively associated with psychiatric disorders.

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