Eat2beNICE

Effects of Nutrition and Lifestyle on Impulsive, Compulsive, and Externalizing Behaviours

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D 1.7 Manuscript 7: a genome-wide by environment interaction study (GWEIS) on impulsivity and compulsivity

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Starting Note

This report is a replacement of the original D.1.7. At the time of grant writing, we had planned to do a genome wide by environment interaction study (GWEIS) in relation to impulsivity but could not pursue this due to slower progress in science than envisioned. GWEIS need extremely large samples, although how large this needs to be is dependent on the effect size that is expected. GWEIS are an extension of GWAS (Genome wide association studies), but the GWAS on impulsivity have since grant writing shown to progress less fast than anticipated, the effects of nutrition on impulsivity/compulsivity identified by us were rather small, and the methodology for GWEIS (so that potentially smaller samples would be needed) has not developed either. Therefore, we have sought a valuable replacement of the planned GWEIS study, using genetics, by studying if resemblence in impulsivity between spouses who live together may be driven by shared diet and lifestyles (so called cohabitation effects) rather than by spouses choosing one another on the basis of their resemblance in impulsivity (so called assortative mating). Findings supporting the former has clinical impliactions. We report on this replacement study here.

Executive Summary

Within Deliverable 1.7 (formerly “a genome-wide by environment interaction study (GWEIS) on impulsivity and compulsivity”), a manuscript has been prepared. The manuscript report on the role of shared diet and lifestyles in spousal similarities of impulsivity and ADHD symptoms.

Previous studies have predominantly investigated the correlations between lifestyle factors and ADHD symptoms in individuals. This study, however, seeks to explore these associations within the context of spouse pairs. Given that most spouses live together, any observed convergence of impulsivity and ADHD symptoms with prolonged relationship duration could indicate the potential role of environmental factors, such as shared diet and lifestyles, in the development of impulsivity and ADHD. Although a limited number of studies have explored the correlations between partners for ADHD, the data used in these previous studies was derived from hospital and psychiatric records, which may have resulted in a biased sample of more severe cases of ADHD. Additionally, these studies failed to examine the underlying mechanisms driving the similarity between spouses. Therefore, we aimed to answer the following questions: 1) Are there significant spousal similarities for impulsivity, ADHD symptoms in the general population? 2) Can spousal similarities be explained by assortative mating, cohabitation effects or both? 3) If cohabitation effects exist, do shared diet and lifestyles play a role in spousal similarities for impulsivity and ADHD symptoms?

In 28,276 spouse pairs identified from Dutch Lifelines cohort study, we observed significant spousal correlations for impulsivity, ADHD, BMI, diet and lifestyles (i.e. current smoking, drinking, sleep duration, psysical activity). We also observed significant spousal correlation for ADHD polygenic risk score (PRS) indicating some degree of assortative mating. In addition, longer relationship was associated with smaller spousal difference so larger similarities for impulsivity, ADHD, diet and lifestyles except sleep, indicating the contribution of cohabitation effects. Furthermore, more similar diet and BMI were associated with more similar impulsivity facet and overall impulsivity score in spouses.

We concluded that there were significant spousal similarities for impulsivity and ADHD symptoms. Cohabitation effects partly explain spousal similarities of impulsivity and ADHD symptoms and shared diet and BMI contribute to spousal similarities of impulsivity. Our study provides a basis for couple-based diet and lifestyle intervention.

Abbreviations

ADHD	Attention-Deficit/Hyperactivity Disorder
PRS	Polygenic risk score
Lifelines	The Lifelines cohort study
FFQ	Food frequency questionnaire

1. Deliverable report

Note: publishers' policies prevent sharing of detailed results prior to publication in a peer-reviewed journal. Detailed results, tables and uncompromised figures will be made available upon acceptance and/or as soon as the publisher's embargo has been lifted.

Spousal similarity refers to the phenomenon that spouse-pairs are generally more phenotypically similar than would be expected by chance. Previous studies suggest that a range of psychiatric disorders such as attention-deficit/hyperactivity disorder (ADHD) are significantly correlated within spouse-pairs (Nordsletten et al., 2016). There exist two primary explanations for the occurrence of spousal similarities (Howe et al., 2019; Peyrot, Robinson, Penninx, & Wray, 2016; Robinson et al., 2017). The first explanation, termed assortative mating, proposes that individuals tend to select partners with similar characteristics, which subsequently leads to initial phenotypic similarity and also similarity of underlying genetic profiles. The second explanation, referred to as cohabitation effects, posits that partners may influence each other's behaviors and common environmental factors, such as shared dietary habits and similar lifestyles may contribute to similar phenotypes in spouses. The presence of cohabitation effects predict that partners would become more similar with longer relationship duration.

Impulsivity is a complex, multidimensional trait that may be defined as 'a predisposition toward rapid, unplanned reactions to internal or external stimuli, with diminished regard to the negative consequences that such reactions may have for the impulsive individual or others' (Moeller, Barratt, Dougherty, Schmitz, & Swann, 2001; Potenza, 2007). Impulsivity is also one of core symptoms of ADHD which is a common neurodevelopmental disorder characterized by hyperactivity and impulsivity, inattention or a combination of both (Faraone et al., 2015).

A limited number of studies have explored the correlations between partners for ADHD, however, the data used in these studies was derived from hospital and psychiatric records, which may have resulted in a biased sample of more severe cases of ADHD (Nordsletten et al., 2016; Steele, Wymbs, & Capps, 2020). Additionally, these studies failed to examine the underlying mechanisms driving the similarity between spouses, particularly the role of shared diet and lifestyles. Therefore, in the present study we aimed to answer the following questions: 1) Are there significant spousal similarities for impulsivity, ADHD symptoms in the general population? 2) Can spousal similarities be explained by assortative mating, cohabitation effects or both? 3) If cohabitation effects exist, do shared diet and lifestyles play a role in spousal similarities for impulsivity and ADHD symptoms?

We conducted the current study in The Lifelines cohort study (Lifelines) which is a multi-disciplinary prospective population-based cohort study examining the health and health-related behaviors of 167,729 persons living in the North of the Netherlands (Sijtsma et al., 2021). Impulsivity was calculated based on 32 selected items of NEO personality index (NEO-PI-R (Costa & McCrae, 1992)) at baseline. 32 selected items included all items constituting the impulsivity facet of the neuroticism scale (narrowly defined impulsivity), the excitement-seeking facet of the extraversion scale, and the deliberateness and self-discipline facets of the conscientiousness scale. Each facet consists of eight items scored on a five-point Likert scale (e.g., "I often do things without thinking"; 1="strongly disagree" to 5="strongly agree") resulting in facet sum scores ranging from 8 to 40. Next, a single principal component was extracted based on Pearson's correlations between the four facet sumscores. The construct was named trait impulsivity (broadly defned impulsivity) after the highest loadings and a single impulsivity-score per subject was derived. ADHD symptoms were assessed with the Dutch version of the ADHD DSM-IV questionnaire including 11 inattention items and 12 hyperactivity-impulsivity items. Attention problems mean score, hyperactivity-impulsivity mean score and ADHD mean score were calculated. Overall diet quality was calculated using a 110-item semi-quantitative food frequency questionnaire (FFQ) (Vinke et al., 2018), and other lifestyle behaviors (i.e., physical activity, sleep duration, smoking, drinking) were calculated based on self-reported questionnaires. ADHD polygenic risk score (PRS) was built using the most recent meta-GWAS of ADHD conducted in

38,691 ADHD cases and 186,843 controls of European ancestry (Demontis et al., 2022) and PRS-PCA approach. For statistical analyses, age-adjusted correlations of impulsivity and ADHD symptoms were calculated between husbands and wives. Then age-adjusted spousal correlation for ADHD PRS was calculated with adjustment of the 10 genetic PCs. Further, we explored if there was an association between longer relationships and larger spousal correlations using a linear regression of marriage duration against spousal differences of impulsivity and ADHD symptoms. Finally, we explored if shared diet and lifestyles explained partner correlations of impulsivity and ADHD using a linear regression of spousal differences of BMI, diet and lifestyles against spousal differences of impulsivity and ADHD symptoms.

In 28,276 spouse pairs identified from Dutch Lifelines cohort study, we observed significant spousal correlations for impulsivity, ADHD, BMI, diet and lifestyles (i.e. current smoking, drinking, sleep duration, psysical activity) (Figure 1). The spousal correlation ranged from 0.071 to 0.216 for impulsivity traits, with the highest correlation for excitement-seeking facet, and ranged from 0.135 to 0.163 for ADHD symptoms. Current smoking (r=0.554), drinking (r=0.394) and diet (r=0.374) have relatively higher spousal correlations among lifestyles. We also observed significant spousal correlation for ADHD PRS (r=0.052, p=0.002) indicating some degree of assortative mating. In addition, longer relationship duration was associated with a smaller spousal difference so larger similarities for impulsivity, ADHD, diet and lifestyles except sleep, indicating the contribution of cohabitation effects (Table 1). Furthermore, more similar diet and BMI were associated with more similar naroowly defined impulsivity and the overall impulsivity score in spouses (Table 2). In conclusion, significant spousal similarities were observed for impulsivity and ADHD symptoms. Cohabitation effects partly explain spousal similarities of impulsivity and ADHD symptoms and shared diet and BMI contribute to spousal similarities of impulsivity, particularly impulsivity facet. Our study provides basis for couple-based diet and lifestyle intervention.

References

Costa, P. T., & McCrae, R. R. (1992). *Revised NEO personality inventory (NEO-PI-R) and NEO five-factor inventory (NEO-FFI). Odessa FL Psychological Assessment Resources*. Odessa, Florida: Psychological Assessment Resources.

Demontis, D., Walters, G. B., Athanasiadis, G., Walters, R., Therrien, K., Farajzadeh, L., … Børglum, A. D. (2022). Genome-wide analyses of ADHD identify 27 risk loci, refine the genetic architecture and implicate several cognitive domains. *MedRxiv*, *15*, 2022.02.14.22270780. https://doi.org/10.1101/2022.02.14.22270780

Faraone, S. V., Asherson, P., Banaschewski, T., Biederman, J., Buitelaar, J. K., Ramos-Quiroga, J. A., … Franke, B. (2015). Attention-deficit/hyperactivity disorder. *Nature Reviews. Disease Primers*, *1*. https://doi.org/10.1038/NRDP.2015.20

Howe, L. J., Lawson, D. J., Davies, N. M., St. Pourcain, B., Lewis, S. J., Davey Smith, G., & Hemani, G. (2019). Genetic evidence for assortative mating on alcohol consumption in the UK Biobank. *Nature Communications*, *10*(1). https://doi.org/10.1038/S41467-019-12424-X

Moeller, F. G., Barratt, E. S., Dougherty, D. M., Schmitz, J. M., & Swann, A. C. (2001). Psychiatric aspects of impulsivity. *American Journal of Psychiatry*, *158*(11), 1783–1793. https://doi.org/10.1176/APPI.AJP.158.11.1783/ASSET/IMAGES/LARGE/J83T1.JPEG

Nordsletten, A. E., Larsson, H., Crowley, J. J., Almqvist, C., Lichtenstein, P., & Mataix-Cols, D. (2016). Patterns of Nonrandom Mating Within and Across 11 Major Psychiatric Disorders. *JAMA Psychiatry*, *73*(4), 354–361. https://doi.org/10.1001/JAMAPSYCHIATRY.2015.3192

Peyrot, W. J., Robinson, M. R., Penninx, B. W. J. H., & Wray, N. R. (2016). Exploring boundaries for the genetic consequences of Assortative mating for psychiatric traits. *JAMA Psychiatry*, *73*(11), 1189–1195. https://doi.org/10.1001/jamapsychiatry.2016.2566

Potenza, M. N. (2007). To do or not to do? The complexities of addiction, motivation, self-control, and impulsivity. *American Journal of Psychiatry*, *164*(1), 4–6. https://doi.org/10.1176/AJP.2007.164.1.4

Robinson, M. R., Kleinman, A., Graff, M., Vinkhuyzen, A. A. E., Couper, D., Miller, M. B., … Visscher, P. M. (2017). Genetic evidence of assortative mating in humans. *Nature Human Behaviour*, *1*(1), 16. https://doi.org/10.1038/s41562-016-0016

Sijtsma, A., Rienks, J., van der Harst, P., Navis, G., Rosmalen, J. G. M., & Dotinga, A. (2021). Cohort Profile Update: Lifelines, a three-generation cohort study and biobank. *International Journal of Epidemiology*. https://doi.org/10.1093/IJE/DYAB257

Steele, C. M., Wymbs, B. T., & Capps, R. E. (2020). Birds of a Feather: An Examination of ADHD Symptoms and Associated Concerns in Partners of Adults with ADHD. *Https://Doi.Org/10.1177/1087054720978553*, *26*(2), 296–306. https://doi.org/10.1177/1087054720978553

Vinke, P. C., Corpeleijn, E., Dekker, L. H., Jacobs, D. R., Navis, G., & Kromhout, D. (2018). Development of the food-based Lifelines Diet Score (LLDS) and its application in 129,369 Lifelines participants. *European Journal of Clinical Nutrition*, *72*(8), 1111–1119. https://doi.org/10.1038/S41430-018-0205-Z

2. Tables and other supporting documents where applicable and necessary

Figure 1. Spousal correlations for impulsivity, ADHD, diet and lifestyles

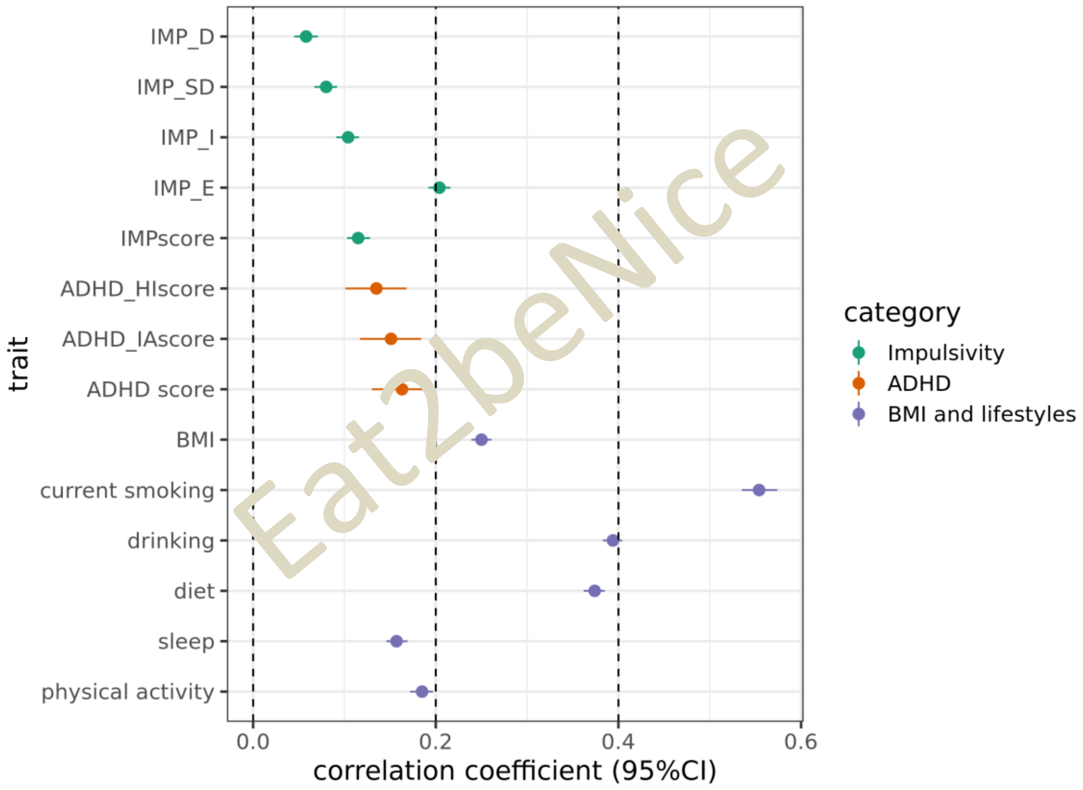

Table 1. Associations between relationship duration and spousal differences

Trait	beta/OR (95% CI)	*P* value	std_Beta
Impulsivity			
IMP score	-0.051 (-0.061, -0.04)	1.55E-21	-0.065
IMP_E	-0.122 (-0.168, -0.075)	3.53E-07	-0.035
IMP_I	-0.207 (-0.248, -0.166)	4.84E-23	-0.067
IMP_D	-0.246 (-0.291, -0.2)	2.10E-26	-0.07
IMP_SD	-0.185 (-0.23, -0.14)	1.03E-15	-0.052
ADHD			
ADHD score	-0.021 (-0.031, -0.011)	3.21E-05	-0.073
ADHD_IAscore	-0.021 (-0.032, -0.01)	0.000152	-0.067
ADHD_HIscore	-0.015 (-0.025, -0.005)	0.004279	-0.048
BMI and lifestyles			
BMI	-0.257 (-0.287, -0.227)	1.55E-62	-0.096
diet	-0.162 (-0.211, -0.113)	8.58E-11	-0.047
physical activity	-13.61 (-16.003, -11.217)	8.78E-29	-0.056
Sleep	0.046 (0.038, 0.054)	1.10E-31	0.068
Drinking	-0.375 (-0.44, -0.309)	2.78E-29	-0.054
Current Smoking (OR)	0.829 (0.802, 0.856)	3.46E-31	-0.59
PRS			
ADHD PRS	-0.006 (-0.029, 0.017)	0.597874	-0.009

Table 2. Associations between shared diet and lifestyles and spousal differences

	Beta (95% CI)	*P* value	std_Beta
Overall impulsivity score			
Education	-0.004 (-0.027, 0.02)	0.770	-0.002
BMI	0.005 (0.001, 0.009)	0.010	0.02
Diet	0.004 (0.001, 0.007)	0.008	0.021
Physical activity	0 (0, 0)	0.398	0.007
Sleep duration	0.015 (0, 0.031)	0.058	0.015
Drinking	-0.001 (-0.003, 0)	0.156	-0.011
Current smoking	-0.014 (-0.045, 0.016)	0.363	-0.007
Impulsivity facet			
Education	-0.044 (-0.138, 0.05)	0.359	-0.007
BMI	0.049 (0.034, 0.064)	3.51E-10	0.049
Diet	0.016 (0.004, 0.027)	0.009	0.02
Physical activity	0 (0, 0)	0.291	0.008
Sleep duration	0.001 (-0.062, 0.063)	0.983	0
Drinking	-0.007 (-0.013, -0.001)	0.019	-0.018
Current smoking	-0.084 (-0.206, 0.037)	0.174	-0.011

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