Eat2beNICE

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

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D 1.1– Manuscript 1: effects of dietary intake and lifestyle across lifespan stratified by sex and SES

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Workpackage leader	Catharina Hartman, UMCG

Author list

Organisation	Name	Contact information
UMCG	Lizanne Schweren	l.j.s.schweren@umcg.nl
UMCG	Catharina Hartman	c.hartman@accare.nl
ORU	Henrik Larsson	henrik.larsson@ki.se
ORU	Lin Li	lin.li@oru.se

Executive Summary

Within Deliverable 1.1 ("Effects of dietary intake and lifestyle across lifespan stratified by sex and SES"), two manuscripts have been prepared. Both manuscripts report on associations between overall diet quality (healthy vs unhealthy dietary habits) and mental health outcomes in the general population of adults. Together, these manuscripts cover both and externalising and internalising mental health problems.

The role of diet in externalising problems, namely attention-deficit/hyperactivity disorder (ADHD), was addressed in a large-scale study in Swedish adults. ADHD is a common neurodevelopmental disorder characterized by inattention or hyperactivity-impulsivity, or both. ADHD is being increasingly recognized as a lifespan disorder, with around two-thirds of childhood ADHD persisting into adulthood. In children and adolescents, but not in adults, males are generally more susceptible to developing ADHD. ADHD is also more common among those with socioeconomic disadvantages, such as low family income and educational under-attainment. In children and adolescent, ADHD symptoms have been associated with frequent consumption of unhealthy food items (e.g. "junk food"), but the link between adult ADHD symptoms and dietary habits is not well established. Therefore, our aim was to identify potentially important patterns of dietary intake related to ADHD symptoms in adults. In a Swedish population-based study, we found that in different age, sex, and SES groups, self-reported symptoms of particularly inattention were positively correlated with unhealthy dietary patterns including high-fat and high-sugar consumption, and with intake of seafood and high-protein foods. Inattention symptoms were negatively correlated with healthy dietary patterns including intake of fruits and vegetables. The same patterns – but weaker – were found for hyperactivity/impulsivity symptoms. We conclude that there are associations between ADHD symptoms and dietary habits in adults, and that these are stable across sex, age and SES groups.

The role of diet in internalising problems, namely depression and anxiety, was addressed in a Dutch general population sample. Stress exposure and neuroticism are risk factors for the development of depression and anxiety. Their effects may be partially mediated by diet: those

exposed to stress and/or those with high levels of neuroticism may be more prone to unhealthy dietary habits, which in turn may contribute to the development of internalizing symptoms. If true, stressed and/or neurotic individuals may prevent the onset or recurrence of internalizing problems by adopting a high-quality diet (consisting of fruits, vegetables, whole-grain products and nuts, among others; and limited consumption of red/processed meat, butter and sugar-sweetened beverages). Dietary interventions for depressed/anxious patients or at-risk groups, aiming to improve overall diet quality, hinge on this idea, but evidence for such a causal pathway is missing. Therefore the aim of our study was to assess whether overall diet quality mediates the effects of stress and neuroticism on the development of internalizing problems. In a longitudinal Dutch population-based study, we found that both stress and neuroticism scores were indeed - albeit weakly - associated with poorer diet quality. However, poor diet quality did not in turn predict mental health problems several years later. We conclude that in the long-term diet quality plays no mediating role in two established pathways to common mental health problems. Therefore, dietary interventions are unlikely to prevent the onset or recurrence of depression and anxiety.

Together, our findings show that in the general population of adults, overall diet quality is associated with symptoms of ADHD, stress, and neuroticism, but not with symptoms of depression or anxiety. It is important to note that the associations we report are cross-sectional. Therefore, the order of events cannot be deducted. Unhealthy dietary habits may lead to an increase in symptoms of inattention, stress or neuroticism, or, alternatively, symptoms of inattention, stress and neuroticism may lead to poorer dietary choices.

Abbreviations

ADHD	Attention-Deficit/Hyperactivity Disorder
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition
FFQ	Food frequency questionnaire
HI	Hyperactivity/impulsivity
IA	Inattention
RCT	Randomized Controlled Trial
SES	Socio-economic status
STAGE	Study of Twin Adults: Genes and Environment

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.

Part 1: the role of diet in externalising problems

Attention-deficit/hyperactivity disorder (ADHD) is a common neurodevelopmental disorder characterized by inattention or hyperactivity-impulsivity, or both (Faraone et al., 2015). For many years, ADHD was thought to be a childhood disorder with an average prevalence of 5% (Sayal et al., 2017). However, ADHD has been increasingly recognized as a lifespan disorder. A systematic review using a thorough assessment of ADHD suggested that around two-thirds of childhood ADHD persists into adulthood (Sibley at al., 2017), resulting in a global prevalence of 2.5% (95% CI: 2.1, 3.1) in adults (Simon et al., 2009). In addition to age, other factors such as sex and socioeconomic status (SES) are also crucial when calculating the prevalence of ADHD. In children and adolescents, males are generally more susceptible to developing ADHD, and exhibits a male-to-female sex ratio from 2.28:1 to 4:1 in different population (Faraone et al., 2015; Yan et al., 2018). However, this sex discrepancy almost disappears in adults (Matte et al., 2015; Weissenberger et al., 2018). A growing body of literature-including clinical samples, epidemiology studies, and meta-analysis, indicates the prevalence of ADHD varies by SES (Rowland et al., 2018). Specifically, strong evidence elucidated that ADHD was more common among those with socioeconomic disadvantages, such as low family income and educational under attainment (Faraone et al., 2015).

Several studies have reported associations between ADHD symptoms and frequent consumption of unhealthy food items (e.g. "junk food"; Ptacek et al., 2016; Del Ponte et al., 2019) in children and adolescents, but the link between adult ADHD symptoms and dietary habits is not well established. This is a major knowledge gap, because dietary habits may play a key role in pathways linking ADHD to health-related outcomes such as metabolic syndromes (e.g., obesity). An advanced understanding of the association between ADHD symptoms and dietary habits could harbour new interventions and non-pharmacological treatments for ADHD. The aim of this study was to identify and elucidate potentially important patterns of dietary intake related to ADHD symptoms in adults across the lifespan and all SES groups in males and females.

We conducted the current Swedish population-based study on ADHD symptoms and food frequency questionnaires in 17,999 individuals from the Study of Twin Adults: Genes and Environment (STAGE). Self-reported ADHD symptoms were obtained via a checklist of 18 DSM-IV symptoms, consisting of nine inattention (IA) items and nine hyperactivity/impulsivity (HI) items. Dietary habits were assessed by a food frequency questionnaire (FFQ), which consisted of 94 food items typically consumed by Swedish adults. We categorized dietary habits into three levels 1) simple food group (fruits, vegetables, dairy, meat and seafood), 2) rich in macronutrients (high-fat food, high-carbohydrate food, high-sugar food and high-protein food), and 3) dietary patterns (healthy food and unhealthy food). We estimated correlations among IA, HI and different dietary groups by using Partial pairwise Pearson's correlation analysis, further stratified by age, sex and SES.

Participants were between 20-47 years of age at the time of assessment (three group were identified in data analysis: 20-29, 30-39, 40-47 years), of which 7,216 (40.1%) were male, with average age of 34.0 years (standard deviation=7.63), and 10,783 (59.9%) were female, with average age of 33.6 years (standard deviation=7.60). SES the participants was indicated by their occupational status: (I) unskilled and semi-skilled workers, (II) skilled workers/assistant non-manual employees, (III) intermediate non-manual collar workers, and (IV) employed and self-employed professionals, higher civil servants, and executives. A majority of the sample was with higher SES (86.55%), in classes II, II and IV.

In different age, sex and SES groups, IA was positively correlated with seafood, high-fat, high-sugar, high-protein food and unhealthy dietary pattern, and negatively correlated with fruits, vegetables and healthy dietary pattern. HI and dietary habits showed similar but weaker patterns compared to IA. High consumption of high-sugar food and unhealthy dietary patterns correlated with IA and HI most strongly in the current adults' sample (Table 2.1.1). In conclusion, we have found evidence for the associations between self-reported trait dimensions of ADHD and various dietary habits in adults, which are stable across sex, age and SES groups. Future longitudinal studies with

various assessments of ADHD and dietary habits are needed to explore the casual associations between ADHD symptoms and dietary habits in adults.

Part 2: the role of diet in internalising problems

Stress exposure and neuroticism are risk factors for the development of anxiety and depression. Their effects may be partially mediated by diet: those exposed to stress and/or those with high levels of neuroticism may be more prone to unhealthy dietary habits, which in turn may contribute to the development of internalizing symptoms (Lopresti et al., 2013). If true, stressed and/or neurotic individuals may prevent the onset or recurrence of internalizing problems by changing their diets. Dietary interventions for depressed/anxious patients or at-risk groups, aiming to improve overall diet quality, hinge on this idea. A high-quality diet consists of fruits, vegetables, whole-grain products and nuts, among others, and limits consumption of red/processed meat, butter and sugar-sweetened beverages (Vinke et al., 2018). In a 2015 systematic review, eight out of 17 whole-diet intervention studies reported positive effects on depression, while nine studies reported no effect (Opie et al., 2015). Mediation via diet quality implies that A) stress exposure and/or neuroticism affects diet quality; and B) diet quality affects the risk of internalizing problems (Figure 2.2.1). Especially the latter path is controversial. Observational studies have shown poorer diet quality in depressed versus non-depressed individuals, although null findings are common as well (Quirk et al., 2013). In a meta-analysis of only prospective studies, poor diet was associated with depression cross-sectionally, but did not predict the development of future depression (Molendijk et al., 2018). The aim of the current study was to assess whether diet quality mediates the effects of stress and neuroticism on the development of internalizing problems.

At baseline, N=121,008 individuals from the general population (age 18-93) reported on past-year stress exposure (long-term difficulties, stressful life-events) and four neuroticism traits (anger-hostility, self-consciousness, impulsivity, vulnerability). Extensive food frequency questionnaire data was used to quantify diet quality. Depression and anxiety were assessed at baseline and follow-up (n=65,342, +3.6 years). We estimated mediated logistic regression models to predict the development of depression and anxiety across time from baseline stress exposure and neuroticism traits via diet quality.

Stress, neuroticism and stress-by-neuroticism interactions predicted mental health problems at follow-up. These effects consisted entirely of direct effects; no mediation effects via diet quality were significant. High stress and high neuroticism scores were - albeit weakly - associated with poorer diet quality. Poor diet quality, in turn, did not predict mental health problems (Figure 2.2.2).

We conclude that diet quality plays no mediating role in two established pathways to common mental health problems. Our findings suggest that dietary interventions may be warranted for stressed and neurotic individuals, but are unlikely to prevent the onset or recurrence of depression and anxiety.

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symptoms among preschoolers in mainland China. Eur J Clin Nutr, 2018.

2. Tables and other supporting documents where applicable and necessary

Table 2.1.1. The correlations with 95% confidence intervals between ADHD symptoms and different dietary habits (adjusted the relatedness of individuals), stratified by age, sex and SES

		IA	HI
Stratified by age		*20-29 years of age (N=2901)*	
1)Food groups	Fruits	-0.10 (-0.14,-0.07)	-0.03 (-0.06,0.01)
	Vegetables	-0.04 (-0.08,-0.01)	-0.00 (-0.04,0.03)
	Dairy	0.01 (-0.02,0.05)	0.01 (-0.02,0.05)
	Meat	0.02 (-0.02,0.06)	0.02 (-0.02,0.05)
	Seafood	0.03 (-0.01,0.07)	0.01 (-0.02,0.05)
2)Food items rich in macro nutrients	High in fat	0.08 (0.04,0.11)	0.03 (-0.01,0.07)
	High in carbohydrates	0.01 (-0.02,0.05)	0.01 (-0.03,0.04)
	High in sugar	0.13 (0.09,0.16)	0.09 (0.05,0.13)
	High in protein	0.03 (-0.01,0.06)	0.03 (-0.01,0.06)
3)Dietary patterns	Unhealthy dietary pattern	0.12 (0.09,0.16)	0.10 (0.06,0.13)
	Healthy dietary pattern	-0.06 (-0.10,-0.03)	-0.01 (-0.05,0.02)
		30-39 years of age (N=3254)	
1)Food groups	Fruits	-0.05 (-0.08,-0.01)	-0.01 (-0.05,0.02)
	Vegetables	-0.05 (-0.08,-0.01)	-0.00 (-0.04,0.03)
	Dairy	0.02 (-0.02,0.05)	0.04 (0.01,0.08)
	Meat	0.02 (-0.02,0.05)	0.01 (-0.02,0.05)
	Seafood	0.04 (0.01,0.08)	0.05 (0.01,0.08)
2)Food items rich in macro nutrients	High in fat	0.03 (-0.01,0.06)	0.04 (0.01,0.08)
	High in carbohydrates	-0.00 (-0.04,0.03)	0.01 (-0.02,0.05)
	High in sugar	0.13 (0.09,0.16)	0.08 (0.04,0.11)
	High in protein	0.03 (-0.01,0.06)	0.05 (0.02,0.08)
3)Dietary patterns	Unhealthy dietary pattern	0.11 (0.08,0.14)	0.06 (0.03,0.10)
	Healthy dietary pattern	-0.04 (-0.08,-0.01)	-0.00 (-0.04,0.03)
		40-47 years of age (N=2576)	
1)Food groups	Fruits	-0.05 (-0.09,-0.01)	-0.03 (-0.07,0.01)
	Vegetables	-0.07 (-0.11,-0.03)	-0.02 (-0.06,0.01)
	Dairy	0.04 (0.00,0.08)	0.02 (-0.02,0.06)
	Meat	-0.01 (-0.05,0.03)	0.01 (-0.03,0.04)
	Seafood	0.02 (-0.02,0.06)	0.06 (0.02,0.10)
2)Food items rich in macro nutrients	High in fat	0.07 (0.04,0.11)	0.02 (-0.02,0.06)
	High in carbohydrates	-0.02 (-0.06,0.02)	-0.01 (-0.05,0.02)
	High in sugar	0.12 (0.08,0.16)	0.08 (0.04,0.12)
	High in protein	0.05 (0.01,0.08)	0.03 (-0.01,0.07)
3)Dietary patterns	Unhealthy dietary pattern	0.10 (0.06,0.13)	0.07 (0.04,0.11)
	Healthy dietary pattern	-0.06 (-0.10,-0.02)	-0.02 (-0.06,0.02)
Stratified by sex		*Male (N=3247)*	
1)Food groups	Fruits	-0.07 (-0.11,-0.04)	-0.05 (-0.08,-0.01)
	Vegetables	-0.06 (-0.10,-0.03)	-0.03 (-0.06,0.00)
	Dairy	0.04 (0.00,0.07)	0.03 (-0.00,0.07)
	Meat	0.00 (-0.03,0.04)	0.04 (0.01,0.08)
	Seafood	0.00 (-0.03,0.04)	0.03 (-0.01,0.06)
2)Food items rich in macro nutrients	High in fat	0.06 (0.03,0.09)	0.03 (-0.01,0.06)
	High in carbohydrates	-0.02 (-0.06,0.01)	-0.02 (-0.05,0.02)
	High in sugar	0.09 (0.06,0.13)	0.10 (0.06,0.13)
	High in protein	0.04 (0.00,0.07)	0.05 (0.02,0.08)
3)Dietary patterns	Unhealthy dietary pattern	0.08 (0.05,0.11)	0.10 (0.06,0.13)
	Healthy dietary pattern	-0.07 (-0.10,-0.03)	-0.04 (-0.07,-0.00)
		Female (N=5484)	
1)Food groups	Fruits	-0.06 (-0.08,-0.03)	-0.02 (-0.04,0.01)
	Vegetables	-0.05 (-0.07,-0.02)	-0.01 (-0.03,0.02)

	Dairy	0.01 (-0.02,0.03)	0.02 (-0.00,0.05)
	Meat	0.00 (-0.02,0.03)	-0.01 (-0.04,0.02)
	Seafood	0.04 (0.02,0.07)	0.04 (0.01,0.07)
2)Food items rich in macro nutrients	High in fat	0.04 (0.02,0.07)	0.03 (0.00,0.06)
	High in carbohydrates	0.01 (-0.02,0.03)	0.01 (-0.02,0.03)
	High in sugar	0.14 (0.11,0.17)	0.08 (0.05,0.10)
	High in protein	0.02 (-0.01,0.05)	0.03 (0.00,0.06)
3)Dietary patterns	Unhealthy dietary pattern	0.12 (0.09,0.15)	0.07 (0.04,0.10)
	Healthy dietary pattern	-0.05 (-0.07,-0.02)	-0.01 (-0.03,0.02)
Stratified by SES		*Low SES (N=1660)*	
1)Food groups	Fruits	-0.08 (-0.13,-0.04)	-0.07 (-0.12,-0.02)
	Vegetables	-0.08 (-0.12,-0.03)	-0.04 (-0.08,0.01)
	Dairy	0.02 (-0.02,0.07)	0.03 (-0.01,0.08)
	Meat	0.03 (-0.02,0.08)	0.01 (-0.04,0.05)
	Seafood	0.02 (-0.03,0.07)	0.03 (-0.01,0.08)
2)Food items rich in macro nutrients	High in fat	0.03 (-0.02,0.08)	0.04 (-0.01,0.09)
	High in carbohydrates	-0.02 (-0.07,0.03)	-0.02 (-0.07,0.03)
	High in sugar	0.15 (0.11,0.20)	0.11 (0.06,0.16)
	High in protein	0.04 (-0.01,0.08)	0.04 (-0.01,0.09)
3)Dietary patterns	Unhealthy dietary pattern	0.13 (0.08,0.18)	0.11 (0.06,0.15)
	Healthy dietary pattern	-0.08 (-0.13,-0.03)	-0.05 (-0.10,-0.00)
		High SES (N=4917)	
1)Food groups	Fruits	-0.04 (-0.07,-0.02)	-0.02 (-0.04,0.01)
	Vegetables	-0.04 (-0.07,-0.02)	-0.01 (-0.04,0.02)
	Dairy	0.01 (-0.01,0.04)	0.03 (-0.00,0.06)
	Meat	-0.00 (-0.03,0.03)	0.00 (-0.02,0.03)
	Seafood	0.03 (0.00,0.06)	0.05 (0.02,0.07)
2)Food items rich in macro nutrients	High in fat	0.06 (0.03,0.09)	0.03 (0.00,0.06)
	High in carbohydrates	-0.01 (-0.03,0.02)	-0.00 (-0.03,0.02)
	High in sugar	0.11 (0.08,0.14)	0.07 (0.04,0.10)
	High in protein	0.02 (-0.00,0.05)	0.04 (0.01,0.07)
3)Dietary patterns	Unhealthy dietary pattern	0.10 (0.07,0.12)	0.06 (0.04,0.09)
	Healthy dietary pattern	-0.04 (-0.07,-0.01)	-0.00 (-0.03,0.02)

IA: Inattention, HI: Hyperactivity-impulsivity

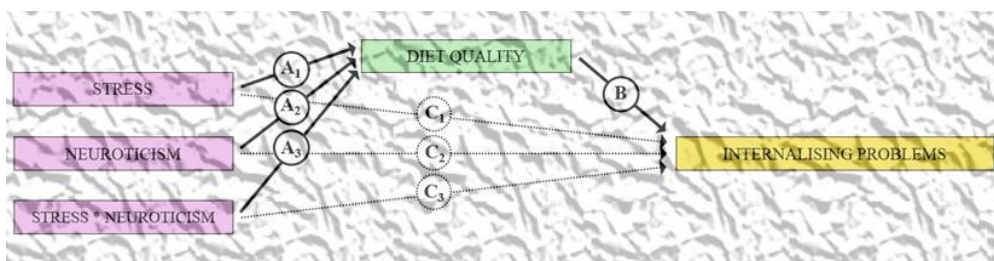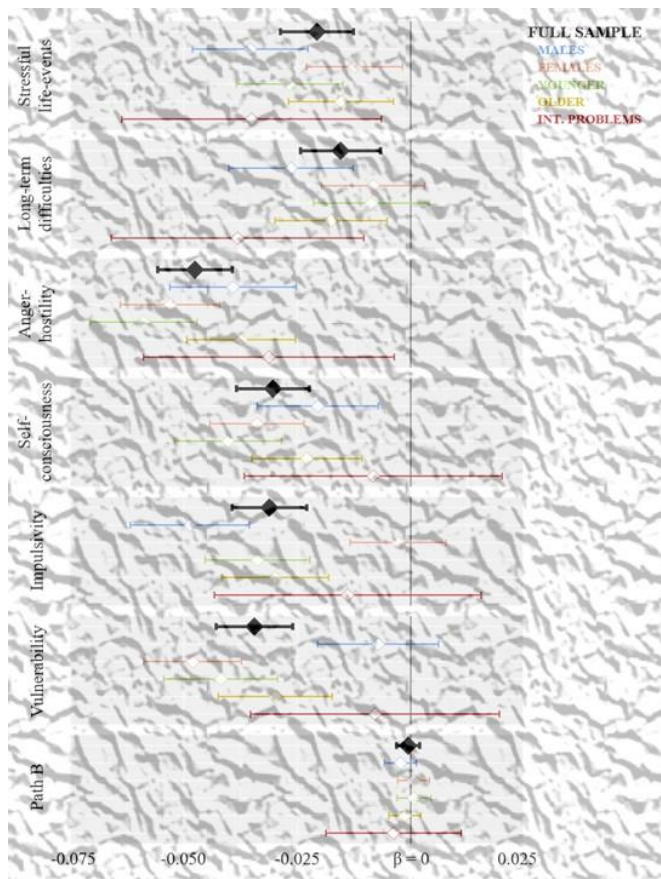**Figure 2.2.1.** Hypothesized (partial) mediation model

Figure 2.2.2. Subgroup analyses of A-paths from stress and neuroticism to diet quality (top six graphs) and the B-path from diet quality to internalizing problems (bottom graph).

3.   Acknowledgement and Disclaimer