Dietary Patterns and Neuropsychological Function in Adolescents: A Cross-sectional and Longitudinal Study
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Additional file 1

Supplementary Methods, Figures, and Tables

Supplementary Methods

Figures

Tables

Methods

Section 1: Neuropsychological outcomes & Covariates

Attention

Assessed with the Attention Network Test (ANT) (41), a computerized test examining sustained attention based on reaction times (RT) to target stimuli. The test consisted of the appearance of five arrows on the screen, and participants had to indicate the direction of the central arrow as fast as possible. The ANT measures three distinct cognitive attention domains: alerting, orienting, and executive control. The alerting component measures the ability to achieve and sustain vigilance by comparing reaction times between no cue and double cue conditions. The orienting component measures the ability to shift attention to a specific spatial location by comparing reaction times between centre cue and spatial cue conditions. The executive control component measures conflict resolution by comparing reaction times between incongruent and congruent flanker conditions. For all components, the outcome is measured in milliseconds, and lower scores indicate better attention performance.

Working Memory

Measured with the N-back task (42), a computer-based test assessing working memory (WM) using series of numbers. The outcome selected for this test was d prime (d'): d′= z (hit rate) – z (false alarm rate). A higher d′ indicates better detection and, thus, a more accurate performance. In this test, a sequence of items is shown, and for each item it must be determined whether the last one shown is identical to the stimulus presented "n" trials back (1-, 2-, 3- and 4-back). These different conditions are known as loads, and in the highest cognitive load (i.e., 4-back) the demands on WM are stronger. For this study, the 4-back test was used.

In the 4-back level, the target was any stimulus identical to the one presented four trials previously. The more correct answers, the higher the score.

Fluid Intelligence

Evaluated using an inductive reasoning subtest (i.e., fluid intelligence) of the Tests of Primary Mental Abilities (PMA-R, the Spanish adaptation) (43). The test consists of choosing a letter from a set of six possible alternatives, underlying a given sequence of letters. The total score is the number of correct item responses. The more correct answers, the higher the score.

Advantageous Decision-Making

Assessed with the Roulettes Task (44), a gambling task adapted from the Cups Task which assesses risky decision-making, specifically whether participants adjust their risky behaviours according to the probabilities and importance of the outcome (cognition influenced by emotion). The Roulettes Task is a game of chance with the goal of making as much money as possible. Two roulettes appear on the screen: each divided into segments with varying amounts of money. The left roulette has one segment with a larger amount, for example $2, while the other segments are empty ($0), making it the risky option since the chance of winning depends on the number of segments. The right roulette is the safe option, with all segments containing the same amount, $1, guaranteeing a win of $1 on each spin. Additionally, roulettes can be red or blue, indicating money loss and gain, respectively. In this study, we focused specifically on the advantageous decision-making (gain) condition as it reflects reward-seeking behaviour and positive risk-taking, which are particularly relevant during adolescence when reward sensitivity is heightened due to ongoing neurodevelopmental changes in the dopaminergic system (45). The gain condition better captures the decision-making processes most pertinent to this developmental stage. The

scores are measured as total risk adjustment to assess risk sensitivity, with values closer to 0 indicating greater risk insensitivity.

Behavioural Problems

A self-reported version of the Strengths and Difficulties Questionnaire (SDQ, Spanish adaptation) (46) was used, which gave a total score of problem behaviour. It consists of 25 questions, organized in a general score of problem behaviour and five sub-scales aimed to assess emotional symptoms, conduct problems, hyperactivity/inattention, peer relationship problems, and pro-social behaviour. For our analyses, the SDQ was grouped to derive internalising (emotional symptoms and peer relationship problems; 10 items) and externalising (conduct problems and hyperactivity/inattention; 10 items) scores, as previously described (47). A higher score indicates a more problematic behaviour.

Attention-Deficit/Hyperactivity Disorder

The attention deficit/hyperactivity disorder (ADHD) DSM-IV form list (48) was completed by the teacher, who answered 18 multiple-choice questions to rate the ADHD performance in a general score of the participant (adolescent). The scores were transformed into the number of symptoms and diagnostic criteria for ADHD. Based on DSM-IV criteria, a binary variable indicating ADHD symptom diagnosis (no/yes) was derived at both baseline and follow-up assessments, with a threshold of 6 or more symptoms in either the inattentive or hyperactive-impulsive domains indicating a positive ADHD symptom diagnosis.

Covariate details

The following variables were included as covariates in the final models: age (continuous, years), sex (male, female), BMI z-score (continuous), maternal ethnicity (Spanish, other), substance use (yes: any use of cigarette, e-cigarette, alcohol, cannabis, or other drugs; no), maternal educational attainment (high school studies or lower, university studies, according to ISCED criteria), physical activity (up to once a week, twice a week, three times a week,

more than three times a week), and annual net household income (low: €21,000–€34,000; moderate: €34,000–€41,000; high: €41,000–€84,000). Diagnosed maternal mental disorder (no, yes) was included as a covariate depending on the specific exposure. These covariates were collected using study-specific questions. For longitudinal analyses, models were further adjusted for randomisation group (control, intervention) and baseline outcome measurement.

Section 2: Sample Preparation and Quantification of Urinary Polyphenols

Urine samples (5 µL) were diluted 1:20 (v/v) with Milli-Q water containing 0.05% formic acid, with abscisic acid-D6 used as the internal standard at a final concentration of 100 ppb. Chromatographic separation was performed on a Kinetex F5 100 Å (50 × 4.6 mm, 2.6 µm) column (Phenomenex), equipped with a SecurityGuard™ UHPLC F5 4.6 mm pre-column, and maintained at 40°C. The mobile phases were 0.05% acetic acid in water (A) and 0.05% acetic acid in acetonitrile (B), using a non-linear gradient at a flow rate of 0.75 mL/min. Metabolites were quantified using calibration curves prepared in synthetic urine; where standards were unavailable, the corresponding aglycone calibration curves were used. Identification and quantification were performed with Agilent MassHunter Software.

Section 3: Development and Validation of a UPF Polyphenol-based Urinary Signature

A polyphenol signature for UPF intake was developed using urinary polyphenol data from 257 participants at six-month follow-up, comprising 61 polyphenols in total. Urinary polyphenols were measured only at follow-up due to financial constraints, but as UPF intake did not significantly change from baseline ($p = 0.473$), these data were suitable for model development.

Urinary polyphenol concentrations equal to zero were recoded as missing and polyphenols with > 20% missing values were excluded from analysis, leaving 19 polyphenols for further analysis. Remaining missing values were imputed using a random forest approach implemented in the missForest R package (v1.5), with imputation quality evaluated by normalized root mean squared error (NRMSE). An inverse normal transformation was then applied to each imputed polyphenol to standardize distributions.

To account for intervention effects, UPF intake was regressed on intervention group within each training set, and the resulting residuals were used as the outcome variable in elastic net regression with all imputed and transformed polyphenol metabolites as predictors. The model was optimised through cross-validation to determine the optimal alpha ($\alpha = 0.85$) and lambda ($\lambda = 0.14$) parameters with the least root mean square error (RMSE = 0.02). Hyperparameters alpha (0.1–1; increment = 0.05) and lambda were selected by leave-one-out cross-validation (LOO-CV) within the training set to minimize root mean squared error.

Polyphenols selected as non-zero predictors in more than 80 out of 100 iterations (80%) were considered stable and retained for further analysis. Coefficients for each stable metabolite were used to construct a weighted composite polyphenol score for each participant, which was subsequently standardised to z-scores. The model underwent internal validation using 1,000 iterations of random train/test splits with a 90/10 split ratio and bootstrap resampling (n = 10,000). The predictive performance of the composite score was evaluated by calculating

the RMSE between observed and predicted UPF intake across 1,000 random train/test splits, using only the stable metabolites as predictors.

Figure S1

Relative contribution of each food group to ultra-processed food and drinks consumption in the MB scenario at baseline (NOVA classification, group 4) in participants of the WALNUTs Smart Snack Trial.

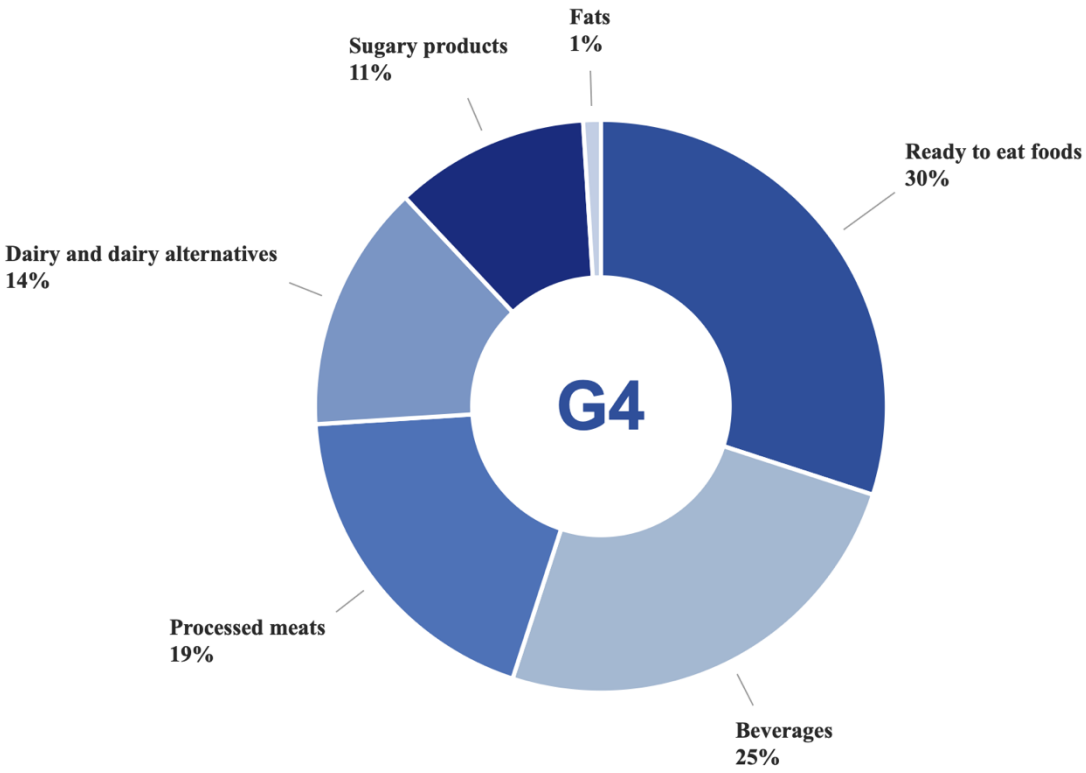


Figure S2

Directed Acyclic Graph illustrating the causal relationships between Mediterranean diet (MD) and neuropsychological function. The minimal sufficient adjustment set includes age, household income, maternal education, maternal ethnicity, physical activity, sex and substance use. All white nodes represent the covariates required to estimate the unbiased total causal effect of MD on neuropsychological outcomes.

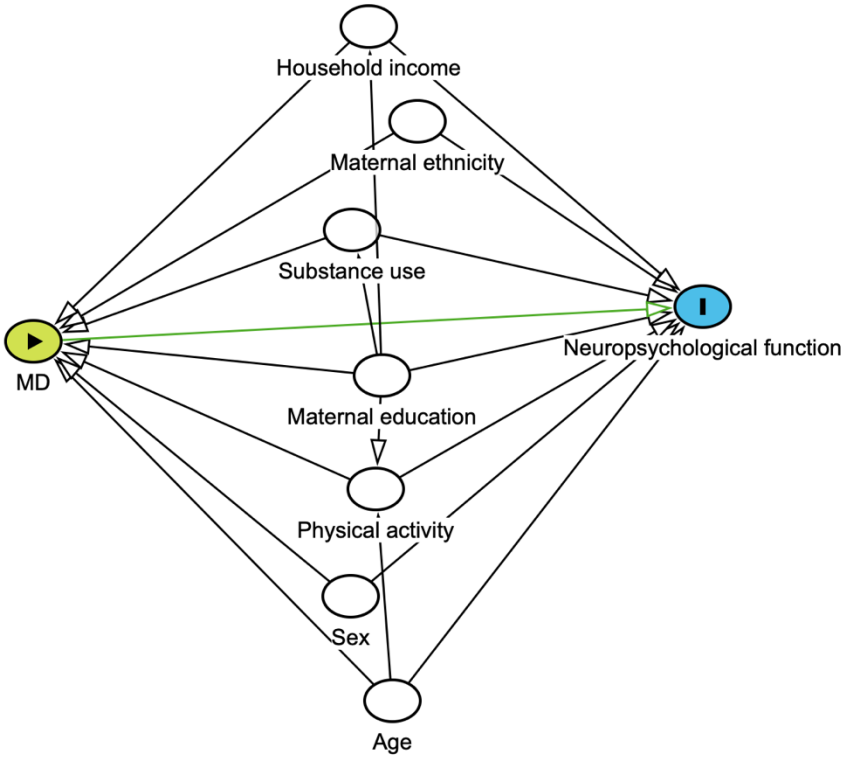


Figure S3

Directed Acyclic Graph illustrating the causal relationships between Ultra-processed Food (UPF) consumption and neuropsychological function. The minimal sufficient adjustment set includes age, household income, maternal education, maternal ethnicity, physical activity, sex, substance use, and maternal mental health disorder. All white nodes represent the covariates required to estimate the unbiased total causal effect of UPF on neuropsychological outcomes.

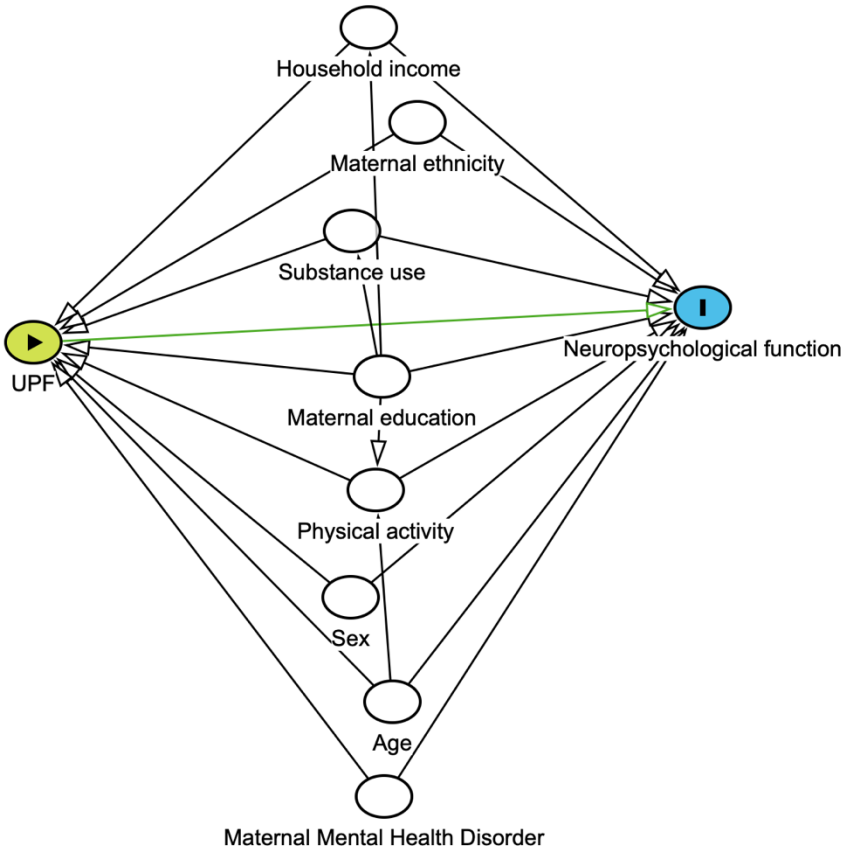
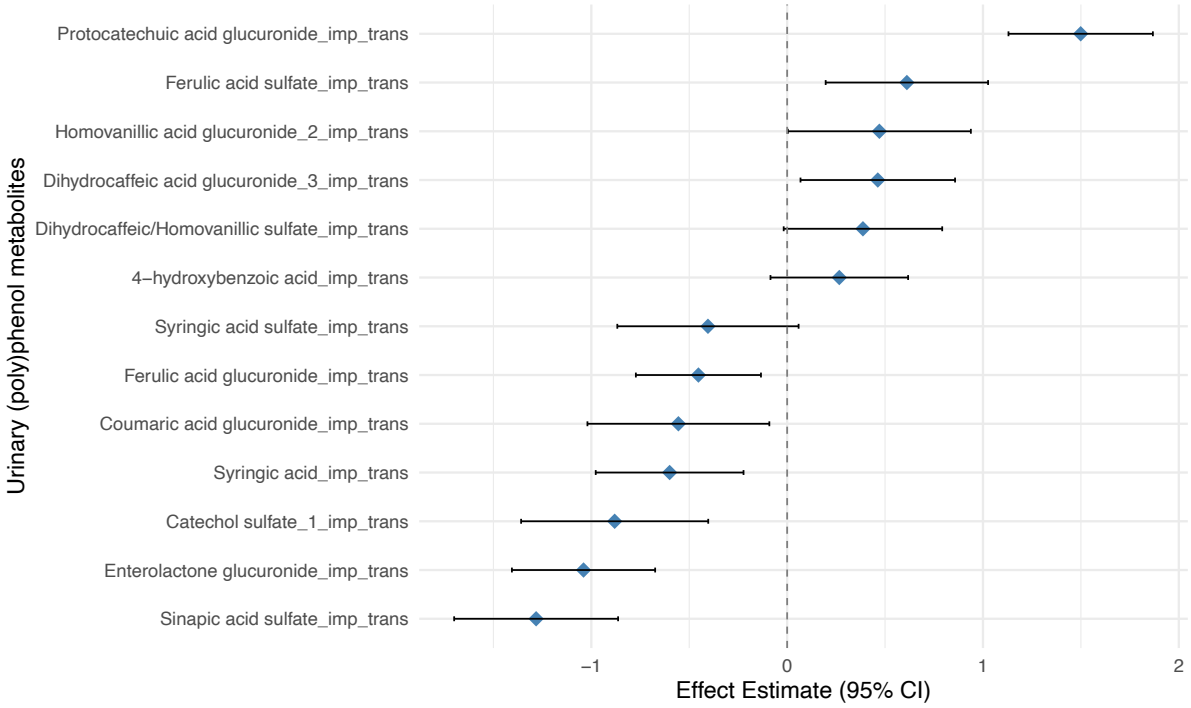


Figure S4

Associations between individual urinary polyphenol metabolites and ultra-processed food consumption. Effect estimates and 95% confidence intervals are shown for each metabolite included in the biomarker signature model[1].



[1] Model: Elastic net regression. Exposure: urinary polyphenol metabolites (n = 13, imputed and inverse-normal transformed). Outcome: ultra-processed food consumption (residuals after regressing on intervention group).

Table S1

Classification of FFQ items according to the NOVA system in the WSS study (MB scenario)

G1: Unprocessed or minimally processed foods	Whole milk, skimmed milk, yogurt, skimmed yogurt, omega-3 eggs, white fish, molluscs, raw vegetables, legumes, orange, apple, watermelon, strawberries, peach, other fruits, walnuts, hazelnuts, almonds, other nuts, seeds, natural fruit juice.
G2: Processed culinary ingredients	Olive oil, other oils, butter.
G3: Processed foods	Hard cheese, low-fat cheese, omelette/fried egg, chicken[a], beef/pork[a], ham, large fatty fish[a], small fatty fish[a], canned fish, cooked vegetables[a], tomato sauce, white bread, whole grain bread, homemade fries, rice/pasta[a], packaged fruit juice.
G4: Ultra-processed foods and drinks	Omega-3 milk drink, vegetable drink, petit-suisse, soya yogurt, frankfurter (hot dog), cold meats, fish derivatives, breakfast cereals, whole grain breakfast cereals, pizza, industrial fries, biscuits and pastries, chocolate pastries, chocolates, chocolate powder, candies, omega-3 butter (spread), mayonnaise, soft drinks, soft drinks (light).

[a] Home-cooked with processed culinary ingredients.

Table S2

Summary of Missing Data in the Original Dataset Prior to Imputation

Variable	Number of Missing Values	Percentage of Missing Values (%)
Age	31	4.8%
BMI-z score	3	0.5%
Substance use	170	26.2%
Physical Activity Frequency	8	1.2%
Maternal Ethnicity	9	1.4%
Maternal Educational Attainment	1	0.2%
Annual Net Household Income	2	0.3%
Maternal Mental Health Disorder	9	1.4%
Variables not listed had no missing data.		

The out-of-bag error was used to evaluate imputation performance. The NRMSE for numeric variables was 0.14 and the Proportion of Falsely Classified for categorical variables was 0.34. The resulting complete dataset was used for all analyses.

Table S3

Comparison of polyphenol distributions before and after data imputation

Comparison of Original and Imputed Data

Variable	Original_Min	Original_1st_Qu	Original_Median	Original_Mean	Original_3rd_Qu	Original_Max	Original_Missing	Imputed_Min	Imputed_1st_Qu	Imputed_Median	Imputed_Mean	Imputed_3rd_Qu	Imputed_Max	Imputed_Missing
Ferulic acid glucuronide	2.442.232	17.021.357	38.175.955	12.259.760	12.219.634	382.867.568	49/278	2.442.232	19.745.836	45.265.112	11.758.871	11.858.629	382.867.568	0/278
Enterodiol glucuronide	4.200.997	1.820.432	5.332.866	1.321.915	1.172.642	29.992.771	44/278	4.200.997	1.820.432	6.046.852	1.286.003	1.165.153	29.992.771	0/278
Syringic acid	16.630.668	7.206.623	7.206.623	1.113.064	1.372.168	7.150.862	42/278	16.630.668	7.206.623	7.206.623	1.045.074	1.244.765	7.150.862	0/278
4-hydroxybenzoic acid	446.630.725	44.663.072	72.878.191	7.432.920	9.086.182	23.515.341	37/278	446.630.725	44.663.072	71.962.969	7.356.288	8.888.531	23.515.341	0/278
Dihydrocaffeic acid glucuronide_3	401.067.510	332.513.485	687.222.177	209.278.375	179.230.508	1.500.000.000	27/278	401.067.510	336.804.567	664.924.752	194.879.892	166.198.116	1.500.000.000	0/278
Hydroxytyrosol sulfate_2	10.565.688	22.690.316	140.720.047	53.219.732	58.482.238	886.542.028	24/278	10.565.688	33.718.352	131.966.349	49.773.055	53.862.379	886.542.028	0/278
Enterolactone glucuronide	2.442.232	11.455.306	25.838.609	4.492.315	4.968.918	48.813.736	14/278	2.442.232	12.238.856	26.363.281	4.433.033	4.932.952	48.813.736	0/278
Protocatechuic acid sulfate	171.425.620	90.695.682	177.075.850	31.213.164	35.224.496	436.777.640	14/278	171.425.620	90.802.832	177.075.850	31.637.818	35.452.179	436.777.640	0/278
Protocatechuic acid glucuronide	65.448.419	26.374.786	43.857.213	6.454.732	8.405.170	40.705.876	10/278	65.448.419	26.240.850	43.669.734	6.420.564	8.354.337	40.705.876	0/278
Hydroxytyrosol sulfate_3	35.661.776	18.203.783	30.715.351	4.781.321	5.269.170	64.634.748	7/278	35.661.776	18.539.151	30.693.921	4.783.609	5.211.297	64.634.748	0/278
Ferulic acid sulfate	2.442.232	79.054.960	189.606.339	30.516.228	37.879.340	542.601.762	5/278	2.442.232	80.395.795	190.122.389	30.906.892	38.440.228	542.601.762	0/278
Sinapic acid sulfate	30.857.576	12.534.319	26.976.569	6.787.212	7.216.029	89.163.399	4/278	30.857.576	12.534.319	26.921.153	6.732.034	7.216.029	89.163.399	0/278
Coumaric acid glucuronide	29.046.543	45.376.477	70.759.124	8.356.474	10.750.555	59.680.369	2/278	29.046.543	45.520.251	70.759.124	8.347.120	10.728.565	59.680.369	0/278
Homovanillic acid glucuronide_2	401.067.510	826.774.987	1.676.063.008	283.843.828	374.073.640	1.500.000.000	2/278	401.067.510	830.727.034	1.668.814.085	282.707.683	372.824.350	1.500.000.000	0/278
Syringic acid sulfate	16.630.668	18.133.986	34.341.723	4.971.872	5.347.045	53.344.058	2/278	16.630.668	17.687.088	34.001.571	4.944.168	5.335.010	53.344.058	0/278
Homovanillic acid	401.067.510	356.087.032	518.062.575	56.298.484	68.280.149	255.236.265	1/278	401.067.510	355.942.443	517.263.554	56.178.377	68.251.096	255.236.265	0/278
Vanillic acid glucuronide	14.326.718	71.929.259	193.426.040	157.489.626	88.562.387	1.500.000.000	1/278	14.326.718	72.279.736	193.603.251	157.133.136	88.390.470	1.500.000.000	0/278
Catechol sulfate_1	156.220.579	1.059.710.248	1.851.905.273	285.309.496	354.712.996	1.500.000.000	0/278	156.220.579	1.059.710.248	1.851.905.273	285.309.496	354.712.996	1.500.000.000	0/278
Dihydrocaffeic/Homovanillic sulfate	401.067.510	1.948.326.672	4.182.767.731	515.519.022	725.008.219	1.500.000.000	0/278	401.067.510	1.948.326.672	4.182.767.731	515.519.022	725.008.219	1.500.000.000	0/278

Table S4

Imputation performance

NRMSE	0.37

Table S5

Baseline Characteristics of Adolescents Included vs Not Included in Analyses

Adolescent Characteristics	Sample	Remainder	P-value	Effect size
Overall	N = 650	N = 121		
Age in years, mean (SD)	13.83 (0.93)	13.97 (0.99)	0.207	-0.15
BMI z score, mean (SD)	0.34 (1.06)	0.43 (1.00)	0.416	-0.09
Sex, %			0.715	Cramér's V 0.01
Male	297 (45.7%)	57 (47.1%)		SMD -0.03
Female	353 (54.3%)	63 (52.1%)		SMD 0.05
Substance Use [3], %			0.328	Cramér's V 0.04
No	232 (35.7%)	17 (14.0%)		SMD 0.52
Yes	248 (38.2%)	25 (20.7%)		SMD 0.39
Physical activity, %			0.831	Cramér's V 0.03
Up to once a week	121 (18.6%)	4 (3.3%)		SMD 0.51
Twice a week	161 (24.8%)	5 (4.1%)		SMD 0.61
Three times a week	168 (25.8%)	3 (2.5%)		SMD 0.71
> Three times a week	192 (29.5%)	5 (4.1%)		SMD 0.72
Maternal Characteristics				
Ethnicity, %			0.706	Cramér's V 0.02
Spanish	537 (82.6%)	26 (21.5%)		SMD 1.55
Other	104 (16.0%)	6 (5.0%)		SMD 0.37
Educational Attainment, %			0.094	Cramér's V 0.06
High school studies or lower	257 (39.5%)	52 (43.0%)		SMD -0.07
University studies	392 (60.3%)	56 (46.3%)		SMD 0.28
Annual Net Household Income, %			0.299	Cramér's V 0.06
Low (€21k-€34k)	217 (33.4%)	10 (8.3%)		SMD 0.65
Moderate (€34k-€41k)	218 (33.5%)	8 (6.6%)		SMD 0.71
High (€41k-€84k)	213 (32.8%)	15 (12.4%)		SMD 0.50
Mental Health Disorder, %			0.407	Cramér's V 0.03
No	572 (88.0%)	29 (24.0%)		SMD 1.69
Yes	69 (10.6%)	5 (4.1%)		SMD 0.25

Abbreviations: BMI: Body Mass Index; SD: Standard Deviation; SMD: Standardised Mean Difference.

[1] For categorical variables, percentages are calculated from the total group size (N=650 for Sample, N=121 for Remainder). The sum of percentages for a given variable may be less than 100% due to missing data.

[2] Continuous variables were compared using a Welch t test (BMI) or Wilcoxon rank sum test (age). Categorical variables were compared using chi squared or Fisher exact tests.

[3] Includes any of the following: cigarette, e-cigarette, alcohol, weed or other drugs.

Table S6

Baseline characteristics of Completers vs Non-completers at six month follow up

Covariates	Completer N = 622 [1]	Non-Completer N = 31 [1]	SMD [2]	P-value [2]
% UPF consumption in g/d	13.55 (8.02)	15.57 (9.56)	-2.01	0.258
KIDMED Index Score	6.83 (2.14)	6.29 (2.22)	0.54	0.196
Sex			0.52	0.096
Male	281 (45.2%)	19 (61.3%)		
Female	341 (54.8%)	12 (38.7%)		
BMI-z score	0.33 (1.04)	0.51 (1.44)	-0.19	0.482
Age, in years	13.82 (0.93)	14.08 (0.86)	-0.26	0.175
Maternal Ethnicity			0.57	0.452
Spanish	513 (83.6%)	27 (90.0%)		
Other	101 (16.4%)	3 (10.0%)		
Adolescent Substance Use	234 (51.2%)	15 (57.7%)	1.30	0.551
Maternal Educational Attainment			0.90	0.851
High school studies or lower	245 (39.5%)	13 (41.9%)		
University studies	376 (60.5%)	18 (58.1%)		
Adolescent Physical Activity Frequency				0.667
Once a week	114 (18.5%)	7 (24.1%)		
Twice a week	154 (25.0%)	8 (27.6%)		
Three times a week	164 (26.6%)	5 (17.2%)		
More than three times a week	184 (29.9%)	9 (31.0%)		
Annual Net Household Income				0.359
Low	205 (33.1%)	13 (41.9%)		
Medium	213 (34.4%)	7 (22.6%)		
High	202 (32.6%)	11 (35.5%)		
Maternal Mental Health Disorder			1.72	0.357
No	550 (89.6%)	25 (83.3%)		
Yes	64 (10.4%)	5 (16.7%)		
Cognitive Outcomes				
Working Memory Score (d′4)	1.80 (1.17)	1.52 (1.16)	0.28	0.287
Alerting Network Score (ANT)	32.01 (37.75)	46.09 (41.72)	-14.08	0.133
Orienting Network Score (ANT)	28.12 (36.14)	31.18 (29.55)	-3.06	0.641
Executive Attention Score (ANT)	67.19 (36.24)	85.02 (52.36)	-17.83	0.128
Fluid Intelligence Score (PMA-R)	16.99 (5.53)	15.91 (5.53)	1.08	0.377
Emotion Recognition Task Score (ERT)	48.64 (5.86)	46.82 (8.39)	1.82	0.323
Advantageous Risk-Taking Score (Roulettes Task)	4.41 (2.46)	4.14 (2.80)	0.27	0.656
Behavioural Outcomes				
Total Behavioural Difficulties Score (SDQ)	10.35 (4.69)	14.00 (4.57)	-3.65	<0.001
Internalising Problems Score (SDQ)	4.16 (2.67)	5.28 (2.81)	-1.11	0.046
Externalising Problems Score (SDQ)	6.19 (3.23)	8.72 (3.30)	-2.54	<0.001
Mental Health Outcomes				
ADHD Symptom Diagnosis			9.09	<0.001
No	514 (91.0%)	11 (52.4%)		
Yes	51 (9.0%)	10 (47.6%)		

Abbreviations: ADHD: Attention-Deficit/Hyperactivity Disorder, BMI: Body Mass Index, SDQ: Strengths & Difficulties Questionnaire, SMD: Standardised Mean Difference.

[1] Mean (SD) or n (%)

[2] Welch Two Sample t-test; Fisher's exact test.

Table S7

Differential attrition analysis for dietary exposure

N	Completion Rate (%)	Strata
164	96.6	UPF Quartile 1
163	95.1	UPF Quartile 2
163	95.7	UPF Quartile 3
163	93.2	UPF Quartile 4
163	93.3	KIDMED Quartile 1
162	94.4	KIDMED Quartile 2
162	98.1	KIDMED Quartile 3
162	95.1	KIDMED Quartile 4

Table S8

Sensitivity analysis of attrition bias using the "Completer" cohort

	Exposure	Estimate (Full Sample, N=653)	Estimate (Completer Sample, N=622)	Percent Change (%)
Cognitive Outcomes				
Advantageous Risk-Taking Score	MD	0.05	0.05	4.3
Alerting Network Score (ANT)	MD	-0.27	-0.11	-58.9
Emotion Recognition Task Score (ERT)	MD	0.00	0.00	-18.6
Executive Attention Score (ANT)	MD	-0.25	0.09	-137.1
Fluid Intelligence Score (PMA-R)	MD	0.01	0.01	4.9
Orienting Network Score (ANT)	MD	-0.39	-0.48	22.1
Working Memory Score (d′4)	MD	-0.02	-0.02	4.9
Advantageous Risk-Taking Score	UPF	-0.02	-0.02	-12.3
Alerting Network Score (ANT)	UPF	0.42	0.40	-5.6
Emotion Recognition Task Score (ERT)	UPF	0.00	0.00	2.6
Executive Attention Score (ANT)	UPF	-0.07	-0.09	21.0
Fluid Intelligence Score (PMA-R)	UPF	0.00	0.00	-4.1
Orienting Network Score (ANT)	UPF	0.19	0.22	19.4
Working Memory Score (d′4)	UPF	-0.01	-0.01	1.5
Behavioural and Mental Health Outcomes				
ADHD Symptom Diagnosis	MD	-0.09	-0.10	12.2
Externalising Problems Score (SDQ)	MD	-0.02	-0.02	11.4
Internalising Problems Score (SDQ)	MD	-0.02	-0.02	-9.6
Total Behavioural Difficulties (SDQ)	MD	-0.02	-0.02	2.1
ADHD Symptom Diagnosis	UPF	0.03	0.04	16.6
Externalising Problems Score (SDQ)	UPF	0.00	0.01	11.6
Internalising Problems Score (SDQ)	UPF	0.01	0.01	13.2
Total Behavioural Difficulties (SDQ)	UPF	0.01	0.01	12.3

Table S9

Longitudinal associations between Mediterranean diet adherence and behavioural and mental health outcomes

	Mediterranean Diet Adherence by Categories				
Outcome	Low-Average	Good β (95% CI)	Continuous β (95% CI)	P-value	FDR [5]
Total Behavioural Difficulties Score (SDQ) [4]					
n =	183	144	327		
Crude	Ref	-0.22 (-1.03, 0.60)	0.11 (-0.09, 0.31)	0.276	0.368
Model 1 [1]	Ref	-0.10 (-0.85, 0.65)	0.07 (-0.11, 0.25)	0.458	0.458
Model 2 [2]	Ref	-0.02 (-0.76, 0.72)	0.09 (-0.01, 0.27)	0.351	0.470
Internalising Problems Score (SDQ) [4]					
n =	183	144	327		
Crude	Ref	-0.52 (-1.01, -0.04)	-0.03 (-0.15, 0.09)	0.655	0.655
Model 1 [1]	Ref	-0.30 (-0.72, 0.13)	-0.05 (-0.15, 0.06)	0.381	0.458
Model 2 [2]	Ref	-0.27 (-0.69, 0.15)	-0.04 (-0.14, 0.07)	0.486	0.486
Externalising Problems Score (SDQ) [4]					
n =	183	144	327		
Crude	Ref	0.31 (-0.23, 0.85)	0.14 (0.01, 0.27)	0.041	0.082
Model 1 [1]	Ref	0.25 (-0.25, 0.76)	0.11 (-0.01, 0.23)	0.076	0.154
Model 2 [2]	Ref	0.31 (-0.20, 0.81)	0.12 (0.00, 0.24)	0.051	0.108
Outcome	Low-Average	Good OR (95% CI)	Continuous OR (95% CI)	P-value	FDR [5]
ADHD incident (no/yes)					
n =	269	185	454		
Crude	Ref	2.03 (0.94, 4.49)	1.32 (1.08, 1.63)	0.009	0.036
Model 1 [1]	Ref	1.86 (0.85, 4.17)	1.27 (1.04, 1.58)	0.023	0.093
Model 2 [2]	Ref	1.72 (0.76, 3.98)	1.24 (1.00, 1.57)	0.054	0.108

Abbreviations: ADHD: Attention-Deficit/Hyperactivity Disorder, CI: Confidence Interval, FDR: False Discovery Rate, OR: Odds Ratio, SDQ: Strengths & Difficulties Questionnaire.

[1] Model 1: Adjusted for sex, age, outcome baseline measurement & RCT group.

[2] Model 2: Model 1 further adjusted for BMI, ethnicity, substance use, maternal educational attainment, physical activity, annual net household income, outcome baseline measurement & RCT group.

[3] All models were estimated using generalised linear models with a Gaussian distribution (identity) for all outcomes, except for ADHD incidence, which was modelled using a logistic link (logit).

[4] Lower scores indicate better performance.

[5] FDR for p-value.

Table S10

Longitudinal associations between Mediterranean diet adherence and cognitive outcomes

	Mediterranean Diet Adherence by Categories				
Outcome	Low-Average	Good β (95% CI)	Continuous β (95% CI)	P-value	FDR [6]
Alerting Network Score (ANT) (ms) [4]					
n =	343	232	575		
Crude	Ref	-0.46 (-8.24, 7.32)	0.22 (-1.57, 2.01)	0.811	0.946
Model 1 [1]	Ref	-0.56 (-6.28, 5.17)	0.49 (-0.83, 1.81)	0.464	0.866
Model 2 [2]	Ref	-0.49 (-6.23, 5.25)	0.46 (-0.87, 1.78)	0.500	0.812
Orienting Network Score (ANT) (ms) [4]					
n =	342	232	574		
Crude	Ref	-2.50 (-10.34, 5.35)	0.22 (-1.58, 2.03)	0.809	0.946
Model 1 [1]	Ref	-1.77 (-7.33, 3.79)	-0.22 (-1.50, 1.07)	0.742	0.866
Model 2 [2]	Ref	-1.86 (-7.46, 3.75)	-0.26 (-1.55, 1.04)	0.696	0.812
Executive Attention Score (ANT) (ms) [4]					
n =	342	232	574		
Crude	Ref	3.88 (-2.77, 10.53)	-0.56 (-2.09, 0.98)	0.476	0.946
Model 1[1]	Ref	-0.91 (-5.22, 3.40)	-0.48 (-1.47, 0.51)	0.343	0.866
Model 2 [2]	Ref	-1.01 (-5.35, 3.34)	-0.54 (-1.54, 0.46)	0.293	0.812
Fluid Intelligence Score (PMA-R) [5]					
n =	341	230	571		
Crude	Ref	-0.23 (-0.83, 0.36)	-0.08 (-0.22, 0.05)	0.233	0.946
Model 1 [1]	Ref	-0.10 (-0.66, 0.47)	-0.02 (-0.15, 0.11)	0.718	0.866
Model 2 [2]	Ref	-0.10 (-0.67, 0.47)	-0.03 (-0.16, 0.11)	0.695	0.812
Working Memory Score (d′4) [5]					
n =	336	226	562		
Crude	Ref	-0.05 (-0.30, 0.20)	0.01 (-0.05, 0.07)	0.758	0.946
Model 1 [1]	Ref	-0.08 (-0.28, 0.12)	0.00 (-0.04, 0.05)	0.939	0.939
Model 2 [2]	Ref	-0.08 (-0.28, 0.12)	0.00 (-0.04, 0.05)	0.928	0.928
Emotion Recognition Task Score (ERT) [5]					
n =	341	231	572		
Crude	Ref	-0.10 (-1.04, 0.84)	-0.00 (-0.22, 0.21)	0.982	0.982
Model 1 [1]	Ref	0.03 (-0.80, 0.87)	0.06 (-0.13, 0.25)	0.549	0.866
Model 2 [2]	Ref	0.06 (-0.78, 0.89)	0.05 (-0.14, 0.24)	0.598	0.812
Advantageous Risk-Taking Score (Roulettes Task) [5]					
n =	343	231	574		
Crude	Ref	0.11 (-0.34, 0.56)	0.03 (-0.08, 0.19)	0.643	0.946
Model 1 [1]	Ref	0.19 (-0.19, 0.57)	0.06 (-0.30, 0.14)	0.207	0.866
Model 2 [2]	Ref	0.17 (-0.21, 0.55)	0.04 (-0.04, 0.13)	0.343	0.812

Abbreviations: ANT: Attentional Network Test, CI: Confidence Interval, FDR: False Discovery Rate, PMA-R: Primary Mental Abilities-Revised.

[1] Model 1: Adjusted for sex, age, outcome baseline measurement & RCT group.

[2] Model 2: Model 1 further adjusted for BMI, ethnicity, substance use, maternal educational attainment, physical activity, annual net household income, outcome baseline measurement & RCT group.

[3] All models were estimated using generalised linear models with Gaussian (identity) distribution for all outcomes.

[4] Lower scores indicate better performance.

[5] Higher scores indicate better performance.

[6] FDR for p-value.

Table S11

Bootstrap estimates of model performance for the metabolic signature predicting ultra-processed food consumption. Table shows R^2 and Pearson correlation coefficient with 95% confidence intervals estimated from 10,000 bootstrap samples.

Metric	Estimate	95% CI
R^2	0.13	0.06, 0.21
Pearson Correlation	0.36	0.25, 0.46

Table S12

Summary of Significant Interactions with Mediterranean Diet

Analysis mode	Outcome Variable	Moderating Variable	Interaction Term	IRR (95% CI)	P-value	FDR
Cross Sectional [1,2]	Emotion Recognition Task Score (ERT) [6]	Sex	MD Score × Sex [Female]	0.99 (0.98, 1.00)	0.023	0.164
Analysis mode	Outcome Variable	Moderating Variable	Interaction Term	β (95% CI)	P-value	FDR
Cross Sectional [1,2]	Working Memory Score (d′4) [6]	Sex	MD Adherence [Good] × Sex [Female]	0.44 (0.06, 0.82)	0.025	0.176
Analysis mode	Outcome Variable	Moderating Variable	Interaction Term	IRR (95% CI)	P-value	FDR
Longitudinal [3,4]	Internalising Problems Score (SDQ) [5]	Sex	MD Adherence [Good] × Sex [Female]	-1.05 (-1.89, -0.21)	0.015	0.061

Abbreviations: CI: Confidence Interval, FDR: False Discovery Rate, IRR: Incidence Rate Ratio, SDQ: Strengths & Difficulties Questionnaire.

[1] Model 2 adjusted for sex, age, BMI, ethnicity, substance use, maternal educational attainment, physical activity & annual net household income.

[2] All models were estimated using generalised linear models with appropriate family distributions: negative binomial (log) for internalising problems and the emotion recognition task; and Gaussian (identity) for working memory.

[3] Model 2: adjusted for sex, age, BMI, ethnicity, substance use, maternal educational attainment, physical activity, annual net household income, baseline outcome measurement & RCT group.

[4] The model was estimated using a generalised linear model with a Gaussian (identity) distribution.

[5] Lower scores indicate better performance.

[6] Higher scores indicate better performance.

*<0.050

Table S13

Summary of Significant Interactions with Mediterranean diet adherence

Analysis mode	Outcome Variable	Moderating Variable	Interaction Term	IRR (95% CI)	P-value	FDR
Cross Sectional [1,2]	Total Behavioural Difficulties Score (SDQ) [4]	% UPF consumption in g/d	MD continuous × % UPF consumption in g/d	1.00 (1.00, 1.00) [5]	0.045	0.139
Analysis mode	Outcome Variable	Moderating Variable	Interaction Term	β (95% CI)	P-value	FDR
Longitudinal [2,3]	Internalising Problems Score (SDQ) [4]	% UPF consumption in g/d	MD continuous × % UPF consumption in g/d	0.02 (0.00, 0.03)	0.011	0.044
Longitudinal [2,3]	Internalising Problems Score (SDQ) [4]	% UPF consumption in g/d	MD (good) × % UPF consumption in g/d	0.07 (0.01, 0.14)	0.023	0.094

Abbreviations: CI: Confidence Interval, FDR: False Discovery Rate, IRR: Incidence Rate Ratio, SDQ: Strengths & Difficulties Questionnaire.

[1] Model adjusted for sex, age, BMI, ethnicity, substance use, maternal educational attainment, physical activity & annual net household income.

[2] Models were estimated using generalised linear models with appropriate family distributions: Negative binomial (log) for behavioural problems and Gaussian (identity) for internalising problems.

[3] Model adjusted for sex, age, BMI, ethnicity, substance use, maternal educational attainment, physical activity, annual net household income, baseline outcome measurement & RCT group.

[4] Lower scores indicate better performance.

[5] IRR is reported as 1.00 due to rounding; the significant p value and negative z score indicate a buffering effect.

Table S14

Summary of Significant Interactions with ultra-processed food consumption

Analysis mode	Outcome Variable	Moderating Variable	Interaction Term	IRR (95% CI)	P-value	FDR
Cross Sectional [1,2]	Total Behavioural Difficulties Score (SDQ) [4]	MD continuous	% UPF consumption in g/d × MD continuous	1.00 (1.00, 1.00) [5]	0.035	0.102
Analysis mode	Outcome Variable	Moderating Variable	Interaction Term	β (95% CI)	P-value	FDR
Longitudinal [2,3]	Internalising Problems Score (SDQ) [4]	MD continuous	% UPF consumption in g/d × MD continuous	0.01 (0.00, 0.03)	0.016	0.067

Abbreviations: CI: Confidence Interval, FDR: False Discovery Rate, IRR: Incidence Rate Ratio, SDQ: Strengths & Difficulties Questionnaire.

[1] Model adjusted for sex, age, BMI, ethnicity, substance use, maternal educational attainment, physical activity, annual net household income & maternal mental health disorder.

[2] Models were estimated using generalised linear models with appropriate family distributions: Negative binomial (log) for behavioural problems and Gaussian (identity) for internalising problems.

[3] Model adjusted for sex, age, BMI, ethnicity, substance use, maternal educational attainment, physical activity, annual net household income, maternal mental health disorder, baseline outcome measurement & RCT group.

[4] Lower scores indicate better performance.

[5] IRR is reported as 1.00 due to rounding; the significant p value and negative z score indicate a buffering effect.