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Impulsivity among healthy adults is associated with diet and fecal microbiota composition

Prokopis Konstanti[1], Kira F. Ahrens[2], Rebecca J. Neumann[2], Michael M. Plichta[2], Carmen Schiweck[2], Alea Ruf[2], Christian J. Fiebach[3], Raffael Kalisch[3,4], Ulrike Basten[3], Michèle Wessa[3], Oliver Tuescher[3], Bianca Kollmann[4,5], Klaus Lieb[3], Alejandro Arias-Vasquez[6,7], Hauke Smidt[1], Andreas Reif[2,8], Silke Matura[2,9] and Clara Belzer[1,9]✉

Impulsivity is an important personality trait that has been associated with unhealthy dietary choices and higher alcohol consumption. In turn, both diet and alcohol can affect gut microbiota composition, which has been recently linked with mental health. Although a few studies have explored the relationship between personality traits and gut microbiota, the interplay between trait impulsivity, diet, and gut microbiota remains underexplored. In the present cross-sectional study, we examine the relationship between impulsivity, diet, and fecal microbiota composition in the LORA (Longitudinal Resilience Assessment) cohort, which included participants of the general population ($N = 913$), without any lifetime diagnosis of mental disorder and no major disease. Fecal samples were analyzed using 16S ribosomal RNA amplicon sequencing, and trait impulsivity was assessed using the UPPS (Urgency-Premeditation-Perseverance-Sensation seeking) questionnaire. UPPS facets were associated with consumption of alcohol, sugary drinks, fruits, vegetables and fiber but not with meat. All the dietary components were associated with overall fecal microbiota composition as determined by beta diversity analyses, but no associations were detected for any of the four UPPS facets. Per genus analysis revealed associations of urgency with three bacterial taxa, premediation with four bacterial taxa and sensation seeking with one bacterial taxon. Notably, the genera *Butyricicoccus* and *Lachnospiraceae* UCG-001 that were negatively associated with urgency were also associated with healthier dietary patterns such as higher fiber, fruits and vegetables consumption and with lower consumption of sugary drinks. Furthermore the bacterium *Eubacterium siraeum* that was associated with higher sensation seeking, was also associated with more frequent alcohol consumption. Overall, our results suggest that impulsivity in neurotypical adults is associated with dietary choices and the relative abundances of specific gut bacteria.

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INTRODUCTION

The personality trait impulsivity is a characteristic or disposition to act without considering the potential consequences [1, 2]. Individuals with high levels of impulsivity are more likely to engage in risky behaviors such as substance abuse, aggression, gambling, and to follow unhealthy dietary patterns [3]. Moreover, the trait impulsivity is considered a key feature for several mental health disorders, such as attention-deficit/hyperactivity disorder (ADHD) or borderline personality disorder [4]. Genetics [5], sex [6], and environmental factors like socioeconomic status [7] have been found to affect impulsivity, while at the neurochemical level, neurotransmitters including dopamine, serotonin, norepinephrine, and glutamate have been reported [8]. However, despite the increasing knowledge on impulsivity, novel, targeted treatment and prevention strategies are lacking.

Recently the role of gut microbiota has been implicated with brain function through the bidirectional communication between the gut and the brain, known as the gut-brain axis (GBA) [9]. Gut microbes can produce several compounds that can interact with the GBA, such as SCFAs, neurotransmitters [10], hormones [11], and also transform bile acid [12], highlighting their important role in the GBA [13, 14]. Of particular importance for impulsivity is the ability of gut microbiota to directly produce neurotransmitters and also regulate the production of neuroactive compounds by the host, such as peripheral serotonin [15] or the satiety-related hormones like ghrelin [16], both of which were linked to impulsivity [17, 18]. Beyond biochemical crosstalk, impulsivity and microbiota might also be associated due to the impact of impulsivity on dietary choices or alcohol consumption since individuals with higher impulsivity are prone to less healthy food

[1]Laboratory of Microbiology, Wageningen University & Research, Wageningen, The Netherlands. [2]Goethe University Frankfurt, University Hospital, Department of Psychiatry, Psychosomatic Medicine and Psychotherapy, Frankfurt, Germany. [3]Neuroimaging Center (NIC), Focus Program Translational Neuroscience (FTN), Johannes Gutenberg University Medical Center, Mainz, Germany. [4]Leibniz Institute for Resilience Research, Mainz, Germany. [5]Department of Psychiatry and Psychotherapy, University Medical Center Mainz, Mainz, Germany. [6]Department of Human Genetics, Donders Institute for Brain, Cognition and Behavior, Radboud University Nijmegen Medical Center, Nijmegen, GA, The Netherlands. [7]Department of Psychiatry, Donders Institute for Brain, Cognition and Behavior, Radboud University Nijmegen Medical Center, Nijmegen, GA, The Netherlands. [8]Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Frankfurt am Main, Germany. [9]These authors jointly supervised this work: Silke Matura, Clara Belzer. ✉email: clara.belzer@wur.nl

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choices and higher alcohol consumption, choosing instant reward over long-term benefits. Hence, studying the relationship between impulsivity and gut microbiota might provide us valuable insights for a deeper understanding of impulsivity.

While a growing body of human studies suggest a role of microbial communities on behaviour [19] and personality traits [20], research into impulsivity is still very limited. The few studies that have been reported, have examined the relationship between gut microbiota and impulsivity mainly from a disease-centered perspective, focussing on impulsivity-associated diseases like ADHD or aggression [21, 22] rather than considering impulsivity as a continuous trait. A systematic review by Gkougka et al. [21] showed differences in microbial composition between people with ADHD compared to unaffected controls, with decreased relative abundances of *Faecalibacterium* being reported in three of the studies. Similar findings were also reported by Langmajerová et al. [22] with reduced relative abundances of *Faecalibacterium* being reported in patients with ADHD and aggressive patients with schizophrenia. Nevertheless, the heterogeneity of the studies in terms of age, methodologies and sample size does not allow for concrete conclusions and there is a necessity for more studies assessing the links between the microbiome and impulsivity.

Although these studies provide valuable initial evidence, focusing solely on pathological states limits our understanding. The relationship between the gut microbiota and impulsivity may differ or be less evident in non-disease conditions. Investigating this link within the general population offers a more comprehensive perspective and helps us understand the potential role of gut bacteria before the onset of impulsivity-associated diseases. Through the present study, we aim to bridge the knowledge gap and study the potential associations between the trait impulsivity, diet, and gut microbiota in the general population.

METHODS

Study design

The samples used for the current study are part of the Longitudinal Resilience Assessment (LORA) study, a population-based, multi-center cohort study in Germany in the cities of Frankfurt am Main and Mainz as previously described [23]. All procedures were approved by the respective Ethical Committees in Mainz (registration number: 837.105.16(10424)) and Frankfurt a. M. (registration number: 244/16), complied with the Declaration of Helsinki (2013), and written informed consent was obtained from all participants. Data collection for the baseline assessment of the study started in 2017 and continued until 2019. Participants were recruited via online or printed advertisements. Inclusion criteria were age 18–50 years, normal or corrected vision, and sufficient knowledge of the German language. The exclusion criteria were lifetime diagnosis of schizophrenia or bipolar disorder, organic mental disorders or substance dependence syndromes, as well as any other current severe axis-I disorders or medical conditions. Participants with known learning disabilities, serious neurological disorders (e.g., tumors in the central nervous system), or participants who had taken part in a clinical trial involving medication in the previous six months were also excluded.

Demographics and assessment of impulsivity, alcohol and diet

Information on the socio-demographics (Table 1) of the subjects was collected through an online database system (secuTrial© electronic data capture system, www.secutrial.com), which adheres to the Guidelines for Good Clinical Practice (GCP). Trait impulsivity was assessed with the UPPS (Urgency, (lack of) Premeditation, (lack of) Perseverance, Sensation Seeking) questionnaire [24]. The four UPPS facets capture: (1) urgency, defined as the tendency to act rashly while faced with intense negative emotional contexts; (2) (lack of) premeditation, defined as the tendency to take into account the consequences of actions before engaging in them; (3) (lack of) perseverance, defined as the ability to remain focused on a task that may be boring and/or difficult; and (4) sensation seeking, considered as a tendency to enjoy and pursue activities that are exciting and open to trying new experiences.

Alcohol consumption was determined using the Alcohol Use Disorder Identification Test (AUDIT) [25]. Height and weight were used for body

Table 1. Sample characteristics.

Categorical Variables	*N* = 913	
Sex	911	
Male		315 (35%)
Female		596 (65%)
Unknown		2
Country of birth	910	
Germany		835 (92%)
Other		75 (8.2%)
Unknown		3
Education	856	
Secondary education and lower		357 (42%)
Technical school		113 (13%)
University		386 45%)
Unknown		57
Civil Status	853	
Single		680 (80%)
Married		154 (18%)
Divorced		12 (1.4%)
Other		7 (0.8%)
Unknown		60
Antibiotics frequency	893	
More than once per month		0 (0%)
Monthly		11 (1.2%)
Rarely		566 (63%)
Never		316 (35%)
Unknown		20
Medication	913	
No		682 (67%)
Yes		231 (33%)
Unknown		0
Vegan or vegetarian	894	
No		765 (86%)
Yes		129 (14%)
Unknown		20
Numerical Variables	***N* = 913**	
Age	911	
Median (IQR)		26 (23, 33)
Mean (SD)		29 (8)
Range		18, 50
Unknown		2
BMI	899	
Median (IQR)		23.4 (21.3, 26.0)
Mean (SD)		24.0 (3.9)
Range		16.3, 42.1
Unknown		14
UPPS urgency	913	
Median (IQR)		20 (16, 24)
Mean (SD)		20 (6)
Range		12, 48
Unknown		0
UPPS (lack of) premeditation	909	
Median (IQR)		24 (21, 28)
Mean (SD)		24 (6)

Table 1. continued

Numerical Variables	N = 913	
Range		11, 44
Unknown		4
UPPS (lack of) perseverance	913	
Median (IQR)		19 (16, 22)
Mean (SD)		19 (5)
Range		10, 37
Unknown		0
UPPS sensation seeking	913	
Median (IQR)		32 (26, 38)
Mean (SD)		32 (8)
Range		12, 48
Unknown		0

mass index calculations (BMI; calculated as weight in kg/m^2). Diet was determined with a specific customized diet frequency questionnaire designed for this study, see Table 2 for further information. In addition to antibiotics, the use of any other medications was also recorded.

Assessment of gut microbiota composition

Fecal samples were collected at home with the OMNIgene gut kit (DNA Genotek Inc. Ottawa, ON, Canada) and sent to the collection sites in Frankfurt a. M. and Mainz within one week after the baseline assessments. Upon arrival, the samples were immediately stored at −80 °C. Bacterial genomic DNA was extracted from 0.25 g of the fecal sample using the repeat bead beating and subsequent DNA isolation using the Maxwell Instrument with a customized kit (AS1220; Promega, Leiden, The Netherlands) [26]. For 16S ribosomal RNA (rRNA) gene sequencing, we used unique barcoded primers, 515F-n and 806R-n, targeting the V4 region of the 16S rRNA gene. The PCR amplification program included 25 cycles as described previously [27]. Amplicon concentration was quantified with Qubit dsDNA BR Assay Kit (Invitrogen, California, USA) and samples were sequenced on a NovaSeq instrument (Novogene Europe, Cambridge, UK). To ensure the quality of the sequence data, technical duplicates, along with negative (no template control samples) and positive (16S rRNA gene DNA mock communities of defined composition) control samples were included in each library. Raw data was processed with the NG-Tax pipeline [28] with default parameters and for taxonomic assignment, the Silva reference database 138.1 was used [29]. Samples with at least 10000 reads were kept for downstream analysis ($n = 913$), resulting in the removal of one sample.

Data analysis

To study the association between impulsivity and dietary data, ordinal regression models were applied using the ordinal package in R [30]. Diet was used as the dependent variable and UPPS facets as an independent variable, including age, sex, BMI, education, and medication in the models. For the microbiota data, analyses were conducted using the genus level data. Alpha diversity indexes were calculated using the R package microbiome [31]. Beta diversity was calculated with the Aitchinson distance method using the centered log-ratio transformed (CLR) genus level data [32]. ADONIS permutational multivariate analysis of variance (PERMANOVA) was performed using the Vegan package [33] and was used to determine the amount of variation explained by different grouping variables. For per feature analysis, we ran linear models (CLR abundance ~ UPPS facet/diet+Age+Sex+BMI+Antibiotics +Education+Medication) using the R package lme4. All analyses were conducted at the genus level including bacterial genera that were detected in at least 25% of the samples (Supplementary Fig. 1). P-values were adjusted using the R package qvalue [34], considering qvalues < 0.15 as significant.

For the mediation analysis, dietary data was tested as the mediator between impulsivity and bacterial taxa. First, we estimated the effect of the UPPS facets on the bacterial taxa; second, we estimated the effect of UPPS facets on diet; and third, we estimated the joint effect of UPPS facets and diet on bacterial taxa. All models were adjusted for age, sex, BMI, antibiotics, education and medication. Mediation was estimated using the R package mediation [35] with 999 simulations.

To predict the functional profiling of the bacterial communities by ancestral state reconstruction using 16S rRNA gene sequences PICRUSt2 was applied [36]. KEGG ontology matrix was further mapped for the gut brain modules (GBMs) as described by Valles-Colomer et al. [37], using the R package Omixer-RPM [38]. The resulting data was CLR transformed and used for downstream data analysis, following the same procedures as with the taxonomy data.

Table 2. Dietary information.

Variable	N = 913	Frequency %
Frequency eating vegetables	893	
Daily		636 (71%)
Weekly		246 (28%)
Monthly		10 (1.1%)
Never		2 (0.2%)
Unknown		20
Frequency eating vegetables with fiber	886	
Daily		126 (14%)
Weekly		587 (66%)
Monthly		166 (19%)
Never		7 (0.8%)
Unknown		27
Frequency eating fruits	889	
Daily		530 (59%)
Weekly		322 (36%)
Monthly		28 (3.1%)
Never		9 (1.0%)
Unknown		24
Frequency eating meat	887	
Daily		215 (24%)
Weekly		459 (51%)
Monthly		85 (9.5%)
Never		128 (14%)
Unknown		26
Sugary drinks	888	
Daily		142 (16%)
Weekly		325 (37%)
Monthly		306 (34%)
Never		115 (13%)
Unknown		25
Alcohol consumption	910	
Never		68 (7.5%)
Monthly or less		179 (20%)
Monthly 2–4 times		433 (48%)
Weekly 2–3 times		206 (23%)
Weekly more than 4 times		23 (2.5%)
Unknown		4

RESULTS

Characteristics of the study population

The characteristics of the 913 subjects included in the present study are presented in Table 1. Participants were predominantly born in Germany (92%), with a median age of 26 years, females represented 65% of the cohort and the median BMI was 23.4 kg/m^2. Dietary information, including the frequency of consumption of vegetables, fiber, fruits, sugary drinks, and alcohol, is presented in Table 2.

Relation between UPPS, alcohol, and diet

We first examined the relationship between UPPS facets with alcohol and diet data. Results showed that higher sensation seeking, and lack of premeditation were related to higher alcohol consumption (Fig. 1A), while higher urgency and sensation seeking were associated with more frequent consumption of sugary drinks (Fig. 1B; Supplementary Table 1). Regarding diet, the most consistent associations were detected between urgency and consumption of fiber (Fig. 1C), while lower sensation seeking was associated with more frequent consumption of fiber (Fig. 1C) and to a lesser extend with fruits and vegetables (Fig. 1D, E). No significant associations were detected between meat consumption and any of the UPPS-facets (Fig. 1F).

Relation between impulsivity and diet with overall fecal microbiota composition

Next, we tested for associations between the study covariates and the variation in the overall fecal microbiota composition. Univariate beta diversity analyses with Aitchison distances showed that age, sex, BMI, education, medication, alcohol consumption, frequency of fruits, fiber and vegetable consumption, and antibiotics were significantly associated with the observed variation in fecal microbiota composition (Fig. 2; Supplementary Table 2). None of the UPPS facets were associated with the observed variation microbiota composition in univariate (Fig. 2; Supplementary Fig. 2) or multivariate models (Supplementary Table 2). The associations between UPPS facets and alpha diversity, as determined by Shannon and number of observed taxa, were also non-significant (Supplementary Fig. 3; Supplementary Table 3).

Associations between bacterial genera with impulsivity and diet

To test for associations between individual genera and the four facets of the UPPS questionnaire linear models were applied. Analysis revealed significant associations between UPPS-urgency and the bacterial genera *Butyricicoccus*, *Lachnospiraceae* UCG-001 and *Ruminococcus* in models adjusted for age, BMI, sex, antibiotics, education and medication (Fig. 3A). Premeditation was positively associated with *Bifidobacterium* and an uncultured member of it and negatively associated with two uncultured Lachnospiraceae taxa (Fig. 3B). Moreover, a positive association between the genus *Eubacterium siraeum* with sensation seeking was detected (Fig. 3C). No associations were detected between (lack of) perseverance with any of the bacterial taxa in any of the models (Supplementary Table 4).

Following, we tested for associations between gut microbiota with the different dietary components. In total 10 bacterial genera were significantly associated with alcohol consumption (Supplementary Table 5; Fig. 4D), 24 bacteria with consumption of sugary drinks (Supplementary Table 5; Fig. 4D), 16 bacterial genera with the frequency of fiber consumption (Supplementary Table 5; Fig. 4D), 27 bacterial genera with the frequency of fruit consumption (Supplementary Table 5; Fig. 4D), 28 bacterial genera with the frequency of vegetable consumption (Supplementary Table 5; Fig. 4D) and 18 with meat consumption (Supplementary Table 5; Fig. 4D). We specifically looked into the associations between the bacteria that were found to be associated with both the UPPS facets and the dietary components. The genera *Butyricicoccus* and *Lachnospiraceae* UCG-001, which were linked with UPPS-urgency (Fig. 3A), were positively associated with frequency of fiber, vegetables, and fruits and negatively with the consumption of sugary drinks. Moreover, *Lachnospiraceae* UCG-001 and *Ruminococcus* were also negatively associated with meat consumption and fiber (Fig. 3D). The bacterial genus *Bifidobacterium* that was associated with premeditation (Fig. 3B) was positively associated with consumption of sugary drinks and negatively with vegetables (Fig. 3D), and the uncultured genus GCA-900066575 (Fig. 3B) from the *Lachnospiraceae* family was associated with premeditation and fruit consumption (Fig. 3D). Finaly, the genus *Eubacterium siraeum* that was positively associated with sensation seeking (Fig. 3C) was also positively associated with higher consumption of alcohol and negatively associated with consumption of sugary drinks and meat (Fig. 3D).

Fiber, sugary drinks and alcohol consumption mediate the relation between UPPS facets and gut microbiota

Since the previous analyses identified associations between gut bacteria with both UPPS facets and diet, we tested for potential mediation effects of diet on the relationship between UPPS facets and gut bacteria. Results showed that consumption of alcohol was found to mediate the relationship between sensation seeking and the bacterium *Eubacterium siraeum* (Fig. 4A). Moreover, fiber partially mediated the relation between UPPS-urgency and *Butyricicoccus* explaining 9% of the direct effect (Fig. 4B), while a marginal significance was observed for fiber as a mediator of the relationship between *Lachnospiraceae* UCG-001 and UPPS-urgency ($p = 0.056$; Supplementary Table 6). Finaly, consumption of sugary drinks significantly mediated the relationship for both *Butyricicoccus* and *Lachnospiraceae* UCG-001 with UPPS-urgency (Fig. 4C, D). No mediation effect was observed for sugary drinks, alcohol, meat, vegetables or fruits with any of the bacteria tested (Supplementary Table 6).

Associations between gut-brain modules and UPPS questionnaire

To test for associations between the functional potential of the gut microbiota and trait impulsivity, we analyse the relationship between the abundance of the Gut-brain-modules with the four facets of the UPPS questionnaire. The GBMs Butyrate synthesis II and Tryptophan degradation were negatively associated with UPPS urgency while Propionate synthesis II was positively associated with UPPS sensation seeking (Supplementary Fig. 4), however after p-value adjustment none of these associations remained significant (Supplementary Table 7).

DISCUSSION

In the present cross-sectional study, the interplay between trait impulsivity, diet, and fecal microbiota composition was studied in a neurotypical German population. Our results showed significant associations between facets of impulsivity with consumption of fiber, meat, sugary drinks, and alcohol, implying that dietary choices are associated with impulsivity. We further built on these findings, exploring their relationship with fecal microbiota composition. Individual bacterial genera, but not the overall microbiota structure, were related to urgency, (lack of) premeditation and sensation seeking. No associations were found with lack of perseverance. Among the genera that were identified by our analyses to be negatively associated with urgency, *Butyricicoccus* and *Lachnospiraceae UCG-001* were also associated with healthier dietary patterns such as lower consumption of sugary drinks and higher consumption of fruits, vegetables and fiber. The bacterium *Eubacterium siraeum* that was positively associated with sensation seeking was also associated with higher alcohol consumption. Mediation analyses revealed that the relation between urgency and gut microbiota is partly mediated by the consumption of sugary drinks and the relation between sensation seeking and *Eubacterium siraeum* is mediated by alcohol consumption. Overall, our results highlight a potential role of impulsivity on both dietary choices and gut microbiota composition.

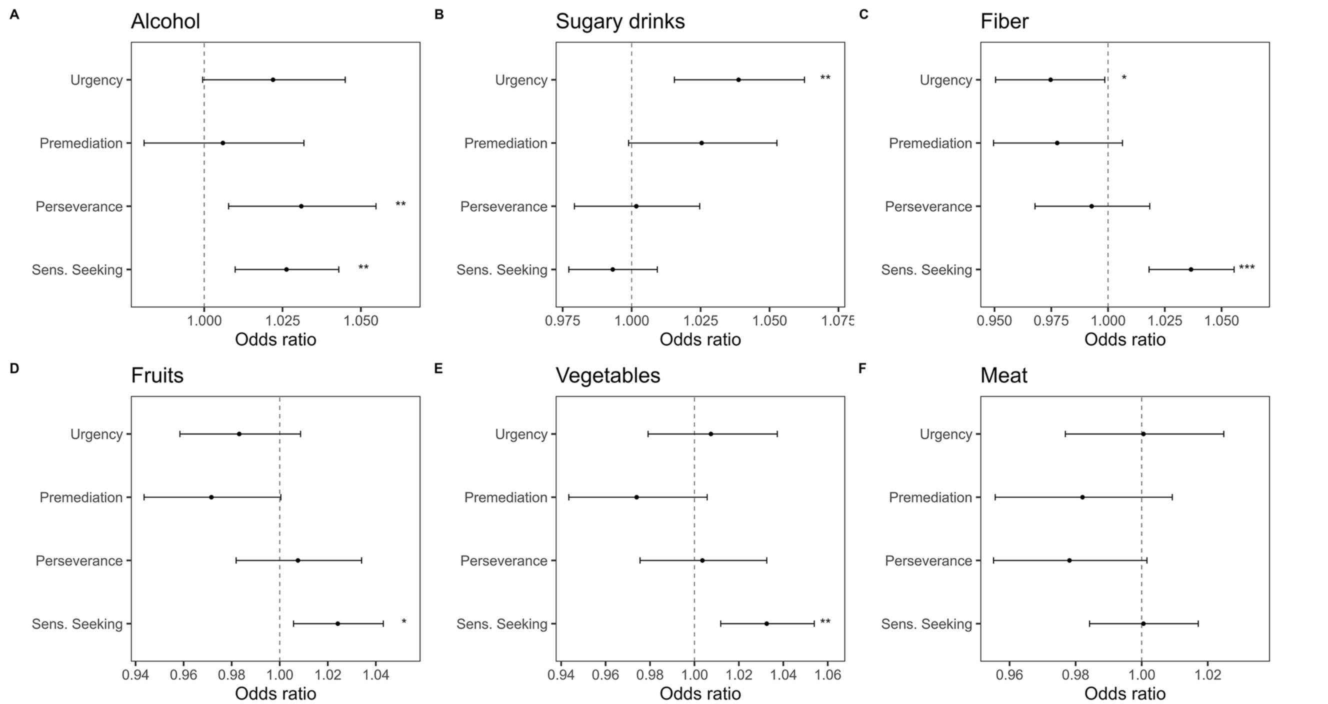

Fig. 1 Associations between UPPS facets and dietary components. Associations between **A** Alcohol, **B** sugary drinks, **C** fiber, **D** fruits, **E** vegetables and **F** meat consumption with the four different UPPS facets, using ordinal regression models, controlling for age, sex, BMI, medication and education. Circles represent regression coefficient, lines the 95% odds ratio and asterisks indicate p-values. Odds ratios above one indicate more frequent consumption and odds ratios below one less frequent consumption. Significance is indicated with *p < 0.05, ** p< 0.01 and ***p<0.001 .

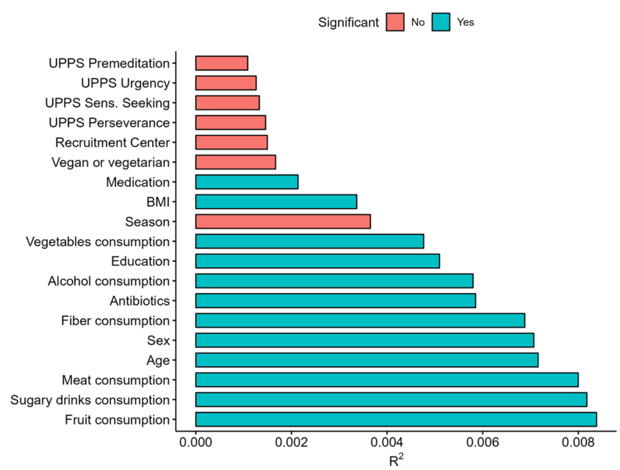

Fig. 2 Results from univariate PERMANOVA analyses using Aitchison distances. Horizontal bars show the amount of variance (R^2) explained by each covariate in univariate models as determined by PERMANOVA tests. Significant covariates (p-value < 0.05) are indicated in light green color, all the tests were performed with 999 bootstraps.

Impulsivity is linked to deficient inhibitory control, and individuals with higher impulsivity have been reported to follow unhealthy dietary choices [39–41]. Among the UPPS facets, urgency is the strongest predictor of psychopathology [42] and has been associated also with unhealthy dietary patterns [41]. In line, our results showed that individuals with higher urgency were consuming sugary drinks more frequently and foods with fiber less frequent, indicating a preference for unhealthy dietary patterns [40,41]. Dietary fiber is an important component of a healthy diet and includes non-digestible polysaccharides that only bacteria can utilise through fermentation, and therefore, are important determinants of the composition and function of the gut microbiota [43]. Hence, one possible scenario is that impulsivity affects gut microbiota composition indirectly via diet and in particular, fiber consumption, a scenario which is also supported by the results from the mediation analysis.

Among the main products of fiber fermentation by intestinal bacteria are SCFAs, such as butyrate. SCFAs can affect the gut-brain axis [44] directly by crossing the blood-brain barrier [45], or indirectly by enhancing cholinergic neurons' contractile response through epigenetic mechanisms [44], via the systemic circulation, or by activating vagal afferents [46]. Our findings show that individuals with higher levels of urgency were consuming fiber less frequently and had lower abundances of the genera *Butyricicoccus* and *Lachnospiraceae UCG-001*. *Butyricicoccus* is a well known butyrate producing bacteria [47], while Lachnospiraceae is a family of bacteria belonging to the phylum Firmicutes and it is one of the most abundant and diverse bacterial families found in the gut microbiota, with many of its members known to be significant butyrate producers, like *Roseburia* and *Faecalibacterium* [48, 49]. In line with our results [50], a previous study from Japan reported higher abundances of uncultured bacteria from the *Lachnospiraceae* in individuals showing high levels of conscientiousness, which is comparable to low levels of impulsivity [51]. In addition, analyses of the GBMs showed trends that higher urgency was negatively associated with Butyrate Synthesis II module. Overall, disruption of the gut bacterial communities due to lower fiber intake in individuals with higher impulsivity levels may predispose them to an imbalanced microbiota composition with limited butyrate production, which in turn can have an effect on overall health.

Validation of these findings from future studies is essential to understand the role of impulsivity on diet and gut microbiota. If indeed neurotypical adults with higher impulsivity are eating fiber less often and exhibit disrupted butyrate metabolism, this could

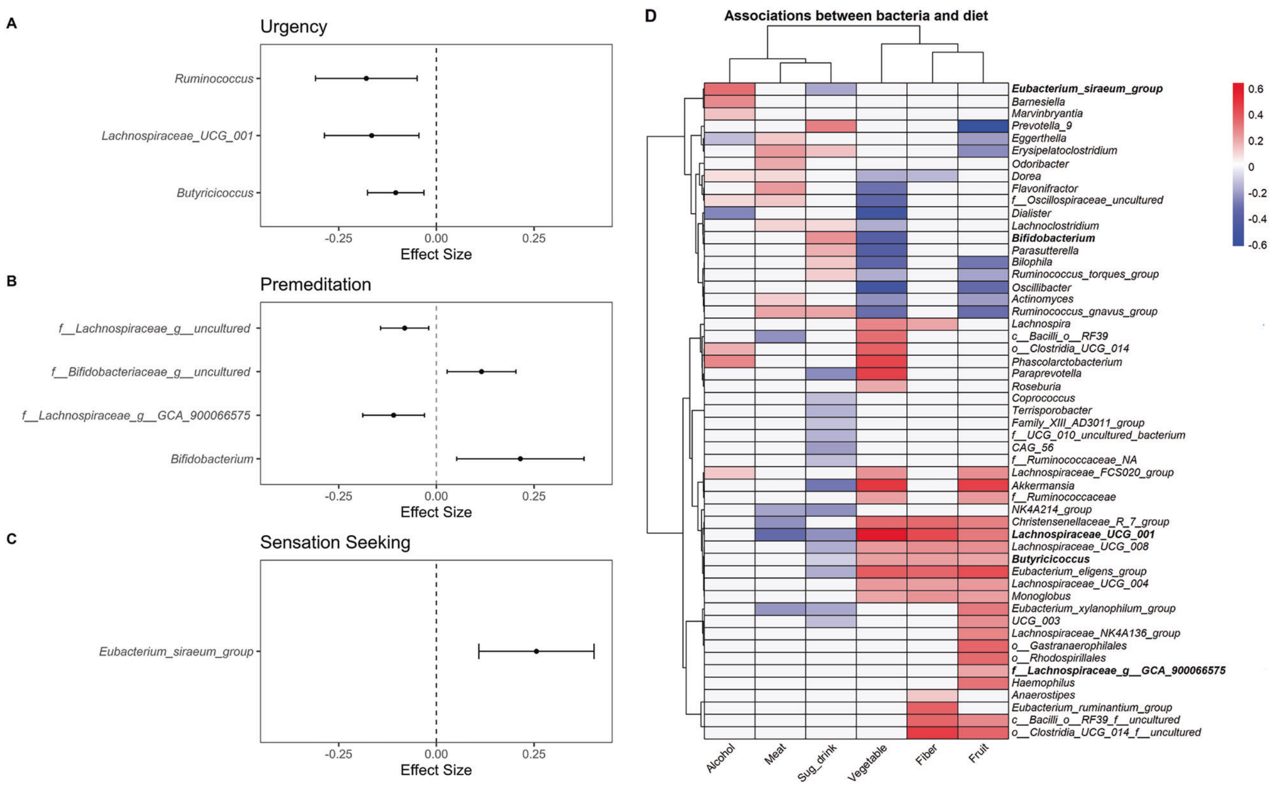

Fig. 3 The relation between gut microbiota with UPPS facets and diet. A Bacterial genera significantly associated with the UPPS-urgency, **B** UPPS-premeditation and **C** UPPS-sensation seeking. **D** Heatmap representing the significant associations between gut microbiota and dietary components. Models were adjusted for age, BMI, sex, antibiotics, education and medication. The options for each dietary components were ordered in ascending order, "never/monthly", "weekly", and" daily", hence a positive association indicate more frequent consumption of the dietary component.

have important implications for preventive measures concerning impulsivity-related disorders. Targeted dietary recommendations aiming to promote healthier dietary choices such as higher fiber intake and lower consumption of sugary drinks, might effectively restore the balance in microbiota composition, thereby enhancing butyrate production and promoting overall health. The latest dietary guidelines, such as those from the DGE (German Nutrition Society), already advocate for high fiber intake in the general population since previous studies suggests that fiber intake in German population are below the recommended intake levels [52, 53]. Increasing dietary fiber intake not only in disease states but also before the onset of impulsivity-related disorders might effectively counteract the negative effects of poor dietary choices associated with increased impulsivity. This approach could foster a healthy gut microbiota composition and support overall mental and physical well-being.

Moreover, the bacteria identified in our study to be associated with impulsivity, have been linked with mental health in previous studies. *Lachnospiraceae UCG-001* was associated with depression in mice studies [54] but also in humans [55], where reduced abundances of *Lachnospiraceae UCG-001* were reported for depression, highlighting its importance for the gut-brain axis. Species within the genus *Butiricicoccus* have been explored as potential new-generation probiotics [56] as they have been associated with anti-inflammatory effects in bowel diseases [57, 58]. Moreover, a recent population-level study identified the genus *Butyricicoccus* to be depleted in people with depression but the effect was non-significant after correction for antidepressant medication [37]. Notably, previous studies have indicated that individuals with newly diagnosed depression may exhibit higher levels of impulsivity [59]. Thus, the decreased abundances of these bacteria may suggest that disruptions in gut microbiota composition precede the development of depression due to impulsivity, potentially contributing to the development of depressive symptoms. Future studies focusing on the relationship between impulsivity and depression might also benefit from examining the microbiota composition of these individuals which could provide important insights for future prevention strategies.

Regarding the relationship between alcohol consumption with impulsivity, in line with previous studies [60], we found a positive association between impulsivity and alcohol consumption. Three out of the four UPPS facets, urgency, lack of premeditation, and sensation seeking were associated with alcohol consumption, showing a consistent association for the different UPPS facets. Moreover, alcohol consumption was significantly associated with fecal microbiota composition also in accordance with previous studies which showed alterations in the gut microbiota composition due to alcohol exposure [61, 62]. We identified the bacterium *Eubacterium siraeum* to be associated higher levels of sensation seeking and alcohol consumption, supporting a tri-partite relation between impulsivity, alcohol consumption, and gut microbiota. Sensation-seeking is the tendency seeking of novel, and intense experiences and while it is not necessarily negative, it has been associated with engagement in risky behaviors such as alcohol abuse [63]. Similar findings were also reported in Carbia et al. [60], however there is a difference in the reported bacteria. This inconsistency might be explained by the differences in sample size, geography and methodology. For instance Carbia et al. used the Barratt Impulsiveness Scale (BIS) [64] which measures different aspects of impulsivity compared to the UPPS dimensions, such as urgency.

The present study attempted to address the directionality of the relation between impulsivity, diet, alcohol, and gut microbiota. However, due to the bidirectional nature of this relationship, it is

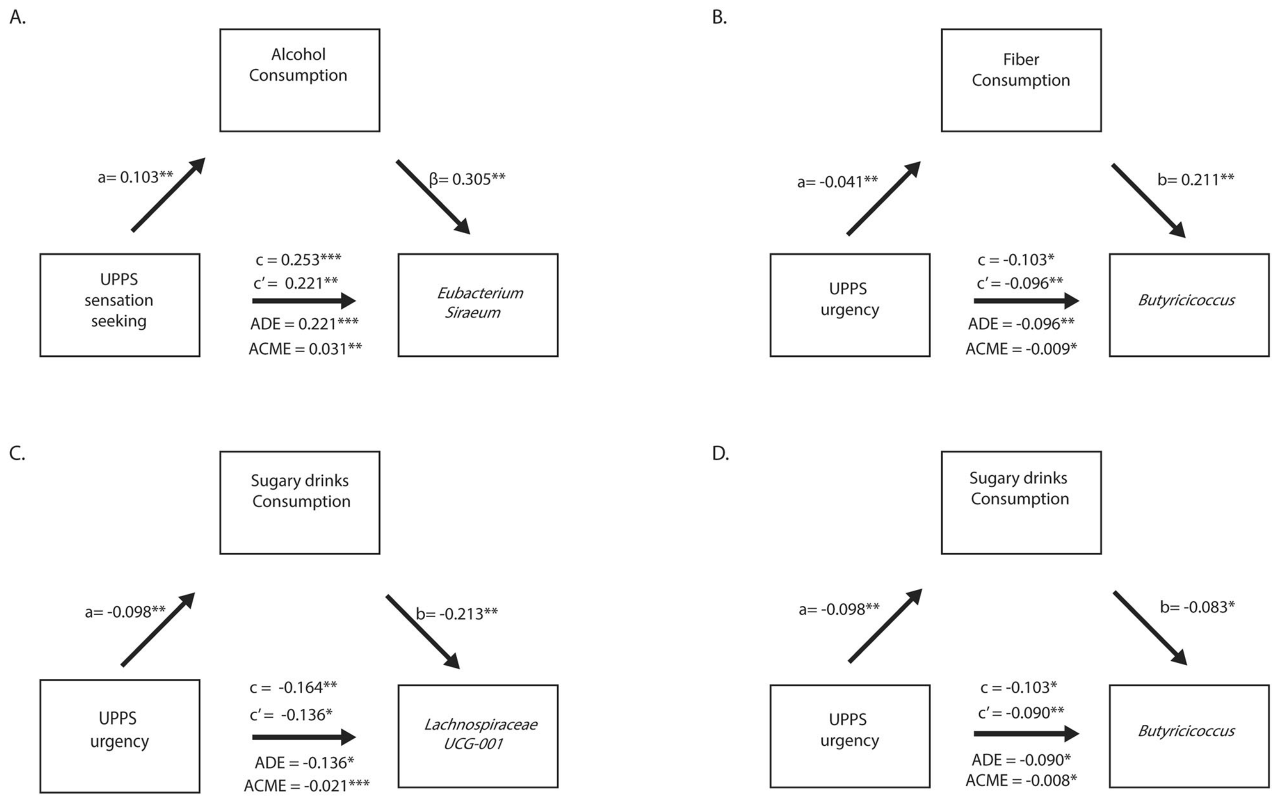

Fig. 4 Dietary components as a mediator between UPPS facets and gut microbiota. Results from the mediation analysis, testing for the mediation effect of dietary components on the relationship between UPPS-facets and gut microbiota. **A**. Consumption of alcohol as a mediator between UPPS-sensation seeking and the bacterial taxa *Eubacterium siraeum*. **B**. Consumption of fiber as a mediator between UPPS-urgency and the bacterial taxa *Butyricicoccus*. Consumption of sugary drinks as a mediator between UPPS-urgency and the bacterial taxa **C**. *Lachnospiraceae* UCG-001 and **D**. *Butyricicoccus*. Coefficients from each model are reported next to the arrows, with the letters a and b. Letters c' and c represent the coefficient with and without the mediator in the model, respectively. ACME: average causal mediated effect, ADE: average direct effect. Significance is indicated with $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$.

challenging to draw causal inferences. While we show that impulsivity can affect gut microbiota composition with dietary components as a mediator, it is also possible that diet can affect impulsivity, with gut microbes as mediators. Although we cannot rule out this possibility, the existing evidence supporting that diet can induce changes in impulsivity is primarily backed by a single animal study, in which a high-fat diet was observed to alter impulsivity levels in rats [65]. Further research in this field will provide a more comprehensive understanding of causality between these two complex systems.

Limitations of our study include the use of the four scale UPPS questionnaire, while a newer version of it is now divided into five scales with urgency dichotomized into negative and positive urgency. Although recent literature suggests that there is a big overlap between negative and positive urgency, we cannot exclude that there is a distinction regarding the association with microbiota composition [66]. Moreover, details on the type of antibiotics, the duration and the last time of use were not collected and might provide further information regarding their influence on microbiota composition. Additionally, including information on the type and quantity of fiber might have offered a more nuanced picture regarding their relation to microbial composition. Finally, longitudinal assessments with multiple sampling of microbiota composition are also important for solid conclusions. In turn, one of the strengths of this study is the large dataset which is important for microbiota analyses due to the high variability in the general population. Moreover, several covariates were collected, that were found to influence the gut microbiota, like age, sex, education, BMI and also antibiotics or other medication.

Impulsivity is an important personality trait, and understanding underlying factors is essential for further advances in the field. Overall, our results suggest that only a few bacterial genera are associated with sensation seeking and urgency –an aspect of impulsivity showing the highest correlations with psychiatric symptoms- and this relationship is mediated by the consumption of alcohol, sugary drinks and fiber. Understanding the relationship between impulsivity, dietary choices, and gut microbiota constitutes one crucial step toward promoting mental health through informed dietary decisions. Ideally, a better understanding of the role of the gut microbiome in non-disease states or primary to the onset of the disease can lead to the development of dietary, lifestyle, or probiotic interventions aimed at modulating the gut microbiome to potentially prevent or delay the onset of impulsivity related disorders.

DATA AVAILABILITY

The sequencing data from the LORA project have been deposited in the European Nucleotide Archive (ENA) under accession number PRJEB89458. The samples included in this study can be identified using the metadata column 'Impulsivity Project'.

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AUTHOR CONTRIBUTIONS

PK, CB, and SM conceptualized the study and designed the experiments. CB and A Reif provided funding for the research. PK supported data acquisition, conducted data analysis, wrote and delivered the first draft of the manuscript. CB, SM and HS provided substantial input into the interpretation of the data and the writing of the first draft; KFA, RJN, CS, and A Ruf supported data acquisition, contributed to experimental design, and provided substantial input in reviewing, editing, and interpreting the data. All authors have read, reviewed and approved the final version of the manuscript.

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COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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Correspondence and requests for materials should be addressed to Clara Belzer.