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Original article

Dietary fiber deficiency as a component of malnutrition associated with psychological alterations in alcohol use disorder

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SUMMARY

Background & aims: Chronic alcohol consumption can cause malnutrition that may contribute to alcohol-induced organ injury and psychological disorders. We evaluated the link between nutrient intake, especially dietary fibers (DF) and different parameters reflecting mental health and well being, namely anxiety, depression, alcohol craving, sociability, fatigue and intestinal comfort in alcohol use disorder (AUD) patients.

Methods: Cross-sectional data from 50 AUD patients, hospitalized for a 3-week detoxification program were used. Three 24-h recalls allowed to calculate dietary habits and nutrient intakes, that was also assessed in healthy subjects (HS). Diet quality was measured using the NOVA score. Psychological factors and intestinal discomfort were evaluated using validated self-administered questionnaires.

Results: Energy intake (excluding alcoholic beverage), total fat, monounsaturated and polyunsaturated fatty acids, protein and DF intakes were lower in AUD subjects compared to HS. Ninety percent of patients had a DF intake below the recommendation. AUD patients consumed more than twice as much ultra-processed food than HS. Fructan intake was negatively associated with anxiety ($p = 0.04$) adjusted for main confounders. Total DF, insoluble, soluble DF and galacto-oligosaccharide intakes were associated with higher sociability score. Soluble DF intake was associated with better satisfaction of bowel function ($p = 0.02$) and a lower intestinal discomfort ($p = 0.04$).

Conclusions: This study reveals that insufficient DF intake is part of AUD-related malnutrition syndrome, and is associated with higher anxiety, lower sociability score and intestinal discomfort. Our results suggest that an adequate intake of DF might be beneficial for recovery from AUD.

Trial registration: NCT03803709, https://clinicaltrials.gov/ct2/show/NCT03803709.

1. Introduction

Alcohol Use Disorder (AUD) is a chronic relapsing disease with significant physical and mental health consequences. It is one of the most common mental disorders affecting 8.6% of men and 1.7% of women worldwide [1]. AUD is associated with mood and social disorders [2,3]. Chronic alcohol consumption leads to metabolic disturbances and is associated with several nutritional deficiencies [4–6]. Indeed, alcohol abuse where alcohol can account for more than 50% of energy intake, compromises key nutrient intake and is one of the main causes of malnutrition in Western countries [7].

Many studies demonstrated that alcohol abuse leads to gastrointestinal symptoms especially diarrhea [8]. It also decreases nutrient absorption and alters liver metabolism, thereby disrupting

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Abbreviations

AUD	Alcohol use disorder
AUDIT	Alcohol use disorder test
BDI	Beck depression inventory
BMI	Body mass index
BSFS	Bristol stool form scale
DF	Dietary fiber
DSM-5	Diagnostic and Statistical Manual of Mental Disorders
EI	Energy intake
FA	Fatty acid
FOS	Fructo-oligosaccharides
GOS	Galacto-oligosaccharides
HS	Healthy subject
MFI	Multidimensional fatigue inventory
MMSE	Mini-mental state examination
MUFA	Monounsaturated fatty acids
OCDS	Obsessive compulsive drinking scale
PF	Processed food
PUFA	Polyunsaturated fatty acids
PSQI	Pittsburgh Sleep Quality Index
SFA	Saturated fatty acids
STAI	State-trait anxiety inventory
UPF	Ultra-processed food

nutrient availability and related physiological processes [4,6]. In addition, alcohol consumption affects eating behaviour that can contribute to malnutrition [9]. Our previous study showed that chronic alcohol abuse is associated with a decrease in energy intake from food, characterized by a reduction in fat and carbohydrate intake [10].

It is now well established that nutrition plays an important role in the development of mental illness. Notably, unbalanced diet or ultra-processed food, characterized by food rich in fat, sugar, salt and additives, is associated with mood disorders, including depression [11–14]. Numerous epidemiological studies have also reported that a diet rich in fibers is associated with a reduced risk of several chronic diseases and a lower prevalence of depressive symptoms [15–17]. Indeed, dietary fibers (DF) is considered a healthy nutrient and the European Food Safety Authority recommends an intake of 25 g per day for adults [18,19]. Dietary fibers with prebiotic properties, such as fructans, are known to have a significant effect on the gut microbiota, which may play a key role due to its potent effects on brain function and behaviour [20–22]. As AUD patients are characterized by alterations of gut microbiota composition [2,23–25] and have significant cognitive, emotional, and social impairments, nutrition could be an important factor to consider in the treatment of patients as it might influence recovery from AUD [26]. However, DF intake has never been studied in the context of AUD. Our hypothesis was that the unbalanced diet of AUD patients and in particular the low fiber intake could have an impact on patients' sociability, mood and alcohol craving. We thus evaluated dietary habits with a special focus on the DF and fructans intake in a population of AUD patients and in healthy subjects (HS). The focus on fructans – including fructo-oligosaccharides (FOS) and other non-digestible oligosaccharides like galacto-oligosaccharides (GOS), is motivated by the fact those prebiotic DF can exert beneficial effects on behaviour in other contexts [20,26].

2. Materials & methods

2.1. Subjects

A total of 50 AUD patients hospitalized for a 3 week-detoxification program in the alcohol-detoxification unit at Saint-Luc Academic Hospital, Brussels, Belgium were recruited. These patients were initially enrolled in a randomized, double-blind, placebo-controlled study assessing the impact of fiber supplementation on the gut–liver–brain axis. The severity of AUD was evaluated using the DSM-5 criteria [27]. Ninety-four percent of patients have been diagnosed as severe AUD (presence of at least 6 symptoms out of 11) and six percent with moderate AUD (presence of 5 symptoms). No other psychiatric diseases have been diagnosed in these patients. All consecutive patients, from October 2018 to December 2019, aged from 18 to 65 years old and who did not suffer from other addictions (except tobacco) were included. Patients were eligible if they had been drinking until the day of admission to the detoxification unit and if they did neither suffer from inflammatory bowel disease, other chronic inflammatory diseases (such as rheumatoid arthritis) or cancer, nor from metabolic disorders such as obesity (BMI$\geq$ 30 kg/m2), diabetes and bariatric surgery, or severe cognitive impairment (MMSE < 24). We also excluded subjects who had taken antibiotics, probiotics, or prebiotics in the 3 months prior to enrolment and those who were taking non-steroidal anti-inflammatory drugs or glucocorticoids within 1 month before inclusion. Patients with known cirrhosis or significant liver fibrosis ($\geq$F2) detected by Fibroscan (>7.6 kPa) at the day of admission were also excluded from the study. Thirteen healthy controls matched for age, gender and BMI with no AUD (Alcohol use disorders test [AUDIT] score <8 in males and <7 in females) were also recruited using flyers posted in Brussel's public setting. The inclusion/exclusion criteria were the same as for AUD patients except for the alcohol related items. The protocol of this study was approved by the "Comité d'éthique Hospitalo-facultaire des cliniques universitaires" (2017/04JUL/354 and 2014/14AOU/438) and all participants provided written informed consent. The study was registered at ClinicalTrials.gov under identification number NCT03803709.

2.2. Dietary assessment

All participants were interviewed on day 2 of alcohol withdrawal by a trained dietician who administered three 24-h dietary recalls (two weekdays and one weekend day in order to limit the source of variance [28]) during a face-to-face interview. The dietician asked the patients who arrived on Monday at the hospital to report their food consumption of the previous Saturday, Friday and Thursday (day -2, -3 and -4 before the inclusion). This procedure is classically used in the hospital because of the difficulty for patients to go back further in their memory. During this interview, food quantities were determined using validated photographs, exact quantity (grams/milliliters) or household measures.

The information collected in these interviews were then entered into the dietary software (Nubel®) to analyze the nutritional values of the diet and the detailed intake of the various macro- and micronutrients. In cases where information was missing from the Nubel software, the French food composition database (CIQUAL 2017) was used to complete the data [29]. Daily mean energy and nutrient intakes were calculated from all dietary records. The results were expressed in quantities and in proportion of total energy intake (EI). The lipid intakes were also expressed in proportion of

total fatty acids (FA). Micronutrient intakes were compared with the dietary guidelines for the Belgian adult population [30].

Twenty-seven categories of foods were formed by summing the amounts of food consumed expressed in grams per day [31]. Vegetables were separated into several classes to estimate the consumption of fructan-rich foods such as bulbs, rhizomes, roots and tubers [32]. The 27 categories were: roots and tubers, bulbs and rhizome, other vegetables, pasta/noodles, rice, potatoes, pulses, fruits, nuts and seeds, eggs, poultry, meat, fish and seafood, pizza/pie or sandwich, processed meat, biscuits or cakes, chocolate, soda and sweets, snack/chips, cheese, other dairy products, cereal products, bread, coffee, tea, fruit or vegetable juices, olive oil.

All foods and beverages were classified according to the NOVA food classification system consisting of four groups (unprocessed foods, culinary ingredients, processed foods and ultra-processed foods) [33]. The Nova score presented in this study excluded alcohol beverages. The proportion of processed foods (PF) and ultra-processed foods (UPF) in the diet (% grams/day of the total diet excluding alcoholic beverage) was calculated for each patient, as well as the frequency of meals (breakfast, morning snack, lunch, afternoon snack, dinner and evening snack).

During the dietary surveys, patients were also asked whether they had eaten alone or accompanied during the 3 meals of the day. From these data we constructed a quantitative score after considering the frequency of meals and the existence of company during meals (number of accompanied meals/total number of meals). The higher the score, the more the patients were used to eat with others.

2.3. Fiber intake

To properly evaluate the different types of fibers ingested, we used a database developed in the FiberTAG project [34]. This database allowed us to calculate insoluble fibers, soluble fibers including fructans (especially fructo-oligosaccharides [FOS]) and galacto-oligosaccharides (GOS). DF content in all food products and ready meals (e.g., pastries, breads) was calculated using the composition of foods from traditional recipes.

2.4. Psychological symptoms assessment

AUD patients were tested for depression, anxiety and alcohol craving with self-reported questionnaires (French versions): the Beck Depression Inventory [BDI] [35], the State-Trait Anxiety Inventory (STAI form YA) [36], and the Obsessive-Compulsive Drinking Scale [OCDS] [37] as described elsewhere [2]. The sociability was tested using the social situation questionnaire that assesses preferences for social (vs. nonsocial) situations. This questionnaire is composed of 28 situations characterized as social or not and pleasant or not. The patient reports how much he wants to do each activity using a Licker scale ranging from 1 to 7. This test is thus composed of 6 sub scores from 1 to 7: social high pleasant, social medium pleasant, social low pleasant and non-social high pleasant, non-social medium pleasant and non-social low pleasant [38]. Fatigue and sleep quality were also assessed using self-report questionnaires. The Multidimensional Fatigue Inventory (MFI-20) is a 20-items questionnaire that covers different dimensions of fatigue: General Fatigue, Physical Fatigue, Mental Fatigue, Reduced Motivation and Reduced Activity [39]. Sleep quality was measured using the Pittsburgh Sleep Quality Index (PSQI). The PSQI measures several aspects of sleep, including subjective sleep quality, sleep latency, sleep duration, usual sleep efficiency, sleep disorders, sleep medication use and daytime dysfunction. The overall score, which we used in this work, is calculated by adding up the seven component scores, resulting in an overall score ranging from 0 to 21. A low score indicates a healthier quality of sleep [40].

2.5. Other variables

Socio-demographic characteristics and anthropometric measures were collected at admission in a face-to-face interview. Age, age of loss of control and duration of drinking habits were reported in years. Marital status was defined as couple/married, divorced/separated or single and educational level as primary, secondary and superior. The amount of alcohol consumed the week before hospitalization was measured in gram per day using the time-line follow back approach [41]. Physical disabilities were assessed using the Health of the Nation Outcome Scales (HoNOS) completed by psychiatrists [42]. Patients with severe cognitive impairments were excluded by using the Mini Mental State Examination (MMSE) [43].

2.6. Gastrointestinal discomfort

Gastrointestinal discomfort was evaluated using a questionnaire initially used to evaluate the symptoms of irritable bowel syndrome [44] for which a French version was developed by gastroenterologists at St Luc hospital. This questionnaire allowed the patients to report the intensity of abdominal pain and bloating, their satisfaction about their intestinal transit and whether gastrointestinal symptoms affected their daily life by using visual analogic scale from 0 to 100. A total score is obtained by adding the 4 scales (abdominal pain, bloating, transit satisfaction and consequences on daily life). The maximum score was 400. A score below 60 indicates normal bowel function, a score between 60 and 139 corresponds to mild symptoms, between 140 and 239 to moderate symptoms and >240 to severe symptoms. Patients also indicated the frequency of stools and completed the Bristol Stool Form Scale (BSFS) [45]. The BSFS is a scale for identifying stool types ranging from the hardest (type 1) to the softest (type 7).

2.7. Statistical analysis

Sociodemographic characteristics and nutritional data between groups were compared using Student's t test or Mann Whitney's test for continuous variables. Categorical variables were analyzed using Chi square or Fisher's test. The effect size and power of the statistical tests were calculated for fiber intake which is the main outcome of the study. Hedges' g were largely higher than 0.8 for total fiber, insoluble and soluble fibers (1.2, 1.6 and 1.2 respectively) and the powers were respectively 92, 95 and 93%, which indicates a high association strength.

Principal component analysis was used to compare the dietary pattern of AUD patients and HS.

To assess which food products contributed to patients' main sources of fibers, quantities of food products were compared across tertiles of total dietary fiber intake using a Jonckheere–Terpstra test.

To address the second objective, bivariate correlation analyses (Pearson's correlation) were performed to assess the relationships between nutrients and psychological outcomes. A relevance association network from the similarity matrix derived from the partial least squares analysis (PLS) was made in order to select the most important nutrients associated with the psychological symptoms [46]. This analysis was performed with macro and micronutrients and the MFI sub-scores and the PSQI score were not included in the analysis because of missing values ($n = 29$). An edge was drawn between two variables if the

estimated correlation coefficient exceeded 0.25. This was performed using the *mixOmics* package. Then, we used linear regression models to confirm the multivariate associations between the nutrients and the psychological measurements. We first adjusted for the age, gender and level of education (model 1). We subsequently added the energy intake, BMI and the smoking status in model 2. Finally, we added the quantity of alcohol consumed per day in model 3.

P values < 0.05 were considered statistically significant.

Statistical analyses were performed using SAS version 9.4, R studio version 3.5.1 and Graphpad Prism 8.0.

3. Results

Forty-nine AUD patients underwent the dietary interview. One outlier was excluded from the analysis because of excessive energy intake (more than 3 standard deviations from the mean). The final population was composed of 48 AUD patients.

We first compared the nutritional intakes of AUD patients with those of HS recruited for this purpose. Then we studied the link between nutrient intakes and psychological outcomes in the same AUD patients.

3.1. Nutritional habits of AUD patients compared to healthy subjects

Socio-demographic data are reported in Table 1. AUD patients and HS were similar in terms of age, sex, BMI and marital status. However, AUD patients were less educated, smoked more and had a lower mean MMSE score than HS. There were no differences in professional status or income sources between AUD patients and HS. In average AUD patients consumed 132 ± 73 g of ethanol/day while HS consumed 7.6 ± 10.4 g/day. Three patients had a HoNOS score of 2 or 3 for physical illnesses or disabilities and the rest had no or minor physical health problem (data not shown).

Meal frequency in AUD patients and healthy controls is shown in Table 1. The number of breakfasts, morning snacks and lunches were lower in AUD subjects compared to controls.

We calculated the NOVA score to evaluate the importance of processed (PF) and ultra-processed food (UPF) in the diet of patients. Patients tended to have a higher NOVA score than HS (2.1 ± 0.7 vs 1.7 ± 0.4, p = 0.0516; Table 1). They consumed

Table 1
Baseline characteristics of healthy subjects and AUD patients in the intervention study.

	HS n = 13	AUD n = 48	p[a]
Sociodemographic characteristics			
Age (y)	46.0 ± 10.9	48.5 ± 11.4	0.52
Female, n (%)	6 (46.1)	18 (35.4)	0.48
Marital status, n (%)			0.12
Couple/married	9 (69.2)	18 (37.5)	
Single	3 (23.1)	22 (45.8)	
Separated/divorced	1 (7.7)	8 (16.7)	
Educational level, n (%)			0.001
Primary	0 (0.0)	5 (10.4)	
Secondary	0 (0.0)	17 (35.4)	
Superior	13 (100.0)	26 (54.2)	
Employment status, n (%)			0.11
Employed	11 (84.6)	27 (56.3)	
Unemployed	1 (7.7)	16 (33.3)	
Retired	1 (7.7)	5 (10.4)	
Income sources			0.10
Professional activity	11 (84.6)	27 (56.2)	
Allocations[b]	1 (7.7)	20 (41.7)	
No income or financial support from family or friends	1 (7.7)	1 (2.1)	
Clinical examination			
Weight (kg)	71.0 ± 10.9	72.6 ± 12.4	0.79
BMI (kg/m^2)	23.6 ± 3.0	24.0 ± 3.3	0.72
MMSE score	29.5 ± 0.5	28.0 ± 2.3	0.01
Smoking, n (%)	2 (15.4)	39 (81.2)	<0.001
Alcohol history			
DSM-5 AUD score	0.0 ± 0.0	8.4 ± 1.8	<0.001
Age of loss of control (y)	–	32.3 ± 11.2	–
Number of alcohol withdrawal cures	–	2.2 ± 2.2	–
Duration of drinking habit (y)	–	15.8 ± 10.7	–
Alcohol consumption (g/d)	7.6 ± 10.4	132.0 ± 73.1	<0.001
AUDIT score	3.1 ± 2.4	–	–
Meal frequency (alcohol not included), n (%)			
Breakfast	13 (100,0)	20 (41.7)	<0.001
Morning snack	7 (53.8)	8 (16.7)	0.01
Lunch	13 (100.0)	36 (75.0)	0.01
Afternoon snack	10 (76.9)	26 (54.2)	0.13
Dinner	13 (100.0)	45 (93.7)	0.22
Evening snack	1 (7.7)	12 (22.9)	0.18
Nova score[c]	1.7 ± 0.4	2.1 ± 0.7	0.05
PF intake[c] **(% of total food intake)**	13.3 ± 5.1	14.1 ± 11.2	0.65
UPF food intake[c] **(% of total food intake)**	13.2 ± 12.9	27.8 ± 23.6	0.04

Values are means ± standard deviation.
AUD, Alcohol use disorders group; AUDIT, Alcohol Use Disorders Test; BMI, Body mass index; CT, Control group; DSM-5, Diagnostic and Statistical Manual of Mental Disorders fifth edition; HS, healthy subjects; MMSE, Mini Mental State Examination.
[a] p values were calculated using a T-test or Mann Whitney Wilcoxon's test and Chi 2 test or Fisher's test for categorical variables.
[b] Invalidity, disability, compensated unemployment, retirement, social integration income.
[c] The Nova score, the percentage of processed and ultra-processed food were calculated without taking into account alcoholic beverages.

significantly more UPF (reached 28% of the total food intake) than HS (Table 1).

The principal component analysis of the food groups revealed that AUD patients ate more pizza, pie or sandwiches, processed meat and sweets and soda and consumed less vegetables, pulses, cereal products, olive oil, nuts and fruits than healthy subjects (Supplementary Fig. 1).

3.2. Actively drinking AUD subjects exhibit insufficient macro and micronutrient intake

Energy intake (EI) provided by food – excluding alcoholic beverages-was significantly lower in AUD than in HS (Fig. 1A). AUD patients consumed less protein and fat than HS when intakes were expressed in g/d (Fig. 1B). When quantified in relative proportions of EI, protein, carbohydrate and fat intakes were all significantly decreased in AUD patients compared to HS (Fig. 1C). AUD patients had lower intakes of any type of fat (saturated fatty acids [SFA], monounsaturated fatty acids [MUFA] and polyunsaturated [PUFA]) compared to HS (Fig. 1E). Among PUFA, both n-6 and n-3 PUFAs (EPA and DHA) intakes were significantly decreased in AUD subjects (Fig. 1E and F). In AUD patients, SFA per total fat was higher than in the HS group ($p = 0.0162$; Supplementary Table 1). AUD patients consumed less cholesterol and trans fat than HS (Supplementary Table 1).

Supplementary Table 2 reports the intake of micronutrients in AUD patients and healthy subjects taking into account alcoholic beverages. The intakes of calcium, selenium, folates and of vitamins B12, C, D and E were significantly lower in AUD patients compared to HS ($p < 0.001$). Nearly 80% of patients had calcium intakes below the Belgian recommendations but the proportion was not different from that of HS (Supplementary Table 2) [30]. Fifty-eight percent of patients had insufficient selenium intake *versus* 23% of HS ($p = 0.0311$). Seventy-one percent and 75% of patients had too low intakes of vitamin B12 and C below the norms, respectively. Fifty-six percent of AUD patient had a folate intake below the recommended value compared to 8% of HS ($p = 0.0017$). Vitamin D and Vitamin E intakes were insufficient for 92% and 85% of AUD patients versus 69% and 23% of HS respectively ($p = 0.0554$ and $p < 0.001$; Supplementary Table 2).

3.3. Actively drinking AUD patients have a low intake of dietary fibers

AUD patients had a lower total (13 g/d), soluble and insoluble dietary fiber intake as compared to HS (Fig. 1G). There were no differences between AUD patients and HS for fructans (Fig. 1D), fructo-oligosaccharides (FOS) (0.9 ± 0.9 g for AUD patients vs 1.1 ± 0.9 g for HS, $p = 0.1234$) and galacto-oligosaccharides (GOS) intake (0.2 ± 0.4 g for AUD patients vs 0.4 ± 0.5g for HS, $p = 0.1322$). Ninety percent of the AUD patients had a DF intake below the recommended value of 25g per day compared to 50% of HS (Fisher's exact test $p = 0.0030$; data not shown).

The Supplementary Table 3 presents the distribution of the food products according to the tertiles of fiber consumed by AUD patients. The patients in the 3rd tertile (high fiber consumers) consumed more roots and tuber, bulbs, vegetables, pulses, potatoes, fruits, bread, coffee, fruit or vegetable juice and olive oil than AUD patients in the 1st tertile (low fiber consumers). The alcohol

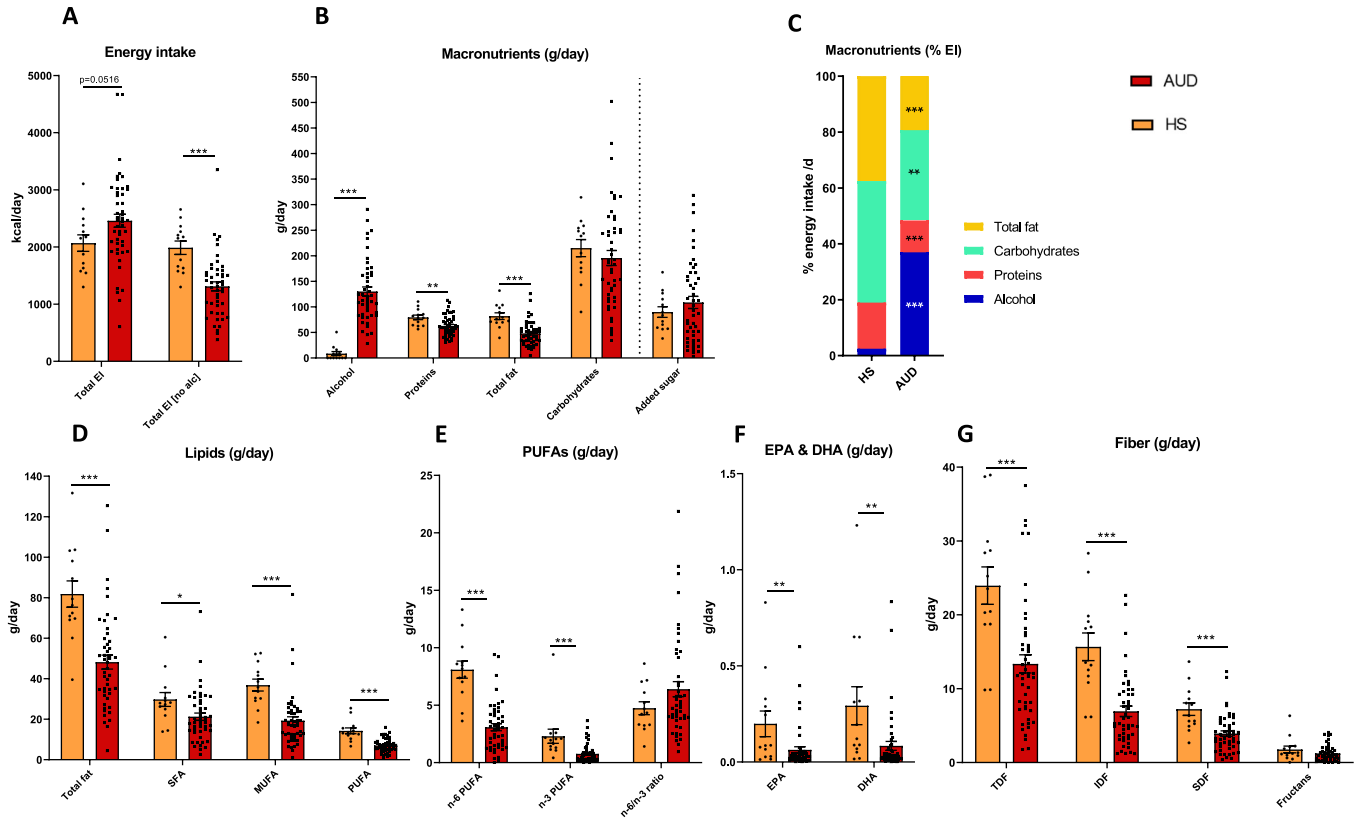

Fig. 1. Values are mean ± SEM. *p < 0.05, **p < 0.01,***p < 0.001. N = 13 for HS group and n = 48 for AUD group.P values were calculated using T test or Mann Whitney Wilcoxon's test. AUD, alcohol use disorder; DHA, Docosahexaenoic acid; EI, energy intake; EPA, Eicosapentaenoic acid; FA, Fatty acid; FOS, Fructo-oligosaccharide; GOS, Galacto-oligosaccharide; HS, healthy subjects; IDF, Insoluble dietary fibers; MUFA, Monounsaturated fatty acids; PUFA, Polyunsaturated fatty acids; SDF, Soluble dietary fibers; TDF, Total dietary fibers.

consumption did not significantly differ between the three groups (Supplementary Table 3).

TDF intake was associated with higher protein and carbohydrate intake ($r = 0.46$, $p = 0.001$; $r = 0.30$, $p = 0.04$) and lower ethanol and UPF intake ($r = -0.38$, $p = 0.009$; $r = -0.31$, $p = 0.03$; Fig. 2). TDF, SDF and fructans were positively correlated with potassium, magnesium, vitamin B1, C and folate intake (Fig. 2).

3.4. Association between nutrient intake and psychological symptoms in AUD patients

Because inadequate nutrition could affect mood, we hypothesized that some nutrients could be involved in the negative emotional state in AUD patients. Therefore, we tested the correlations between nutrient intake, UPF and psychological symptoms

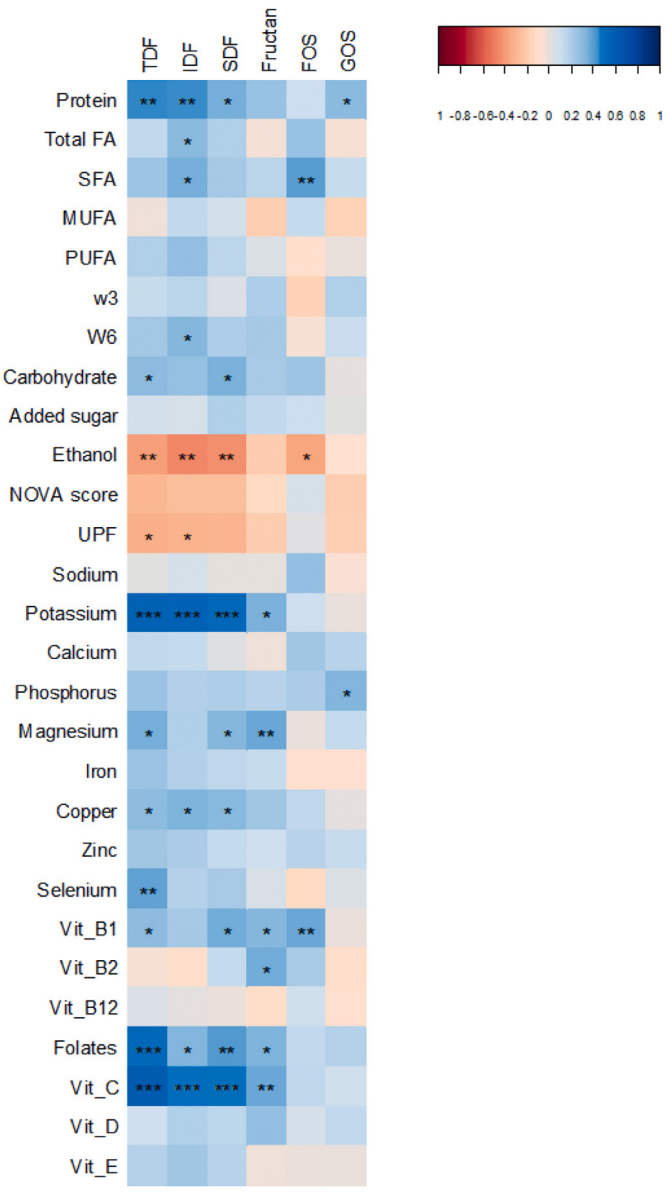

Fig. 2. Pearson partial correlations adjusted for total energy intake. N = 48. *p < 0.05, **p < 0.01, ***p < 0.001. AUD, Alcohol use disorder; FA, Fatty acid; FOS, Fructo-oligosaccharide; GOS, Galacto-oligosaccharide; HS, healthy subjects; IDF, Insoluble dietary fibers; MUFA, Monounsaturated fatty acids; PUFA, Polyunsaturated fatty acids; SDF, Soluble dietary fibers; TDF, Total dietary fibers; UPF, ultra-processed food.

(Fig. 3). Our results revealed a positive correlation between the proportion of UPF in the diet and the obsessive sub-score of alcohol craving scale, the sleep quality and the mental fatigue scores meaning that patients who consumed high quantity of UPF had higher obsessive thoughts about alcohol, a higher mental fatigue and a lower sleep quality (Fig. 3A). A tendency was observed between the proportion of UPF in the diet and the depression score ($r = 0.32$; $p = 0.0555$). Positive correlations were observed between n-6 PUFA, n-3 PUFA and the sociability score. Total fat and MUFA intakes were associated with a better sleep quality and less physical fatigue. Negative correlations were also found between potassium intake and depression, anxiety, sleep quality and physical fatigue scores (Fig. 3B). Magnesium intake was negatively correlated with the general and physical fatigue scores while vitamin B12 was positively correlated with depression and mental fatigue scores (Fig. 3B). TDF, SDF, IDF and GOS intakes were associated with higher score of sociability and fructan intake with a lower anxiety (Fig. 3A). Meaning that patients who consumed more fiber wanted to do more social activities and were less anxious.

In order to highlight the most relevant associations between nutrients and mood we performed a PLS analysis (Fig. 3C). It confirmed that, among all macro and micronutrients, DF were the most correlated with psychological outcomes. Indeed, this analysis revealed that fructan, n-6 PUFA and potassium intakes were negatively associated with the anxiety score. TDF, SDF and IDF intakes were associated with sociability (Fig. 3C).

Finally, we wanted to confirm these associations using multivariate linear models in order to take into account the different confounding factors (Table 2). When we adjusted for potential confounders, TDF, IDF, SDF and GOS were significantly associated with a higher sociability score regardless of the model suggesting a minimal confounding effect (Table 2 and Supplementary Table 4). After adjustment for sociodemographic factors, a significant inverse association was observed between fructan intake and anxiety score. This association remained significant after adjustment for energy intake, smoking habits, BMI (model 2) and alcohol consumption (model 3). Indeed, higher fructan intake was related to a decreased level of anxiety (Table 2). We did not find any significant association between the other types of fiber and the anxiety score. However, the sociability score was negatively correlated with anxiety score ($r = -0.43$, $p = 0.002$; data not shown). For the n-6 PUFAs, the associations did not reach significance when the different confounding factors were taken into account (Supplementary Table 4). Potassium intake was associated with a decreased depression score but only in models 2 and 3. The association was no longer observed between potassium intake and anxiety after taking into account the different confounding factors (Supplementary Table 4).

We also wanted to investigate whether eating alone or accompanied could be linked to a poor nutritional quality and more severe psychological symptoms in AUD. To do so we constructed a correlation matrix. We found that eating accompanied was positively correlated with the sociability score ($r = 0.33$, $p = 0.03$). No association were found between nutrients or UPF intakes and sharing a meal (Supplementary Fig. 2).

3.5. Association between nutrient intake gastrointestinal discomfort in AUD patients

We compared the gastrointestinal symptoms of AUD patients with those of HS. Almost the half of the patients suffered from abdominal pain while no HS reported pain (data not shown). AUD patients were less satisfied about their bowel function (48.5 ± 29.7 vs 75.5 ± 29.6, $p = 0.006$; Supplementary Fig. 3B) and reported that their symptoms had more impact on their daily life (33.8 ± 29.8 vs 10.9 ± 19.6 $p = 0.008$; Supplementary Fig. 3C). The total score of

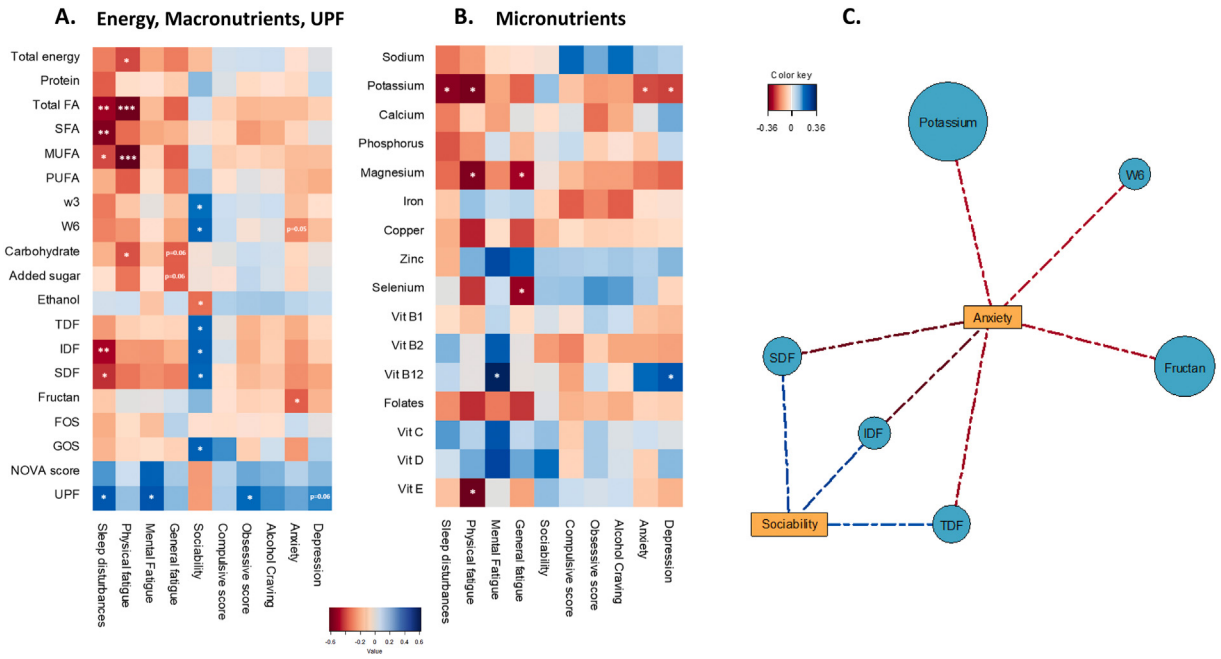

Fig. 3. Pearson correlations. N = 48 for all the parameters (excepted for fatigue and sleep disturbances scores n = 29). *p < 0.05, **p < 0.01, ***p < 0.001. A. Correlations between the energy, macronutrient and UPF intakes and the psychological outcomes. B. Correlations between the micronutrients and the psychological outcomes. C. Relevance associations network of partial least squares analysis with macro/micronutrients and psychological symptoms (excepted fatigue scores). A cutoff value of 0.25 was applied. AUD, Alcohol use disorder; FA, Fatty acid; FOS, Fructo-oligosaccharide; GOS, Galacto-oligosaccharide; HS, healthy subjects; IDF, Insoluble dietary fibers; MUFA, Monounsaturated fatty acids; PUFA, Polyunsaturated fatty acids; SDF, Soluble dietary fibers; TDF, Total dietary fibers; UPF, ultra-processed food.

Table 2
Associations between dietary fiber intake and psychological measurements in AUD patients.

	TDF	p	IDF	p	SDF	p	Fructans	p
	β [95% CI]		β [95% CI]		β [95% CI]		β [95% CI]	
Depression								
Model 1[a]	−0.04 [−0.46; 0.38]	0.84	−0.10 [−0.83; 0.62]	0.77	−0.76 [−2.12; 0.60]	0.26	−1.48 [−4.77; 1.82]	0.37
Model 2[b]	−0.07 [−0.56; 0.42]	0.77	−0.15 [−0.99; 0.68]	0.71	−1.04 [−2.63; 0.54]	0.19	−1.74 [−5.37; 1.88]	0.34
Model 3[c]	−0.07 [−0.62; 0.47]	0.79	−0.17 [−1.12; 0.78]	0.72	−1.26 [−3.06; 0.52]	0.16	−1.77 [−5.37; 1.98]	0.34
Anxiety								
Model 1[a]	−0.30 [−0.82; 0.22]	0.26	−0.67 [−1.56; 0.22]	0.14	−1.33 [−3.02; 0.35]	0.12	−4.44 [−8.38; −0.50]	0.03
Model 2[b]	−0.38 [−0.99; 0.22]	0.21	−0.85 [−1.87; 0.17]	0.10	−1.71 [−3.68; 0.25]	0.08	−5.07 [−9.38; −0.75]	0.02
Model 3[c]	−0.25 [−0.92; 0.41]	0.44	−0.65 [−1.81; 0.50]	0.26	−1.36 [−3.58; 0.86]	0.22	−4.62 [−9.03; −0.21]	0.04
Sociability								
Model 1[a]	0.05 [0.01; 0.10]	0.02	0.09 [0.006; 0.17]	0.04	0.16 [0.01; 0.32]	0.04	0.26 [−0.12; 0.64]	0.18
Model 2[b]	0.07 [0.02; 0.12]	0.01	0.11 [0.02; 0.20]	0.02	0.23 [0.05; 0.40]	0.01	0.32 [−0.09; 0.73]	0.13
Model 3[c]	0.07 [0.01; 0.13]	0.02	0.11 [0.01; 0.21]	0.04	0.22 [0.02; 0.42]	0.03	0.27 [−0.15; 0.70]	0.19
Alcohol Craving								
Model 1[a]	−0.03 [−0.22; 0.17]	0.78	−0.07 [−0.41; 0.27]	0.67	−0.18 [−0.82; 0.46]	0.57	−0.01 [−1.57; 1.54]	0.98
Model 2[b]	−0.08 [−0.30; 0.14]	0.47	−0.16 [−0.53; 0.22]	0.40	−0.41 [−1.12; 0.31]	0.26	−0.24 [−1.89; 1.41]	0.77
Model 3[c]	−0.02 [−0.26; 0.22]	0.85	−0.05 [−0.47; 0.36]	0.79	−0.23 [−1.04; 0.57]	0.55	−0.02 [−1.69; 1.65]	0.98

N = 48 for all the parameters.IDF, Insoluble dietary fibers; SDF, Soluble dietary fibers; TDF, Total dietary fibers.
[a] Linear model adjusted for age, gender, educational level.
[b] Linear model adjusted for age, gender, educational level, energy intake, BMI, tobacco.
[c] Linear model adjusted for age, gender, educational level, energy intake, BMI, tobacco, alcohol consumption.

intestinal discomfort was significantly higher in AUD patients compared to HS (129.0 ± 82.1 vs 51.2 ± 68.8, p = 0.002; Supplementary Fig. 3E). There was no difference concerning bloating intensity and stool frequency. The consistency of stool evaluated by the BSFS was significantly different between the two groups. AUD patients were more likely to report a score of 6 and 7 and less likely to report a score of 4 (Supplementary Fig. 3F).

We then tested the link between gastrointestinal symptoms and macronutrients in AUD patients. We found a positive correlation between the satisfaction of bowel function and the intake of SDF (r = 0.35, p = 0.02; Supplementary Fig. 4A). A negative correlation was observed between the total score of GI discomfort and the intake of SDF (−0.32, p = 0.04; Supplementary Fig. 4B).

4. Discussion

This study describes the dietary habits and nutrient intakes of actively drinking AUD patients compared to healthy individuals and evaluates the link between nutritional intakes, especially DF and psychological outcomes.

We confirmed that AUD patients displayed disorganized food habits compare to HS. As previously described by our group, AUD

patients had less frequent breakfast and lunch [10]. The energy intake provided from food sources was significantly lower in AUD patients, alcohol accounting for 37% of their total energy intake. Consequently, AUD patients ate less of all macronutrients (lipids, proteins, carbohydrates). These results corroborate previous studies suggesting that energy derived from alcohol replaces energy from other macronutrients [10,47,48]. The decrease in energy and macronutrient intake could be explained by an alteration in the balance of appetite regulatory peptides [10,49,50]. Several studies have also shown an increase in leptin levels in AUD patients and a decrease in ghrelin compared to controls [10,51–53]. AUD is associated with negative emotional state and depressive symptoms that could also affect energy intake and food choices [54,55].

Total, MUFA, n-6 and n-3 PUFAs were lower in AUD patients than in HS. This is due to a reduction in the consumption of fish, nuts, seeds, dairy products and beneficial fats like olive oil. Few studies have explored the relationship between alcohol consumption and fat intake and have shown a decrease in SFA, MUFA and PUFA in heavy drinkers and binge-drinkers [48,56]. In addition, numerous studies reviewed by Borsoleno et al. have shown that ethanol alters the absorption and metabolism of lipids leading to essential lipid deficiency [57]. Therefore, a decrease in essential fat intake, together with alterations of their absorption, could lead to several metabolic and neurobiological alterations that could favor mood and cognitive disturbances [57–60]. Furthermore, n-3 PUFA supplementation in substance abusers reduces anger and anxiety level in a 3-month trial [61]. Our results reveal positive correlations between n-3 and n-6 PUFAs and sociability and negative correlations with anxiety score. However, these associations do not persist when taking into account potential confounding factors like sociodemographic characteristics, BMI, energy intake and tobacco use. The observation of a relationship between lipid metabolism dysregulation and the importance of symptoms of AUD as well as changes in myelin synthesis has recently been highlighted by a translational study from our research group [62]. Together, these data stress the importance of lipid intake and metabolism in the development of AUD.

Our data show correlations between UPF, depression, mental fatigue, alcohol craving and sleep quality in AUD patients. Two large French and Spanish cohorts have highlighted a positive association between depressive symptoms and the consumption of UPF in global population and university graduates respectively [12,63].

We also observed a lower intake of calcium, selenium, folate, vitamin B12, C, D and E. These deficiencies are common in patients suffering from chronic alcohol abuse [4,64] and may affect the cardiovascular, skeletal and nervous systems [4,65]. Potassium intake in active AUD patients was inversely associated with depression score, which is in line with previous studies in general population and elderly [66,67].

The originality of our work is to demonstrate that total dietary fiber, soluble and insoluble fiber intakes were lower in AUD patients compare to HS. To our knowledge, the fiber intake has never been studied in AUD patients. A Finnish study showed that heavy drinkers, in the general population, had lower fiber intake compared to non-drinkers [68]. A recent study reveals that higher DF consumers have a 30% decrease in all cause and cardiovascular related mortality [69]. In addition, most DF – in particular the fermented ones-interact with the gut microbiota and DF is one of the most important nutrients that modulates the gut microbiota composition [18]. We have already shown that the gut microbiota of alcoholic patients is altered [2]. It has been shown in animal studies that gut microbiota could influence anxiety and social behaviour [62,70,71]. In humans, microbial changes caused by fermented foods induce changes in mood [20,72]. Interestingly, our work reveals that fructan intake is associated with a decreased anxiety score and TDF, SDF, IDF and GOS intakes with an increased sociability score. Several studies support the link between DF and/or prebiotic intake and depression. A study performed in 3394 older Chinese adults revealed that TDF intake is associated with a decreased prevalence of depressive symptoms [73]. GOS supplementation, associated with a gluten and casein free diet, induces a significant improvement in anti-social behaviour in autism spectrum disorders children [74]. SDF and IDF intakes are associated with better sleep quality in our work. Few studies have investigated the relationship between fiber intake and sleep quality. One study in 26 adults found that low fiber intake and high SFA and sugar intake was associated with poor sleep quality [75]. This is not in total agreement with our study since in our study sample, SFAs is associated with a better quality of sleep.

The mechanisms linking psychological outcomes and DF are not fully understood but it could involve a plethora of pathways and molecules [20]. For example, it has been shown that fermentable fibers (fructans and galactans) are able to stimulate short chain fatty acid production which can act as neuroactive metabolites and consequently have an impact on the brain and behaviour [76–80]. This supports the interest to evaluate the microbiome of these patients.

Our results show a great variability in the AUD population. The vast majority of patients have an overall nutritional deficit, but some patients have a nutritional profile close to HS. Nutritional advice should therefore target a sub-population of AUD patients.

In our population of AUD patients those who consumed their meals alone had a lower sociability score but no association was found with nutrient or UPF intakes. Our results are not in line with those of two other studies which showed in a population of Koreans and Australian that eating alone was associated with a lower food quality [81,82].

We observed that DF intakes, particularly SDF were associated with less gastro-intestinal discomfort in our population of AUD patients. Clinical and experimental studies have demonstrated that SDF may cause bloating, but they also improved functional gastrointestinal disorders [83–85]. The authors stated that their beneficial effect could be explained by their secondary effect on the gut microbiota, inflammation as well as on gut permeability [86]. Increasing fiber intake in alcoholic patients could be a way of reducing their intestinal discomfort. However, DF supplementation has never been tested in the context of AUD.

Our study presents some limitations. The cross-sectional design of the study does not exclude the risk of reverse causality. Indeed, a poor quality diet may be the result of psychological alterations, rather than a causal factor. Then, we used of 3 day-recall which can be subject to memory bias. However, the dietician used the multiple-pass interviewing to limits this bias [87]. In addition, this approach allows us to capture intra-individual variation in dietary intakes and therefore to better estimate the eating habits than with a single 24 h recall. Our population of healthy subjects is limited; all the subjects have a high level of education which can have an impact on nutritional intake [88]. Nonetheless, the nutrient intakes of those control subjects are comparable to those of a Belgian study conducted in more than 3000 persons, relating protein, fat and carbohydrate intake [89]. Furthermore, the power calculation for the comparison of dietary fiber intakes indicates high association strength to consider our data as valuable in this protocol.

5. Conclusion

To conclude, our study showed that DF intake is insufficient in AUD patients and is related to anxiety and social impairment. In AUD, depression, anxiety and social impairment are interrelated and can lead to relapse after withdrawal [90,91]. The relapse being a real problem in AUD patients, nutrition – and namely the focus on

dietary fiber intake, appears as a key factor to take into account to improve the psychological symptoms of AUD patients and to promote the maintenance of abstinence. Further prospective and interventional studies are needed to evaluate the effects of DF as part of a more balanced diet on metabolic and psychological symptoms of AUD patients, and test whether it may be used as an additional treatment option in this pathology.

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Authors' contributions

Conceptualization & design: SL, NMD, PdT, PS, AMN.
Data curation: CA, VT, SL, VC, NMD, AMN, PdT, PS.
Formal analysis: CA, VT, SL, NMD, AMN, LBB.
Funding acquisition: NMD, PdT, PS.
Investigation: CA, SL, PS.
Methodology: SL, NMD, PdT, PS, AMN, HP.
Project administration: SL,AMN, NMD, PdT, PS.
Resources: NMD, PdT, PS.
Software: CA, VT.
Supervision: NMD, PdT, SL, PS.
Validation: SL, NMD, AMN, PdT, PS, LBB.
Writing original draft: CA, SL, NMD.
Writing review & editing: CA, SL, NMD, AMN, PdT, PDC, PS, LBB, HP.

All authors read and approved the final manuscript.

Conflicts of interest

The authors declare no competing interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.clnu.2021.03.029.

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