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Fructoholism in adults: The importance of personalised care in metabolic dysfunction-associated fatty liver disease

To the Editor:

Herein, we report the case of a 64-year-old woman followed-up by an endocrinology clinic since 2001, for a metabolic syndrome characterised by abdominal adiposity, type 2 diabetes, dyslipidaemia and hypertension. Due to the development of liver test disturbances in 2020, the patient was referred to hepatology. Transient elastography revealed steatosis and a stage F1 fibrosis (Table 1). With those positive diagnostic criteria, the diagnosis of metabolic dysfunction-associated fatty liver disease (MAFLD) was made.[1] Other causes of steatosis were excluded. Therefore, the disease also corresponds to non-alcoholic fatty liver disease (NAFLD). The patient denied any major consumption of alcohol, sweetened beverages, or other processed food, but on thorough history mentioned an excessive consumption of fruits, oscillating between 1 and 3 kilograms every day. The patient was referred to the psychiatry consultation. Initial psychiatric evaluation using the Yale Food Addiction Scale (YAFS)[2] was positive for food addiction, with clinically significant distress and 4 out of 7 positive criteria for addiction (Table 1). Psychiatric follow-up consisted of psychotherapy sessions of 45 minutes every 3 weeks and continuation of selective serotonin reuptake inhibitor (SSRI) treatment. After a period of 6 months, we found a reduction of fruit consumption, a reduction of insulin resistance and a normalisation of liver blood tests and elasticity (Table 1). Evaluation of food addiction using the YAFS after 1 year of follow-up was negative for the diagnosis, only 1 positive criterion remained (Table 1).

Retrospectively, in the past 20 years, the patient had met several times with dietitians, who proposed standardised hypocaloric menus. However, she did not receive personalised dietetic care and never had a follow-up with the dietitians. Over 20 years, the patient's weight remained excessive but stable, with a BMI oscillating between 27.2 and 29.9 kg/m^2. During psychotherapy sessions, the patient said that she felt her addiction to fruits was never taken seriously by medical professionals. She reported being more often questioned and warned by professionals about other sugar sources in her diet and about alcohol. The patient rapidly committed to the psychotherapeutic care and managed to progressively reduce her consumption below 1 kilogram per day, with periods of total abstinence lasting several days and periods of relapse.

Table 1. Evolution of biological, transient elastography and insulin therapy values before and after psychotherapeutic intervention.

	Baseline	Month 6	Month 12
Body weight (kg)	81	79.2	81.7
BMI (kg/m^2)	29.0	28.4	29.3
Waist circumference (cm)	108	107	111
HbA1c (%)	6.9	6.4	6.9
Basal insulin therapy (U/day)	34	20	30
AST (IU/L)	43	19	26
ALT (IU/L)	48	15	33
GGT (IU/L)	55	65	32
CAP (dB/m)	358	ND	330
E (kPa)	7.7	ND	5.3
YAFS (number of positive criteria)	4	1	1

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CAP, controlled attenuation parameter; E, elasticity; GGT, gamma glutamyltransferase; YAFS, Yale addiction food scale.

Food addiction is emerging as an entity that shows numerous similarities with substance use disorders. These parallels are found on different levels: biological, psychological (*e.g.* excessive preoccupation with the product, impaired control and impulsivity, altered reward sensitivity) and behavioural (*e.g.* relapse, using more than intended).

Studies have shown that fructose is a major mediator of steatosis.[3] The term "fructoholism" has already been proposed in children to define "the consumption of a substance (fructose) that can cause psychological and physical damage, and fructoholic liver disease".[4] Compared to glucose, fructose induces less feelings of satiety and more interest in prospective food consumption, as shows a functional magnetic resonance imaging study.[5] Fructose also has a different metabolic pathway. Acute fructose intake increases the availability of carbohydrate substrates for *de novo* lipogenesis in the liver and induces an upregulation of pro-lipogenic mechanisms, which favour effective hepatic lipid synthesis and accumulation.[3] Thus, fructose is both a substrate and an inducer of hepatic *de novo* lipogenesis.

Parallels can be established between excessive consumption of fructose and of ethanol. From a metabolic point of view, fructose and ethanol both lead to hepatic insulin resistance, dyslipidaemia and hepatic steatosis. Both produce reactive oxygen species, which lead to inflammation and hepatocyte damage, and consequently to fibrosis.[6] Finally, fructose consumption can lead to endogenous ethanol production through endogenous fermentation by fungi or bacteria in the gastrointestinal tract. A recent study reported that high alcohol-producing *Klebisella pneumoniae* was found in 60% of patients with NAFLD.[7] Furthermore, transfer of this bacteria into mice resulted in steatosis, suggesting increased levels of alcohol-producing bacteria might be a cause of NAFLD in humans.[7]

NAFLD is becoming the primary cause of liver disease in Western countries and a major economic concern due to the rise in its associated costs.[8] The treatment of NAFLD focuses on lifestyle interventions such as diet and physical exercise. However, in the long run, it has been estimated that less than 10% of patients maintain these dietary changes sufficiently for the hepatic fibrosis to regress. As reported in the recent "patient guideline",[9] up to 25% of patients with NAFLD suffer from depression and/or

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an eating disorder, and treating one condition in isolation could potentially aggravate the other. A recent study in patients with type 2 diabetes showed that continuous nutritional counselling could increase orthorexic traits and paradoxically create an excessive intake of healthy foods, without any weight loss or better metabolic control.[10] Our clinical example (although reporting a probably rare observation) supports this and shows that NAFLD-MAFLD can be the result of complex behavioural addictions that require a global multidisciplinary and patient-centred approach.

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Authors' contributions
All authors have contributed to the clinical follow-up of the patient and the data collection. Nicolas Lanthier conceived the idea of the present manuscript and supervised the project. Mélissa Salavrakos wrote the article with critical feedback from all authors.

Patient consent statement
The patient agreed to the publication of this manuscript and gave her signed consent.

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