

## Nutritional Status of Depressive Patients

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### Abstract

Depression is a multifactorial disease and nutrition is an important environmental factor in its development and progression.

**Methods:** This is a retrospective study of 50 depressed patients recruited from the outpatient department of psychiatry in Tunisia, as well as 50 controls. Both groups were matched for age and sex

**Results:** A pathological waist circumference was found in 84% of cases against 78% of controls  $p=0.02$ . Our patients had a significantly higher intake of carbohydrates and sucrose compared to controls  $p=0.0001$ ,  $p=0.02$ , and significantly lower protein intake ( $p=0.0001$ ), lipids ( $p=0.0001$ ), SFA ( $p=0.01$ ), MUFA ( $p=0.003$ ), EPA ( $p=0.02$ ), fibers ( $p=0.05$ ), iron ( $p=0.0001$ ), zinc ( $p=0.02$ ), vitamin B9 ( $p=0.0001$ ), vitamin B1 ( $p=0.02$ ) vitamin C ( $p=0.02$ ), calcium ( $P=0.004$ ). In addition, controls consumed significantly more blue fish, hard cheeses and Olive oil than the patients respectively. Plus the depression was severe, according to the PHQ9 score, plus the intakes were significantly lower in: proteins, carbohydrates, alpha linoleic acid Calcium, consumption of butter and cheese spread, and when depression was certain, according to the HAD, intakes of protein, w3, alpha linoleic acid, corn oil and soybean were low.

**Conclusions:** Our study revealed a very frequent deficit in micro and macronutrients in depressed patients. Some of these deficits, in particular Omega 3, were significantly associated with the severity of depression.

**Keywords:** Depression; Nutrition; Omega 3; Omega 6

### Introduction

World health organization (WHO) considers depression as the most frequent psychiatric illness. Indeed, today, 350 million people worldwide are affected by depression [1]. A Tunisian study of psychiatric disorders following the revolution showed that depression was the most prevalent psychiatric disorder with a prevalence of 30.8% [2].

Depression has a multifactorial origin involving physiological, social, genetic, psychological and environmental factors [3]. Current evidence highlights the crucial role of nutrition as an important environmental factor in the development and progression of depression [2,4-7].

The relationship between diet and depression has been much written, on the one hand diet can be a risk factor for the onset, development and severity of depression, and on the other hand, depression itself can lead to changes in lifestyle [8].

Several authors have noted that deficiency in certain micronutrients such as vitamin B9, vitamin D [4], selenium [5], zinc [6], polyunsaturated fatty acids(PUFA) such as omega 3 [7] and Omega 6 is associated with depression.

The objectives of our study are to evaluate the nutritional status of depressed patients compared to a control group and to detect a

possible deficiency in some micro and / or macronutrients in the depressed.

### Methods

This is a retrospective cross-sectional study of 50 depressed patients recruited from the outpatient department of psychiatric hospital in Tunis from November 10 to December 16, 2016, as well as 50 randomized controls with no known psychiatric history, recruited during the same period. Both groups were matched for age and sex.

We included in our study adult patients with depression who were diagnosed by psychiatrists according to the criteria of the DSM IV [9]. In addition, we excluded from our study: pregnant or nursing women, patients with psychiatric disorders other than depression, diabetics, patients on diet or under corticosteroids.

Patients underwent an interrogation concerning their pathology. To assess the depressive state of the patients two scores were used the score hospital anxiety and depression scale" HAD " [10,11] and the patient health questionnaire" PHQ 9 " [12,13].

Anthropometric measurements were taken and were interpreted according to the WHO criteria for BMI and a WC (waist circumference) was pathological if >80 cm in women and 94 cm in men.

The score " MUST ": The Malnutrition Universal Screening Tool (MUST) was also used in our study [14-16].

A feeding history was carried out to assess the typical dietary habits of the two groups. This survey details the inputs, meals, snacks, nature and proportion of food consumed. The amount of food was estimated using a photographic manual that the patient used to bring us closer to the portion actually taken [17]. The results of the survey were then analyzed using the computer software "BILNUT, version 2.01-1990" to evaluate the spontaneous nutritional intakes.

A frequency of consumption of certain foods was noted from food history, targeting foods rich in vitamin D, omega 3 and omega 6. The calculation of omega 3 was split on these different precursors namely EPA (eicosapentaenoic acid), DHA (docosahexaenoic acid) and alpha linolenic acid (Fatty acid C18: 3), the various results were summed in order to obtain the fraction of omega 3 consumed. Similarly for Omega 6 which was calculated based on the alpha linoleic acid intake (Fatty acid C18: 2). These different elements were calculated manually using the food composition table (CIQUAL 2016) [18]. The dietary intake of our population were compared to the recommended nutritional intake RNI of the general adult population [19-21].

The statistical analysis was carried out using statistical software (PSPP) using the Chi-square test for the comparison of qualitative variables and the T-Student test for the comparison of the quantitative ones. We started with a comparative study between the two groups of depressed patients and the control group. The percentages were compared by the Pearson chi-square test, and if this test was invalid, by Fisher's exact bilateral test. The comparison of 2 means was carried out by the Student t test for independent series or by the Mann-Whitney test according to the distribution of the variables. The comparison of 2 averages was carried out by the Student t test for matched series or by the Wilcoxon matched test according to the distribution of the variables. In all cases, the threshold of statistical significance p was set at 0.05.

## Results

The general characteristics of the population are summarized in Table 1. The majority (72%) of the patients had only one episode of depression and 28% of the patients attempted suicide, 12% of which were repeated. In our population, only 20 depressed (40%) reported a psychiatric family history. Our sample consisted of 11 new consultants (22%) who had not yet been treated, for the rest, 66% were under anti-depressive treatment and 22% required anxiolytics. For the others, 66% were on antidepressants and 46% on anxiolytics.

The mean waist circumference (WC) of the patients was 98.34 ± 10 cm versus 91.77 ± 18.09 cm for the controls (p=0.02). The mean BMI of the patients was 28.21 ± 6.02 Kg/m<sup>2</sup> and that of the controls at 28.10 ± 5.15 Kg/m<sup>2</sup> (Table 2). In our study, a BMI > 25 Kg/m<sup>2</sup> was present in 74% of the patients versus 69.3% of the controls (p=0.31). The weight was higher for almost half of the depressed (52%) with an average of 8.22 kg and a maximum of 24 kg. After the diagnosis of depression, weight loss affected 36% of depressed patients with an average of 7.76 kg lost. The maximum weight loss was 32 kg. The MUST score did not show a risk of under nutrition in the majority of patients (Figure 1).

| Variables                                | Patients                  | controls                  | p*    |        |
|--|---------------------------|---------------------------|-------|--------|
| Average age (years) ± standard deviation | 45.08 ± 14,24             | 44.72 ± 13.2              | 0.87  |        |
| Gender (n)                               | Females: 34<br>Males : 16 | Females : 33<br>Males: 17 | 0.83  |        |
| Level of education (%)                   | Illiterate                | 16                        | 6     |        |
|  | Primary level             | 40                        | 6     |        |
|  | Secondary level           | 32                        | 48    |        |
|  | Higher level              | 10                        | 38    | 0.0001 |
| Marital status (%)                       | Professional training     | 2                         | 2     |        |
|  | Single                    | 18                        | 18    |        |
|  | Married                   | 68                        | 76    | 0.48   |
|  | Divorced                  | 6                         | 0     |        |
| Profession (%)                           | Widower                   | 8                         | 6     |        |
|  | Unemployment              | 34                        | 22    |        |
|  | Student                   | 2                         | 6     |        |
|  | Official                  | 50                        | 70    | 0.03   |
| Clothing habits (%)                      | Daily                     | 2                         | 2     |        |
|  | retirement                | 2                         | 0     |        |
| Women's Cycle (n)                        | Headscarf                 | 83                        | 58    | 0.02   |
|  | Regular                   | 9                         | 22    | 0.01   |
| Physical activity (%)                    | Menopause (n)             | 17                        | 10    | 0.37   |
|  | low                       | 66                        | 34    |        |
|  | average                   | 34                        | 62    | 0.001  |
| Duration of exposition to the sun (min)  | Intense                   | 0                         | 4     |        |
| Tabacco (%)                              | 38.20                     | 46.5                      | 0.29  |        |
| Alcool (%)                               | 66                        | 34                        | 0.001 |        |
| Drugs (n)                                | 14                        | 0                         | 0.006 |        |
|  | 3                         | 0                         | 0.08  |        |

**Table 1:** Distribution of the population according to its general characteristics.

|                        | Depressed |    | controls |    |
|------------------------|-----------|----|----------|----|
|                        | n         | %  | n        | %  |
| Undernutrition class 2 | 1         | 2  | 0        | 0  |
| Normal corpulence      | 12        | 24 | 15       | 30 |
| Overweight             | 18        | 36 | 18       | 36 |
| Obesity Class 1        | 14        | 28 | 10       | 20 |
| Obesity Class 2        | 3         | 6  | 6        | 12 |
| Obesity Class 3        | 2         | 4  | 1        | 2  |

**Table 2:** Distribution of population by body mass index (BMI).

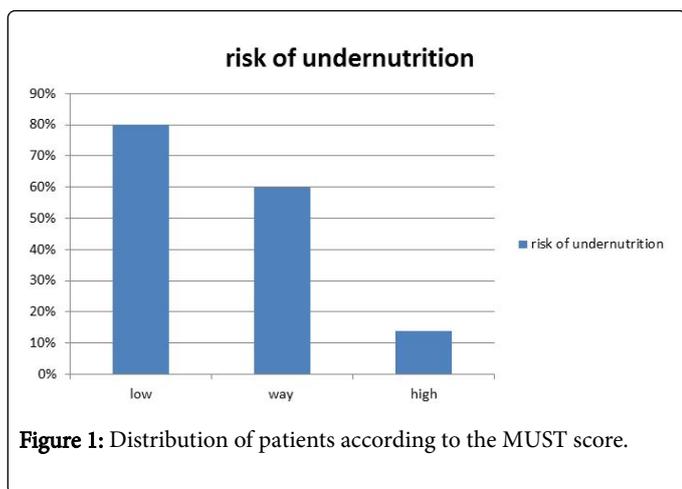


Figure 1: Distribution of patients according to the MUST score.

For the patients, a pathological WC was found in 84% of the cases against 78% of the controls. Depressed men had significantly more abdominal obesity than controls (18% versus 14%) (p=0.001).

The results of the food surveys are summarized in Tables 3-7 and Figures 2 and 3.

|                                 | Patients | Controls | p      |
|---------------------------------|----------|----------|--------|
| Average caloric intake (Kcal/d) | 1985.34  | 2186.5   | 0.19   |
| Carbohydrate (% TEI)            | 52.79    | 44.65    | 0.0001 |
| Sucrose (% TEI)                 | 11.52    | 8.61     | 0.02   |
| Total proteins (g/kg iw /d) *   | 0.86     | 1.19     | 0.0001 |
| Protein (% TEI)                 | 11.19    | 13.75    | 0.0001 |
| Lipids (% TEI)                  | 36.05    | 41.37    | 0.0001 |
| SFA (% Lipids)                  | 8.88     | 10.16    | 0.01   |
| MUFA (% Lipids)                 | 15.62    | 18.82    | 0,003  |
| PUFA (% lipids)                 | 11.52    | 12.38    | 0.32   |
| Cholesterol (mg/day)            | 191.48   | 294.42   | 0.1    |

\*iw: ideal weight; TEI= total energy intake; SFA=saturated fatty acid; MUFA=monounsaturated fatty acid

Table 3: Average Intakes of Calories and Macronutrients.

|                              | patients    | controls     | P *  |
|------------------------------|-------------|--------------|------|
| Alpha linolenic acid (g / d) | 2,5 ± 1,71  | 2,44 ± 2,88  | 0.9  |
| EPA (mg / day)               | 12 ± 0,21   | 24 ± 0,33    | 0.02 |
| DHA (mg / day)               | 19 ± 0,29   | 30 ± 0,37    | 0.09 |
| Omega 3 (% TEI)              | 1,34 ± 0,78 | 1,09 ± 0,7   | 0.76 |
| Omega 6 (% TEI)              | 9,5 ± 4,73  | 10,39 ± 3,77 | 0.3  |

Table 4: Mean fatty acid intake.

|                      | Patient          | Controls         | P *    |
|----------------------|------------------|------------------|--------|
| Fibers (g / d)       | 13,43            | 16.57            | 0.05   |
| Iron (mg / day)      | 7.16<br>8.74     | 10.53<br>10.48   | 0.0001 |
| Magnesium (mg / day) | 254.96<br>285.06 | 263.34<br>262.18 | 0.75   |
| Zinc (mg / d)        | 5.76             | 7.06             | 0.02   |
| Folic acid (µg / d)  | 148.98<br>153.69 | 228.92<br>232.18 | 0.0001 |
| Vitamin B1 (mg / d)  | 0.73             | 0.92             | 0.02   |
| Vitamin C (mg / d)   | 65.34            | 115.94           | 0.02   |
| Phosphorus (mg / d)  | 817.7            | 1129.96          | 0,001  |
| Potassium (mg / d)   | 2010.1           | 2393.64          | 0.03   |
| Calcium (mg / day)   | 568.22<br>578.81 | 756.94<br>749.88 | 0,004  |
| Vitamin D (µg / d)   | 2.55             | 3.03             | 0.27   |
| Sodium (mg / day)    | 1102.94          | 1290.62          | 0.12   |
| Water (ml / d)       | 1010             | 1100             | 0.41   |

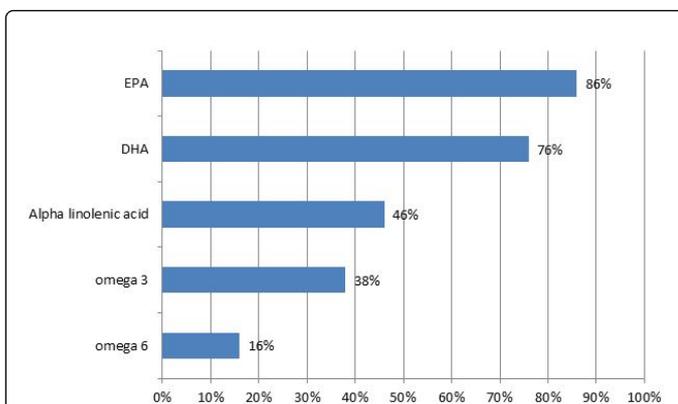
Table 5: Mean Intakes of Micronutrients and Dietary Fiber.

| (Number of servings per week) | patients | controls | P     |
|-------------------------------|----------|----------|-------|
| Blue fish                     | 0.9      | 1.7      | 0.02  |
| Hard cheese                   | 0.38     | 1.22     | 0,009 |
| Yogurt                        | 2.1      | 1.92     | 0.72  |
| eggs                          | 4.56     | 5.64     | 0.06  |
| Olive oil                     | 2.38     | 4.42     | 0,001 |
| Corn oil                      | 1.54     | 3.64     | 0,002 |

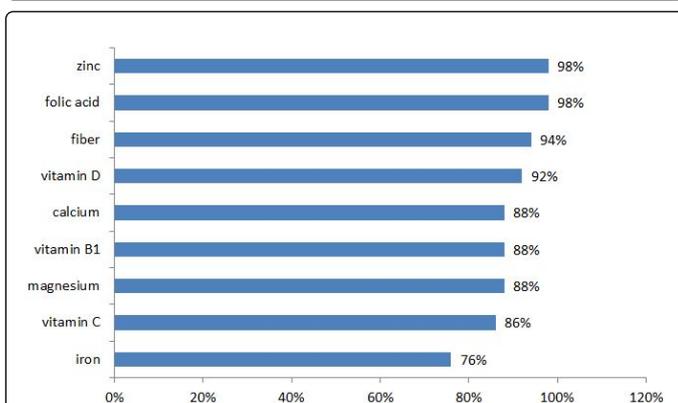
Table 6: Comparison of the frequency of weekly consumption of certain foods in our population.

|                             | Absence of symptomatology | Symptomatology doubtful | Symptomatology certain | P *   |
|-----------------------------|---------------------------|-------------------------|------------------------|-------|
| BMI (kg / m <sup>2</sup> )  | 34.81                     | 25.416                  | 27.76                  | 0.01  |
| Protein (g / d)             | 6052                      | 52.27                   | 48.76                  | 0.03  |
| W3 (g / d)                  | 37                        | 3.9                     | 2.3                    | 0.03  |
| Alpha linoleic acid (g / d) | 37.39                     | 22.66                   | 18.46                  | 0,002 |
| Corn oil (ml / week)        | 149.8                     | 0                       | 41.1                   | 0.03  |
| Soybean oil (ml / week)     | 261.4                     | 838.5                   | 150.36                 | 0,009 |

Table 7: Association between nutritional profile and HAD score.



**Figure 2:** Percentage of patients with insufficient intake of essential fatty acids by daily energy intake [18,19].



**Figure 3:** Percentage of patients with insufficient intake of micronutrients by Daily energy intake.

The majority of patients (72%) were taking vitamin E and iron supplements but the difference was not significant with controls ( $p=0.26$ ).

The association between the severity of the depression sought by the HAD scores and the food survey results was noted in Table 7.

The more severe the depression, according to the PHQ9 score, the significantly lower the intakes of protein, carbohydrates, alpha linolenic acid, calcium, consumption of butter and spread, respectively  $p=0.03$ ;  $0.01$ ;  $0.04$ ;  $0.02$ ;  $0.004$  and  $0.005$ . The rest of the nutritional parameters did not show any significant results with PHQ-9.

There were no differences between the macro and micronutrients intake of the patients according to their treatment or between the patients already treated and the newest one.

## Discussion

The mean WC of the patients was significantly higher than the controls ( $p=0.02$ ). Our results were consistent with those of Correia et al. [22] who found that 69% of depressed patients had waist circumference above normal values. Zhao et al. [23] found that in overweight or obese adults, abdominal obesity was significantly associated with an increased likelihood of having severe depressive

symptoms. The cohort of Lasserre et al. [24] who followed 3054 participants for 5.5 years showed that only patients with depression increased their waist size during follow-up. However, other studies have found contradictory results, notably those of Turley [25] and Hach [26] who did not find significant relationships between a high waist circumference and depression.

The protein intake in patients was  $0.86$  g/kg ideal weight per day, i.e.  $55.53$  g/day. This was significantly lower than that of controls ( $p=0.0001$ ). In our study, 66% of our patients were protein-deficient, in contrast to the Pourghassem study where 11.4% of patients had insufficient protein intake [27]. Some studies agree that amino acids (tryptophan, phenylalanine, tyrosine and methionine) are useful in the treatment of many mental disorders such as depression [28,29], since some essential amino acids are involved in the synthesis of Neurotransmitters and neuro-modulators [30]. Tryptophan even improves the quality of sleep [28,31].

Patients' carbohydrate intake was 52.79% of the total energy intake (TEI). These intakes estimated at  $249.91$  g/day were significantly greater than controls ( $p=0.0001$ ). Our results are comparable to Gülşah Kaner [32] and Ben Smail [33]. In Iran, a contribution of  $318.6$  g/d was found in the study of Pourghassem Gargari [27], whose purpose was to determine the relationship between nutrient intake and the severity of depression. The consumption of carbohydrates increases the release of serotonin, involved in several functions such as sleep, pain sensitivity and mood control [34-36]. As a result, many patients have an appetite for carbohydrates after major depressive episodes [37].

The daily intake of PUFA patients and controls was well below the recommendations with a non-significant difference between the two groups. Several studies have demonstrated the benefits of PUFA supplementation for depression [38,39]. Notably the study by Venna et al. [40]. Where supplementation of PUFA had an antidepressant effect that was explained by molecular changes at the hippocampus.

The majority of our patients (82%) had lower intakes of cholesterol compared to recommended dietary intakes. Different physiopathological explanations have been given, in particular, that a low cholesterol level could negatively affect the mood by a direct effect on the serotonin system [41]. Others have explained the association between depression and cholesterol levels by the fact that it has an essential role in the structure and functioning of the cell membrane and can also affect neurotransmission, thus cholesterol deficiency in neuronal membranes may also have a direct impact on dendritic growth [42], synapses [43] and even neuronal survival [44]. On the other hand, other studies [45-47] refuted these explanations.

In our study, the majority of patients had inadequate intake of EPA (86%), and they consumed significantly less EPA than controls ( $p=0.02$ ). Numerous studies have examined the beneficial effect of EPA on depression: the study by Demosthenes et al. [48] among 453 men and 400 women showed that elevated plasma EPA concentrations were associated with low depression. Martin [49] conducted a meta-analysis examining the effect of omega-3 supplementation on depression. He showed that EPA may be more effective than DHA in treating depression. As an important membrane component, EPAs have beneficial effects on the brain by modulating the neuroimmune and apoptotic pathways, modifying membrane function and competing with omega 6, precursors of inflammatory mediators [50].

In our patients, we observed a deficiency of alpha linolenic acid (46%), and omega 3 (38%). Their intakes were lower than the controls but the results were not statistically significant. These results are

similar to the study by Hakkarainen et al. [51] performed on 29,133 men aged 50-69 who found that there was no association between dietary intake of omega-3 fatty acids, Depressed mood and major depressive episodes. Indeed, the relationship between omega 3 and depression has been the subject of several studies [52,53]. A meta-analysis of the effects of omega 3 on depression concluded that there was evidence of the effect of omega 3 on mood [54,55]. The results of the study by Rees et al. [56] showed that women with low omega-3 intakes were six times more likely to develop perinatal depression than women with adequate omega-3 intakes. A prospective study from 54,662 American women from 1996 to 2006 demonstrated that  $\alpha$ -linolenic acid (ALA) intake was inversely associated with the risk of depression [57].

The mean intake of zinc in our patients was significantly lower than the controls ( $p=0.02$ ) with 98% of the patients with a deficiency of intake. The study of Styczeń et al [6] carried out in 2017 showed that serum zinc levels in patients with depressive episodes were significantly lower than those in controls ( $p=0.003$ ). Zinc is the most concentrated trace element in the brain, especially in the hippocampus and cerebral cortex. It contributes to the structure of the nervous system and contributes to the proper functioning of the brain. Zinc deficiency can influence cerebral homeostasis and can lead to impaired behavior and mental functions [58]. Many studies have shown that in depression there is an imbalance between the main excitatory systems (Glutamatergic) and inhibitors (GABA) and administration of antagonists of the glutamatergic system, including zinc, has shown antidepressant effect in clinical studies [59].

The average intake of folic acid in patients was significantly lower than the control with a deficiency of intake which affected 98% of the patients. A study of 9670 participants showed that low folate intake was associated with depression [60]. In fact, folate deficiency was associated with low levels of 5-hydroxyindoleacetic acid (5-HIAA), a metabolite of serotonin, in the cerebrospinal fluid [61].

Our results showed that patients had a significantly lower calcium intake than controls and 88% of them don't meet their needs. The more severe the depression was according to the pHq9 and the calcium intakes were low. Calcium activates the enzyme tryptophan hydroxylase which intervenes in the metabolic pathways of serotonin synthesis [62].

The mean iron intake of the patients was significantly lower than the controls. Inadequate intake was found in 76% of patients. Iron plays an important role in the oxygenation of the brain parenchyma, the synthesis of several neurotransmitters such as dopamine and serotonin as well as enzymes of the nervous system, namely tyrosine hydroxylase and tryptophan hydroxylase [63].

Mean intake of vitamin B1 in patients was significantly lower than in controls ( $p=0.02$ ), an inadequate intake was found in 88% of patients. Zhang et al. [64] found that lower thrombocytopenia levels of thiamine (free thiamine, thiamine mono phosphate (TMP), and thiamine di phosphate (TDP)) were associated with a higher prevalence of depressive symptoms. Thiamine di phosphate (TDP), the most bioactive form of thiamine, is a coenzyme in glucose metabolism crucial for secretion of serotonin [65].

The consumption of blue fish was significantly higher in controls than in patients. A meta-analysis by Li et al. [66] showed that high consumption of fish could reduce the risk of depression. Several studies have shown an inverse relationship between fish consumption and depression, as many other studies [67-70]. In the cross-sectional

study of Smith et al. [71] conducted from 2009 to 2011, consumption of fish was examined continuously using a frequency questionnaire: women who ate fish  $\geq 2$  times / week at the start of the study had a 25% lower risk of depression than those who ate fish  $<2$  times / week. Fish is an important source of PUFA (omega 3). Parletta et al. [72] have shown that omega-3 play an important role in the growth of axons, increase the fluidity and flexibility of the brain's cell membrane, improve the function of neurotransmitters such as serotonin and dopamine. They play an important role in the endothelial function, they increase the transport of glucose, they promote the synthesis of neuroprotectin D1 (NDP1) and therefore a large fish intake can thus prevent depression.

The intake of hard cheeses was higher in controls ( $\geq 1$  time / week) than in patients ( $<1$  time/week). Different studies have suggested that high dairy consumption is associated with better brain function and mood [73], cheese consumption was associated with a lower prevalence of cognitive deficit [74] despite their low PUFA and MUFA content. Changes in the extracellular concentration of calcium can affect the excitability of cells involved in the emotional regulation [75] and thus a correct intake of cheese, an important source of calcium, can be protective against these changes.

According to our study, patients consumed less olive oil than controls. Reverse associations between depression and the Mediterranean diet (rich in olive oil) have been demonstrated in several studies [76,77]. In the prospective study of kyrozis et al. [78] spreading over 13 years, the depression score was negatively associated with food intake of MUFA and their main source the olive oil. This has been justified in other studies by the fact that this consumption could improve the binding of serotonin to its receptors [79]. In addition to these antioxidant properties, olive oil increases and maintains the activity of the steryl-CoA 9-desaturase enzyme, or  $\Delta 9$ -desaturase (whose activity allows to pass from stearic acid, saturated, To oleic acid), and thus maintains the physicochemical properties of neuronal membranes [80].

However, there are some limitations to our study: this is a retrospective study that involved a small sample from which the causal link is difficult to establish, and we were not able to perform biological investigations.

## Conclusion

Our study has highlighted severe reduced intake in micronutrients that are certainly related to the installation of depression and its potential gravity.

Therefore, the imperative of nutritional care for depressed patients associated with psychiatric care is of crucial importance. These aspects are completely ignored in the treatment of depressed patients. These patients should be advised of the nutritional dimension of their pathology and thus adopt a healthy lifestyle with adequate diet and regular physical activity to effectively prevent and treat overweight or obesity and metabolic comorbidity.

This management will allow regular monitoring of anthropometric measurements to avoid weight gain and will involve a nutritional evaluation to detect deficiencies and/or excess intake of macro and micronutrients which may aggravate the symptomatology of depression.

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