Journal of Affective Disorders 172 (2015) 403–409

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research Report

Serum triglycerides, but not cholesterol or leptin, are decreased in suicide attempters with mood disorders

Maria da Graça Cantarelli [a], Patrícia Nardin [b], Andréia Buffon [c], Murilo Castilhos Eidt [d], Luiz Antônio Godoy [e], Brisa S. Fernandes [b], Carlos-Alberto Gonçalves [a,b,*]

[a] Post Graduate Program in Neuroscience, Federal University of Rio Grande do Sul,Porto Alegre, Brazil
[b] Laboratory of Calcium Binding Proteins in the Central Nervous System, Post Graduate Program in Biochemistry, Federal University of Rio Grande do Sul, Porto Alegre, Brazil
[c] Faculty of Pharmacy, Federal University of Rio Grande do Sul, Porto Alegre, Brazil
[d] Study Center José de Barros Falcão, Porto Alegre, Brazil
[e] São José Psychiatric Clinic, Porto Alegre, Brazil

ARTICLE INFO

Article history:
Received 8 October 2014
Accepted 14 October 2014
Available online 22 October 2014

Keywords:
Cholesterol
Mood affective disorders
Leptin
Suicide
Triglycerides

ABSTRACT

Background: Many peripheral biomarkers, including low cholesterol and its fractions, have been examined to identify suicidal behavior. Herein, we assessed serum lipid profile and some proteins putatively associated with suicidal behavior in subjects with mood disorder (bipolar disorder or major depressive disorder) with a recent suicide attempt and with no lifetime history of suicide attempts.
Methods: Fifty subjects had presented an episode of attempted suicide during the last 15 days, and 36 subjects had no history of any suicide attempt. We measured total cholesterol, HDL, LDL and triglycerides as well as serum leptin, brain-derived neurotrophic factor (BDNF), S100B and C-reactive protein (CRP).
Results: Individuals that had attempted suicide presented decreased body mass index (BMI) and waist circumference. After adjusting for these confounders, we found that triglycerides were decreased in attempted suicide subjects. We found no differences among total cholesterol, LDL, and HDL or leptin, S100B, CRP and BDNF.
Limitations: This is a cross-sectional study, and we cannot therefore assess whether a decrease in triglycerides caused a mood episode with suicidal ideation that led to a suicide attempt or if the presence of a mood episode originated a loss of appetite and consequent loss of weight, therefore decreasing triglyceride levels.
Conclusions: These results do not support the hypothesis that lower levels of cholesterol are associated with suicidal behavior in a mood disorder sample. However, our data support the idea that adiposity is differentiated in these patients (reduced BMI, waist circumference and serum triglycerides), which could lead to an altered communication between the adipose tissue and brain.

1. Introduction

Suicide is a public health problem of high complexity, annually causing a premature loss of approximately one million lives worldwide (Bertolote and Fleischmann, 2002; Pompili et al., 2013), and generating a wave of psychic events in family, friends and society that are often irreparable. Many studies have searched for and proposed biological markers that might be linked to suicidal behavior and could be used as an additional tool for prevention and therapeutic actions (Arango et al., 2003; Asellus et al., 2010; De Luca et al., 2005; Lee and Kim, 2011; Marcinko et al., 2008; Pandey, 2013). Many peripheral markers have been investigated in persons vulnerable to suicide, including low serum cholesterol and its fractions (Atmaca et al., 2002; Chang et al., 2012; Coryell and Schlesser, 2007; Jee et al., 2011; Jokinen et al., 2010; Lee and Kim, 2003; Olie et al., 2011; Papadopoulou et al., 2013; Troisi, 2009). This is intriguing, considering that persons with mood disorders [particularly bipolar disorder (BD)] have an increased prevalence of metabolic syndrome, which includes obesity, increased waist circumference and hyperlipidemia (Fagiolini et al., 2005; Nousen et al., 2014; Vancampfort et al., 2013). However, the biochemical connection reported between obesity and suicidal behavior (Dutton et al., 2013; Mukamal and Miller, 2009) demands further characterization, not only with regard to the serum lipid profile, but in relation to proteins associated with adipose tissue, such as leptin (Eikelis et al., 2006).

The link between low cholesterol and suicidal behavior is not clear, but the association between cholesterol and mental illness has

* Correspondence to:Post Graduate Program in Biochemistry, Universidade Federal do Rio Grande do Sul, Ramiro Barcelos, 2600-anexo, 90035-003, Porto Alegre, RS Brazil. Fax: +55 51 3308 5535.
E-mail address: casg@ufrgs.br (C.-A. Gonçalves).

http://dx.doi.org/10.1016/j.jad.2014.10.033

attracted the interest of researchers for over a century (Cruickshank and Tisdall, 1916; Poynder and Russell, 1926; Weston, 1915). Two meta-analyses summarize our current knowledge regarding cholesterol and suicidal behavior. Firstly, longitudinal studies show that individuals with lower cholesterol levels do have a slightly, but statistically significant, increased risk of completing suicide (Lester, 2002); secondly, cholesterol-lowering treatments, such as statins, have not been shown to increase non-illness mortality (including accidents, trauma and suicide) (Muldoon et al., 2001).

We analyzed the lipid profiles of subjects with mood disorders [BD and major depressive disorder (MDD)] and with a recent suicide attempt and in subjects with no lifetime history of suicide attempt. We aimed to determine whether total cholesterol, its fractions and triglycerides were decreased in subjects that had attempted suicide, as well as to investigate serum levels of other proteins putatively associated with suicidal behavior: leptin (Atmaca et al., 2008), S100B protein (Falcone et al., 2010), brain-derived neurotrophic factor (BDNF) (Pandey et al., 2010) and C-reactive protein (CRP) (De Berardis et al., 2008).

2. Methods and materials

2.1. Subjects and measurement

Eighty-six subjects with mood disorders (BD and MDD), according to DSM-IV criteria, were enrolled in the study upon admission to the São José Clinic, an inpatient psychiatric unit in Porto Alegre, Brazil, from April 2010 to December 2012. Of those, 50 had presented a suicide attempt during the last 15 days, and 36 had no lifetime history of suicide attempt. Suicide attempts were considered as "situations in which a person performs a life-threatening behavior with the intent of jeopardizing his or her life, or to give the appearance of such intent" (Beck et al., 1973; Brundin et al., 2007). All study participants underwent a general physical examination that showed no evidence of ongoing infection. Individuals on antibiotics and anti-inflammatory medications were excluded from the study. Demographic data and somatic diagnoses for the study participants are shown in Table 1. All subjects were on psychiatric medication for their current mood episode at the moment of sample collection. According to the criteria of Traskman et al. (1981), suicide attempters were further divided into two subgroups: 20 subjects with a violent attempt (5 subjects with a knife wound, 1 subject jumping from a high place, 1 with a firearm, 7 that had tried to hang themselves, and 6 that had thrown themselves in front of a vehicle in movement), and 30 with a non-violent attempt (medication ingestion and/or a superficial wrist cut). This study was approved by our local Ethical Review Board for human studies (UFRGS, 18153) in accordance with the 1964 Declaration of Helsinki. All subjects provided their written informed consent before being enrolled in this study.

2.2. Biochemical measurements

All subjects were fasted overnight. Venous blood samples were drawn from the antecubital vein at 08:00 a.m. After whole blood was obtained, the serum was separated by centrifugation at 3000 rpm for 15 min and was then aliquoted at −80 °C until analyses to determine the serum levels of cholesterol and triglycerides, as well as leptin, S100B protein, brain-derived neurotrophic factor (BDNF) and C-reactive protein (CRP).

Total cholesterol, HDL, LDL and triglyceride levels were determined by colorimetric assays using Labtest Diagnostica Kits, as indicated by the manufacturer, and employing the Labmax 240® equipment from Labtest Diagnóstica (Minas Gerais, Brazil). Serum S100B was measured by sandwich ELISA, as described previously (Leite et al., 2008). BDNF and leptin were measured by sandwich ELISA kits from Millipore (MA, USA). CRP was measured by a high sensitivity turbidimetric immunoassay kit from Biotécnica (Minas Gerais, Brazil), using the Labmax 240® for absorbance reading (Labtest Diagnostica, Minas Gerais, Brazil).

2.3. Statistical analysis

Statistical analyses were performed using SPSS 17.0 for Windows. All continuous variables are presented as means ± standard deviation (SD) or medians and interquartile range, as appropriate. Categorical variables are presented as the raw number and percentage (%). χ^2 and Fisher's test were used to evaluate associations between categorical variables, as appropriate. For the comparisons of continuous variables among groups, we employed the independent t test for parametric variables, and the Mann–Whitney test for non-parametric variables. For analyses of total cholesterol, LDL, HDL, triglycerides, BDNF, and leptin we used the analysis of covariance (ANCOVA). Length of illness and of current episode, sex, use of anticonvulsants or selective serotonin reuptake inhibitor (SSRI), body mass index (BMI), and waist circumference were used as covariates. As leptin was a highly skewed variable, we applied a logarithmic transformation in order to use parametric methods. S100 and CRP were highly skewed and not suitable for mathematical transformations, and therefore we used non-parametrical methods. Pearson's and Spearman's correlations coefficients were used to analyze the correlations between parametric and non-parametric continuous variables, respectively. We also analyzed the effect of the presence of suicide attempt as a moderator in the correlations. Two-tailed p values <0.05 were considered to be statistically significant.

3. Results

A total of 86 subjects with mood disorders were included in this study. Fifty subjects had presented an episode of suicide attempt during the last 15 days, and 36 subjects had no lifetime history of suicide attempt. The characteristics of the sample are summarized in Table 1. All subjects were on current psychiatric medication at the time of the suicide attempt and at the time of blood withdrawal. The frequencies of the types of psychiatric medication were similar between both groups, except for the use of anticonvulsants and SSRI antidepressants, which were higher in the subjects without any suicide attempt. Subjects with a recent suicide attempt had decreased BMI and waist circumference, when compared to subjects that had not attempted suicide. We identified the presence of T2DM (Type 2 diabetes mellitus) and hypothyroidism in subjects without any history of suicide attempt. After adjusting for length of illness and of current episode, sex, use of anticonvulsants and SSRI, BMI, and waist circumference, we found that triglycerides were decreased in attempted suicide subjects when compared to subjects without any suicide attempt (103.45 ± 31.72 vs. 144.15 ± 74.48, $p=0.001$) (Fig. 1). We found no differences among total cholesterol, LDL, and HDLbetween subjects with and without any suicide attempt.

Moreover, there were no differences among BDNF, S100B, CRP, and leptin between those attempted suicide and non-suicide subjects (Table 2). In addition, we found no difference in total cholesterol, LDL, HDL, triglycerides, BDNF, S100B, CRP, and leptin when analyzing the suicide attempters, according to the violence of the act (data not shown).

We found a positive correlation between leptin and length of illness ($r=0.24$, $p=0.03$), leptin and waist circumference ($r=0.32$, $p=0.003$), and between leptin and BMI ($r=0.48$, $p=0.001$). The correlation between leptin and BMI is clearly observed in subjects with and without suicide attempt (Fig. 2A). There were positive

Table 1
Characteristics of subjects with and without a history of suicide attempt.

Characteristic	With suicide attempt ($n=50$)	Without suicide attempt ($n=36$)	*P* value
Socio-demographics			
Male/female[a]	11/39	12/24	**0.048***
Age, years[b]	27.83 ± 12.21	32.28 ± 13.91	0.120
Education level, years[b]	10.27 ± 3.15	12.17 ± 3.09	0.064
Psychiatric disorder			
Pathology[a]			
Bipolar disorder	37	29	0.323
Current mania	23	16	0.658
Current depression	14	13	0.658
Major depressive disorder	13	7	0.323
Presence of psychosis[a]	21	8	0.133
Length of illness, years[c]	10.0 (3.0–20.0)	18.0 (11.0–30.0)	**0.032***
Length of current episode, days[c]	25.0 (15.0–60.0)	60.0 (30.0–180.0)	**0.046***
Family history of psychiatric disorder[a]	31	33	0.780
Current psychiatric medication[a]			
Antidepressants			
SSRI	7	14	**0.020***
Others	14	13	0.680
Lithium	15	11	0.570
Anticonvulsants	21	29	**0.021***
Antipsychotics			
Typical	28	17	0.280
Atypical	27	21	0.475
Metabolic characteristics			
BMI[b]	24.61 ± 4.77	28.13 ± 6.41	**0.001***
Waist circumference (cm)[b]	81.14 ± 9.48	96.68 ± 17.17	**0.049***
T2DM[d]	0	2	0.310
Hypothyroidism[d]	0	2	0.310

Abbreviations: SSRI, selective serotonin reuptake inhibitor; BMI, body-mass index; T2DM, Type 2 diabetes mellitus.

* Columns show means ± standard deviation (SD) for all categories except male sex, presence of psychosis, pathology, current psychiatric medication, family history of psychiatric disorder, and presence of T2DM or hypothyroidism, which are presented as raw data. Length of illness and current episode are shown as median and interquartile range.

[a] Chi-square test.
[b] Independent *t* test.
[c] Mann–Whitney test.
[d] Fisher's exact test.

correlations between CRP and waist circumference ($r_0=0.32$, $p=0.003$), and CRP and BMI ($r_0=0.38$, $p=0.001$). However, the presence of a suicide attempt did not act as a moderator in these correlations (Table 3). Moreover, we found no correlation between S100B and BDNF with any clinical characteristic, including BMI and length of illness.

With regard to the serum triglycerides (the parameter that differed between subjects with and without a history of suicide attempt) we found no correlations between triglycerides and BMI ($r=0.12$, $p=0.261$), triglycerides and waist circumference ($r=0.17$, $p=0.098$), or triglycerides and length of illness ($r=0.08$, $p=0.454$). The lack of correlation between triglycerides and BMI, observed in mood disorder subjects with and without a history of suicide, is shown in Fig. 2B.

4. Discussion

In contrast to current hypothesizes reported in the literature, we did not find any relationship between low total cholesterol and its fractions and suicidal behavior in patients with mood disorders. However, this lack of relationship is in agreement with some other studies in the literature (Almeida-Montes et al., 2000; Asellus et al., 2010; Paplos et al., 2012; Park et al., 2013; Persons et al., 2012) and our data are in accordance with two other independent and contemporary studies in individuals with BD and MDD, where no differences were found in serum cholesterol content (Baek et al., 2014; D'Ambrosio et al., 2012). We did not find any difference in total cholesterol, HDL or LDL. Commonly, psychiatric patients, particularly with BD and MDD, have elevated BMI and other metabolic abnormalities, which contribute to metabolic syndrome (Carpiniello et al., 2012; Fiedorowicz et al., 2008; Lopresti and Drummond, 2013). Herein, we found some differences between suicide attempters and non-attempters in the sample of mood disorders studied, particularly with regard to BMI and waist circumference, which were both reduced in suicide attempters. In agreement with these body parameters, the suicide attempters exhibited lower serum triglycerides. It is important to emphasize that the difference found in serum triglycerides (and not in cholesterol) in suicide attempters was adjusted for gender and BMI, which is generally underestimated in other cross-sectional studies of suicidality [see Zhang (2011)].

Three demographic data parameters deserve consideration in our sample; gender, length of illness and current episode and current medication. The gender difference regarding risk of suicide attempt is well known. Worldwide the risk of attempted suicide is higher in females (Borges et al., 2010; Rihmer et al., 2013). Accordingly, our study included more females than males with a history of attempted suicide. Furthermore, the average time between the onset of disease and the current suicide attempt was 10 years. This period has been considered to present a higher risk of suicide in patients with both BD and MDD (Tondo et al., 2003; Tsai et al., 2002). The use of SSRI and anticonvulsants was lower in suicide attempters. Atypical antipsychotics and anticonvulsants (particularly valproate) contribute to insulin resistance and obesity (Pylvanen et al., 2006; Verrotti et al., 2009). Notably, we did not find any differences in the use of antipsychotic drugs between suicide attempters and non-attempters. Triglyceride levels were decreased in subjects without suicide attempt even after adjusting for the use of anticonvulsants and SSRI. However, since ours is a cross-sectional study, we cannot

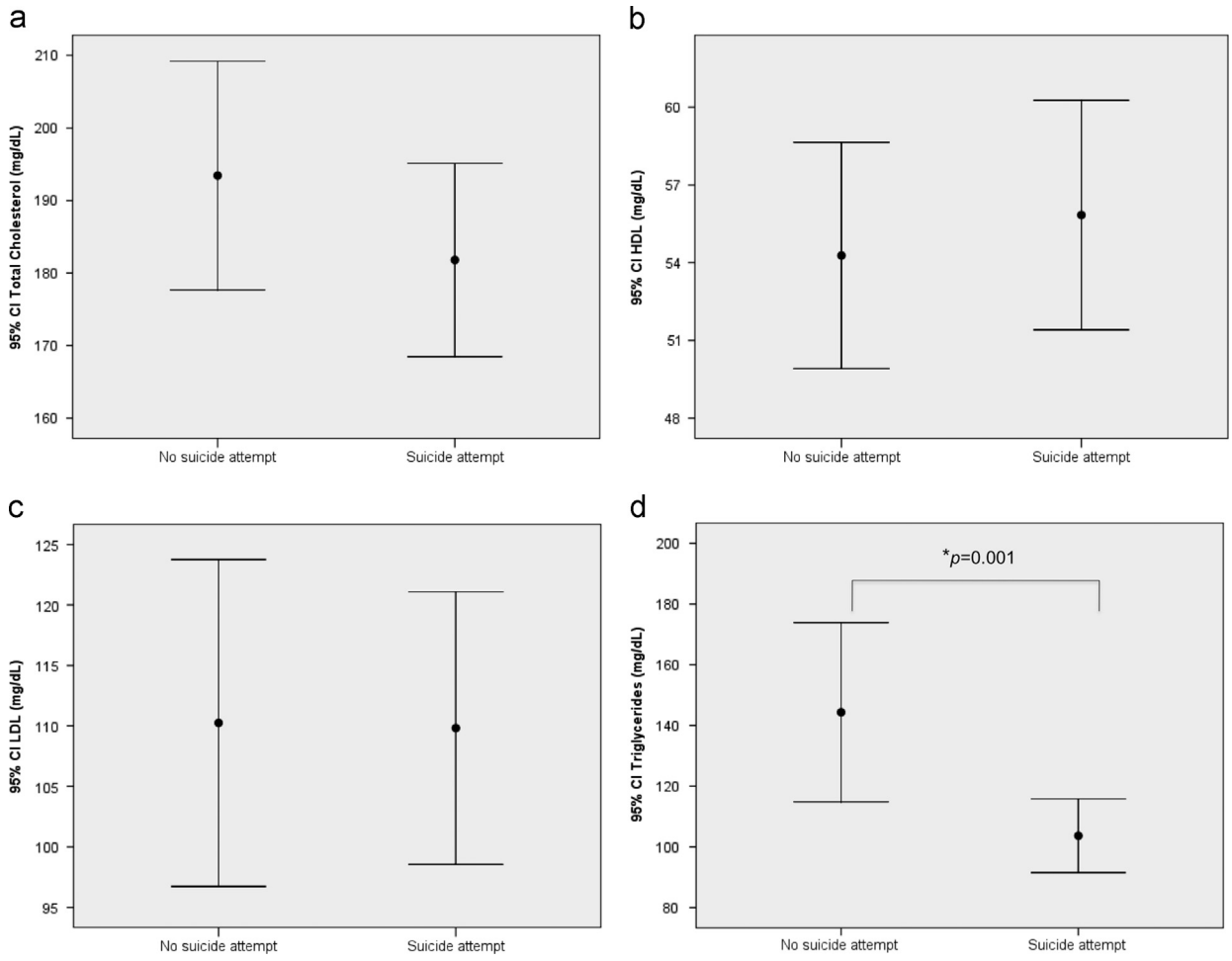

Fig. 1. Fasting serum lipid profile in subjects with and without a history of suicide attempt. (a) Total cholesterol, 181.00 ± 53.71 vs. 193.00 ± 44.70, respectively, $p=0.406$. (b) LDL cholesterol, 109.90 ± 44.97 vs. 111.55 ± 36.12, respectively, $p=0.504$. (c) HDL cholesterol, 54.50 ± 18.54 vs. 55.39 ± 13.13, $p=0.810$, and (d) Triglycerides, 103.45 ± 31.72 vs. 144.15 ± 74.48, $p=0.001$. Data are shown as mean ± standard deviation. Figure shows the mean and the 95% confidence interval (CI) of the mean. Analysis of covariance (ANCOVA) with length of illness and of current episode, sex, use of anticonvulsants and SSRI, BMI, and waist circumference as covariates.* denotes $p < 0.05$.

Table 2
BDNF, S100B, CRP, and leptin in subjects with and without a history of suicide attempt.

	With suicide attempt (*n*=50)	**Without suicide attempt (*n*=36)**	***P*** value
BDNF, pg/ml[a]	1070.94 ± 371.29	1045.38 ± 672.07	0.60
S100B, ng/ml[b]	3.00 (1.00–7.00)	3.50 (1.00–7.75)	0.85
CRP, mg/l[b]	4.00 (1.00–9.00)	3.50 (2.00–6.00)	0.89
Leptin, ng/ml[a,c]	2.74 ± 1.12	3.05 ± 1.19	0.65

Abbreviations: BDNF, brain-derived neurotrophic factor; CRP, C-reactive protein.
[a] Independent *t* test, mean and standard deviation.
[b] Mann–Whitney test, median and interquartile range.
[c] Log-transformed variable.

rule out that the use of anticonvulsant drugs, which were more prevalent in the non-attempter group, contributed to the discrepancy observed in BMI and serum triglyceride levels. In another study regarding BD, decreased cholesterol and triglycerides were observed in suicide attempters (Vuksan-Cusa et al., 2009). Interestingly, in Vuksan-Cusa's study the sample was free of psychotropic medication, reinforcing the idea that medication is not the sole contributor to changes in lipid profile.

It has been proposed that a decreased serotonergic activity could result in a poorer inhibition of impulsivity and, consequently, suicidal behavior (Arango et al., 2002; Mann, 2013). In our study, we observed that the prescription of SSRI in persons without suicide attempts was higher than in those with suicide attempts. This difference in prescribing may be secondary to a possible association between the class of SSRI, particularly fluoxetine, with violence and suicide (Gunnell and Ashby, 2004; Hammad et al., 2006; Marcinko, 2007; Walsh and Dinan, 2001), although no consensus regarding the direct relationship between antidepressant use and development of suicidal ideation or behavior exists (Fazel et al., 2007; Hammad et al., 2006; Miller et al., 2014; Walsh and Dinan, 2001). More recently, the serotonergic system, widely established as being linked to suicidality (Arango et al., 1995; Jokinen et al., 2009; Traskman et al., 1981), has been studied in the area of genetics and presented interesting results. For example, the presence of sequence variants in HTR5A (serotonin type 5A receptor gene) was strongly associated with high plasma levels of triglycerides (Zhang et al., 2010) and associations between lower HDL cholesterol levels with depression were also modified by a 5-HTTLPR (serotonin transporter gene linked promoter region) polymorphism; however this association was only significant in the presence of one or more copies of the s (short) allele (Kim et al., 2011).

Some studies have suggested that lower cholesterol can be more linked to violent suicide attempts than suicidality itself [e.g. (Atmaca et al., 2008)]. We did not find a significant difference in

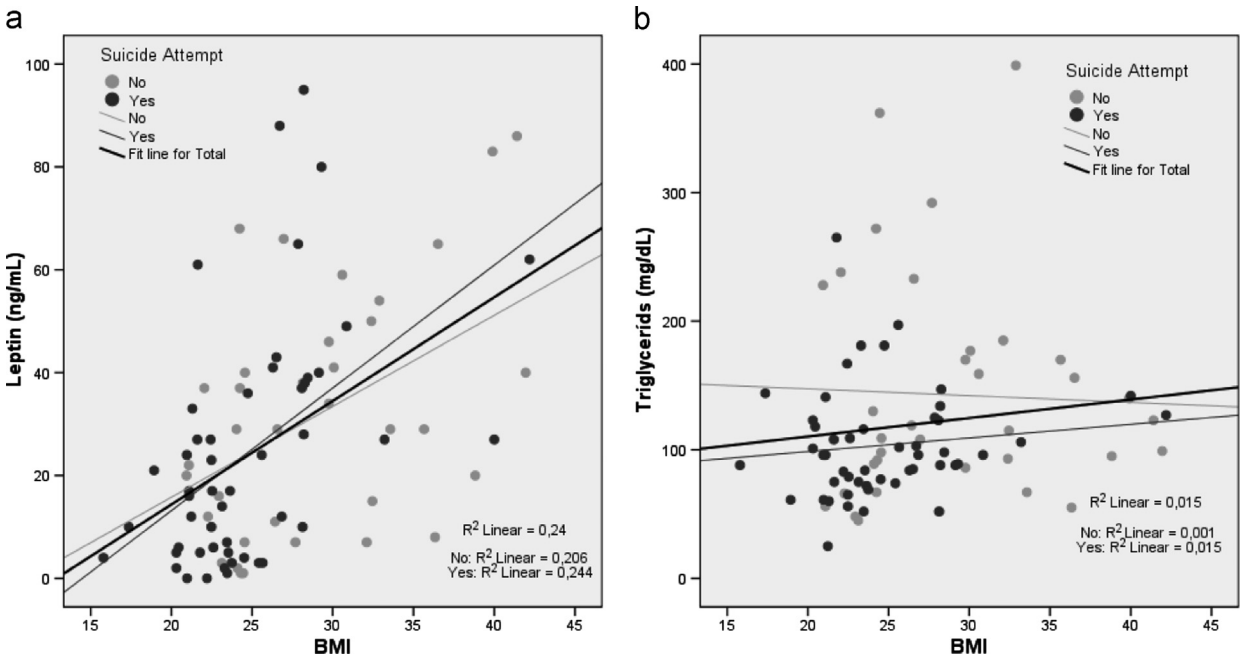

Fig. 2. Correlations between leptin or triglycerides with body-mass index (BMI). A positive correlation between leptin and BMI is observed (in a, $r=0.48$), but no correlation between triglycerides and BMI (in b, $r=0.12$). History of suicide attempt is not a moderator of the correlations ($p>0.05$).

Table 3
Analysis of a "history of suicide attempt" as a moderator of the correlations between body-mass index and length of illness in years with C-reactive protein, leptin, brain-derived neuotrophic factor (BDNF), protein S100B, and lipidic profile.

	R* values with suicide attempt ($n=50$)	***R* values without suicide attempt ($n=36$)***	***P*** value
BMI vs. BDNF	0.17	−0.15	0.472
BMI vs. CRP	0.38	0.45	0.563
BMI vs. Leptin	0.45	0.39	0.555
BMI vs. S100B	0.08	−0.05	0.549
Length of illness vs. BDNF	−0.26	−0.06	0.289
Length of illness vs. CRP	0.01	0.15	0.782
Length of illness vs. Leptin	0.19	0.25	0.878
Length of illness vs. S100B	0.16	−0.06	0.281

* Columns show Pearson's correlation (r). The P values refers to the effect of the presence of suicide attempt as a moderator to the correlations.

serum cholesterol between violent and non-violent attempters, in agreement with a previous study in BD (D'Ambrosio et al., 2012). We also did not find any difference in triglyceride levels between violent and non-violent suicide attempters.

This study also evaluated other markers related to adiposity, namely leptin, CRP and S100B (Eikelis et al., 2006; Steiner et al., 2010a). BDNF was also investigated because it is widely involved in body energetic homeostasis and commonly associated with psychiatric disorders with an elevated rate of suicide (Fernandes et al., 2013, 2011; Marosi and Mattson, 2014).

Serum leptin, an adipocyte-derived protein regulator of food intake, has a positive correlation with BMI [e.g. (McConway et al., 2000)]. Leptin (together with cholesterol) was found to be reduced in suicidal patients, compared to healthy controls (Atmaca et al., 2008, 2002). In addition, low levels of cerebrospinal leptin were found in female suicide attempters with major depression (Westling et al., 2004), in agreement with reduced levels of brain leptin observed in suicide victims (Eikelis et al., 2006). However, serum leptin was not altered in pregnant women with a higher suicide risk (Farias et al., 2013). Herein, we found a positive correlation of leptin with BMI in our sample, but no difference was found in serum leptin between patients with and without a history of suicide. This finding contends the idea that serum leptin may act as a suicidality marker in patients with mood disorders. Moreover, we did not find an association between CRP and a history of suicide in patients with mood disorders. However, the positive correlation between CRP and BMI and CRP and waist circumference in these patients reinforces the idea that a systemic inflammatory process (including adipose tissue) may contribute to the pathophysiology of mood disorders (Kling et al., 2007).

No differences were observed in serum BDNF and S100B between mood disorder subjects with and without a history of suicide. Moreover, no correlation was found between these proteins and the anthropomorphic signals of adiposity observed in these patients (BMI or waist circumference) or these proteins and the length of illness. Serum BDNF was reduced in suicidal individuals soon after an attempted suicide (Dawood et al., 2007), in agreement with the changes in brain BDNF and its receptors observed in postmortem studies of depressive patients (Lee and Kim, 2011). Our sample included patients with suicide attempts during the last 15 days, time enough to "recover" possible decreases in the peripheral levels of BDNF associated with a suicidal attempt. However, further studies are necessary to clarify this question. S100B increments have been reported in many conditions of brain injury and neurodegenerative diseases (Kleindienst et al., 2007; Rothermundt et al., 2003). Serum S100B protein comes from the brain and from other non-neural sources, particularly adipose tissue (Goncalves et al., 2010, 2008). In fact, serum S100B levels in humans appear to closely reflect adipose tissue mass (Gross et al., 2010; Steiner et al., 2010a). Some studies have shown elevated levels of serum S100B in episodes of mood disorders, and these elevations were more evident in major depressive disorder than in bipolar disorder (Schroeter and Steiner, 2009). We found elevated levels of S100B (compared to those of healthy individuals) [e.g. (Andreazza et al., 2007; Schroeter et al., 2011)], but no difference was found between patients with and without a

history of suicide attempt. Moreover, no correlation was found with BMI. Interestingly, this lack of correlation was also observed in schizophrenic patients and attributed to insulin resistance in these patients (Steiner et al., 2010b). However, augmented S100B was correlated with the severity of suicidal ideation in adolescents with psychosis or mood disorders (Falcone et al., 2010). As such, this matter demands further studies.

Our study presents some limitations; firstly, our sample is probably underpowered to detect a difference in total cholesterol between subjects with and without a history of suicide attempt. However, in support of our analysis, another cross-sectional study of a sample of schizophrenic patients, also adjusted for gender and BMI, found no association between cholesterol and suicidal behavior (Huang and Wu, 2000). Secondly, all subjects were on medication and a higher number of non-suicidal persons were on anticonvulsants, drugs known to increase insulin resistance; however, we adjusted for this type of medication in our analysis. Thirdly, ours was a cross-sectional study, and we cannot therefore assess whether a decrease in triglycerides caused a mood episode with suicidal ideation that led to a suicide attempt or if the presence of a mood episode originated a loss of appetite and consequent loss of weight, therefore decreasing triglyceride levels.

Taken together our data suggest that suicide attempters with mood disorders exhibit less adiposity, expressed as a reduced BMI, waist circumference and serum triglycerides, when compared to non-attempters. Our data opposed the idea that serum leptin, CRP and S100B could represent the markers of suicidality in patient with mood disorders. However, further studies are investigating these and other markers related to adiposity, such as ghrelin (Atmaca et al., 2006), are necessary not only to diagnose such behavior, but for the follow-up of treatment of psychiatric diseases with elevated rates of suicide.

5. Conclusions

We did not find any decrease in serum cholesterol when comparing suicide attempters with non-attempters in a sample of subjects with mood disorders. However, we found a reduced adiposity in suicide attempters, as indicated by reduced BMI, waist circumference, and peripheral triglycerides. These data do not support the hypothesis that lower levels of cholesterol are associated with suicidal behavior. Moreover, although peripheral levels of leptin, BDNF, S100B and CRP may be associated with mood disorders, we did not find any difference in the levels of these proteins in subjects that had a history of suicide, or not. However, our data contribute to the idea that adiposity is differentiated in these patients, which could lead to an altered adipose tissue–brain communication.

Role of funding source

This work was supported by the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), MS/Ministry of Health (Project 6845-4) and INCT – National Institute of Science and Technology for Brain Diseases, Excitotoxicity and Neuroprotection of the Brazilian government.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgments

We would like to thank Nurses Míriam Daniela da Silva Porciúncula, Marta Ziziane Dorneles Wachter, Rosa Amélia Espíndola Gomes and Jorge Correia da Silva for technical support and collection of blood samples. This work was supported by the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), MS/Ministry of Health (Project 6845-4) and INCT – National Institute of Science and Technology for Brain Diseases, Excitotoxicity and Neuroprotection (Project 573677/2008-5) of the Brazilian government.

References

Almeida-Montes, L.G., Valles-Sanchez, V., Moreno-Aguilar, J., Chavez-Balderas, R.A., Garcia-Marin, J.A., Cortes Sotres, J.F., Hheinze-Martin, G., 2000. Relation of serum cholesterol, lipid, serotonin and tryptophan levels to severity of depression and to suicide attempts. J. of Psychiatry Neurosci. 25, 371–377.

Andreazza, A.C., Cassini, C., Rosa, A.R., Leite, M.C., de Almeida, L.M., Nardin, P., Cunha, A.B., Cereser, K.M., Santin, A., Gottfried, C., Salvador, M., Kapczinski, F., Goncalves, C.A., 2007. Serum S100B and antioxidant enzymes in bipolar patientsJ. Psychiatr. Res. 41, 523–529.

Arango, V., Huang, Y.Y., Underwood, M.D., Mann, J.J., 2003. Genetics of the serotonergic system in suicidal behavior. J.Psychiatr. Res. 37, 375–386.

Arango, V., Underwood, M.D., Gubbi, A.V., Mann, J.J., 1995. Localized alterations in pre- and postsynaptic serotonin binding sites in the ventrolateral prefrontal cortex of suicide victims. Brain Res. 688, 121–133.

Arango, V., Underwood, M.D., Mann, J.J., 2002. Serotonin brain circuits involved in major depression and suicide. Prog. Brain Res. 136, 443–453.

Asellus, P., Nordstrom, P., Jokinen, J., 2010. Cholesterol and CSF 5-HIAA in attempted suicide. J.Affect. Disord. 125, 388–392.

Atmaca, M., Kuloglu, M., Tezcan, E., Ustundag, B., 2008. Serum leptin and cholesterol values in violent and non-violent suicide attempters. Psychiatry Res. 158, 87–91.

Atmaca, M., Kuloglu, M., Tezcan, E., Ustundag, B., Gecici, O., Firidin, B., 2002. Serum leptin and cholesterol values in suicide attempters. Neuropsychobiology 45, 124–127.

Atmaca, M., Tezcan, E., Parmaksiz, S., Saribas, M., Ozler, S., Ustundag, B., 2006. Serum ghrelin and cholesterol values in suicide attempters. Neuropsychobiology 54, 59–63.

Baek, J.H., Kang, E.S., Fava, M., Mischoulon, D., Nierenberg, A.A., Yu, B.H., Lee, D., Jeon, H.J., 2014. Serum lipids, recent suicide attempt and recent suicide status in patients with major depressive disorder. Prog. Neuro-psychopharmacol. Biol. Psychiatry 51, 113–118.

Beck, A.T., Frederick, C.J., Perlin, S., Pokorny, A.D., Schulman, R.E., 1973. Classification and nomenclatureSuperintendent of Documents, U.S.. In: Superintendent of Documents, U.S., Resnik, H.L.P., Hathorne, B.C. (Eds.), Suicide Prevention in the Seventies. Government Printing Office, Washington, D.C., pp. 7–12.

Bertolote, J.M., Fleischmann, A., 2002. A global perspective in the epidemiology of suicide. Suicidology, 6–8.

Borges, G., Nock, M.K., Haro Abad, J.M., Hwang, I., Sampson, N.A., Alonso, J., Andrade, L.H., Angermeyer, M.C., Beautrais, A., Bromet, E., Bruffaerts, R., de Girolamo, G., Florescu, S., Gureje, O., Hu, C., Karam, E.G., Kovess-Masfety, V., Lee, S., Levinson, D., Medina-Mora, M.E., Ormel, J., Posada-Villa, J., Sagar, R., Tomov, T., U.d.a, H., Williams, D.R., Kessler, R.C., 2010. Twelve-month prevalence of and risk factors for suicide attempts in the World Health Organization World Mental Health Surveys. J. Clin. Psychiatry 71, 1617–1628.

Brundin, L., Bjorkqvist, M., Petersen, A., Traskman-Bendz, L., 2007. Reduced orexin levels in the cerebrospinal fluid of suicidal patients with major depressive disorder. Eur. Neuropsychopharmacol. 17, 573–579.

Carpiniello, B., Pinna, F., Velluzzi, F., Loviselli, A., 2012. Mental disorders in patients with metabolic syndrome. The key role of central obesity. Eat. Weight Disord. 17, e259–e266.

Chang, S.S., Wen, C.P., Tsai, M.K., Lawlor, D.A., Yang, Y.C., Gunnell, D., 2012. Adiposity, its related biologic risk factors, and suicide: a cohort study of 542,088 taiwanese adults. Am. J. Epidemiol. 175, 804–815.

Coryell, W., Schlesser, M., 2007. Combined biological tests for suicide prediction. Psychiatry Res. 150, 187–191.

Cruickshank, J., Tisdall, C.J., 1916. The cholesterol content of the serum in mental diseases. Br. J. Psychiatry 62, 168–173.

D'Ambrosio, V., Salvi, V., Bogetto, F., Maina, G., 2012. Serum lipids, metabolic syndrome and lifetime suicide attempts in patients with bipolar disorder. Prog. Neuro-Psychopharmacol. Biol. Psychiatry 37, 136–140.

Dawood, T., Anderson, J., Barton, D., Lambert, E., Esler, M., Hotchkin, E., Haikerwal, D., Kaye, D., Lambert, G., 2007. Reduced overflow of BDNF from the brain is linked with suicide risk in depressive illness. Mol. Psychiatry 12, 981–983.

De Berardis, D., Serroni, N., Campanella, D., Carano, A., Gambi, F., Valchera, A., Conti, C., Sepede, G., Scali, M., Fulcheri, M., Salerno, R.M., Ferro, F.M., 2008. Alexithymia and its relationships with C-reactive protein and serum lipid levels among drug naive adult outpatients with major depression. Prog. Neuro-psychopharmacol. Biol. Psychiatry 32, 1982–1986.

De Luca, V., Tharmalingam, S., King, N., Strauss, J., Bulgin, N., Kennedy, J.L., 2005. Association study of a novel functional polymorphism of the serotonin transporter gene in bipolar disorder and suicidal behaviour. Psychopharmacology 182, 128–131.

Dutton, G.R., Bodell, L.P., Smith, A.R., Joiner, T.E., 2013. Examination of the relationship between obesity and suicidal ideation. Int. J. Obes. 37, 1282–1286.

Eikelis, N., Esler, M., Barton, D., Dawood, T., Wiesner, G., Lambert, G., 2006. Reduced brain leptin in patients with major depressive disorder and in suicide victims. Mol. Psychiatry 11, 800–801.

Fagiolini, A., Frank, E., Scott, J.A., Turkin, S., Kupfer, D.J., 2005. Metabolic syndrome in bipolar disorder: findings from the Bipolar Disorder Center for Pennsylvanians. Bipolar Disord. 7, 424–430.

Falcone, T., Fazio, V., Lee, C., Simon, B., Franco, K., Marchi, N., Janigro, D., 2010. Serum S100B: a potential biomarker for suicidality in adolescents? PLoS one 5, e11089.
Farias, D.R., Pinto Tde, J., Teofilo, M.M., Vilela, A.A., Vaz Jdos, S., Nardi, A.E., Kac, G., 2013. Prevalence of psychiatric disorders in the first trimester of pregnancy and factors associated with current suicide risk. Psychiatry Res. 210, 962–968.
Fazel, S., Grann, M., Ahlner, J., Goodwin, G., 2007. Suicides by violent means in individuals taking SSRIs and other antidepressants: a postmortem study in Sweden, 1992–2004. J. Clin. Psychopharmacol. 27, 503–506.
Fernandes, B.S., Berk, M., Turck, C.W., Steiner, J., Goncalves, C.A., 2013. Decreased peripheral brain-derived neurotrophic factor levels are a biomarker of disease activity in major psychiatric disorders: a comparative meta-analysis. Mol. Psychiatry.
Fernandes, B.S., Gama, C.S., Cereser, K.M., Yatham, L.N., Fries, G.R., Colpo, G., de Lucena, D., Kunz, M., Gomes, F.A., Kapczinski, F., 2011. Brain-derived neurotrophic factor as a state-marker of mood episodes in bipolar disorders: a systematic review and meta-regression analysis. J. Psychiatr. Res. 45, 995–1004.
Fiedorowicz, J.G., Palagummi, N.M., Forman-Hoffman, V.L., Miller, D.D., Haynes, W. G., 2008. Elevated prevalence of obesity, metabolic syndrome, and cardiovascular risk factors in bipolar disorder. Ann. Clin. Psychiatry 20, 131–137.
Goncalves, C.A., Leite, M.C., Guerra, M.C., 2010. Adipocytes as an important source of serum S100B and possible roles of this protein in adipose tissue. Cardiovasc. Psychiatry Neurol. 2010, 790431.
Goncalves, C.A., Leite, M.C., Nardin, P., 2008. Biological and methodological features of the measurement of S100B, a putative marker of brain injury. Clin. .Biochem. 41, 755–763.
Gross, S., Homan van der Heide, J.J., van Son, W.J., Gans, R.O., Foell, D., Navis, G., Bakker, S.J., 2010. Body mass index and creatinine clearance are associated with steady-state serum concentrations of the cell damage marker S100B in renal transplant recipients. Med. Sci. Monit.: Int. Med. J. Exp. Clin. Res. 16, CR318–CR324.
Gunnell, D., Ashby, D., 2004. Antidepressants and suicide: what is the balance of benefit and harm. Br. Med. J. 329, 34–38.
Hammad, T.A., Laughren, T.P., Racoosin, J.A., 2006. Suicide rates in short-term randomized controlled trials of newer antidepressants. J. Clin. Psychopharmacol. 26, 203–207.
Huang, T., Wu, S., 2000. Serum cholesterol levels in paranoid and non-paranoid schizophrenia associated with physical violence or suicide attempts in Taiwanese. Psychiatry Res. 96, 175–178.
Jee, S.H., Kivimaki, M., Kang, H.C., Park, I.S., Samet, J.M., Batty, G.D., 2011. Cardiovascular disease risk factors in relation to suicide mortality in Asia: prospective cohort study of over one million Korean men and women. Eur. Heart J. 32, 2773–2780.
Jokinen, J., Nordstrom, A.L., Nordstrom, P., 2009. CSF 5-HIAA and DST non-suppression–orthogonal biologic risk factors for suicide in male mood disorder inpatients. Psychiatry Res. 165, 96–102.
Jokinen, J., Nordstrom, A.L., Nordstrom, P., 2010. Cholesterol, CSF 5-HIAA, violence and intent in suicidal men. Psychiatry Res. 178, 217–219.
Kim, J.M., Stewart, R., Kim, S.W., Shin, I.S., Yang, S.J., Yoon, J.S., 2011. Cholesterol and serotonin transporter polymorphism interactions in late-life depression. Neurobiol. Aging 32, 336–343.
Kleindienst, A., Hesse, F., Bullock, M.R., Buchfelder, M., 2007. The neurotrophic protein S100B: value as a marker of brain damage and possible therapeutic implications. Prog. Brain Res. 161, 317–325.
Kling, M.A., Alesci, S., Csako, G., Costello, R., Luckenbaugh, D.A., Bonne, O., Duncko, R., Drevets, W.C., Manji, H.K., Charney, D.S., Gold, P.W., Neumeister, A., 2007. Sustained low-grade pro-inflammatory state in unmedicated, remitted women with major depressive disorder as evidenced by elevated serum levels of the acute phase proteins C-reactive protein and serum amyloid A. Biol. Psychiatry 62, 309–313.
Lee, B.H., Kim, Y.K., 2011. Potential peripheral biological predictors of suicidal behavior in major depressive disorder. Prog. Neuro-psychopharmacol. Biol. Psychiatry 35, 842–847.
Lee, H.J., Kim, Y.K., 2003. Serum lipid levels and suicide attempts. Acta Psychiatr. Scand. 108, 215–221.
Leite, M.C., Galland, F., Brolese, G., Guerra, M.C., Bortolotto, J.W., Freitas, R., Almeida, L.M., Gottfried, C., Goncalves, C.A., 2008. A simple, sensitive and widely applicable ELISA for S100B: methodological features of the measurement of this glial protein. J. Neurosci. Methods 169, 93–99.
Lester, D., 2002. Serum cholesterol levels and suicide: a meta-analysis. Suicide Life-threat. Behav. 32, 333–346.
Lopresti, A.L., Drummond, P.D., 2013. Obesity and psychiatric disorders: commonalities in dysregulated biological pathways and their implications for treatment. Prog. Neuro-psychopharmacol. Biol. Psychiatry 45, 92–99.
Mann, J.J., 2013. The serotonergic system in mood disorders and suicidal behaviour. Philos. Trans. R. Soc. Lond. B: Biol. Sci. 368, 20120537.
Marcinko, D., 2007. Antidepressants and suicidality: the basis of controversies. Psychiatr. Danub. 19, 238–240.
Marcinko, D., Marcinko, V., Karlovic, D., Marcinko, A., Martinac, M., Begic, D., Jakovljevic, M., 2008. Serum lipid levels and suicidality among male patients with schizoaffective disorder. Prog. Neuro-Psychopharmacol. Biol. Psychiatry 32, 193–196.
Marosi, K., Mattson, M.P., 2014. BDNF mediates adaptive brain and body responses to energetic challenges. Trends Endocrinol. Metab.: 25, 89–98.
McConway, M.G., Johnson, D., Kelly, A., Griffin, D., Smith, J., Wallace, A.M., 2000. Differences in circulating concentrations of total, free and bound leptin relate to gender and body composition in adult humans. (Pt 5). Ann. Clin. Biochem. 37, 717–723.
Miller, M., Pate, V., Swanson, S.A., Azrael, D., White, A., Sturmer, T., 2014. Antidepressant class, age, and the risk of deliberate self-harm: a propensity score matched cohort study of SSRI and SNRI users in the USA. CNS Drugs 28, 79–88.
Mukamal, K.J., Miller, M., 2009. BMI and risk factors for suicide: why is BMI inversely related to suicide? Obesity 17, 532–538.
Muldoon, M.F., Manuck, S.B., Mendelsohn, A.B., Kaplan, J.R., Belle, S.H., 2001. Cholesterol reduction and non-illness mortality: meta-analysis of randomised clinical trials. Br. Med. J. 322, 11–15.
Nousen, E.K., Franco, J.G., Sullivan, E.L., 2014. Unraveling the mechanisms responsible for the comorbidity between metabolic syndrome and mental health disorders. Neuroendocrinology.
Olie, E., Picot, M.C., Guillaume, S., Abbar, M., Courtet, P., 2011. Measurement of total serum cholesterol in the evaluation of suicidal risk. J. Affect. Disord. 133, 234–238.
Pandey, G.N., 2013. Biological basis of suicide and suicidal behavior. Bipolar Disord. 15, 524–541.
Pandey, G.N., Dwivedi, Y., Rizavi, H.S., Ren, X., Zhang, H., Pavuluri, M.N., 2010. Brain-derived neurotrophic factor gene and protein expression in pediatric and adult depressed subjects. Prog. Neuro-Psychopharmacol. Biol. Psychiatry 34, 645–651.
Papadopoulou, A., Markianos, M., Christodoulou, C., Lykouras, L., 2013. Plasma total cholesterol in psychiatric patients after a suicide attempt and in follow-up. J. Affect. Disord. 148, 440–443.
Paplos, K., Havaki-Kontaxaki, B., Ferentinos, P., Dasopoulou, M., Kontaxakis, V., 2012. Alexithymia, depression and serum lipids in suicide attempters. Psychiatriki=Psychiatriki 23, 149–152.
Park, S., Yi, K.K., Na, R., Lim, A., Hong, J.P., 2013. No association between serum cholesterol and death by suicide in patients with schizophrenia, bipolar affective disorder, or major depressive disorder. Behav. Brain Funct. 9, 45.
Persons, J.E., Coryell, W.H., Fiedorowicz, J.G., 2012. Cholesterol fractions, symptom burden, and suicide attempts in mood disorders. Psychiatry Res. 200, 1088–1089.
Pompili, M., Gonda, X., Serafini, G., Innamorati, M., Sher, L., Amore, M., Rihmer, Z., Girardi, P., 2013. Epidemiology of suicide in bipolar disorders: a systematic review of the literature. Bipolar Disord. 15, 457–490.
Poynder, E.G.T., Russell, R.J., 1926. The Cholesterol Content of the Cerebro-Spinal Fluid in Certain Mental Diseases. British Journal of Psychiatry 72, 62–66.
Pylvanen, V., Pakarinen, A., Knip, M., Isojarvi, J., 2006. Insulin-related metabolic changes during treatment with valproate in patients with epilepsy. Epilepsy Behav. 8, 643–648.
Rihmer, Z., Gonda, X., Torzsa, P., Kalabay, L., Akiskal, H.S., Eory, A., 2013. Affective temperament, history of suicide attempt and family history of suicide in general practice patients. J. Affect. Disord. 149, 350–354.
Rothermundt, M., Peters, M., Prehn, J.H., Arolt, V., 2003. S100B in brain damage and neurodegeneration. Microsc. Res. Tech. 60, 614–632.
Schroeter, M.L., Steiner, J., 2009. Elevated serum levels of the glial marker protein S100B are not specific for schizophrenia or mood disorders. Mol. Psychiatry 14, 235–237.
Schroeter, M.L., Steiner, J., Mueller, K., 2011. Glial pathology is modified by age in mood disorders – a systematic meta-analysis of serum S100B in vivo studies. J. Affect. Disord. 134, 32–38.
Steiner, J., Schiltz, K., Walter, M., Wunderlich, M.T., Keilhoff, G., Brisch, R., Bielau, H., Bernstein, H.G., Bogerts, B., Schroeter, M.L., Westphal, S., 2010a. S100B serum levels are closely correlated with body mass index: an important caveat in neuropsychiatric research. Psychoneuroendocrinology 35, 321–324.
Steiner, J., Walter, M., Guest, P., Myint, A.M., Schiltz, K., Panteli, B., Brauner, M., Bernstein, H.G., Gos, T., Herberth, M., Schroeter, M.L., Schwarz, M.J., Westphal, S., Bahn, S., Bogerts, B., 2010b. Elevated S100B levels in schizophrenia are associated with insulin resistance. Mol. Psychiatry 15, 3–4.
Tondo, L., Isacsson, G., Baldessarini, R., 2003. Suicidal behaviour in bipolar disorder: risk and prevention. CNS Drugs 17, 491–511.
Traskman, L., Asberg, M., Bertilsson, L., Sjostrand, L., 1981. Monoamine metabolites in CSF and suicidal behavior. Arch. Gen. Psychiatry 38, 631–636.
Troisi, A., 2009. Cholesterol in coronary heart disease and psychiatric disorders: same or opposite effects on morbidity risk? Neuroscience and Biobehav. Rev. 33, 125–132.
Tsai, S.Y., Kuo, C.J., Chen, C.C., Lee, H.C., 2002. Risk factors for completed suicide in bipolar disorder. J. Clin. Psychiatry 63, 469–476.
Vancampfort, D., Vansteelandt, K., Correll, C.U., Mitchell, A.J., De Herdt, A., Sienaert, P., Probst, M., De Hert, M., 2013. Metabolic syndrome and metabolic abnormalities in bipolar disorder: a meta-analysis of prevalence rates and moderators. Am. J. Psychiatry 170, 265–274.
Verrotti, A., la Torre, R., Trotta, D., Mohn, A., Chiarelli, F., 2009. Valproate-induced insulin resistance and obesity in children. Horm. Res. 71, 125–131.
Vuksan-Cusa, B., Marcinko, D., Nad, S., Jakovljevic, M., 2009. Differences in cholesterol and metabolic syndrome between bipolar disorder men with and without suicide attempts. Prog. Neuro-Psychopharmacol. Biol. Psychiatry 33, 109–112.
Walsh, M.T., Dinan, T.G., 2001. Selective serotonin reuptake inhibitors and violence: a review of the available evidence. Acta Psychiatr. Scand. 104, 84–91.
Westling, S., Ahren, B., Traskman-Bendz, L., Westrin, A., 2004. Low CSF leptin in female suicide attempters with major depression. J. Affect. Disord. 81, 41–48.
Weston, P.G., 1915. The cholesterol content of cerebrospinal fluid. J. Med. Res. 33, 119–126.
Zhang, J., 2011. Epidemiological link between low cholesterol and suicidality: a puzzle never finished. Nutr. Neurosci. 14, 268–287.
Zhang, Y., Smith, E.M., Baye, T.M., Eckert, J.V., Abraham, L.J., Moses, E.K., Kissebah, A.H., Martin, L.J., Olivier, M., 2010. Serotonin (5-HT) receptor 5A sequence variants affect human plasma triglyceride levels. Physiol. Genomics 42, 168–176.