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Low total cholesterol and low-density lipoprotein associated with aggression and hostility in recent suicide attempters

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ABSTRACT

Low cholesterol levels have been correlated with both suicidal and aggressive behavior in psychiatric patients. Few studies have investigated associations between serum lipid profiles and both aggressive state and trait. Fifty-two psychiatric medication-free inpatients were included in this study after a suicide attempt. Composite scores of "State Aggression" and "Trait Aggression" were calculated using relevant items from the Comprehensive Psychopathological Rating Scale and the Karolinska Scales of Personality. State Aggression was significantly and negatively correlated with total cholesterol (TC) and low-density lipoprotein (LDL). Trait Aggression was also significantly and negatively correlated with LDL, but not TC. There were small but significant mediation effects of severity of anxiety symptoms on the relationship between State Aggression and TC as well as LDL. In exploratory analyses we found that low cholesterol was also associated with personality traits of hostility. Moreover, low cholesterol was more robustly associated with personality trait items related to interpersonal aggression, as opposed to items related to irritability or more indirect, non-overt aggression. Our findings suggest that low cholesterol is associated with both state and trait aggression in suicide attempters. Future mechanistic studies are warranted to better understand the relationship between low cholesterol and high aggression in suicide attempters.

1. Introduction

More than three decades ago, when cholesterol-lowering therapies were introduced, concerns were expressed about potential side effects, including aggressive and suicidal behavior (Engelberg, 1992). Since then, both cohort studies and case reports have further supported associations between cholesterol-lowering medications and aggression and irritability, as well as depression and anxiety (Cham et al., 2016; Golomb et al., 2004; Olson et al., 2008). Consistent with this, low blood levels of cholesterol have been linked to violent (Golomb, 1998; Repo-Tiihonen et al., 2002) and aggressive (Virkkunen and Penttinen, 1984) behavior. These findings have been replicated across various clinical and non-clinical samples. For instance, low cholesterol has been associated with antisocial personality (Virkkunen, 1979, 1983), violent crime in the general population (Golomb et al., 2000), violent behavior in psychiatric inpatients (Mufti et al., 1998) and aggressive and disruptive behavior in school-age children (Zhang et al., 2005). Low cholesterol has also been associated with attempted suicide, completed suicide, and suicidal ideation (Lester, 2002; Wu et al., 2016), although there is significant heterogeneity across studies and also several negative reports (Pompili et al., 2012; Pompili et al., 2010). It has been suggested that aggressive symptoms and personality traits may be key features of certain "suicidal endophenotypes" (Courtet et al., 2011). A better understanding of the biology behind aggressive symptoms and personality traits in suicidal individuals could open up for improved preventive and therapeutic strategies. While some have found that cholesterol is lower in violent compared to non-violent suicide attempters (Alvarez et al., 2000), the relationship between total cholesterol (TC) as well as other lipid sub fractions and aggressive symptoms and personality traits in recent suicide attempters has not been well studied.

In the present study, we therefore analyzed serum lipid levels following a suicide attempt and related these to aggressive symptom state and personality traits. In exploratory analyses, we also correlated lipid sub fractions to individual symptom rating scale items and personality trait subscales related to aggression and hostility. Based on existing literature, we hypothesized that lower cholesterol would be associated with higher composite scores on trait and state aggression.

2. Methods

All subjects gave written informed consent to participate and the study was approved by Lund University Medical Ethics Committee.

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2.1. Subjects

Fifty-two psychiatric inpatients were included after a recent suicide attempt. Between the suicide attempt and the blood draw, patients underwent a washout period (13 ± 10 days) during which time they did not receive any antidepressants, antipsychotics, mood stabilizers or ADHD medications. No benzodiazepines were administered at least 9 h before blood sampling. Patients with any severe medical illness were excluded. None were prescribed cholesterol-lowering treatment. Nineteen (37%) had a history of a previous suicide attempt ("repeater") prior to the current attempt. Seventeen patients (33%) had made a violent suicide attempt and 35 (67%) a non-violent attempt. Drug-overdoses, single wrist cutting or a combination of both are considered non-violent suicide attempts, while all other methods (e.g. hanging, use of firearms or several deep knife cuts) are classified as violent (Traskman et al., 1981).

2.2. Psychiatric assessments

The Diagnostic and Statistical Manual of Mental Disorders, Third Edition-Revised (Spitzer et al., 1987) was used for diagnostic assessments. On the day of the blood sampling, participants were evaluated with the Comprehensive Psychopathological Rating Scale (CPRS) (Asberg et al., 1978). The CPRS symptom rating is based on a semi-structured interview where the psychiatrist asks open and general questions and the patient is encouraged to describe his/her condition in his/her own words. The reliability and validity of the CPRS have been demonstrated in previous studies (Asberg and Schalling, 1979; Jacobsson et al., 1978)

We extracted the Montgomery-Åsberg Depression Rating Scale (MADRS) (Montgomery and Asberg, 1979) and the Brief Scale for Anxiety (BSA) (Tyrer et al., 1984) from the CPRS in order to assess depressive and anxiety symptoms respectively.

The Karolinska Scales of Personality (KSP) (Gustavsson, 1997) is a self-report personality inventory that was used to assess aggressive personality traits. The KSP consists of 135 items grouped into 15 subscales, each item given as a statement with a four-point response format. A 5 factor model according to Schalling et al. (1987) was used.

2.3. Lipid profile assay

After the wash-out period and a night of fasting and bed rest, venous blood samples from antecubital vein were collected at 8 a.m. in tubes containing EDTA. The samples were immediately placed on ice and centrifuged at 4 °C and 3000 g for 10 min to separate plasma from cellular components within 1 h of collection. Details of the analysis of serum TC, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides (TG) levels have been described previously (Engstrom et al., 1995).

2.4. Statistics

All statistical analyses were conducted using SPSS statistical software version 21.0. Spearman's rho was used for correlations. Mann-Whitney *U* test was used for groupwise comparisons. All statistical analyses were tested for two-tailed level of significance. Alpha-level of significance was set at $p < 0.05$ and p-values < 0.1 were considered trends. Mediation analyses were carried out using the PROCESS tool for SPSS (Hayes, 2012). For indirect effects, bias-corrected and accelerated bootstrap confidence intervals (BCa CI) are given (Efron and Tibshirani, 1993).

In order to minimize the risk of Type 1 statistical error due to multiple comparisons (Babyak, 2004), we calculated a composite score of CPRS item 4 ("Hostile feelings, reported") and CPRS item 43 ("Hostility, observed") to assess "State Aggression". Based on the same rationale we summarized scores on the following KSP subscales to assess "Trait Aggression": "Verbal Aggression", "Indirect Aggression" and "Irritability". CPRS items 4 and 43 (State Aggression) and the items included in the KSP subscales comprising Trait Aggression are described in detail in Tables 1 and 2.

Table 1
Items 4 and 43, extracted from the Comprehensive Psychopathological Rating Scale. "State aggression" was calculated as a composite score of these items.

4. Hostile Feelings (reported)
Representing anger, hostility and aggressive feelings regardless of whether acted or not. Rate according to intensity, frequency and the amount of provocation tolerated. Inability to feel angry is scored zero on this item.
0 – Not easily angered
1 – Easily angered. Reports hostile feelings, which are easily dissipated
2 – Reacts to provocation with excessive anger or hostility
3 – Persistent anger, rage, or intense hatred which is difficult or impossible to control
43. Hostility (observed)
Representing irritability, angry looks, words, or actions. Rate by intensity and frequency, and the small amount of provocation that elicits the response and the time taken to quieten.
0 – No evident hostility
1 – Querulous, touchy and irritable on provocation. Occasional angry glances
2 – Pugnacious, quarrelsome, very aggressive gestures, but can be calmed down
3 – Threatening behavior or actual physical violence

In addition to primary analyses, testing the relationship between lipid levels and State and Trait Aggression, we also carried out exploratory analyses relating lipid levels to the individual CPRS items and KSP subscales described above, as well as the related KSP factor "Hostility" (comprising KSP subscales "Suspicion" and "Guilt") (Schalling et al., 1987).

3. Results

Clinical and demographic variables are summarized in Table 3. Age, BMI and gender were not associated with any of the dependent variables (State Aggression or Trait Aggression) (all $p > 0.1$). State and Trait Aggression did not correlate significantly (rho = 0.23, $p = 0.11$).

Table 2
Karolinska Scale of Personality (KSP) items included in subscales "Verbal Aggression", "Indirect Aggression" and "Irritability". We calculated "Trait aggression" as a composite of these subscales. Answers are on a four-point Likert scale from "Does not apply at all" (1) to "Applies completely" (4).

Verbal aggression items
Item # 15 - Even when my anger is aroused, I don't use "strong language" (inverse scoring)
Item # 95 – I can't help getting into arguments when people disagree with me
Item # 123 – If somebody annoys me, I am apt to tell him what I think of him
Item # 126 – When I get mad, I say nasty things
Item # 129 – When people yell at me, I yell back
Indirect aggression items
Item # 23 - When I am mad, I sometimes slam doors
Item # 31 – I can get mad enough to throw things
Item # 43 – Since the age of ten, I have never had a temper tantrum (inverse scoring)
Item # 87 – I sometimes spread gossip about people I don't like
Item # 132 – When I am angry, I sometimes sulk
Irritability items
Item # 3 – Sometimes people bother me just by being around
Item # 39 – I am irritated a great deal more than people are aware of
Item # 99 – I can't help being a little rude to people I don't like
Item # 111 – I am always patient with others (inverse scoring)
Item # 115 – I don't let a lot of unimportant things irritate me (inverse scoring)

Table 3
Clinical, demographic and biological characteristics of the sample.

Females/males	27/25
Repeaters/non-repeaters	19/33
Violent/non-violent attempts	17/35
Days between suicide attempt and blood draw	13.0 ± 10.0 (range 5–57)
Age	39.2 ± 14.0
BMI	24.3 ± 4.83
Principal Axis I diagnosis (% substance abuse co-morbidity)	
Mood disorders	29 (14)
Anxiety disorders	0 (0)
Psychotic disorders	1 (0)
Adjustment disorders	13 (0)
Substance use disorders	3 (100)
Other diagnoses	2 (0)
No diagnosis	4 (0)
Axis II comorbidity Yes/No[1]	28/22
Cluster A	3
Cluster B	14
Cluster C	4
Not Otherwise Specified	7
Serum cholesterol (nmol/l)	
TC	4.9 ± 1.1
LDL	3.1 ± 1.0
HDL	1.2 ± 0.3
TG	1.2 ± 0.6

Interval data are presented as mean ± SD.
Abbreviations: *BMI:* Body Mass Index*; TC*: Total cholesterol; *LDL*: Low-density lipoprotein; *HDL*: High-density lipoprotein; *TG*: Triglycerides. [1]Data regarding Axis II diagnosis is missing in two patients.

3.1. Primary analyses

State Aggression was significantly and negatively correlated with TC (rho = −0.42, $p = 0.002$) and LDL (rho = −0.46, $p = 0.001$), but not with TG (rho = −0.01, $p = 0.97$) or HDL (rho = 0.03, $p = 0.84$). Trait Aggression was significantly and negatively correlated with LDL (rho = −0.30, $p = 0.04$), but not with TC (rho = −0.13, $p = 0.38$), HDL (rho = 0.08, $p = 0.61$) or TG (rho = 0.01, $p = 0.96$). Correlations between State Aggression and TC and LDL as well as between Trait Aggression and LDL are shown in Fig. 1.

3.2. Mediation analyses

We wanted to test if severity of anxiety or depressive symptoms mediated the relationship between low TC and State Aggression as well as between low LDL and Trait and State aggression. BSA scores correlated negatively with LDL (rho = −0.31, $p = 0.03$) and TC (rho = −0.26, $p = 0.07$) and positively with State (rho = 0.35, $p = 0.01$) and Trait aggression (rho = 0.24, $p = 0.09$). MADRS did not correlate significantly with LDL, TC, State or Trait Aggression (all $p > 0.28$). Based on these bivariate analyses, we tested BSA scores as a potential mediator. We found significant mediation effects of BSA on the association between LDL and State Aggression (standardized beta = −0.09, 95% BCa CI [−0.28, −0.01]) and between TC and State Aggression (standardized beta = −0.09, 95% BCa CI [−0.25, −0.01]). There was no significant mediation effect of BSA scores on the association between LDL and Trait Aggression (standardized beta = −0.07, 95% BCa CI [−0.26, 0.03]).

3.3. Exploratory analyses

Exploratory analyses were performed for correlations between serum lipid levels and individual CPRS items and KSP subscales included in the primary analyses, as well as KSP factor Hostility (summarized in Table 4). Briefly, LDL showed robust and negative correlations with KSP subscale Verbal Aggression (rho = −0.38, $p < 0.01$), CPRS item 4 (Hostile feelings, reported) (rho = −0.44, $p < 0.01$), and KSP factor Hostility (rho = −0.32, $p < 0.05$) while TC showed a negative correlation with CPRS item 4 (Hostile feelings, reported) (rho = −0.38, $p < 0.01$).

Violent suicide attempters did not differ significantly from non-violent on any of the aggression measures or lipid levels (all $p > 0.05$). Repeaters and non-repeaters did not differ significantly on any of the aggression measures or lipid levels ($p > 0.35$).

4. Discussion

We here report negative associations between serum total cholesterol (TC) as well as low-density lipoprotein (LDL) with a compound variable of aggressive state, furthermore we report a negative association between LDL and a compound variable of aggressive personality traits, in 52 recent suicide attempters. Interestingly, severity of anxiety symptoms partly mediated the relationship between lipid levels and State Aggression, but not Trait Aggression. Moreover, in exploratory analyses, low LDL showed a more robust association with personality subscales related to interpersonal aggression, as opposed to items related to irritability or more indirect, non-overt aggression. Additionally, low LDL was associated with increased hostility, which has previously been found to, together with increased anxiety, predict violent behavior in psychiatric inpatients (Amore et al., 2008; Palmstierna et al., 1989).

In the present study we considered trait and state separately when relating severity of aggression to serum lipid levels. Previous studies of the State-Trait Anger Expression Inventory (Spielberger, 1988), have found a relative independence of the state and trait anger subscales (Fuqua et al., 1991), suggesting that it is meaningful to separate these two constructs in statistical analyses. This is in line with our finding of a small and non-significant correlation between our constructs of Trait and State Aggression. State here, refers to a temporary condition invoked by characteristics of the immediate situation, while trait refers to a more stable predisposition to react with an angry or aggressive response to a wider range of stimuli. Specific psychological traits, such as aggressiveness and impulsivity, have been associated with suicidality (Gvion and Apter, 2011). While some believe that impulsivity and aggression overlap to the extent that they should be considered together, as a single phenotype (Seroczynski et al., 1999), others argue they represent two distinct latent dimensions (Critchfield et al., 2004). Impulsivity has also been associated with serum lipid levels. Loas et al. found that, among psychiatric patients of whom approximately 1/3 had attempted suicide, HDL levels were positively correlated with impulsivity (Loas et al., 2016). Similarly, Pozzi et al. found, in a large sample of healthy young men, that impulsivity was associated with high HDL but also lower total cholesterol (Pozzi et al., 2003). Future studies should attempt to tease apart the effects of aggression and impulsivity on proposed biological markers of suicidal behavior.

In exploratory analyses, we found that LDL correlated more strongly with the KSP subscale Verbal Aggression than Indirect Aggression or Irritability. The Verbal Aggression subscale comprises items related to more overt or relational aggression, whereas the items included in the two other Trait Aggression subscales focus more on indirect, covert aggression. Overt and interpersonal aggressive behavior may be higher up on an “aggression continuum” than covert aggression, thus our findings are consistent with a dose-response relationship, with lower cholesterol being associated with more severe or frequent aggressive behaviors. Partly in line with such a dose-response relationship, Hillbrand et al. found that, in a cohort of male forensic inpatients, although the entire group had lower cholesterol levels compared to a control sample, those with the lowest levels engaged in more frequent aggressive behaviors than those with medium-high cortisol levels (Hillbrand et al., 1995).

Both psychological and biological mediators linking low cholesterol to aggression are currently unknown. In the present study, we found that severity of anxiety symptoms mediated the relationship between low LDL as well as TC and State aggression. Based on preclinical and

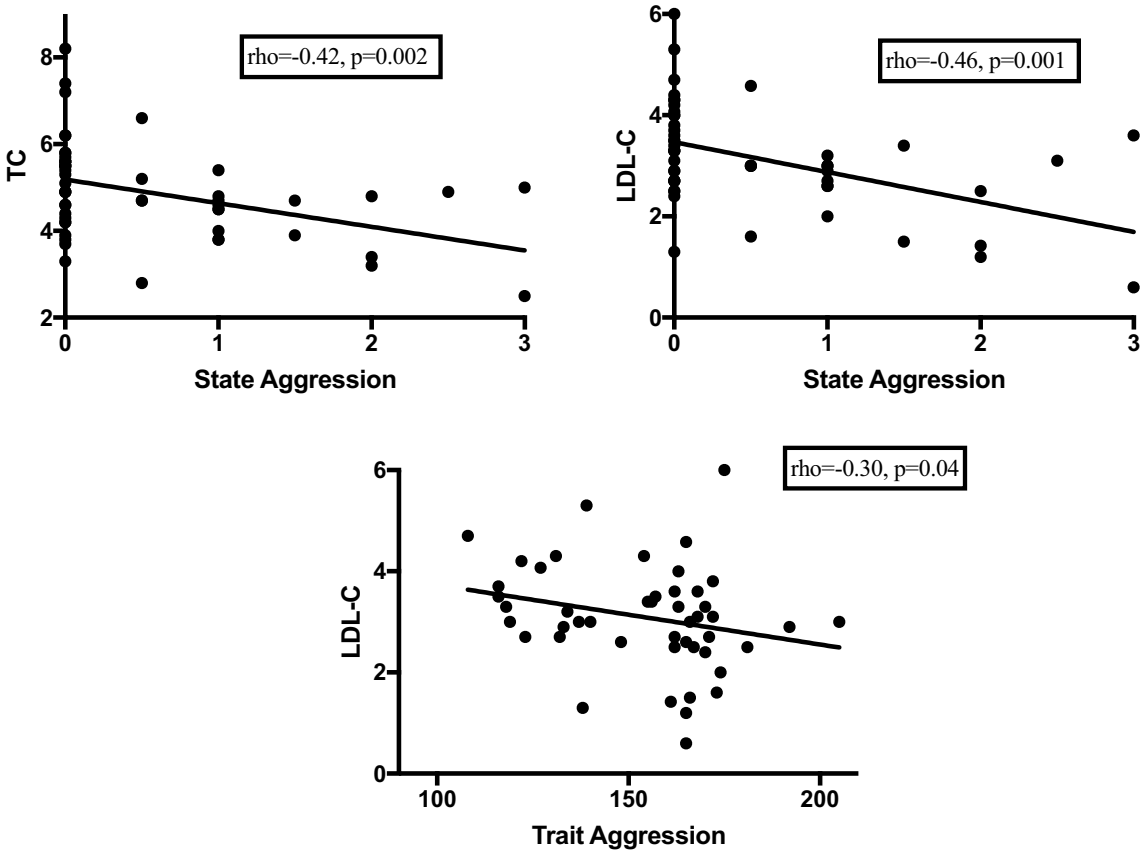

Fig. 1. Correlations (Spearman's rho) between State Aggression and TC as well as LDL, and between Trait Aggression and LDL.

Table 4
Correlations between lipid biomarkers, individual CPRS items and KSP subscales.

	LDL	HDL	TC	TG
KSP subscale Verbal Aggression	−0.38**	0.06	−0.21	−0.01
KSP subscale Indirect Aggression	−0.04	0.10	0.05	−0.08
KSP subscale Irritability	−0.26(*)	0.03	−0.12	0.06
CPRS item "Hostile feelings, reported"	−0.44**	0.09	−0.38**	−0.08
CPRS item "Hostility, observed"	−0.23	−0.12	−0.25(*)	0.30*
KSP factor Hostility	−0.32*	0.22	−0.15	−0.12

Spearman's rho correlation coefficients are given.
Abbreviations: *KSP*: Karolinska Scales of Personality; *CPRS*: Comprehensive Psychopathological Rating Scale; *LDL*: Low-density lipoprotein; *HDL*: High-density lipoprotein; *TC:* Total Cholesterol; *TG*: Triglycerides
** $p < 0.01$;
* $p < 0.05$;
(*) $p < 0.1$.

clinical data indicating that anxiety and aggression share common risk factors as well as underlying neurobiological mechanisms, it has been hypothesized that aggression and violence may, in some cases, develop via increased anxiety (Neumann et al., 2010). This is consistent with case reports linking statin treatment not only to the development of aggressive behavior, but also to anxiety (Cham et al., 2016). *In vitro* studies show that statin-induced cholesterol depletion leads to a decrease in specific ligand binding to the serotonin$_{1A}$ receptor, known for its role in anxiety and stress-related disorders (Shrivastava et al., 2010), highlighting the importance of cholesterol and other lipids in maintaining structure and function of membrane proteins and receptors. Indeed, much focus has been on the potential link between low cholesterol, serotonergic hypofunction and violence and aggression (Wallner and Machatschke, 2009). Serum cholesterol has been shown positively associated with cerebrospinal fluid (CSF) levels of serotonin metabolite 5-hydroxyindoleacetic acid (5-HIAA) in individuals who later completed suicide (Jokinen et al., 2010). Consistent with this, other studies have shown that violent suicide attempters display lower CSF 5-HIAA (Traskman et al., 1981) as well as lower cholesterol in serum (Alvarez et al., 2000) and in frontal cortex grey matter (Lalovic et al., 2007). Although we were not able to test any biological mediation models in our study, we hope that this will be the focus of future studies in the field, in order to improve our understanding of the mechanisms.

A major strength of the study was that all patients were free from psychotropics. This is important since such medications could influence both aggression and cholesterol levels (Noordam et al., 2015). Our study comes with some limitations, such as the relatively small sample size and we did not adjust for multiple comparisons. Also, we analysed only peripheral cholesterol, an important limitation given that cholesterol metabolism in the brain is independent from that in the blood due to the blood brain barrier (Zhang and Liu, 2015). It is also possible that low peripheral cholesterol is part of a larger metabolic pattern including also increased insulin sensitivity and hypoglycaemia affecting brain function and aggressive behavior (Golomb et al., 2002). Moreover, we assessed lipid levels within a cohort where illness and stress related malnutrition or malabsorption could have influenced our results, as seen with depression or substance abuse. We also note that physical injury or its medical treatment, sometimes associated with a suicide attempt, may affect serum lipid levels. Although we cannot completely rule out that this may have had an impact on our results, the non-significant relationship between lipid levels and the use of a violent method speaks against this. Moreover, a previous study found that cholesterol levels remain low in suicide attempters even several months after the suicide attempt (Papadopoulou et al., 2013), suggesting that this finding is independent of the potential physical injury associated

with the suicide attempt *per se*. Finally, while the main aim of our study was to investigate the association between aggression and lipid markers, lower ratings on the CPRS items used to capture State Aggression might have reflected hostile feelings rather than overt aggression. Future studies relating lipid markers to aggression should attempt to tease apart overt aggression from related emotions such as hostility and anger. While our approach of creating a CPRS-item compound for State Aggression has the advantage of limiting the number of statistical tests, this particular approach has not been validated in previous studies and our results should therefore be considered preliminary and in need of replication.

In conclusion, our results indicate negative associations between serum total cholesterol and State Aggression as well as between LDL and both State and Trait Aggression in recent suicide attempters. Future studies, with comparable constructs of aggression, are needed to further interpret these relations and examine any clinical implications.

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References

Alvarez, J.C., Cremniter, D., Gluck, N., Quintin, P., Leboyer, M., Berlin, I., Therond, P., Spreux-Varoquaux, O., 2000. Low serum cholesterol in violent but not in non-violent suicide attempters. Psychiatry Res. 95, 103–108.

Amore, M., Menchetti, M., Tonti, C., Scarlatti, F., Lundgren, E., Esposito, W., Berardi, D., 2008. Predictors of violent behavior among acute psychiatric patients: clinical study. Psychiatry Clin. Neurosci. 62, 247–255.

Asberg, M., Montgomery, S.A., Perris, C., Schalling, D., Sedvall, G., 1978. A comprehensive psychopathological rating scale. Acta Psychiatr. Scand. Suppl. 5–27.

Asberg, M., Schalling, D., 1979. Construction of a new psychiatric rating instrument, the Comprehensive Psychopathological Rating Scale (CPRS). Prog. Neuropsychopharmaco.l 3, 405–412.

Babyak, M.A., 2004. What you see may not be what you get: a brief, nontechnical introduction to overfitting in regression-type models. Psychosom. Med. 66, 411–421.

Cham, S., Koslik, H.J., Golomb, B.A., 2016. Mood, personality, and behavior changes during treatment with statins: a case series. Drug Saf. Case Rep. 3, 1.

Courtet, P., Gottesman, I.I., Jollant, F., Gould, T.D., 2011. The neuroscience of suicidal behaviors: what can we expect from endophenotype strategies? Transl. Psychiatry 1. https://doi.org/10.1038/tp.2011.6.

Critchfield, K.L., Levy, K.N., Clarkin, J.F., 2004. The relationship between impulsivity, aggression, and impulsive-aggression in borderline personality disorder: an empirical analysis of self-report measures. J. Pers. Disord. 18, 555–570.

Efron, B., Tibshirani, R., 1993. An Introduction to the Bootstrap. Chapman & Hall, New York.

Engelberg, H., 1992. Low serum cholesterol and suicide. Lancet 339, 727–729.

Engstrom, G., Alsen, M., Regnell, G., Traskman-Bendz, L., 1995. Serum lipids in suicide attempters. Suicide Life-Threat. Behav. 25, 393–400.

Fuqua, D.R., Leonard, E., Masters, M.A., Smith, R.J., Campbell, J.L., Fischer, P.C., 1991. A Structural-analysis of the state-trait anger expression inventory. Educ. Psychol. Meas. 51, 439–446.

Golomb, B.A., 1998. Cholesterol and violence: is there a connection? Ann. Intern. Med. 128, 478–487.

Golomb, B.A., Kane, T., Dimsdale, J.E., 2004. Severe irritability associated with statin cholesterol-lowering drugs. QJM 97, 229–235.

Golomb, B.A., Stattin, H., Mednick, S., 2000. Low cholesterol and violent crime. J. Psychiatr. Res. 34, 301–309.

Golomb, B.A., Tenkanen, L., Alikoski, T., Niskanen, T., Manninen, V., Huttunen, M., Mednick, S.A., 2002. Insulin sensitivity markers: predictors of accidents and suicides in Helsinki heart study screenees. J. Clin. Epidemiol. 55, 767–773.

Gustavsson, J.P., 1997. Stability and validity of self-reported personality traits: contributions to the evaluation of the Karolinska scales of personality, Stockholm.

Gvion, Y., Apter, A., 2011. Aggression, impulsivity, and suicide behavior: a review of the literature. Arch. Suicide Res. 15, 93–112.

Hayes, A.F., 2012. PROCESS: a versatile computational tool for observed variable mediation, moderation, and conditional process modeling.

Hillbrand, M., Spitz, R.T., Foster, H.G., 1995. Serum cholesterol and aggression in hospitalized male forensic patients. J. Behav. Med. 18, 33–43.

Jacobsson, L., von Knorring, L., Mattsson, B., Perris, C., Edenius, B., Kettner, B., Magnusson, K.E., Villemoes, P., 1978. The comprehesive psychopathological rating scale–CPRS–in patients with schizophrenic syndromes. Inter-rater reliability and in relation to Martens' S-scale. Acta Psychiatr. Scand. Suppl. 271, 39–44.

Jokinen, J., Nordstrom, A.L., Nordstrom, P., 2010. Cholesterol, CSF 5-HIAA, violence and intent in suicidal men. Psychiatry Res. 178, 217–219.

Lalovic, A., Levy, E., Luheshi, G., Canetti, L., Grenier, E., Sequeira, A., Turecki, G., 2007. Cholesterol content in brains of suicide completers. Int. J. Neuropsychopharmacol. 10, 159–166.

Lester, D., 2002. Serum cholesterol levels and suicide: a meta-analysis. Suicide Life Threat. Behav. 32, 333–346.

Loas, G., Dalleau, E., Lecointe, H., Yon, V., 2016. Relationships between anhedonia, alexithymia, impulsivity, suicidal ideation, recent suicide attempt, C-reactive protein and serum lipid levels among 122 inpatients with mood or anxious disorders. Psychiatry Res. 246, 296–302.

Montgomery, S.A., Asberg, M., 1979. A new depression scale designed to be sensitive to change. Br. J. Psychiatry 134, 382–389.

Mufti, R.M., Balon, R., Arfken, C.L., 1998. Low cholesterol and violence. Psychiatr Serv. 49, 221–224.

Neumann, I.D., Veenema, A.H., Beiderbeck, D.I., 2010. Aggression and anxiety: social context and neurobiological links. Front. Behav. Neurosci. 4, 12.

Noordam, R., Aarts, N., de Keyser, C.E., Hofman, A., Stricker, B.H., Visser, L.E., 2015. Antidepressants with a high serotonin reuptake transporter affinity and serum lipid levels in a population-based study in older adults. J. Psychopharmacol. 29, 1112–1118.

Olson, M.B., Kelsey, S.F., Matthews, K.A., Bairey Merz, C.N., Eteiba, W., McGorray, S.P., Cornell, C.E., Vido, D.A., Muldoon, M.F., 2008. Lipid-lowering medication use and aggression scores in women: a report from the NHLBI-sponsored WISE study. J. Womens Health (Larchmt.) 17, 187–194.

Palmstierna, T., Lassenius, R., Wistedt, B., 1989. Evaluation of the Brief Psychopathological Rating Scale in relation to aggressive behavior by acute involuntarily admitted patients. Acta Psychiatr. Scand. 79, 313–316.

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.

Pompili, M., Gibiino, S., Innamorati, M., Serafini, G., Del Casale, A., De Risio, L., Palermo, M., Montebovi, F., Campi, S., De Luca, V., Sher, L., Tatarelli, R., Biondi, M., Duval, F., Serretti, A., Girardi, P., 2012. Prolactin and thyroid hormone levels are associated with suicide attempts in psychiatric patients. Psychiatry Res. 200, 389–394.

Pompili, M., Innamorati, M., Lester, D., Girardi, P., Tatarelli, R., 2010. Nearly lethal resuscitated suicide attempters have no low serum levels of cholesterol and triglycerides. Psychol. Rep. 106, 785–790.

Pozzi, F., Troisi, A., Cerilli, M., Autore, A.M., Lo Castro, C., Ribatti, D., Frajese, G., 2003. Serum cholesterol and impulsivity in a large sample of healthy young men. Psychiatry Res. 120, 239–245.

Repo-Tiihonen, E., Halonen, P., Tiihonen, J., Virkkunen, M., 2002. Total serum cholesterol level, violent criminal offences, suicidal behavior, mortality and the appearance of conduct disorder in Finnish male criminal offenders with antisocial personality disorder. Eur. Arch. Psychiatry Clin. Neurosci. 252, 8–11.

Schalling, D., Asberg, M., Edman, G., Oreland, L., 1987. Markers for vulnerability to psychopathology: temperament traits associated with platelet MAO activity. Acta Psychiatrica Scandinavica 76, 172–182.

Seroczynski, A.D., Bergeman, C.S., Coccaro, E.F., 1999. Etiology of the impulsivity/aggression relationship: genes or environment? Psychiatry Res. 86, 41–57.

Shrivastava, S., Pucadyil, T.J., Paila, Y.D., Ganguly, S., Chattopadhyay, A., 2010. Chronic cholesterol depletion using statin impairs the function and dynamics of human serotonin(1A) receptors. Biochemistry 49, 5426–5435.

Spielberger, C.D., 1988. Manual For the State-Trait Anger Expression Inventory. Psychological Assessment Resources, Odessa, FL.

Spitzer, R.L., Williams, J.B.W., American psychiatric association, 1987. Diagnostic and Statistical Manual of Mental disorders: DSM-III-R, 3. ed. The Assoc.; Press Syndicate of the Univ., Washington Cambridge.

Traskman, L., Asberg, M., Bertilsson, L., Sjostrand, L., 1981. Monoamine metabolites in CSF and suicidal behavior. Arch. Gen. Psychiatry 38, 631–636.

Tyrer, P., Owen, R.T., Cicchetti, D.V., 1984. The brief scale for anxiety: a subdivision of the comprehensive psychopathological rating scale. J. Neurol. Neurosurg. Psychiatry 47, 970–975.

Virkkunen, M., 1979. Serum cholesterol in antisocial personality. Neuropsychobiology 5, 27–30.

Virkkunen, M., 1983. Serum cholesterol levels in homicidal offenders. A low cholesterol level is connected with a habitually violent tendency under the influence of alcohol. Neuropsychobiology 10, 65–69.

Virkkunen, M., Penttinen, H., 1984. Serum cholesterol in aggressive conduct disorder: a preliminary study. Biological. Psychiatry 19, 435–439.

Wallner, B., Machatschke, I.H., 2009. The evolution of violence in men: the function of central cholesterol and serotonin. Prog. Neuropsychopharmacol. Biol. Psychiatry. 33, 391–397.

Wu, S., Ding, Y., Wu, F., Xie, G., Hou, J., Mao, P., 2016. Serum lipid levels and suicidality: a meta-analysis of 65 epidemiological studies. J. Psychiatry Neurosci. 41, 56–69.

Zhang, J., Liu, Q., 2015. Cholesterol metabolism and homeostasis in the brain. Protein Cell 6, 254–264.

Zhang, J., Muldoon, M.F., McKeown, R.E., Cuffe, S.P., 2005. Association of serum cholesterol and history of school suspension among school-age children and adolescents in the United States. Am. J. Epidemiol. 161, 691–699.