

## The Importance of Cholesterol in Psychopathology: A Review of Recent Contributions

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### ABSTRACT

**Aim:** The aim of this study was to describe systematically recent studies that show the importance of cholesterol in psychopathology. **Methods:** This study was a review. The following databases were searched for relevant published articles on human studies: MEDLINE, Web of Science, EBSCOhost Academic Search Complete, and Psychology and Behavioral Sciences Collection (papers from January 2012 to March 2016). **Results:** Eighteen recent papers were selected, and thematic dimensions showing correlations between cholesterol and behavioral and psychopathological variables were depression, suicide, personality, and aggression. **Conclusion:** This paper demonstrates that recent research corroborates the idea that cholesterol plays an important role in governing behavior and psychopathology in humans. Deepening the studies in this field could be a promising avenue for future research, with implications for treating people with behavior or mental health problems.

**Key words:** Cholesterol, human behavior, psychopathology

### INTRODUCTION

Necessary for the healthy functioning of cells, cholesterol is a soft, fat-like, waxy substance that is moved around in the bloodstream by lipoproteins. Elevated levels of low-density lipoprotein (LDL or “bad” cholesterol) in the blood contribute to the formation of plaque in the arteries, which make them less flexible and increase the risk of blood clots. In contrast, high-density lipoprotein (“good” cholesterol) carries cholesterol away from arteries back to the liver where it is processed out of the body. Finally, triglycerides, a form of fat made by the body, are typically considered

the third component of lipoprotein profiles; as with LDL, elevated levels of triglycerides contribute to the development of atherosclerosis.<sup>[1]</sup>

Abnormal or pathological serum lipid levels have been identified as important risk factors for coronary heart disease.<sup>[2,3]</sup> Substantial individual variations in lipid levels suggest that psychological factors might affect these levels. Therefore, a considerable amount of effort has been devoted to understanding the factors, from the cellular to the psychological, that contribute

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to high (and low) levels of cholesterol. Interest in the interface between psychological variables and cholesterol levels has focused mainly on the context of mood and anxiety disorders<sup>[4]</sup> and suicide.<sup>[5]</sup>

A body of research spanning several decades has identified a significant association between cholesterol levels and serious behavioral problems, wherein individuals with lower overall levels of cholesterol display significantly higher levels of antisocial and violent criminal behavior than their counterparts.<sup>[6]</sup> Along the same lines, several studies have shown that individuals with lower levels of cholesterol are more likely to score higher on measures of aggression and anger<sup>[7]</sup> and have a higher risk of displaying impulsive and violent suicidal behaviors<sup>[8]</sup> to name just a few.

Although there is strong evidence that cholesterol is involved in the occurrence of psychological symptoms, it must be remembered that cholesterol itself does not directly cause behaviors but may induce chemical changes, affecting the likelihood of certain behavioral outcomes as a result of modulation of particular neural pathways. Furthermore, cholesterol is only one of a myriad of influences on human behavior such as cognition and environmental circumstances.

Scientists are limited in that they cannot perform experimental procedures in humans. As such, we should remember that correlation does not necessarily indicate causation, and in many studies, such assumptions have been made. Before experiments can be done to investigate these correlations, we need to be sure that the types of behavioral variables we are looking into are cholesterol-dependent and eliminate other factors that could confound the results. Therefore, the purpose of this review is to describe systematically recent studies that show the importance of cholesterol in human behavior and psychopathology.

## METHODS

### Search strategies

I searched MEDLINE, Web of Science, EBSCOhost Academic Search Complete, and Psychology and Behavioral Sciences Collection (from January 2010 to March 2016). As a search criterion, I used the following: cholesterol, serum lipids, behavior, mental health, psychopathology, aggression, suicide, and depression. No language restriction was applied.

### Selection criteria

I limited my search to full text, published articles, and human studies from the past 6 years. Abstracts, case reports, and editorials were excluded. I also retrieved relevant references of included studies for

my search. All studies that investigated the association between cholesterol levels and human behavior and psychopathology were considered.

### Qualitative data synthesis

The primary analysis was conducted by organizing obtained research by thematic dimension: authorship, country, number of human participants, short description of methods, and main results.

## RESULTS

Table 1 illustrates the systematic review process of identifying and describing relevant studies that demonstrate associations between cholesterol and behavioral and psychopathological variables. This section reports on 18 recent papers, and thematic dimensions showing correlations between these variables were depression, suicide, personality, and aggression.

## DISCUSSION

Cholesterol has long been associated with various behaviors and mental health problems. This review highlights the latest key issues in lipidology and behavior and then provides a brief summary of the research into various associations between cholesterol and personality and psychopathology. Some evidence in support of the assumption is found for the following indicators: Depression, suicide, personality, and aggression; however, some critical issues regarding cholesterol-behavior/psychopathology relationships are also raised. Lipoproteins do not directly change behavior; they influence the expression of behavior within appropriate environmental/social contexts. When studying human behaviors, identifying which environmental/social contexts might be important remains a significant challenge to researchers trying to identify cholesterol-behavior/psychopathology relationships.

Research questions concerning the activational effects of cholesterol can now be more easily addressed because it is simple and relatively cheap to measure levels of circulating cholesterol and compare levels of observed behaviors and/or psychopathology. Bioavailable cholesterol can be measured in blood, and such testing can be conducted outside of a laboratory setting in various groups (e.g., patients, athletes) with basic training and equipment.

As it was observed from this review, different research paradigms can be adopted. The most commonly used was correlational – associating the level of cholesterol with a certain behavioral characteristic.

**Table 1: List of 18 references from 2012 to 2016 associating cholesterol levels with behavioral and psychopathological variables**

Thematic dimension	Main topic	Authorship	Country	Number of human participants	Short description of methods	Main results
Depression	Depression	Schwartz <i>et al.</i> <sup>[9]</sup>	USA	379 volunteers	Depressive symptoms were measured using the CES-D scale. Fasting blood samples were collected to determine each respondent's TGs, HDL, and TC levels. LDL-C levels were determined using the Friedewald formula	HDL-C levels were negatively and significantly associated with depressive symptoms
	Depression	Teofilo <i>et al.</i> <sup>[10]</sup>	Brazil	238 pregnant women	Depressive symptoms were assessed using the EPDS. Serum concentrations (mg/dL) of TGs, TC, and LDL-C; HDL-C were the main exposures	HDL-C concentrations were inversely associated with PDS scores
	Depression	Patra <i>et al.</i> <sup>[11]</sup>	India	30 depressive patients and 30 healthy matched control subjects	TC, LDL and HDL-C, and TG levels of both patient and control group	The serum TC and LDL-C levels were found to be significantly lower in study group than that of control group
	Major depressive disorder	Lehto <i>et al.</i> <sup>[12]</sup>	Finland	Depressed patients ( $n=88$ ) and a group of healthy controls ( $n=88$ )	SCID and depressed participants reported the duration of their symptoms The serum levels of TC, HDL-C, LDL-C, TG, and non-HDL, and the ratios of LDL-C/HDL and TC/HDL-C were assessed	MDD subjects with a long symptom duration (3 years) had lower levels of HDL-C compared with healthy controls or MDD subjects with a symptom duration < 3 years
	Depressive symptoms	Fang <i>et al.</i> <sup>[13]</sup>	USA	Healthy young adult women ( $n=225$ )	Depressive symptoms were assessed with the 20-item CES-D scale, and a fasting blood sample was obtained for serum lipid levels, including TC, HDL-C and LDL-C	Results indicated a modest negative association between depressive symptoms and LDL-C levels
	Depressive Symptoms	Liang <i>et al.</i> <sup>[14]</sup>	China	1529 participants (age $\geq 60$ years)	Data were collected through an interview, clinical examinations, and laboratory tests	Elevated depressive symptoms were associated with lipid profile characterized by high cholesterol, high TGs, low HDL-C, high LDL-C, and dyslipidemia
Suicide	Recent suicide attempt	Baek <i>et al.</i> <sup>[15]</sup>	South Korea	555 subjects with major depressive disorder	MINI with the suicidality module. At the evaluation visit, serum lipid profiles were measured including TC, TG, LDL, HDL, and VLDL	Low serum TG, high HDL, and VLDL levels were associated with recent suicide attempt or recent suicide status
	Suicide ideation	Marcinko <i>et al.</i> <sup>[8]</sup>	Croatia	Male suicidal patients ( $n=20$ ) with BPD and male nonsuicidal patients ( $n=20$ ) with BPD	Blood samples were collected from all subjects at 8.00 am after an overnight fasting, and serum concentration of cholesterol was determined enzymatically, immediately after the blood collection. The BPRS14 was administered to assess a broad range of psychopathology	Results showed that serum cholesterol levels did not differ significantly between suicidal and nonsuicidal BPD patients and healthy controls
	Suicide attempt	Plana <i>et al.</i> <sup>[16]</sup>	Spain	66 psychiatric patients and 54 patients with no history of suicide attempts	Levels of cholesterol were obtained from the blood samples collected upon admission, after overnight fasting. Control subjects (nonsuicide attempts) were paired with case subjects (suicide attempts) according to psychiatric diagnosis, age, and gender	Cholesterol levels were significantly lower in attempted suicide patients than in controls, supporting the hypothesis that lower cholesterol levels might be associated with suicidal behavior in patients with similar acute phase of their disorder

Contd...

**Table 1: Contd...**

Thematic dimension	Main topic	Authorship	Country	Number of human participants	Short description of methods	Main results
Personality	Five-Factor Model	Sutin <i>et al.</i> <sup>[4]</sup>	Italy	Community-based sample ( $n=5532$ )	Cholesterol and TG levels assessed and completed a comprehensive personality questionnaire, the NEO-PI-R	Low conscientiousness and traits related to impulsivity were associated with lower HDL-C and higher TGs
	Five-Factor Model	Schwartz <i>et al.</i> <sup>[9]</sup>	USA	379 volunteers	Fasting blood samples were collected to determine each respondent's TGs, HDL, and TC levels. LDL cholesterol levels were determined using the Friedewald formula	HDL-C levels had a marginally significant effect on neuroticism
	Five-Factor Model	Armon <sup>[2]</sup>	Israel	Individuals who underwent a health examination at two points of time, T1 ( $n=3835$ ) and T2 ( $n=2283$ ), about 2.5 years apart	Personality was assessed by the Five-Factor Model. Health, socioeconomic status and healthy lifestyle behaviors (smoking intensity, physical activity, and body weight) were controlled	Personality factors of neuroticism, extraversion and conscientiousness were each significantly associated with HDL-C and triglyceride, both concurrently and over time
	Five-Factor Model	Pereira <i>et al.</i> <sup>[17]</sup>	Portugal	A convenience sample of 52 individuals	The NEO-PI-R (Portuguese version). Regarding the serum determinations, the following parameters were quantified: TC, LDL, HDL, TGs and glucose	Results showed that there was a negative correlation between extroversion and total levels of cholesterol, as well as LDL; a negative correlation between neuroticism and LDL
	Impulsivity	Troisi <sup>[18]</sup>	Italy	301 psychiatric patients	BIS-11 and the POMS. On the same day of psychometric assessment, blood samples were analyzed for TC and HDL-C	Lower TC levels were associated with increased attentional impulsivity
	Personality traits	Roh <i>et al.</i> <sup>[19]</sup>	South Korea	1701 young Korean women	Lipid levels, including TC, HDL-C, and TG, were measured in all subjects after an overnight fast. Personality traits were measured using NEO-PI-R for the Five-Factor Model of personality	Angry hostility, self-consciousness, vulnerability to stress, activity, and straightforwardness were associated with HDL-C levels. Activity, positive emotion, esthetics, actions, and deliberation were associated with TG
	Personality traits	Hengartner <i>et al.</i> <sup>[20]</sup>	Switzerland	171 participants	A short form of the Big Five Inventory was completed. TC levels and LDL-C were measured with an enzymatic colorimetric assay analysis using a kit from Roche	A notable association was found between neuroticism and TC
Aggression	Anger expression	Schwartz <i>et al.</i> <sup>[9]</sup>	USA	379 volunteers	A 22-item self-control measure was constructed using responses from the Wave2 self-administered questionnaire. Fasting blood samples were collected to determine each respondent's TGs, HDL, and TC levels. LDL-C levels were determined using the Friedewald formula	HDL-C levels had a nonsignificant effect on both anger expression and self-control
	Violent behavior	Asellus <i>et al.</i> <sup>[5]</sup>	Sweden	81 suicide attempters	Blood samples were collected in a controlled setting from the antecubital vein after the participants had been fasting overnight. KIVS was used	In patients with serum cholesterol below median, the correlation between exposure to violence as a child and used adult violence was significant, while in patients with serum cholesterol above median, the correlation between exposure to violence as a child and expressed violent behavior as an adult was not significant

CES-D – Center for Epidemiological Studies Depression; HDL-C – High-density lipoprotein cholesterol; LDL-C – Low-density lipoprotein cholesterol; EPDS – Edinburgh Postnatal Depression Scale; TC – Total cholesterol; SCID – Structured Clinical Interview for DSM-IV; TGs – Triglycerides; MINI – Mini International Neuropsychiatric Interview; VLDL – Very low-density lipoprotein; BPRS – Brief Psychiatric Rating Scale; BIS-11 – Barratt Impulsiveness Scale-Version 11; POMS – Profile of Mood States; KIVS – Karolinska Interpersonal Violence Scale; BPD – Borderline personality disorder; MDD – Major depressive disorder; NEO-PI-R – Revised NEO Personality Inventory

More experimental designs should also be adopted, whereby cholesterol levels can be (a) compared between different groups, (b) compared within the same individuals in different situations, or (c) directly manipulated via cholesterol therapy.

This paper demonstrates that recent research corroborates the idea that cholesterol plays an important role in governing behavior and psychopathology in humans. Hence, can variations in circulating cholesterol activate changes in aspects of behavior and mental health? This is a pertinent question in light of the likelihood in the future of a substantial uptake of cholesterol.

## CONCLUSION

Deepening the studies in this field could be a promising avenue for future research, with implications for treating people with behavior or mental health problems. It is clear that an enormous amount of work remains to completely understand the relationships between cholesterol and human behavior. Traditional research questions have focused on the role of cholesterol in behaviors, but it is becoming increasingly aware that this is not a simple linear relationship; the social context and intrapsychic factors might also play a significant role in determining cholesterol levels. This “chicken and egg” problem remains a key issue, and there are many questions that remain to be addressed and many variables that need to be considered. We are currently in an exciting period where cholesterol analyses are becoming cheaper and easier to conduct so that more endocrinology and behavioral scientists can begin to get involved in attempting to address these important questions.

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### Conflicts of interest

There are no conflicts of interest.

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