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Article

Genetic and Environmental Influences on Blood Pressure and Serum Lipids Across Age-Groups

Ke Miao[1,2], Yutong Wang[1,2], Weihua Cao[1,2], Jun Lv[1,2], Canqing Yu[1,2], Tao Huang[1,2], Dianjianyi Sun[1,2], Chunxiao Liao[1,2], Yuanjie Pang[1,2], Runhua Hu[1,2], Zengchang Pang[3], Min Yu[4], Hua Wang[5], Xianping Wu[6], Yu Liu[7], Wenjing Gao[1,2] and Liming Li[1,2]

[1]Department of Epidemiology and Biostatistics, School of Public Health, Peking University, Beijing, China, [2]Key Laboratory of Epidemiology of Major Diseases (Peking University), Ministry of Education, Beijing, China, [3]Qingdao Center for Disease Control and Prevention, Qingdao, China, [4]Zhejiang Center for Disease Control and Prevention, Hangzhou, China, [5]Jiangsu Center for Disease Control and Prevention, Nanjing, China, [6]Sichuan Center for Disease Control and Prevention, Chengdu, China and [7]Heilongjiang Center for Disease Control and Prevention, Harbin, China

Abstract

Aging plays a crucial role in the mechanisms of the impacts of genetic and environmental factors on blood pressure and serum lipids. However, to our knowledge, how the influence of genetic and environmental factors on the correlation between blood pressure and serum lipids changes with age remains to be determined. In this study, data from the Chinese National Twin Registry (CNTR) were used. Resting blood pressure, including systolic and diastolic blood pressure (SBP and DBP), and fasting serum lipids, including total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and triglycerides (TGs) were measured in 2378 participants (1189 twin pairs). Univariate and bivariate structural equation models examined the genetic and environmental influences on blood pressure and serum lipids among three age groups. All phenotypes showed moderate to high heritability (0.37–0.59) and moderate unique environmental variance (0.30–0.44). The heritability of all phenotypes showed a decreasing trend with age. Among all phenotypes, SBP and DBP showed a significant monotonic decreasing trend. For phenotype-phenotype pairs, the phenotypic correlation (Rph) of each pair ranged from −0.04 to 0.23, and the additive genetic correlation (Ra) ranged from 0.00 to 0.36. For TC&SBP, TC&DBP, TG&SBP and TGs&DBP, both the Rph and Ra declined with age, and the Ra difference between the young group and the older adult group is statistically significant ($p < .05$). The unique environmental correlation (Re) of each pair did not follow any pattern with age and remained relatively stable with age. In summary, we observed that the heritability of blood pressure was affected by age. Moreover, blood pressure and serum lipids shared common genetic backgrounds, and age had an impact on the phenotypic correlation and genetic correlations.

Keywords: Heritability; blood pressure; serum lipids; genetic; twin study

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Hypertension, especially high systolic blood pressure (SBP), is widely recognized as a risk factor for cardiovascular disease, with 10.8 million deaths worldwide in 2019 (GBD 2019 Risk Factors Collaborators, 2020). Dyslipidemia is defined as abnormal serum lipid levels, including low levels of high-density lipoprotein cholesterol (HDL-C) and elevated levels of serum total cholesterol (TC), triglycerides (TGs) and low-density lipoprotein cholesterol (LDL-C).

Both hypertension and dyslipidemia are risk factors for damage to the vessel wall damage. Dyslipidemia directly affects blood pressure (Ruixing et al., 2009). First, dyslipidemia reduces the elasticity of the blood vessel wall and causes an increase in SBP. It causes excessive lipid molecules to stimulate the elastic components of the arterial wall, resulting in the production of large amounts of extracellular matrix and inflammatory mediators, such as interleukins and chemokines. These inflammatory mediators and lipids eventually form atheromatous plaques locally with platelets in the arterial wall. Finally, in terms of hemodynamics, the increase in lipid molecules in the blood will increase the viscosity of the blood, slow down the flow of blood in the blood vessels, and make it difficult for peripheral blood to flow back into the heart, resulting in an increase in both SBP and diastolic blood pressure (DBP). However, no definitive evidence has indicated that hypertension can directly cause dyslipidemia (Hurtubise et al., 2016). The elasticity of the blood vessel wall in middle-aged and older adults is weakened, SBP is prone to increase. And the low metabolic rate of middle-aged and elderly people may lead to abnormality of hepatic lipid metabolism, resulting in dyslipidemia. In addition, some hypertension drugs, such as thiazide diuretics and β-blockers, have adverse effects on lipid metabolism, which may further promote the occurrence of dyslipidemia (Deshmukh et al., 2008).

Both blood pressure and serum lipids are affected by genetic and environmental factors. In general, blood pressure increases

Corresponding author: Wenjing Gao; Email: pkuepigwj@126.com; Liming Li; Email: lmlee@vip.163.com

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with age. At the same time, the pattern of serum lipids changes dramatically with age, especially in the following four life periods: infancy, adolescence, female menopause, and old age (Snieder et al., 1999). These specific age trends indicate that the effect of genetic and environmental factors changes with age (Snieder et al., 1999). In addition, evidence from epidemiological studies has found a positive correlation between blood pressure and serum lipids (Lepira et al., 2005; Tang et al., 2022; Zhang et al., 2007), and the correlation also decreases with age (Bønaa & Thelle, 1991). In previous twin studies, it was found that there was a moderate or low genetic correlation between blood pressure and serum lipids (Benyamin et al., 2007; Duan et al., 2011; Panizzon et al., 2015; Zhang et al., 2009). However, most previous studies did not consider the effect of age on genetic correlation, and it is unclear how the influence of genetic and environmental factors on the correlation between blood pressure and serum lipids changes with age.

Therefore, we aimed to quantify genetic and environmental contributions to blood pressure and serum lipids. The degree to which the genetic and environmental contributions are shared for blood pressure and serum lipids was explored using twins in the Chinese National Twin Registry (CNTR). Furthermore, we studied the changes in different age groups.

Method

Study Population

The participants were from the CNTR, the largest twin registration system in China, which has been detailed elsewhere (Gao et al., 2019). The study data from thematic surveys of the CNTR between 2013 and 2017 included a questionnaire survey (demographic information and medication history), physical examination (blood pressure) and blood sampling (biochemical tests). This study received ethical approval from the Biomedical Ethics Committee at Peking University, Beijing, China. All participants provided written informed consent.

Twins who are 18 years old and over were included. Exclusion standards were as follows: (1) twins with missing key variables, such as age and zygosity; (2) twin pairs who were raised separately for more than one year before the age of 5; (3) opposite-sex twin pairs; (4) twins who had been taking hypolipidemic agents in the previous month; and (5) pregnant women and their cotwins. Ultimately, this study divided 2378 participants (1189 twin pairs) into three age groups based on age: young ($\leq$ 5 years old), middle-aged (46 to 55 years old), and older adults (>55 years old); see Figure 1.

Measurements of Blood Pressure

Blood pressure of the right arm was measured twice in a sitting position using an electronic sphygmomanometer after at least 5 minutes of rest. A third blood pressure measurement was taken if the difference between the first two blood pressures was greater than 10 mmHg. The average of the two measurements with the closest values was taken as the mean blood pressure. Blood pressure needed to be adjusted if antihypertensive drugs were taken, and 10 mmHg and 15 mmHg were added to the measured DBP and SBP respectively (Tobin et al., 2005).

Measurements of Serum Lipids

The peripheral blood was collected after at least 12 hours of fasting. The blood samples were stored in a portable blood refrigerator box at 4 °C. Then, a desktop frozen centrifugal machine was used to separate the serum and blood cells for 20 minutes at 2500 rpm. Separated serum was used to detect serum lipids according to the same testing process and standards.

Twin Zygosity

The CNTR used the 'Peas in the Pod Questionnaire' (PPQ) to judge the zygosity of twins, which asks about the degree of similarity of twins. Compared with genetic data, the accuracy of this method can reach 87% (Wang et al., 2015).

Data Analysis

All data analyses were conducted using R (4.0.2) software, and structural equation models (SEM) were performed using the OpenMx (2.18.1) package of R. For serum TC, TG, HDL-C and LDL-C showing a nonnormal distribution, a natural logarithm transformation was carried out. For each trait, individuals with blood pressure or serum lipid value that exceeded ±3 standard deviation (*SD*) from the mean and their co-twins were removed. The models were adjusted for age and sex; $p < .05$ indicated statistical significance.

Structural Equation Modeling

The SEM was utilized to evaluate the genetic and environmental factors influencing a trait. This approach partitions the variation into four components: additive genetic component (A), unique environmental component (E), dominant genetic component (D) and common environmental component (C). Since only twins reared together are included, the effects of C or D cannot be estimated simultaneously in the same model due to the confounding of these components (Rijsdijk & Sham, 2002). As it is dependent on the pattern of correlations between MZ and DZ twins, an ACE or ADE model was chosen. C is calculated when the MZ correlation is less than twice the DZ correlation, while D is calculated if the MZ correlation is more than the DZ correlation. Then A, C or D were gradually dropped to fit the submodels. Using likelihood ratio tests, we compared ACE or ADE models and the submodels with the saturated models. The criteria for the suitable model was the $p > .05$ and the lowest Akaike information criterion (AIC) value.

Univariate Structural Equation Modeling

We constructed the univariate SEM for blood pressure and serum lipids in the three age groups. The proportion of the variance of A in the overall variation was defined as heritability.

We fitted homogeneity models among the three age groups to examine whether the variance components could be equal. A likelihood ratio test was performed between the homogeneity models and the suitable models in the total population and if $p < .05$, we could judge that the homogeneity model was unacceptable. Based on the homogeneity models, heritability estimates in the three age groups and the 95% confidence intervals (CI), we observed whether heritability changed with age.

Bivariate Structural Equation Modeling

Based on the suitable models of univariate SEM, bivariate SEM was fitted in the three age groups. The bivariate Cholesky model was used to calculate the genetic correlation coefficient (Ra) and

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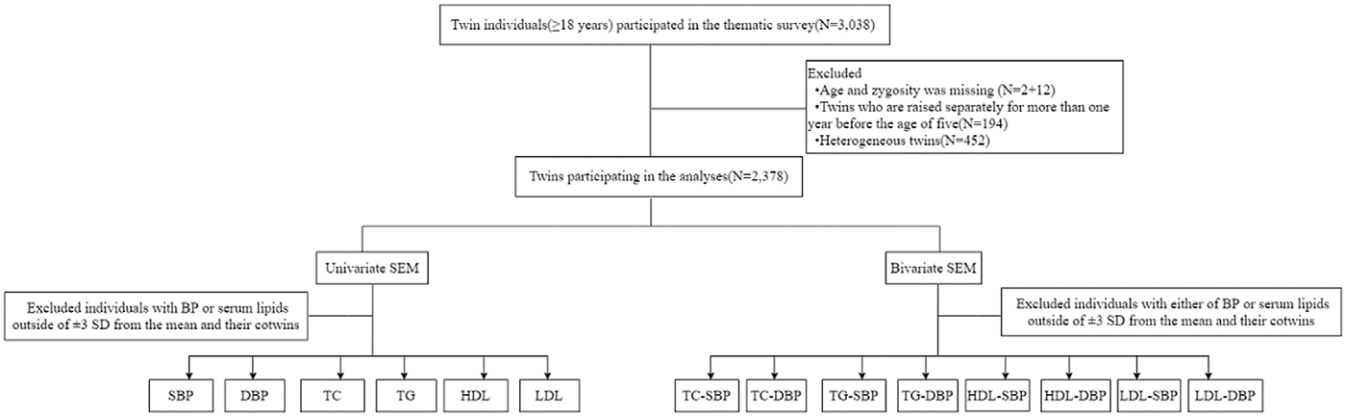

Figure 1. Flow chart of the study population and data analysis.
Note: SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol. SEM, structural equation model; SD, standard deviation

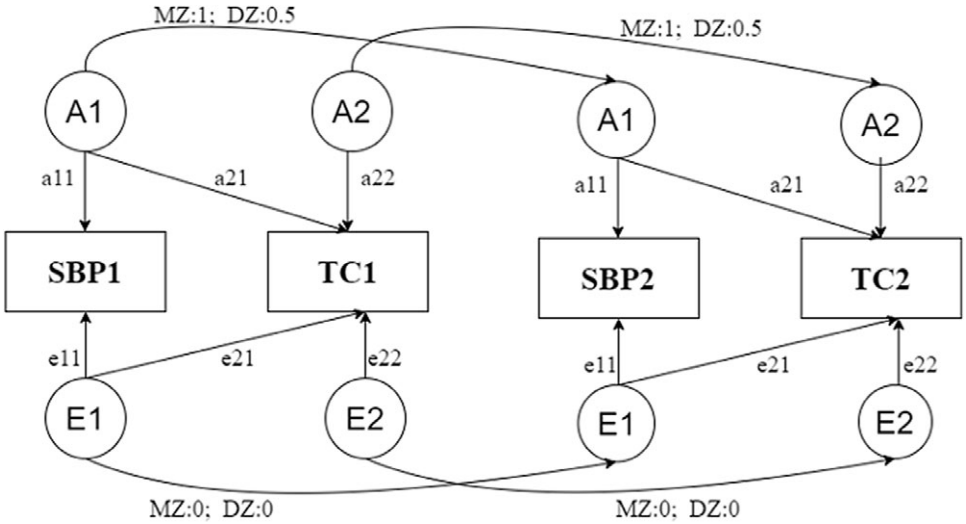

Figure 2. Bivariate Cholesky model for SBP and TC as examples.
Note: The observed phenotypes of twin 1 and twin 2 are in boxes, and the latent variables are in circles. SBP, systolic blood pressure; TC, total cholesterol; a11, the effect of the additive genetic component on SBP; e11, the effect of the unique environmental component on SBP; a21, the combined effect of the additive genetic component on SBP; a22, the effect of additive genetic component on TC; e22, the effect of the unique environmental component on TC.

environmental correlations coefficient (Re) between BP and serum lipids indicators (Figure 2)

Like univariate SEM, we constructed homogeneity models pairwise for each of the three age groups with equal variance components between two age groups. We compare the homogeneity model with the suitable model for each age group using a likelihood ratio test. If $p < .05$, the homogeneity model was considered unacceptable. Examining the model fitting effect, the selection criteria of the suitable models and the criteria for determining whether different age groups are the same refer to the univariate SEM.

Results

Sample Characteristics

A total of 2378 (1189 pairs) adult twins were included in this study, of which 840 pairs (70.6%) were MZ. The average age of all participants was 48.2 ± 12.1 years old, and 68.5% were male. SBP and DBP increased with age among the three age groups, while no age-dependent trend was observed in serum lipid indicators (Table 1).

Heritability of Blood Pressure and Serum Lipids

In the total population and the three age groups, the model-fitting process is shown in Supplementary Tables S1–S5. In the total population, except for TGs, the suitable models for other phenotypes were ACE models, and the suitable model for TGs was AE model (Supplementary Table 4). The heritability was 0.39 for SBP, 0.39 for DBP, 0.45 for TC, 0.59 for TGs, 0.47 for HDL-C and 0.37 for LDL-C (Table 2).

Among the three age groups, we chose AE models as the suitable models for phenotypes. The homogeneity model for only SBP and DBP could be accepted ($p < .001$; Supplementary Table 4), indicating that heritability is not equal among the three age groups. Since unique environmental variation increased, the heritability of SBP and DBP declined in the older adult group compared to the younger group. For TC and TGs, heritability point values at different age groups showed a downward trend as genetic variation declined and environmental variation increased. Still, the heritability difference was insignificant ($p > .05$). Genetic and environmental variation of HDL-C and LDL-C was similar among the three groups, so the heritability remains relatively stable with age (Figure 3, Supplementary Figure S1).

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Table 1. Characteristics of the study participants ($N = 2378$)

Characteristic	Overall	≤45 years old	46–55 years old	>55 years old
No.	2378	934	848	596
Age (years)	48.2 (12.1)	36.2(6.6)	50.4 (2.8)	63.7 (5.9)
Sex/zygosity(%)				
MZF	560 (23.5)	242(25.9)	200 (23.5)	118 (19.8)
MZM	1120 (47.1)	364(39.0)	410 (48.4)	346 (58.0)
DZF	188 (8.0)	86(9.2)	76 (9.0)	26 (4.4)
DZM	510 (21.4)	242(25.9)	162 (19.1)	106 (17.8)
Blood pressure				
SBP(mmHg)	134.4 (22.5)	125.2(18.1)	135.8 (21.3)	146.9 (23.8)
DBP(mmHg)	82.6 (13.9)	79.0(13.3)	84.5 (13.8)	85.6 (13.6)
Serum lipid				
TC(mmol/L)	4.8 (4.2,5.4)	4.8(4.1,5.3)	4.9 (4.3,5.5)	4.8 (4.2,5.4)
TGs(mmol/L)	1.4 (0.9,2.1)	1.4(0.9,2.3)	1.4 (1.0,2.2)	1.3 (0.9,1.9)
LDL-C(mmol/L)	2.5 (2.0,3.0)	2.4(2.0,2.9)	2.6 (2.1,3.1)	2.5 (2.0,3.0)
HDL-C(mmol/L)	1.3 (1.1,1.5)	1.3(1.1,1.5)	1.3 (1.1,1.6)	1.4 (1.1,1.6)

Note: SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; MZF, monozygotic female; MZM, monozygotic male; DZF, dizygotic female; MZM: monozygotic male. Data are reported as the mean (standard deviation) for blood pressure indicators and the median (interquartile range) for serum lipid indicators.

Table 2. Parameter estimates (95% CI) from the univariate model of blood pressure and serum lipids in the total population

Phenotype	A (95% CI)	C (95% CI)	E (95% CI)	h2 (95% CI)	e2 (95% CI)
SBP	0.31 (0.16, 0.49)	0.13 (0.00, 0.29)	0.36 (0.33, 0.40)	0.39 (0.20, 0.59)	0.44 (0.40, 0.49)
DBP	0.35 (0.19, 0.54)	0.17 (0.00, 0.33)	0.38 (0.35, 0.42)	0.39 (0.21, 0.59)	0.42 (0.38, 0.47)
TC	0.45 (0.28, 0.64)	0.18 (0.00, 0.33)	0.36 (0.33, 0.40)	0.45 (0.29, 0.64)	0.37 (0.33, 0.41)
TGs	0.59 (0.52, 0.66)	0.00 (0.00, 0.00)	0.42 (0.38, 0.46)	0.59 (0.54, 0.63)	0.41 (0.37, 0.46)
HDL-C	0.45 (0.30, 0.63)	0.22 (0.05, 0.38)	0.29 (0.26, 0.32)	0.47 (0.31, 0.65)	0.30 (0.27, 0.33)
LDL-C	0.37 (0.21, 0.56)	0.25 (0.08, 0.41)	0.37 (0.33, 0.41)	0.37 (0.21, 0.56)	0.37 (0.33, 0.41)

Note: SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol. A, additive genetic component; E, unique environmental component. h2, heritability, that is, the ratio of A to the total variance; e2, the proportion of E to the total variance.

Genetic and Environmental Correlation between Blood Pressure and Serum Lipids Indicators

There were eight phenotype-phenotype pairs of blood pressure and serum lipid indicators. For each of them we chose the AE model as the binary Cholesky decomposition model according to the suitable model of univariate SEM. The model-fitting process is shown in Supplementary Tables S6–S9. Therefore, the phenotypic correlation (Rph) was decomposed into additive genetic correlation (Ra) and unique environmental correlation (Re).

In total populations, the Rphs were 0.15 for TC&SBP, 0.17 for TGs&SBP, 0.11 for LDL-C&SBP, −0.04 for HDL-C&SBP, 0.19 for TC&DBP, 0.23 for TGs&DBP, 0.16 for LDL-C&DBP and −0.08 for HDL-C&DBP. For these phenotypes-phenotypes pairs, the Ra ranged from 0.00 to 0.36. 0–85% of the phenotypic correlations were determined by genetic factors, and the remaining 15–100% were explained by environmental factors (Table 3).

Among the age groups, Rph and Ra of each phenotype-phenotype pair showed the same change trend. For TC&SBP, TC&DBP, TGs&SBP and TGs&DBP, both the Rph and Ra declined with age, and the difference of Ra between the young group and the older adult group was statistically significant ($p < .05$) according to the 95% CI and the unacceptable homogeneity models (Figures 4 and 5, Supplementary Table S9). However, for LDL-C&DBP, HDL-C&SBP, and HDL-C&DBP, the lowest Ra and Rph appeared in the middle age group. The rE did not follow any pattern with age, and the differences in Re among the three age groups for all phenotype-phenotype pairs were not statistically significant according to the point value of Re and their 95% CI (Figure 5).

Discussion

To our knowledge, age plays a crucial role in genetic and environmental influences on blood pressure and serum lipids. As expected, the heritability and genetic correlations of most

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Table 3. Parameter estimates (95% CI) from the bivariate model of blood pressure and serum lipid in total population

Phenotype1	Phenotype2	Rph (95% CI)	Ra (95% CI)	Re (95% CI)	Pa (95% CI)	Pe (95% CI)
SBP	**TC**	0.15 (0.10, 0.20)	0.09 (0.00, 0.41)	0.19 (0.01, 0.34)	0.22 (0.00, 0.96)	0.78 (0.04, 1.00)
	TGs	0.17 (0.12, 0.21)	0.28 (0.16, 0.46)	0.09 (0.05, 0.15)	0.70 (0.50, 0.85)	0.30 (0.15, 0.50)
	LDL-C	0.11 (0.06, 0.15)	0.00 (0.00, 0.33)	0.16 (0.00, 0.25)	0.00 (0.00, 1.00)	1.00 (0.00, 1.00)
	HDL-C	−0.04 (−0.08, 0.00)	−0.07 (−0.22, 0.00)	−0.02 (−0.11, 0.00)	0.73 (0.00, 1.00)	0.27 (0.00, 1.00)
DBP	**TC**	0.19 (0.14, 0.23)	0.22 (0.00, 0.50)	0.16 (0.01, 0.37)	0.50 (0.00, 0.97)	0.50 (0.03, 1.00)
	TGs	0.23 (0.19, 0.27)	0.36 (0.24, 0.54)	0.14 (0.08, 0.19)	0.69 (0.55, 0.81)	0.31 (0.19, 0.45)
	LDL-C	0.16 (0.11, 0.21)	0.04 (0.00, 0.38)	0.23 (0.02, 0.35)	0.09 (0.00, 0.91)	0.91 (0.09, 1.00)
	HDL-C	−0.08 (−0.12, −0.03)	−0.17 (−0.32, 0.00)	−0.02 (−0.16, 0.00)	0.85 (0.00, 1.00)	0.15 (0.00, 0.58)

Note: Ra, genetic correlation between 2 phenotypes; Re, unique environmental correlation between 2 phenotypes; Rph, phenotypic correlation between two phenotypes; Pa, percentage of genetic contributions to the correlation between two phenotypes; Pe, percentage of environmental contributions to the correlation between two phenotypes; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

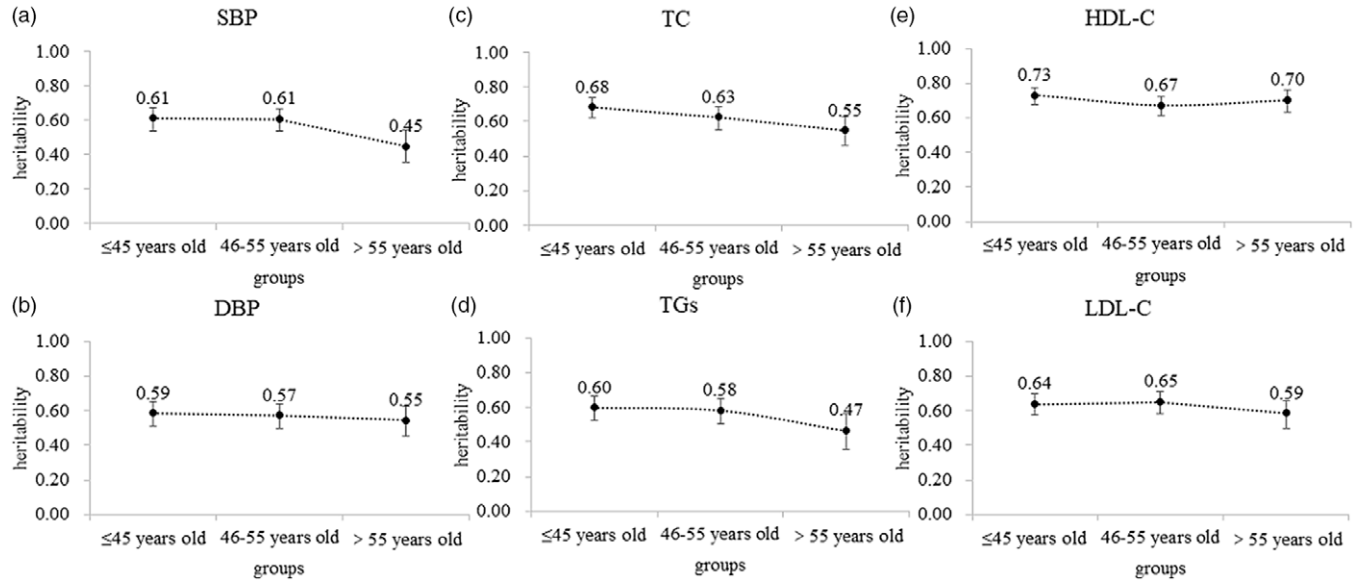

Figure 3. Heritability of blood pressure and serum lipids by three age groups.
Note: SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TGs, triglycerides; LDL-C,low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.

phenotype and phenotype-phenotype pairs decreased with age. However, some heritability or genetic correlations still reached extreme values in the middle-aged group.

Univariate analysis showed that the overall heritability of blood pressure and serum lipid indicators was estimated to be moderate to high, suggesting that these phenotypic variations were mainly due to genetic effects, which is consistent with previous findings (Jermendy et al., 2011; Liao et al., 2017; Liao et al., 2015; Snieder et al., 1999). The environmental factors that lead to phenotypic variation are mainly the unique environment rather than the common environment, which may be because most of the participants in this study were middle-aged and elderly, and the shared environmental exposure of twins may no longer play a significant role (Benyamin et al., 2007). We found that the heritability of SBP and DBP declined with age. The unacceptable homogeneity models support this hypothesis. Differences in the heritability across age groups may reflect the cumulative effect of the unique environment, such as smoking, drinking and exercising (Heller et al., 1993; Province et al., 1989). Alternatively, these results may reflect cohort differences. In line with previous studies (Snieder et al., 1999), the heritability of TC, TG, HDL-C and LDL-C remains relatively stable with age. However, other studies found that the heritability of serum lipids fluctuates with age, possibly due to the age-dependent expression of lipid-related genes (Heller et al., 1993; Simino et al., 2014). In addition, women enter menopause in this age group (46−55 years old; Marlatt et al., 2022). In this period, LDL-C levels rise rapidly, while HDL-C levels fall (Marlatt et al., 2022; Snieder et al., 1999) when a lack of ovarian hormones affects lipid metabolism. It may be due to the complex changes in genetic and environmental factors that lead to stability in heritability. The role of unique environmental factors such as lifestyle becomes increasingly important as age increases. Thus, unique environmental factors should be given more attention at a young age to prevent or slow disease progression.

Most previous studies have analyzed blood pressure and serum lipid indicators separately. Few have investigated genetic and

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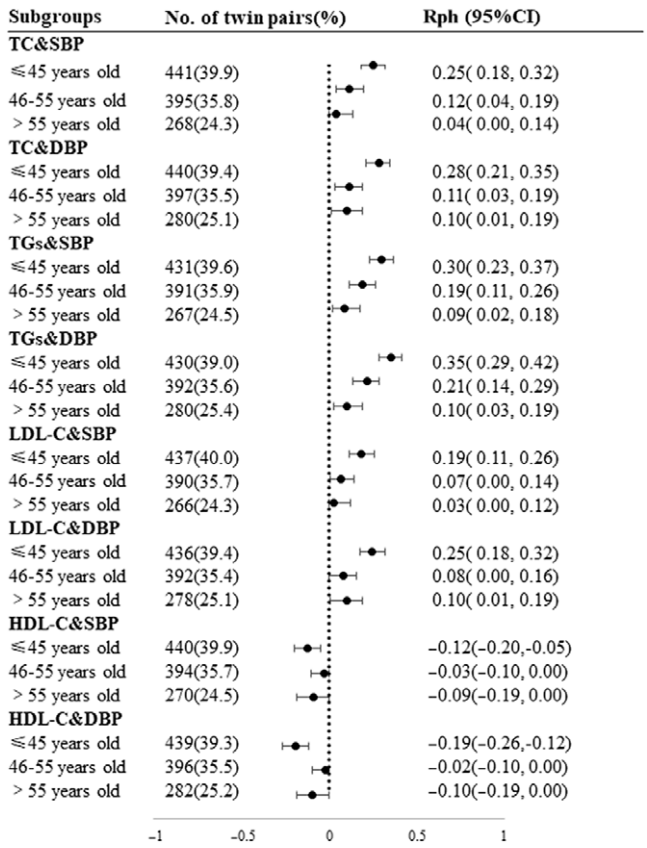

Figure 4. Phenotypic correlation (95% CIs) from the best-fitting bivariate AE model of blood pressure and serum lipid in three age groups.
Note: Rph, phenotypic correlation between two phenotypes; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

environmental correlations in metabolic syndrome subphenotypes, including blood pressure, TG and HDL-C, instead of the four serum lipid indicators (Benyamin et al., 2007; Duan et al., 2011; Panizzon et al., 2015; Zhang et al., 2009). We found a weak genetic correlation (0.00−0.36) between blood pressure and serum lipids through bivariate analysis, consistent with previous twin studies (Benyamin et al., 2007; Duan et al., 2011; Panizzon et al., 2015; Zhang et al., 2009). Genetic correlation provides epidemiological evidence for exploring the overlapping genes between blood pressure and serum lipids. The trend may indicate the change in genetic effects of overlapping genes over time. A genetic correlation of 1.00 or −1.00 suggests that the genetic effects on the two traits overlap entirely, while a genetic correlation of zero indicates that completely different genes affect the two traits. Apart from genetic correlation, the percentage of genetic contributions to the correlation between two phenotypes (Pa) reflects the magnitude of genetic influences on phenotypes. This study found that genetics contributed significantly (0−85%) to the correlation between blood pressure and serum lipids, suggesting that genes affecting blood pressure overlap with genes affecting serum lipids. A large genomewide association study (GWAS; Willer et al., 2013) found that 20 and 29 loci associated with lipid levels were associated with SBP and DBP respectively, of which the BRAP gene (Kim et al., 2016) and the SLC39A8 gene (Yao et al., 2015) were duplicated in other studies. Another GWAS on Koreans found that *BRAP, ACAD10,* and *ALDH2* were genes shared by SBP and DBP with TGs, HDL-C and LDL-C respectively (Kim et al., 2016). Two other GWAS on the pleiotropy of coronary heart disease risk loci found that the *SH2B3* gene was the locus associated with SBP, DBP, HDL-C, and LDL-C (CARDIoGRAMplusC4D Consortium et al., 2013; Webb et al., 2017). These genomic studies support our findings that there are overlapping genes between blood pressure and serum lipids.

In the bivariate analysis of age groups, as expected, the phenotypic correlation between serum lipids and blood pressure generally declined with age, and the phenotypic correlation was highest in the young group. Considering that dyslipidemia in China has a higher prevalence and lower awareness, treatment and control rates than hypertension (Pan et al., 2016), we should pay more attention to the serum lipid levels of hypertensive patients to detect dyslipidemia early. Similarly, the genetic correlation of TC, TG and blood pressure phenotype-phenotype pairs declined with age. This shows that the genetic effect decreases, and the environmental effect increases with age. Compared with the results of a study using young twins with an average age of 21.31 years old (McCaffery et al., 1999), the proportions of genetic correlations to total phenotypic correlations (Pa) of TC&SBP, TC&DBP, TGs&SBP and TGs&DBP in the youth twin study (Pa = 93%, 77%, 90% and 100% respectively) were greater than those in our study (Pa = 22%, 50%, 70% and 69% respectively), indirectly indicating that age has a moderating effect on the genetic correlations of these phenotype-phenotype pairs. It is physiologically plausible that age modulates the magnitude of genetic correlations. Aging leads to cumulative exposure to lifestyle choices, such as smoking, alcohol consumption, diet and exercise, which may affect the regulation of blood pressure (Hart & Charkoudian, 2014), lipid metabolism (Liu & Li, 2015) and the expression of lipid-related genes (Simino et al., 2014).

Both univariate and bivariate results indicate that unique environmental factors play an increasingly important role in the heritability of traits or the phenotypic correlations of phenotype pairs with age. A study comparing the differences in environmental factors between dyslipidemia and hypertension in the Guangxi Zhuang population in China found that common risk factors for hypertension and dyslipidemia included age, total energy and total fat intake (Ruixing et al., 2009). In addition, smoking (Handa et al., 1990), alcohol consumption (Handa et al., 1990; Wakabayashi, 2009), and BMI (Wakabayashi, 2009) are also common risk factors for dyslipidemia and hypertension. These environmental risk factors specifically accumulate with age. Therefore, common risk factors can be intervened early to prevent and control dyslipidemia and hypertension simultaneously.

Our study focuses on the heritability and genetic correlation between blood pressure and serum lipids, and we also attempted to explore the effect of age on heritability and genetic correlation. However, our study also has limitations. First, although our sample size is sufficient to detect the change trends with age, a larger sample size is required for gender-stratified analysis. Second, this study is cross-sectional and cannot directly use correlation to make causal inferences.

Conclusion

In conclusion, our study shows the importance of genetic and independent environmental factors in the correlation of blood pressure with serum lipids. It shows the influence of age on genetic and independent environmental contributions. Genetic factors play a more significant role in the correlation between blood pressure and serum lipids in young age, whereas cumulative

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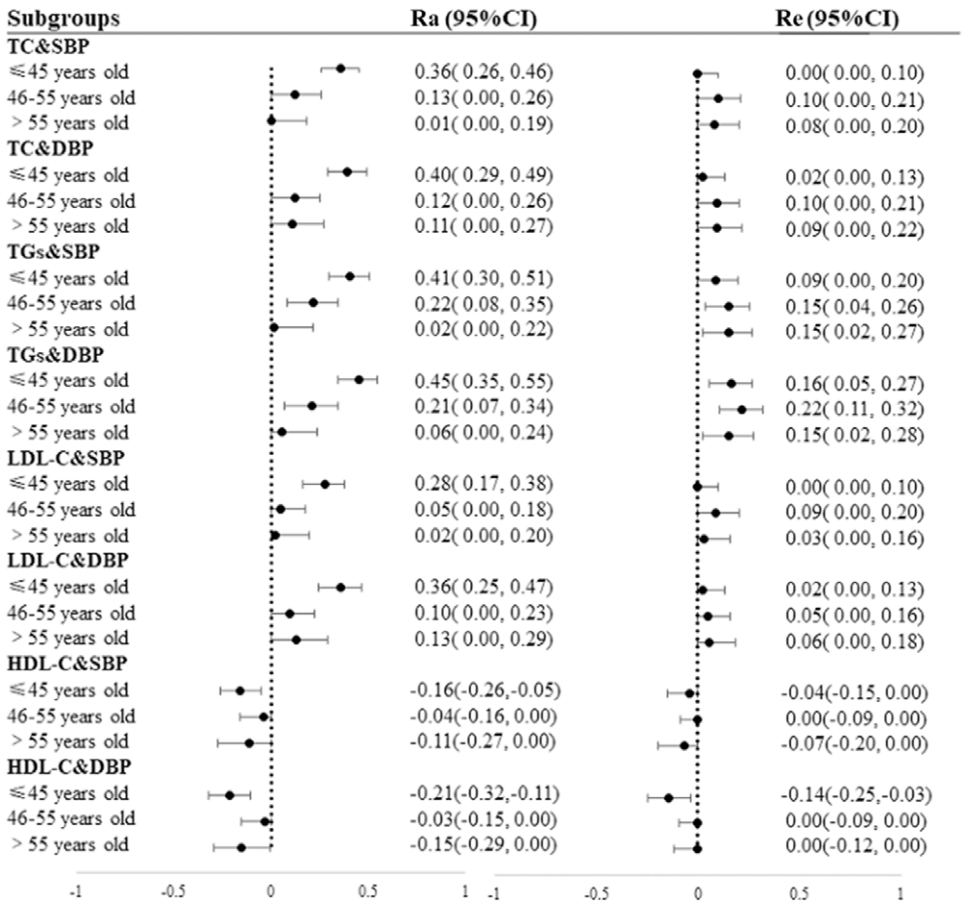

Figure 5. Genetic and environmental correlation (95% CI) from the best-fitting bivariate AE model of blood pressure and serum lipid in three age groups.
Note: Ra, genetic correlation between two phenotypes; Re, unique environmental correlation between two phenotypes; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

unique environmental effects play a more substantial role in old age. Studies of common genes or epigenetic loci between blood pressure and blood lipids should consider using younger participants. Patients with hypertension or dyslipidemia should pay more attention to their own blood pressure and serum lipids and take intervention measures for common risk factors. Furthermore, more prospective studies are needed to validate our findings, and further studies are required to identify specific genes that affect blood pressure and serum lipids.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/thg.2023.25.

Data availability statement. The datasets generated during and analyzed during the current study are not publicly available but are available from the corresponding author at reasonable request.

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Author contributions. Wenjing Gao: conceptualization, methodology, writing - review & editing; Zengchang Pang, Min Yu, Hua Wang, Xianping Wu, and Yu Liu: Investigation; Yutong Wang, Weihua Cao, Jun Lv, Canqing Yu, Shengfeng Wang, Tao Huang, Dianjianyi Sun, Chunxiao Liao, Yuanjie Pang and Runhua Hu: Writing — review and editing; Liming Li: supervision, project administration, funding acquisition; Ke Miao: software, writing original draft

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Competing interests. The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

Ethics statement. This study was granted by the Biomedical Ethics Committee at Peking University, Beijing, China (approval number: IRB00001052-13022, IRB00001052-14021). All participants provided written informed consent when investigated. All methods were carried out in accordance with the relevant guidelines and regulations.

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