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Shared genetic effects of emotion and subcortical volumes in healthy adults

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ABSTRACT

Ample studies have reported a strong association between emotion and subcortical volumes; still, the underlying mechanism regarding this relation remains unclear. Using a twin design, the current study aimed to explore the intrinsic association between emotion and subcortical volumes by examining their phenotypic, genetic, and environmental correlations. We used a group dataset of 960 individuals from the Human Connectome Project (234 monozygotic twins, 145 dizygotic twins, 581 not twins, males = 454, age = 22–37 years). We found that both emotion and subcortical volumes were heritable. Of the 17 emotional traits, 13 were significantly phenotypically correlated with the volumes of multiple subcortical regions. There was no environmental correlation between emotion and subcortical volumes; however, we found a genetic overlap between overall emotional traits and caudate volume. Taken together, our results showed that emotion and subcortical volumes were heritable and closely related. Although the caudate has been often studied with execution of movement, given that the caudate volume is genetically associated with diverse emotional domains, such as negative affect, psychological well-being, and social relationships, it may suggest that the caudate volume might also be an important factor when studying the brain basis of emotion.

1. Introduction

The brain basis of emotion has been studied extensively to discover how the brain is associated with emotion (Lindquist et al., 2012; Pierce and Péron, 2020). Notably, a large body of studies has demonstrated a strong link between emotion and subcortical structures, such as the volumes of the basal ganglia, amygdala, and hippocampus (Dennison et al., 2015; DeYoung et al., 2010; Kim et al., 2008; Uono et al., 2017; Videbech and Ravnkilde, 2004). Yet, little is known about whether this connection is due to shared genetic or environmental factors. Understanding the genetic and environmental associations may shed light on the fundamental association between emotion and subcortical volume.

Previous studies have consistently reported a close relation between emotion and subcortical volume. For instance, lower levels of positive affect were associated with smaller hippocampal volume, whereas higher levels of negative affect were related to smaller amygdala volume (Dennison et al., 2015). Reduced hippocampal volume is associated with neuroticism, stress (DeYoung et al., 2010; McEwen, 1999), and depression (Videbech and Ravnkilde, 2004). The putamen volume showed a negative correlation with recognition of fearful facial expressions (Uono et al., 2017). Women with major depressive disorders showed reduced caudate volume (Kim et al., 2008). However, these studies have focused only on the phenotypic relation between emotion and subcortical volume; therefore, it is difficult to demonstrate whether shared genetic or environmental factors drive their associations. Moreover, several prior studies have discovered that emotion and subcortical volume are heritable (den Braber et al., 2013; Han and Adolphs, 2020; Kremen et al., 2010), which indicates that they are influenced by genetics. Thus, investigating the genetic and environmental relation between emotion and subcortical volume is necessary.

Twin design may be ideal for discovering genetic and environmental association, as it takes genetic and environmental factors into account separately. Different from dizygotic (DZ) twins, which share 50% of their genes, monozygotic (MZ) twins share 100% of their genes (Han and Adolphs, 2020). Therefore, if MZ twins differ in individual traits (i.e., height, intelligence), it would be mainly due to differences

Abbreviations: DZ, dizygotic; FDR, false discovery rate; HCP, Human Connectome Project; IRB, Institutional Review Board; MZ, monozygotic; NIH, National Institutes of Health; PANAS, Positive Affect and Negative Affect Schedule; PROMIS, Patient-Reported Outcomes Measurement Information System; SOLAR, Sequential Oligogenic Linkage Analysis Routines.

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Table 1
Descriptive statistics for monozygotic (MZ) twins, dizygotic (DZ) twins, and not twin

	MZ (N = 234)	DZ (N = 145)	Not Twin (N = 581)	Total (N = 960)
Sex, male (N, %)	102 (43.6)	61 (42.1)	291 (50.1)	454 (47.3)
Age, years (M, SD)	29.26 (3.27)	28.99 (3.43)	28.34 (3.90)	28.66 (3.71)
Race, White (N, %)	198 (84.6)	125 (86.2)	403 (69.4)	726 (75.6)

in the environmental factors rather than the genetic factors. To date, genetic associations between several traits have been discovered with such twin designs (Dager et al., 2015; Valk et al., 2020). For example, Valk et al. (2020) found that personality traits are genetically associated with cortical structure, such as cortical thickness and surface area. Dager et al. (2015) also found a genetic overlap between amygdala volume and alcohol use disorders' risk factors. However, despite the heritability of emotion and subcortical volume, little is known about the genetic link between various emotional traits and subcortical volume.

The present study investigated the genetic influences on various emotional functions and subcortical volumes. Considering this, heritability analyses using Sequential Oligogenic Linkage Analysis Routines (SOLAR) (Almasy and Blangero, 1998) were performed for each emotional trait and subcortical volume. We further performed bivariate analyses to examine the phenotypic, genetic, and environmental correlation between emotion and subcortical volumes.

2. Material and methods

2.1. Participants

We used the Human Connectome Project (HCP) S1200 release dataset (http://www.humanconnectomeproject.org/), which consists of 1206 healthy individuals (MZ = 298, DZ =188, Not Twin = 720). Since HCP aims for a pool that can represent the general population regarding behavioral, ethnic, and socioeconomic diversity, the term "healthy" is broadly defined. The participants' zygosity was verified by genotyping. More detailed sets of inclusion and exclusion criteria can be found in Van Essen et al. (2013). The use of behavioral and imaging data from the HCP project was approved by the Institutional Review Board (IRB) and Ethics Committee (AJIRB-BMR-EXP-21-122) of Ajou University Hospital.

The HCP dataset provides the National Institutes of Health (NIH) Toolbox Emotion Battery and estimated volume values for each subcortical area. Of the 1206 individuals, individuals who had a complete set of these behavioral and imaging data were included in our study. We further excluded single MZ twins (N = 22) and individuals with missing data on zygosity (N = 2), resulting in a final sample size of 960 participants (MZ = 234, DZ = 145, Not Twin = 581). We removed single MZ twins since SOLAR requires the data for MZ pairs when loading the pedigree data. Also, the size of single MZ twins is about 2% of the final sample size (N=960) – which is not that large – so we decided to remove them from our analyses. The DZ twins were included in the analyses as they share 50% of their genes. Although the singletons do not directly contribute to the estimation of genetic parameters, they were included in the analyses due to the possibility of a more precise estimation of mean and variance effects (Liu et al., 2019). The sample included 454 men and 506 women, with a mean age of 28.66 years (standard deviation = 3.71, range = 22–37). Brief demographics are presented in Table 1.

2.2. Behavioral data

The NIH Toolbox Emotion Battery was used to comprehensively assess emotions. It consists of four core domains: negative affect, psychological well-being, stress and self-efficacy, and social relationships, which are critical components of individuals' emotions. In this study, we analyzed all 17 subdomains from the domains at which each participant's level of agreement was reported using a 5-point Likert scale. All the subdomains and their descriptive statistics are listed in Table 2.

The NIH Toolbox Emotion Battery covers broad aspects of emotion and, thus, is an effective measurement to broadly assess individuals' emotions broadly (Salsman et al., 2013). Moreover, the NIH Toolbox Emotion Battery shows a close relationship with other large NIH initiatives, such as the Patient-Reported Outcomes Measurement Information System (PROMIS; www.healthmeasures.net/explore-measurement-systems/promis) and Quality of Life Outcomes in Neurological Disorders (www.neuro-qol.org). Certainly, several item banks related to depression, anxiety, and anger in PROMIS and the questionnaires of negative affect domain in the NIH Toolbox are drawn from the same pool of questions (Salsman et al., 2013). This overlap with other measurements not only allows researchers to have a shared metric for important emotional concepts but also provides strong evidence when considering the generalizability of our results.

2.3. Image acquisition and preprocessing

The subcortical regions, such as the thalamus, basal ganglia (i.e., the caudate, putamen, pallidum, and accumbens area), hippocampus, and amygdala, were included as regions of interest in our study (Fig. 1).

Briefly, high-resolution (0.7-mm isotropic voxels) structural imaging data were acquired using a customized Siemens 3-T Connectome Skyra with a 32-channel head coil at Washington University. Subcortical volume estimates were extracted using automatic segmentation in FreeSurfer 5.3.0 (https://surfer.nmr.mgh.harvard.edu/). Participants who passed the HCP quality control and assurance standards were included in our study (Marcus et al., 2013). More details can be found in (Glasser et al., 2016; Van Essen et al., 2013).

2.4. Heritability estimation and statistical analyses

SOLAR was used to estimate the heritability and genetic correlation of emotion and subcortical volume. SOLAR uses the maximum likelihood estimation, which can handle pedigrees of arbitrary size and complexity; thus, it is a flexible and large-scale imaging genetic analysis software package (Kochunov et al., 2019). It decomposes phenotypic variance for each phenotype into additive genetic variance and unique (= individual specific) environmental variance as an additive genetic and unique environment model, where covariance within each pedigree and kinship relations are considered (Fig. 1) (Kochunov et al., 2019).

After decomposition of each variance, heritability (h^2) was estimated as the proportion of the phenotypic variance (σ^2_p), which can be attributed to additive genetic variance (σ^2_g). Bivariate analysis was performed to estimate the shared genetic influence (i.e., genetic correlation), phenotypic correlation, and environmental correlation between emotion and subcortical volumes. For this, SOLAR software decomposed the total phenotypic correlation into the genetic (ρ_g) and environmental (ρ_e) component using the following formula: $\rho_{p=}\ \rho_g\sqrt{(h^2_1\ h^2_2)} + \rho_e\sqrt{[(1–h^2_1)(1–h^2_2)]}$, where h^2_1 and h^2_1 indicate the heritability of emotional traits and subcortical volumes, respectively. If the genetic correlation coefficient is significantly different from zero, then there is a genetic overlap between the two variables.

In our study, the effects of sex and age were regressed out in all analyses, and the effect of z-transformed total intracranial volume was ad-

Table 2
Domain and descriptive statistics of the National Institutes of Health Toolbox Emotion Battery

Domain	Subdomain	MZ Mean (SD)	DZ	Not Twin	Total
Negative affect	Anger-affect	45.98 (8.61)	47.99 (8.11)	48.33 (7.96)	47.70 (8.20)
	Anger-hostility	49.20 (8.49)	49.68 (8.53)	50.99 (8.57)	50.36 (8.57)
	Anger-aggression	49.84 (7.25)	50.80 (8.30)	52.68 (9.08)	51.70 (8.63)
	Fear-affect	49.49 (8.09)	49.95 (7.07)	50.39 (8.09)	50.10 (7.95)
	Fear-somatic arousal	51.06 (8.01)	51.47 (7.74)	52.27 (8.35)	51.86 (8.19)
	Sadness	45.49 (7.97)	46.54 (7.23)	46.30 (8.02)	46.14 (7.90)
Psychological well-being	Life satisfaction	55.40 (9.18)	54.44 (9.70)	54.43 (9.02)	54.67 (9.17)
	Meaning and purpose	51.98 (8.80)	51.41 (9.17)	52.17 (8.69)	52.01 (8.79)
	Positive affect	50.46 (7.15)	49.36 (7.70)	50.40 (8.15)	50.26 (7.85)
Social relationships	Friendship	50.50 (9.01)	50.12 (8.39)	50.53 (9.14)	50.46 (8.99)
	Loneliness	50.51 (9.04)	50.90 (8.41)	51.19 (8.47)	50.98 (8.60)
	Perceived hostility	47.96 (8.97)	47.27 (8.09)	49.22 (8.25)	48.62 (8.44)
	Perceived rejection	48.24 (8.76)	47.44 (8.38)	48.60 (8.58)	48.34 (8.59)
	Emotional support	52.10 (9.49)	50.73 (9.08)	51.29 (9.54)	51.40 (9.46)
	Instrumental support	48.24 (9.16)	48.33 (8.83)	47.80 (9.04)	47.99 (9.03)
Stress and self-efficacy	Perceived stress	47.64 (9.11)	47.04 (7.73)	48.68 (9.40)	48.18 (9.11)
	Self-efficacy	50.93 (7.57)	50.05 (8.09)	51.32 (8.56)	51.03 (8.26)

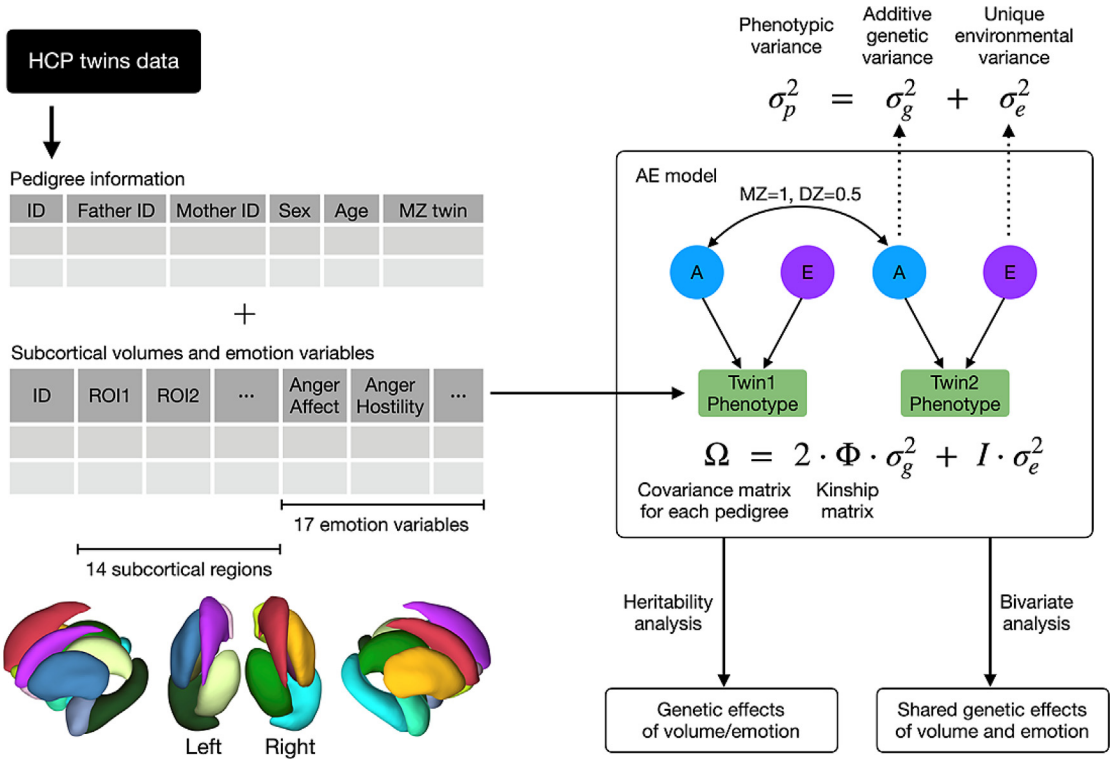

Fig. 1. Schematic overview of the study. Additive genetic and unique environment model implemented in Sequential Oligogenic Linkage Analysis Routines software was applied to decompose phenotypic variance into additive genetic and unique environmental variance for each phenotype (i.e., estimated volume from 14 subcortical regions and observed values from 17 emotion variables). Based on this decomposition, heritability and bivariate analysis were further performed to investigate the genetic effects of volumes and emotion and their associations. All phenotypic data and pedigree information used in our study were acquired from the Human Connectome Project twin dataset.

ditionally regressed out when examining subcortical volume. All behavioral and structural imaging traits were inversely normalized to conform to the assumptions of normality (Kochunov et al., 2019). We reported heritability results with a Bonferroni correction ($p < 0.05$), which was done for the 17 emotional traits ($p < 0.05/17$) and 14 subcortical volumes ($p < 0.05/14$), respectively. Regarding the bivariate model results, levels of false discovery rate (FDR) < 0.05 and < 0.1 were determined to be significant in addressing multiple comparison problems. Specifically, FDR was applied on phenotypic correlation results (17×14), genetic correlation results (17×14), and environmental correlation results (17×14), respectively. FDR thresholding controls the expected proportion of false positives only among traits that exhibit significance (Genovese et al., 2002).

3. Results

3.1. Heritability analyses

According to our heritability analyses, both emotional traits and subcortical volumes were influenced by genetics ($p < 0.05$, Bonferroni corrected) (Tables 3 and 4).

Table 3
Heritability of emotional traits

Domain	Subdomain	Heritability	*p*-value(uncorrected)	FDR-adjusted *p*-value	Bonferroni- adjusted *p*-value
Negative affect	Anger-affect	.23	1.3×10^{-4}	2.0×10^{-4}	2.23×10^{-3}
	Anger-hostility	.31	2.0×10^{-7}	8.5×10^{-7}	3.4×10^{-6}
	Anger-aggression	.36	6.0×10^{-7}	1.7×10^{-6}	1.02×10^{-5}
	Fear-affect	.25	3.71×10^{-5}	7.88×10^{-5}	6.31×10^{-4}
	Fear-somatic arousal	.19	4.6×10^{-4}	6.0×10^{-4}	7.89×10^{-3}
	Sadness	.29	5.9×10^{-6}	1.43×10^{-5}	1.0×10^{-4}
Psychological well-being	Life satisfaction	.23	1.2×10^{-4}	2.0×10^{-4}	2.17×10^{-3}
	Meaning and purpose	.24	5.97×10^{-5}	1.0×10^{-4}	1.02×10^{-3}
	Positive affect	.20	1.9×10^{-3}	2.0×10^{-3}	3.27×10^{-2}
Social relationships	Friendship	.40	6.27×10^{-10}	1.07×10^{-8}	1.07×10^{-8}
	Loneliness	.36	1.65×10^{-9}	1.40×10^{-8}	2.81×10^{-8}
	Perceived hostility	.24	1.2×10^{-4}	2.0×10^{-4}	2.06×10^{-3}
	Perceived rejection	.20	8.65×10^{-4}	9.0×10^{-4}	1.47×10^{-2}
	Emotional support	.23	5.93×10^{-5}	1.0×10^{-4}	1.01×10^{-3}
	Instrumental support	.23	2.1×10^{-4}	3.0×10^{-4}	3.56×10^{-3}
Stress and self-efficacy	Perceived stress	.36	5.19×10^{-9}	2.94×10^{-8}	8.82×10^{-8}
	Self-efficacy	.33	3.00×10^{-7}	1.02×10^{-6}	5.1×10^{-6}

Table 4
Heritability of subcortical volumes

Subcortical volume	Heritability	*p*-value (uncorrected)	FDR-adjusted *p*-value	Bonferroni- adjusted *p*-value
Left thalamus	.51	1.85×10^{-17}	1.85×10^{-17}	2.59×10^{-16}
Right thalamus	.63	2.86×10^{-30}	6.67×10^{-30}	4.00×10^{-29}
Left caudate	.81	8.53×10^{-43}	5.97×10^{-42}	1.19×10^{-41}
Right caudate	.79	5.26×10^{-40}	1.84×10^{-39}	7.37×10^{-39}
Left putamen	.65	1.64×10^{-31}	4.59×10^{-31}	2.29×10^{-30}
Right putamen	.84	5.40×10^{-54}	7.56×10^{-53}	7.56×10^{-53}
Left pallidum	.58	4.22×10^{-22}	5.91×10^{-22}	5.91×10^{-21}
Right pallidum	.66	4.27×10^{-27}	8.54×10^{-27}	5.97×10^{-26}
Left accumbens area	.55	1.07×10^{-19}	1.17×10^{-19}	1.50×10^{-18}
Right accumbens area	.58	2.91×10^{-20}	3.70×10^{-20}	4.08×10^{-19}
Left hippocampus	.53	1.09×10^{-19}	1.17×10^{-19}	1.52×10^{-18}
Right hippocampus	.82	5.96×10^{-42}	2.78×10^{-41}	8.34×10^{-41}
Left amygdala	.60	5.77×10^{-25}	1.01×10^{-24}	8.08×10^{-24}
Right amygdala	.64	2.21×10^{-24}	3.44×10^{-24}	3.09×10^{-23}

Among the emotional traits, fear-somatic arousal in the negative affect domain showed the lowest heritability ($h^2 = 0.19$, $p = 4.6 \times 10^{-4}$), while friendship in the social relationships domain showed the highest heritability ($h^2 = 0.40$, $p = 6.27 \times 10^{-10}$). Consistent with the previous findings (den Braber et al., 2013; Kremen et al., 2010; Rentería et al., 2014), the heritability estimates for subcortical volumes ranged from 0.51 to 0.84, indicating high heritability. Note that a heritability value close to 0 indicates low genetic effects, whereas a heritability value close to 1 indicates high genetic effects. The values less than 0.20, 0.21–0.40, and greater than 0.40 are empirically considered low, moderate, and high heritability, respectively (Bailey, 2014). We described the heritability for each subcortical volume and emotion in Fig. 2.

3.2. Phenotypic correlation analyses

Volumes at multiple subcortical regions showed significant correlations with scores of eight emotional traits with FDR < 0.05 (13 emotional traits with FDR < 0.1). Eight emotional traits included anger-affect, anger-hostility, fear-affect, fear-somatic arousal, life satisfaction, meaning and purpose, perceived hostility, and perceived hostility, which are visually detailed in Fig. 3.

Specifically, in the negative affect domain, the anger-affect score showed a positive correlation with the right putamen volume ($\rho_p = .11$, $p < .001$) and left hippocampal volume ($\rho_p = .10$, $p < .01$). Anger-hostility scores were positively correlated with the volumes of the bilateral caudate nuclei (left: $\rho_p = .12$, $p < .001$; right: $\rho_p = .11$, $p < .01$). Fear-affect score was positively associated with left hippocampal volume ($\rho_p = .11$, $p < .01$). Fear-somatic arousal score was positively correlated with left pallidum volume ($\rho_p = .11$, $p < .01$).

Among the psychological well-being domains, life satisfaction score was negatively correlated with the volumes of the bilateral caudate (left: $\rho_p = -.11$, $p < .01$, right: $\rho_p = -.10$, $p < .01$). Meaning and purpose score showed a negative correlation with the left caudate volume ($\rho_p = -.11$, $p < .001$).

In the social relationships domain, perceived hostility score was positively associated with the volumes of the bilateral thalamus (left: $\rho_p = .14$, $p < .0001$, right: $\rho_p = .11$, $p < .001$) and the right putamen ($\rho_p = .11$, $p < .01$). The perceived rejection score was positively correlated with the left caudate volume ($\rho_p = .11$, $p < .01$) and right putamen volume ($\rho_p = .11$, $p < .01$).

3.3. Genetic and environmental correlation analyses

Subsequently, we examined the genetic and environmental correlations between emotion and subcortical volumes to evaluate whether these associations affect phenotypic correlations. Of the 13 emotional traits that showed significant phenotypic correlations at the FDR 0.1 level, six emotional traits were significantly genetically correlated with subcortical volumes (Table 5 and Fig. 3). We did not find an environmental correlation between emotion and subcortical volumes.

In the negative affect domain, anger-hostility score was positively correlated with the left caudate volume ($\rho_g = .29$, $p < .01$). In the psychological well-being domain, the life satisfaction score showed a negative association with the right caudate volume ($\rho_g = -.30$, $p < .01$). Meaning and purpose also showed a negative correlation with the right caudate volume ($\rho_g = -.29$, $p < .01$). In the social relationships domain, loneliness score was positively associated with the left caudate volume ($\rho_g = .27$, $p < .01$), and the emotional support score was negatively cor-

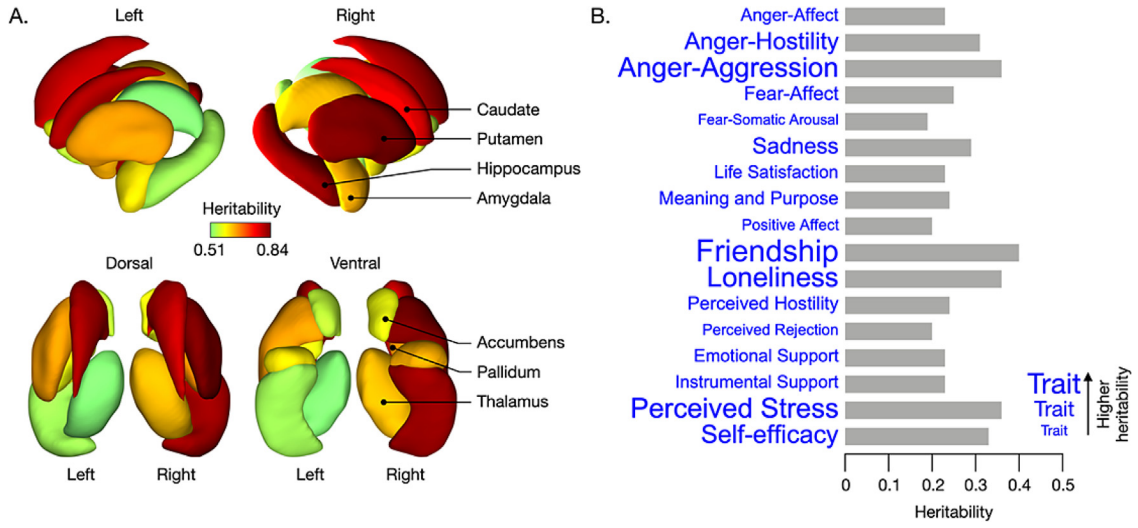

Fig. 2. Genetic effects of subcortical volumes and emotional traits. A. Heritability map for 14 subcortical regions. B. Heritability plot for 17 emotional traits, where larger text and bar plot each represents higher heritability and the value for each trait. In our study, all subcortical volumes and emotional traits were highly heritable ($p < 0.05$, Bonferroni corrected).

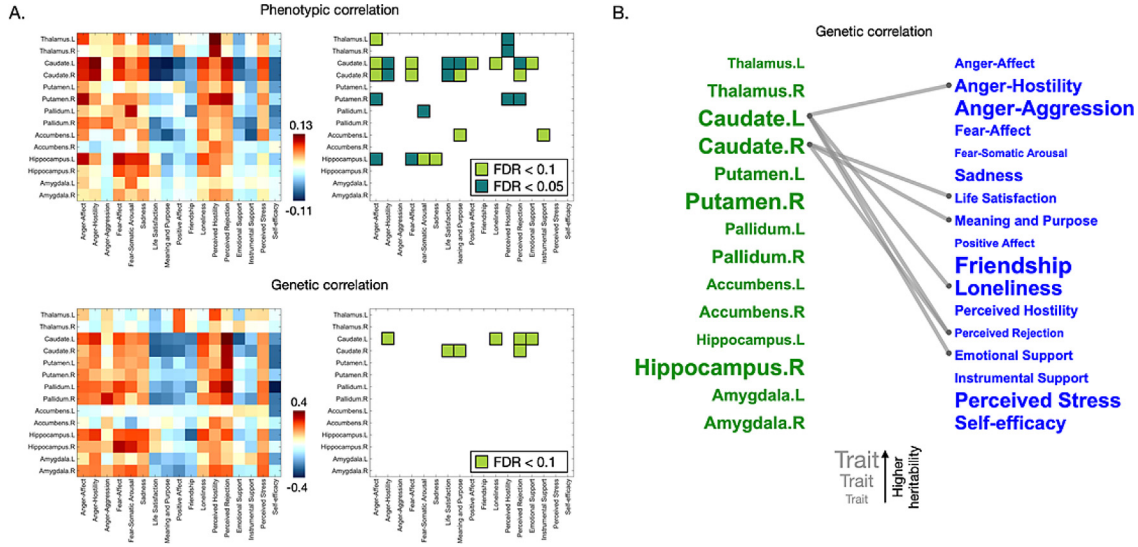

Fig. 3. Shared genetic effects of subcortical volumes and emotional traits. A. Left column: Phenotypic and genetic correlation matrix between subcortical volumes and emotional traits, which were estimated using bivariate analysis. Right column: The box indicates significant correlation with false discovery rate < 0.05 or < 0.1. B. Summary of genetic effects for subcortical volumes, emotional traits, and their associations. Larger text represents higher heritability for each phenotype, and each line indicates significant shared genetic effects between two different phenotypes.

related with the left caudate volume ($\rho_g = -.31$, $p < .01$). The perceived rejection score showed a positive correlation with the volumes of the bilateral caudate (left: $\rho_g = .40$, $p < .001$, right: $\rho_g = .34$, $p < .01$).

3.4. Supplementary analysis

To investigate more deeply about the association between the caudate volume and emotion, we additionally analyzed the phenotypic and genetic association between the emotional traits (See Supplementary Table1 and 2). A lot of emotional traits showed significant phenotypic and genetic correlations ($p < 0.05$, Bonferroni corrected). Notably, regarding the six emotional traits that were significantly genetically associated with the caudate volume (i.e., anger-hostility, life satisfaction, meaning and purpose, loneliness, perceived rejection, and emotional support), we found significant genetic associations between loneliness and anger-hostility, perceived stress, and emotional support. The emotional support and meaning and purpose also showed significant genetic correlation.

4. Discussion

In the present study, we investigated the heritability of various emotional traits and subcortical volumes in large twin HCP data. We also explored the existence of phenotypic, genetic, and environmental correlations between them using SOLAR. We found that all emotional traits and subcortical volumes were heritable. Additionally, most emotional traits were phenotypically correlated with the subcortical volumes. Notably, the caudate volume was genetically correlated with six emotional characteristics (i.e., anger-hostility, life satisfaction, meaning and purpose, loneliness, perceived rejection, and emotional support).

Table 5
Phenotypic and genetic correlations between emotion and subcortical volume

Phenotypes		Phenotypic correlation			Genetic correlation		
Subcortical volume	Emotion	Correlation	*p*-value	FDR	Correlation	*p*-value	FDR
Left thalamus	Anger-affect	0.085	0.010	0.09	0.121	0.383	0.584
	Perceived hostility	0.138	0.00003	0.008	0.246	0.372	0.255
Right thalamus	Perceived hostility	0.115	0.001	0.034	0.105	0.083	0.584
Left caudate	Anger-affect	0.097	0.004	0.062	0.234	0.022	0.184
	Anger-hostility	0.125	0.0003	0.034	0.286	0.001	0.065
	Fear-affect	0.098	0.004	0.062	0.251	0.012	0.116
	Life satisfaction	−0.106	0.002	0.034	−0.290	0.009	0.116
	Meaning and purpose	−0.115	0.001	0.034	−0.260	0.011	0.116
	Positive affect	−0.086	0.011	0.096	−0.246	0.041	0.209
	Loneliness	0.095	0.006	0.063	0.267	0.001	0.065
	Perceived rejection	0.109	0.001	0.034	0.404	0.0005	0.057
	Emotional support	−0.087	0.010	0.090	−0.309	0.003	0.079
Right caudate	Anger-affect	0.094	0.006	0.063	0.130	0.223	0.429
	Anger-hostility	0.110	0.001	0.034	0.201	0.027	0.201
	Fear-affect	0.088	0.010	0.090	0.188	0.070	0.255
	Life satisfaction	−0.103	0.002	0.038	−0.305	0.006	0.098
	Meaning and purpose	−0.096	0.005	0.063	−0.287	0.005	0.090
	Perceived rejection	0.100	0.003	0.051	0.345	0.004	0.081
Right putamen	Anger-affect	0.111	0.001	0.034	0.196	0.042	0.209
	Perceived hostility	0.105	0.002	0.034	0.210	0.031	0.201
	Perceived rejection	0.110	0.001	0.034	0.274	0.010	0.116
Left pallidum	Fear-somatic arousal	0.106	0.001	0.034	0.223	0.117	0.290
Left accumbens area	Meaning and purpose	−0.087	0.010	0.090	−0.017	0.900	0.959
	Instrumental support	−0.087	0.010	0.090	0.079	0.553	0.700
Left hippocampus	Anger-affect	0.105	0.002	0.034	0.219	0.097	0.272
	Fear-affect	0.106	0.001	0.034	0.231	0.074	0.256
	Fear-somatic arousal	0.092	0.005	0.063	0.249	0.080	0.263
	Sadness	0.093	0.005	0.063	0.247	0.037	0.209

Note. Bold fonts indicate significant genetic correlation at the false discovery rate (FDR) 0.1 level. *p*-value = uncorrected *p*-value, FDR = adjusted *p*-value

4.1. Heritability analyses

We found that all subcortical areas generally showed moderate to high heritability of their volumes. Naturally, this may support the hypothesis that subcortical volumes are largely determined by genes. The highest heritability estimate was observed for the right putamen ($h^2 = 0.84$, $p = 5.40\times10^{-54}$) and the lowest estimate for the left thalamus ($h^2 = 0.51$, $p = 1.85\times10^{-17}$). Similarly, several previous studies have reported high heritability estimates for the putamen volume (Kremen et al., 2010; Wright et al., 2002; Yoon et al., 2011) and moderate heritability estimates for the thalamus volume (Yoon et al., 2011). However, heritability estimates for the thalamus volume varied between 0 and 0.8 (den Braber et al., 2013; Kremen et al., 2010; Wright et al., 2002). These discrepancies in the heritability estimates for subcortical volume could be due to the sample size, age, sex, or other factors related to the characteristics of the participants.

It seems that all emotional traits were influenced by genetic effects. To date, despite substantial evidence supporting a close association between emotion and subcortical volume, only a few studies have examined the heritability of emotion (Gatt et al., 2014; Han and Adolphs, 2020; Jang et al., 2004; Stubbe et al., 2005; Zheng et al., 2016). However, instead of including various emotional traits, these studies focused only on a few aspects of emotion, such as well-being, depressive symptoms, life satisfaction, or negative affect (Gatt et al., 2014; Jang et al., 2004; Stubbe et al., 2005; Zheng et al., 2016). Although Zheng et al. (Zheng et al., 2016) investigated the heritability of both positive and negative affect using the Positive Affect and Negative Affect Schedule (PANAS) scale, they reported that positive affect was not heritable, which contradicts our findings. Han and Adolphs (2020) investigated the heritability of all emotional traits provided by the same HCP dataset as our study; however, they found that life satisfaction was not heritable. This inconsistency may be attributed to the difference in sample size since Han and Adolphs (2020) included 1189 participants from the HCP dataset, while we had 960 participants in total. Taken together, in contrast with these previous results, we found that both negative and positive emotions are heritable. This significant finding may provide insights for the future studies regarding the genetic effects on negative and positive emotions.

4.2. Phenotypic and genetic correlation between emotion and subcortical volumes

In line with previous studies (Gilam et al., 2018; Ismaylova et al., 2018; Pohlack et al., 2012), it was observed that the volume of the limbic area (i.e., thalamus and hippocampus) was phenotypically related to diverse negative emotional traits, such as anger-affect, fear-affect, fear-somatic arousal, sadness, and perceived hostility. Still, the findings from previous studies may not be sufficient to draw a concrete conclusion regarding the connection between limbic volume and emotion, as most studies included few emotional traits, such as anger or fear (Gilam et al., 2018; Pohlack et al., 2012). Ismaylova et al. (Ismaylova et al., 2018) found an association between reduced hippocampal volume and daily negative mood using PANAS; however, their sample size was significantly small ($N = 42$) and the participants' mood states were based on a daily diary, which might not be suitable for assessing the participants' overall emotional conditions. Therefore, our results may provide strong evidence for strengthening the phenotypic relation between limbic volume and negative emotional traits. Still, we did not find a significant association between emotional traits and the amygdala, which is an interesting result given that the amygdala is frequently reported to show a strong association with emotion (Adolphs et al., 1994; Kim and Hamann, 2007; LeDoux, 2003; Murray, 2007).

Additionally, this study showed that emotional traits were phenotypically related to areas of the basal ganglia (i.e., the caudate, putamen, pallidum, and accumbens area), which are well known to be the key regions in emotion regulation and processing (Herrero et al., 2002; Pierce and Péron, 2020). Our findings further suggest that although the basal ganglia is related to the emotion process in general,

stronger associations may exist between specific subcortical regions and emotional traits. For instance, we found that the pallidum volume, which is classically known to participate in motor control (Albin et al., 1989; Smith et al., 1998), was specifically associated with fear-somatic arousal. Since the NIH assessment for fear-somatic arousal assesses the participants' somatic problems (e.g., dizziness, heart pounding, and muscle tension), our results may well reflect the link between the emotional trait and the subcortical region's function. Additionally, we found a significant relation between the putamen volume and negative emotional traits (i.e., anger-affect, perceived hostility, and perceived rejection). Given that the putamen serves an important function in individuals' emotion recognition (Uono et al., 2017), it may suggest that the putamen plays a more prominent role in recognizing those negative emotional traits than other traits. It was also observed that accumbens area was associated with positive emotion (i.e., instrumental support and meaning and purpose), which is consistent with the results of previous studies showing that the accumbens area is responsive to rewards, specifically for positive reinforcement (e.g., money, positive value) (Knutson et al., 2001; Monk et al., 2008; Reynolds and Berridge, 2002).

In basal ganglia structures, notably, we found that the caudate was associated with diverse emotional traits, including both positive and negative emotions (i.e., anger-affect, anger-hostility, fear-affect, life satisfaction, meaning and purpose, positive affect, loneliness, perceived rejection, and emotional support), whereas other subcortical regions were associated with either positive or negative emotional traits. Moreover, the caudate was the only region that shared genetic traits with emotional traits (i.e., anger-hostility, life satisfaction, meaning and purpose, loneliness, perceived rejection, and emotional support), implying that the phenotypic correlations with such traits and the caudate volume are partly genetically determined. Although we have found our results with relatively moderate level of significance (i.e., FDR < 0.1), this level could be sufficiently acceptable for identifying genetic correlations since it was applied only for strictly significant phenotypic correlations. Therefore, it is plausible to demonstrate that the caudate may have a predominant influence on emotion in general. As this study did not measure genetic factors, it is difficult to identify which genetic factors are specifically shared between the caudate volume and emotional traits. Our finding may contradict with the previous finding (Van't Ent et al., 2017). Van't Ent et al. (2017) studied the associations between subjective well-being and subcortical volumes but did not find a significant phenotypic and genetic link between the caudate volumes and subjective well-being. This could be due to the differences in statistical methods since we used SOLAR while Van't Ent et al. (2017) used linear mixed model to measure phenotypic association and ADE model in OpenMx for genetic association. Additionally, Van't Ent et al. (2017) recruited MZ, DZ, and siblings and added their genetic relatedness as a random effect to the linear mixed model. These choices of different statistical analyses may have yielded different outcomes with our findings. Nevertheless, our findings are promising in that only a few studies have currently investigated the relation between the caudate volume and emotion (Dennison et al., 2015; Taren et al., 2013). Taren et al. (2013) reported a significant link between reduced caudate volume and higher dispositional mindfulness; however, mindfulness is "related" to well-being and does not directly measure individuals' well-being or positive emotion. Although Dennison et al. (2015) found that positive affect predicted the volume reduction in the caudate over time using PANAS, the sample only included adolescents of small size ($N = 89$). Thus, our findings highlight the importance of the caudate in individuals' diverse emotional traits and may serve as a crucial step in further investigating the genetic association between the caudate volume and emotional traits.

Furthermore, given that the caudate has been repeatedly studied in the context of cognition or mental disorders, such as schizophrenia, bipolar disorder, obsessive-compulsive disorder, and depression (Beyer et al., 2004; Kim et al., 2008; Krishnan et al., 1992; Rajarethinam et al., 2007; Robinson et al., 1995; Voelbel et al., 2006), it is also possible to assume that these mental disorders may be associated with the emotional traits that were found to be genetically related to the caudate volume in our study. Indeed, several prior studies have reported an association between depression and loneliness (Erzen and Çikrikci, 2018; Wei et al., 2005) and between schizophrenia and life satisfaction (Fervaha et al., 2016; Ponizovsky et al., 2003). Emotional support from close people has also been found to be a protective factor for individuals' psychological health (Johnson et al., 1999; Reblin and Uchino, 2008; Slavin and Rainer, 1990). Further studies on the association between the caudate, emotion, and mental disorders will be necessary to elucidate the underlying mechanism of the brain basis of mental disorders.

4.3. Limitation and methodological considerations

This study has some limitations. First, the current study mainly focused on subcortical volume; however, emotion is also related to other brain structures and functions, such as cortical thickness, surface area, and functional connectivity. Future studies will be required to consider such features when examining heritability and shared genetic influences with emotion. Second, we used self-report measures to assess emotional traits; therefore, there is a possibility that the participants' bias may have influenced our results. Including other measures (e.g., parental reports and observational methods) is recommended for future studies to increase the validity and reliability of the results. Third, our study measured individuals' emotional traits; however, it might not be the same as emotion regulation or recognition. Investigating emotion regulation or recognition may also be one way to fully capture the association between emotion and subcortical volume. Fourth, our analyses were based on AE model, which excludes the effects of shared environment, and thereby may leave the possibility of overestimated heritability and genetic correlation. However, the HCP data do not have a clear measure to indicate a common environment since the subjects were not asked about their rearing environment. Although the mother, father and family ID information are present, this does not imply that the subjects grew up in the same households. Therefore, we chose AE model instead of ACE model to prevent the spurious effects of shared environment. Finally, the effect sizes for the emotional traits were low to moderate, as well as for the phenotypic and genetic correlation between the emotional traits and subcortical volumes. These results indicate that there are other factors that influence the emotional traits and their associations with subcortical volumes. Since only a few studies have investigated the genetic influence on emotional traits, further study will be necessary to clearly identify the genetic basis of emotional traits and brain volumes.

5. Conclusion

To the best of our knowledge, our study is the first to examine the phenotypic and genetic link between diverse emotional traits and subcortical volume using a large twin sample drawn from the HCP. Our findings provide strong evidence that individuals' emotion and subcortical volume are both heritable and closely related. We found that the caudate volume is associated with emotional health in general, but also plays a crucial role in discovering the genetic basis of such emotional traits. Furthermore, by including a variety of emotional traits, we were able to capture a wide spectrum of emotional health. As emotion and subcortical volume are related to mental disorders, the current study may provide insights into the genetic basis of mental disorders and how emotional problems and subcortical volume can develop into mental disorders.

Declaration of Competing Interest

None.

Credit authorship contribution statement

Seung Yun Choi: Conceptualization, Methodology, Formal analysis, Investigation, Writing – original draft, Writing – review & editing, Visualization. **Sang Joon Son:** Conceptualization, Writing – review & editing, Funding acquisition. **Bumhee Park:** Conceptualization, Methodology, Investigation, Visualization, Funding acquisition, Supervision, Writing – review & editing.

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Data and code availability

All data and codes used in our study were obtained from the HCP website (http://www.humanconnectomeproject.org/) and SOLAR software website (http://solar-eclipse-genetics.org/index.html).

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Supplementary materials

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