

# Relationships among stress, emotional intelligence, cognitive intelligence, and cytokines

Ye-Ha Jung, PhD<sup>a</sup>, Na Young Shin, PhD<sup>b</sup>, Joon Hwan Jang, MD, PhD<sup>a,c</sup>, Won Joon Lee, MD<sup>d</sup>, Dasom Lee, MA<sup>a</sup>, Yoobin Choi, BS<sup>a</sup>, Soo-Hee Choi, MD, PhD<sup>a,e,\*</sup>, Do-Hyung Kang, MD, PhD<sup>f,\*</sup>

## Abstract

The brain has multiple functions, and its structures are very closely related to one another. Thus, the brain areas associated with stress, emotion, and intelligence are closely connected. The purpose of this study was to investigate the multiple associations between stress and emotional intelligence (EI), between EI and intelligence quotient (IQ), between cytokines and stress, and between cytokines and IQ. We measured the stress, EI, cognitive intelligence using IQ, and cytokine levels of 70 healthy subjects. We also analyzed the association of cytokines with IQ according to hemispheric dominance using the brain preference indicator (BPI). We found significant negative correlations between stress and the components of EI, such as emotional awareness and expression, emotional thinking, and emotional regulation. High levels of anger, which is a component of stress, were significantly related to poor emotional regulation. Additionally, emotional application was positively correlated with full-scale IQ scores and scores on the vocabulary, picture arrangement, and block design subtests of the IQ test. High IL-10 levels were significantly associated with low stress levels only in the right-brain-dominant group. High IL-10 and IFN-gamma levels have been associated with high scores of arithmetic intelligence. TNF-alpha and IL-6 were negatively associated with vocabulary scores and full-scale IQ, but IL-10 and IFN-gamma were positively associated with scores on the arithmetic subtest in left-brain-dominant subjects. On the other hand, IL-10 showed positive correlations with scores for vocabulary and for vocabulary and arithmetic in right-brain-dominant subjects. Furthermore, we found significant linear regression models which can show integrative associations and contribution on emotional and cognitive intelligence. Thus, we demonstrated that cytokines, stress, and emotional and cognitive intelligence are closely connected one another related to brain structure and functions. Also, the pro-inflammatory cytokines TNF-alpha and IL-6 had negative effects, whereas the anti-inflammatory cytokines (e.g., IL-10 and IFN-gamma) showed beneficial effects, on stress levels, and multiple dimensions of emotional and cognitive intelligence. Additionally, these relationships among cytokines, stress, and emotional and cognitive intelligence differed depending on right and left hemispheric dominance.

**Abbreviations:** BPI = brain preference indicator, EI = emotional intelligence, HPA axis = hypothalamo-pituitary-adrenocortical axis, IQ = intelligence quotient, SRI = stress response inventory.

**Keywords:** cytokines, emotional intelligence, intelligence quotient, hemispheric dominance, functional connection, stress

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<sup>a</sup> Department of Psychiatry, Seoul National University Hospital, Seoul, <sup>b</sup> College of Humanities, Kyonggi University, Suwon, <sup>c</sup> Department of Medicine, Seoul National University College of Medicine, <sup>d</sup> Department of Psychiatry, Kangdong Sacred Heart Hospital, <sup>e</sup> Department of Psychiatry, Seoul National University College of Medicine and Institute of Human Behavioral Medicine, SNU-MRC, <sup>f</sup> Emotional Information and Communication Technology Association, Seoul, Republic of Korea.

\* Correspondence: Do-Hyung Kang, Emotional Information and Communication Technology Association, 508, Samseong-ro, Gangnam-gu, Seoul, Republic of Korea (e-mail: basuare@daum.net), Soo-Hee Choi, Department of Psychiatry, Seoul National University College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul, 03080, Republic of Korea (e-mail: soohchoi@snu.ac.kr).

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## 1. Introduction

Stress can be defined as a real or anticipated disruption of homeostasis or an anticipated threat to well-being.<sup>[1]</sup> It has been established that psychosocial stressors are related to disease development, and psychosocial interventions have proven useful for treating stress-related disorders and may influence the course of chronic diseases.<sup>[2]</sup> Emotional intelligence (EI) plays a role as a moderator of the relationship between stress and psychological health,<sup>[3]</sup> as it promotes the adoption of proactive and effective coping strategies when dealing with stress.<sup>[4]</sup> EI is the ability of individuals to recognize their own and others' emotions, to use emotional information to guide their thinking and behavior, and to discriminate among different feelings and label them appropriately.<sup>[5]</sup> Higher EI is significantly related to lower stress and burnout,<sup>[6,7]</sup> and EI influences stress levels, ability to perform tasks, and effectiveness when working with others.<sup>[8]</sup> The relationship between cognitive impairment and stress-related exhaustion has been established,<sup>[9]</sup> and process-based cognitive training has been provided to patients with stress-related exhaustion.<sup>[10]</sup> Intelligence quotient (IQ) and EI are essential to human cognitive control processes.<sup>[11]</sup> Although, stress, emotional intelligence, and cognitive intelligence were closely connected, complex relationships among them have little known in these area. Thus, we focused on the dynamic associations between stress and EI, between EI and IQ and between stress and IQ in the same subjects at the same time.

In addition, cytokines are important in health and disease, specifically immune responses, inflammation, trauma, cancer and, etc.<sup>[12–14]</sup> On the other hand, immune reactions of neuronal bodies and glial cells are also implicated in the survival and conditioning of neurons to regenerate severed nerves, showing the role of inflammation and cytokines in peripheral nerve regeneration.<sup>[15]</sup> In addition, some of the cognitive deficits associated with inflammation may in part be related to inflammation-induced reductions in adult hippocampal neurogenesis, indicating that immune-reactive cells in the brain can support or disrupt neural processes depending on the phenotype and behavior of the cells in cognition and behavior.<sup>[16]</sup> Peripheral inflammatory responses can affect the brain, as neuroinflammation contributes to the increase in neurotoxic kynurenine pathway metabolites, and pro-inflammatory cytokines can also exert direct neurotoxic effects on specific brain regions.<sup>[17]</sup> The frontal brain regions involved in cognition and affect appear to be selectively affected by exposure to community violence, which has been associated with lower IQ scores.<sup>[18]</sup> Therefore, considering that cognitive functions or cognitive deficits associated with inflammation may be associated with some cytokines, we investigated the relationships between cytokines and cognitive intelligence in this study. Furthermore, stress is related to the hypothalamo–pituitary–adrenocortical (HPA) axis and inflammatory reactivity,<sup>[19,20]</sup> and many pro-inflammatory cytokines have a markedly activating influence on the HPA axis.<sup>[21]</sup> IL-6 and IL-1 $\beta$  have been associated with stress,<sup>[22]</sup> and restraint stress significantly decreased IFN- $\gamma$  production in rats.<sup>[23]</sup> Thus, we also focused on the relationships between stress-related cytokines and cognitive intelligence.

The effects of hemispheric lateralization on affective responses, emotion, language, and dexterity have been well established.<sup>[24]</sup> Indeed, structural laterality is associated with cognition and mood,<sup>[25]</sup> and the hemispheric lateralization of certain cognitive abilities in the human brain is beneficial for functioning.<sup>[26]</sup> The central nervous system plays a crucial role in the body's stress-related mechanisms, and stress may induce abnormalities in the sympathetic nervous system and HPA axis. Emotion is related to a group of structures at the center of the brain known as the limbic system, which includes the hypothalamus, cingulate cortex, hippocampi, and other structures. And, both IQ and EI are related to human cognitive control processes.<sup>[11]</sup> Thus, stress, emotion, and intelligence are structurally and functionally closely related to one another.

Therefore, we investigated associations among stress, EI, and IQ and then examined correlations between cytokines and these variables, suggesting hypothetical interactions among them (Supplementary Figure 1, <http://links.lww.com/MD/C940>). Additionally, we investigated these relationships according to hemispheric dominance.

## 2. Method

### 2.1. Subjects

We measured the stress, EI, IQ, and cytokine levels of 70 healthy subjects. Five subjects had no answer in most of items in Stress Response Inventory (SRI) and one subject in Brain Preference Indicator (BPI). So we analyzed with 65 subjects except 5 subjects in related data. The Structured Clinical Interview for DSM-IV-nonline patient version was used to assess psychiatric disorders. Exclusion criteria included history of psychosis, bipolar disorder,

major depressive disorder, substance abuse or dependence, significant head injury, seizure disorder, or mental retardation. This study was approved by the Institutional Review Board of Seoul National University Hospital, and informed consent was obtained from all participants.

### 2.2. Stress Response Inventory (SRI)

This experiment used 22 questions derived from the original SRI questionnaire.<sup>[27]</sup> Each question was scored on a Likert-type scale including “not at all” (0), “somewhat” (1), “moderately” (2), “very much” (3), or “absolutely” (4). The 22 questions were categorized into 3 simplified stress factors: somatization, depression, and anger.<sup>[28]</sup>

### 2.3. Emotional intelligence (EI)

EI was measured using the Korean version of the instrument<sup>[29]</sup> developed based on the ability model of EI.<sup>[30]</sup> EI was measured with 50 questions categorized into 5 simplified factors of emotional awareness and expression, empathy, emotional thinking, emotional application, and emotional regulation. Each of these 5 simplified factors consisted of 10 questions describing different feelings and emotions. Each question was scored on a 5-point Likert-scale of “not at all” (1), “somewhat” (2), “moderately” (3), “very much” (4), or “absolutely” (5). Each factor was scored, and higher scores indicated greater EI.

### 2.4. Intelligence quotient (IQ)

We used an abbreviated form of the Korean version of the Wechsler Adult Intelligence Scale<sup>[31]</sup> consisting of the vocabulary, arithmetic, block design, and picture arrangement subtests to estimate the full-scale IQ.<sup>[32]</sup> We adopted the abbreviated form to decrease participants' cognitive fatigue and improve their cooperativeness. In addition to the above 4 scales, digit span was also administered to measure verbal working memory.

### 2.5. Cytokine assays

TNF-alpha and IL-6 (R&D Systems, Minneapolis, MN) and IFN-gamma and IL-10 (Pierce Endogen, Rockford, IL) levels were measured using enzyme-linked immunosorbent assay (ELISA) kits. Absorbance was measured at 450 nm in a microplate reader (Versamax; Molecular Devices, Sunnyvale, CA). All plasma samples were coded so that investigators could perform the assay under blind conditions. All measurements were run in triplicate, and the statistical analysis relied on the average values obtained after subtracting the average of the blanks.

### 2.6. Brain preference indicator (BPI)

The BPI, a self-administered test to determine hemispheric dominance, consists of items that were normed on data obtained from EEG tests on dominance administered at the Biofeedback Institute of Denver.<sup>[33]</sup> In its final form, the self-administered version has been given to more than 500 people in so-called Wonder seminars. The results of this self-administered test have been shown to be correlated with comparable laboratory tests.<sup>[33]</sup> Subjects select the item that most closely represents their attitude or behavior. We deleted questions with multiple-choice answers and eliminated question 3; thus, the final self-administered test

**Table 1**  
Demographic characteristics and the levels of stress, EI, IQ, BPI and cytokines of the participants.

	Healthy controls (N=70)	
	Male/Female	N
	mean	SD
Age	25.68	3.89
SRI	16.75	12.23
EI	167.94	19.99
Emotional awareness and expression	34.34	5.38
Empathy	34.40	5.09
Emotional thinking	32.86	5.05
Emotional application	33.00	4.84
Emotional regulation	33.16	5.63
IQ	114.13	11.22
Vocabulary IQ	12.97	1.63
Digit span IQ	12.83	2.23
Picture arrange IQ	12.39	1.82
Block design IQ	13.64	2.48
Arithmetic IQ	12.79	2.63
BPI	4.68	0.79
TNF-alpha	28.27	72.95
IL-6	6.90	24.18
IFN-gamma	5.29	6.53
IL-10	22.14	43.66

BPI=brain preference indicator, EI=emotional intelligence, IQ=intelligence quotient, SRI=Stress Response Inventory.

consisted of 32 questions. The answer to each question was assigned a score, and the sum of the average scores for all items ranged from 1 to 9. Average scores of 1 or 9 indicated high lateralization. In this study, we divided left-brain-dominant (<5) and right-brain dominant (>5), based on the middle average score 5.

**2.7. Data analysis**

Student’s t-tests were used to analyze differences between 2 groups, and Pearson’s correlation coefficients were used to

analyze relationships between variables; p-values less than 0.05 were considered statistically significant.

**3. Results**

**3.1. Study participants**

Table 1 summarizes the demographic characteristics of the subjects, which shows the levels of stress, EI, IQ, BPI, and cytokines of the participants.

**3.2. Associations among stress, EI, and IQ**

Our investigation of the relationships between stress and EI revealed negative correlations between stress and emotional awareness and expression ( $r=-0.324, P=.008$ ), emotional thinking ( $r=-0.394, P=.001$ ), and emotional regulation ( $r=-0.386, P=.001$ ) (Fig. 1A, C, E). On the other hand, there were no significant correlations between stress and empathy and emotional application (Fig. 1B and D). High levels of anger were significantly associated with low levels of emotional regulation ( $r=-0.284, P=.022$ , Fig. 2). Our investigation of the correlations between emotion and IQ showed that emotional application was the only one of the 5 factors of EI to have positive correlations with the vocabulary ( $r=0.292, P=.014$ ), picture arrangement ( $r=0.290, P=.015$ ), block design ( $r=0.252, P=.035$ ), and full-scale IQ ( $r=0.240, P=.045$ ) scores (Fig. 3A–D). Interestingly, there was no significant correlation between stress and IQ, although stress was significantly correlated with EI and EI was significantly correlated with IQ.

**3.3. Linear regression models for relationships among cytokines, stress, and IQ**

We conducted linear regression analysis to elucidate relationships among the dependent variables and the independent variables including cytokines, stress, EI and IQ. We found linear regression models for understanding on complex and dynamic associations

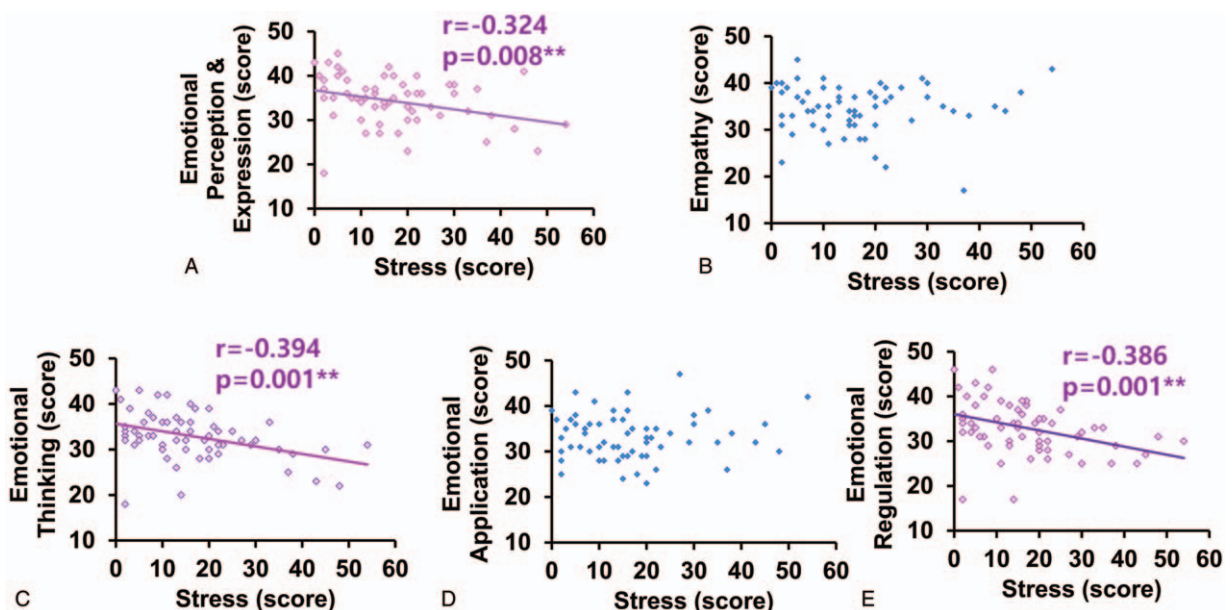


Figure 1. The correlations between stress and EI. (A–E) n=65. EI=emotional intelligence.



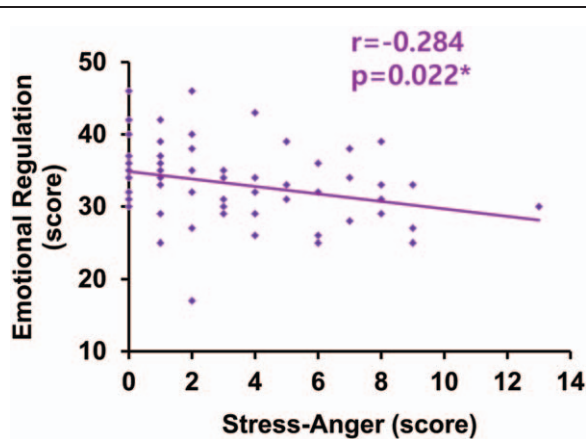


Figure 2. Association of anger in stress with emotional regulation. n=65.

between them. The regression model for the full-scale IQ is “ $Y = 0.208X_1 - 0.337X_2 + 0.291X_3 + 91.751$ ” (Y: the full-scale IQ,  $X_1$ : IL-10,  $X_2$ : IL-6,  $X_3$ : emotional application), indicating positive effects of IL-10 and emotional application and negative effects of IL-6 on the full-scale IQ in the total subjects ( $r = 0.402$ , adjusted  $R^2 = 0.123$ ,  $P = .009^{**}$ ; Fig. 4A). And, the regression model for EI is “ $Y = -0.218X_1 - 0.196X_2 - 2.986X_3 - 4.858X_4 + 6.397X_5 + 174.765$ ” (Y: EI,  $X_1$ : somatization stress,  $X_2$ : depression stress,  $X_3$ : vocabulary IQ,  $X_4$ : arithmetic IQ,  $X_5$ : vocabulary and arithmetic IQ), indicating positive effects of vocabulary and arithmetic IQ and negative effects of somatization and depression stress, and each vocabulary IQ or arithmetic IQ in the total subjects ( $r = 0.553$ , adjusted  $R^2 = 0.247$ ,  $P = .001^{**}$ , Fig. 4B). Additionally, we found linear regression models for understanding on complex and dynamic associations between them according to right-brain and left-brain dominance groups. In the left-brain dominance group, emotional thinking was affected negatively by somatization and depression stress, but

positively by cognitive intelligence, showing regression model of “ $Y = -0.321X_1 - 0.324X_2 + 0.239X_3 + 27.500$ ” (Y: ET,  $X_1$ : somatization stress,  $X_2$ : depression stress,  $X_3$ : Total VPBA) ( $r = 0.623$ , adjusted  $R^2 = 0.343$ ,  $P < 0.000^{***}$ ; Fig. 5A). On the other hand, the full-scale IQ was affected negatively by anger stress, but positively by emotional application, showing the regression model of “ $Y = -0.331X_1 + 0.535X_2 + 70.241$ ” (Y: the full-scale IQ,  $X_1$ : anger stress,  $X_2$ : emotional application) in the right-brain dominance group ( $r = 0.583$ , adjusted  $R^2 = 0.263$ ,  $P = .029^*$ ; Fig. 5B). And, emotional thinking was affected positively by IL-10 and vocabulary and arithmetic IQ, but affected negatively by IL-6, each vocabulary and arithmetic IQ, showing the regression model of “ $Y = 0.664X_1 - 0.382X_2 - 3.755X_3 - 4.447X_4 + 6.403X_5 + 37.297$ ” (Y: Emotional Thinking,  $X_1$ : IL-10,  $X_2$ : IL-6,  $X_3$ : vocabulary IQ,  $X_4$ : arithmetic IQ,  $X_5$ : vocabulary and arithmetic IQ) ( $r = 0.752$ , adjusted  $R^2 = 0.430$ ,  $P = .013^*$ ; Fig. 5C).

**3.4. Correlations between stress and cytokines, and between cytokines and IQ**

Next, we investigated the associations of cytokines with stress and IQ. First, we investigated the correlations between stress and cytokines. High IL-10 levels were significantly associated with low stress levels only in the right-brain-dominant group ( $r = -0.599$ ,  $P = .005$ , Fig. 6A). Second, we analyzed correlations between cytokines and IQ. High scores on the arithmetic subtest were associated with high levels of IFN-gamma ( $r = 0.280$ ,  $P = .019$ ) and IL-10 ( $r = 0.304$ ,  $P = .011$ ) (Fig. 6B and C).

**3.5. Correlations between cytokines and IQ in the right-brain- and left-brain-dominance groups**

We also analyzed the association of cytokines with intelligence according to hemispheric dominance using the BPI. Low scores on the vocabulary subtest were correlated with high levels of TNF-alpha ( $r = -0.300$ ,  $P = .041$ ) and IL-6 ( $r = -0.331$ ,  $P = .023$ )

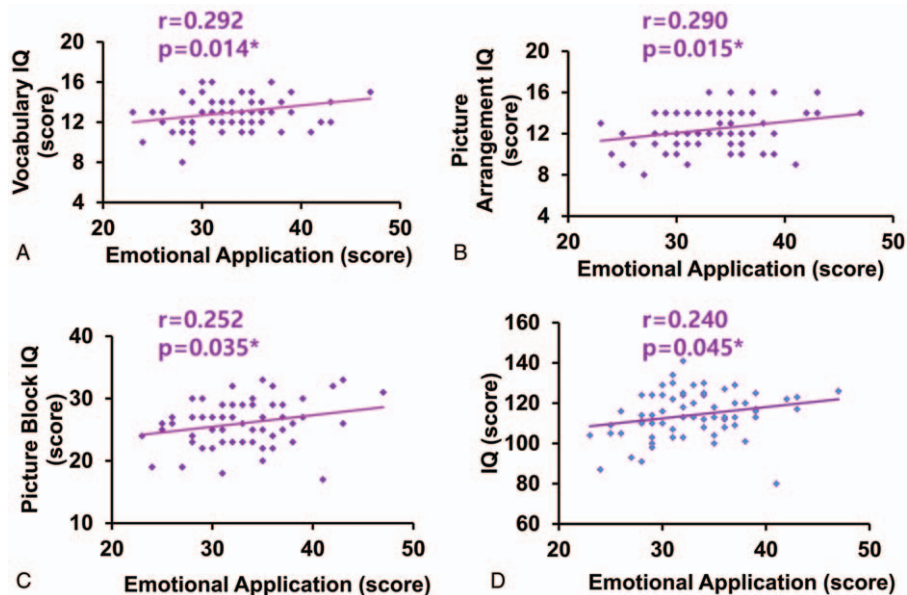
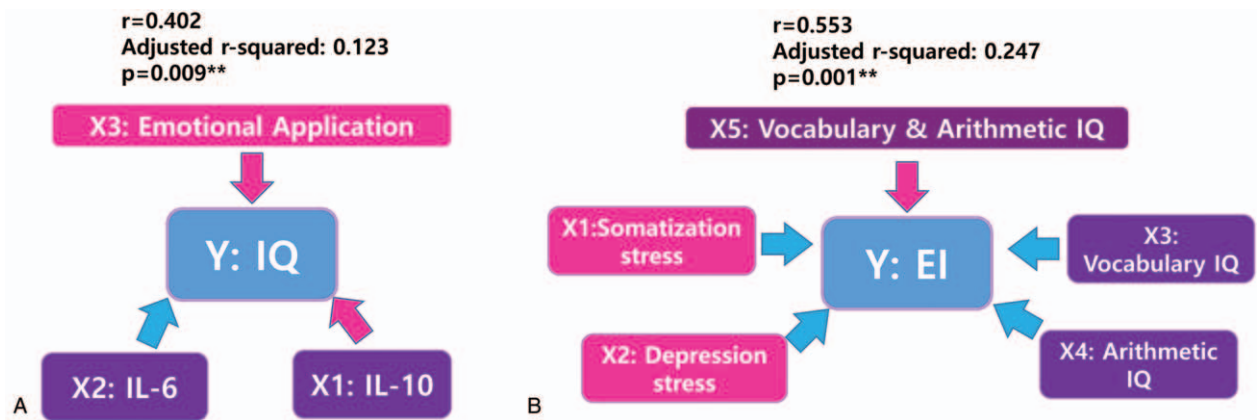


Figure 3. Correlations between emotional application and IQ. (A–D) n=70, IQ=intelligence quotient.



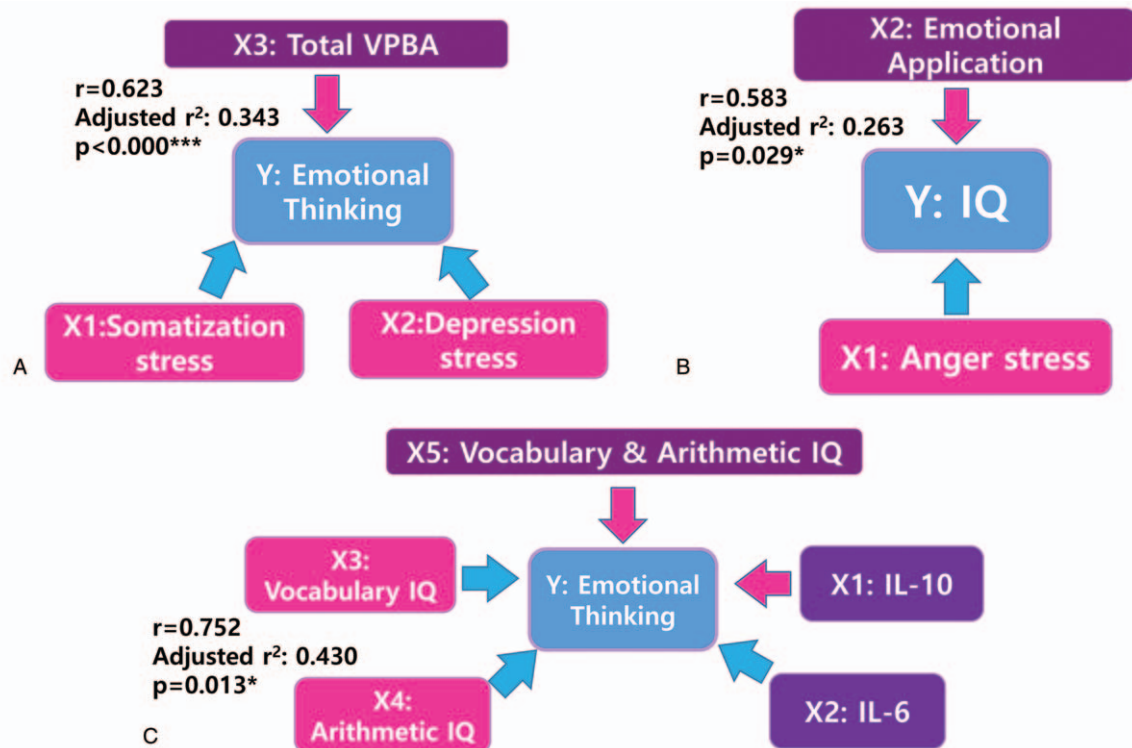
**Figure 4.** Linear regression models for understanding EI and IQ in the total subjects. A, B) Blue arrows: negative contribution, Pink arrows: positive contribution. (A)  $n=70$ ,  $Y=0.208X_1 - 0.337X_2 + 0.291X_3 + 91.751$ , Y: IQ,  $X_1$ : IL-10,  $X_2$ : IL-6,  $X_3$ : Emotional Application. (B)  $n=65$ ,  $Y=-0.218X_1-0.196X_2-2.986X_3-4.858X_4+6.397X_5+174.765$ , Y: EI,  $X_1$ : somatization stress,  $X_2$ : depression stress,  $X_3$ : vocabulary IQ,  $X_4$ : arithmetic IQ,  $X_5$ : vocabulary and arithmetic IQ. EI=emotional intelligence, IQ=intelligence quotient.

(Fig. 7A and B) in left-brain-dominant subjects. Moreover, high full-scale IQ was related to low levels of the pro-inflammatory cytokine IL-6 ( $r=-0.327$ ,  $P=.025$ , Fig. 7C). On the other hand, high scores on the arithmetic subtest were positively correlated with high levels of IFN-gamma ( $r=0.363$ ,  $P=.012$ ) and IL-10 ( $r=0.307$ ,  $P=.036$ ) in left-brain-dominant subjects (Fig. 7D and E). Similarly, high levels of the anti-inflammatory cytokine IL-10 were associated with high scores on the vocabulary ( $r=0.467$ ,

$P=.028$ ) and vocabulary + arithmetic ( $r=0.443$ ,  $P=.039$ ) subtests in right-brain-dominant subjects (Fig. 8A and B).

#### 4. Discussion

We found that stress was associated with EI and EI was related to IQ. Through linear regression analysis, we elucidated the integrative contribution on the full-scale IQ, representing positive



**Figure 5.** Linear regression model for EI and IQ in the right and left-dominance groups. (A–C) Blue arrows: negative contribution, Pink arrows: positive contribution. (A) Left-brain dominance group, (B, C) right-brain dominance group. (A)  $n=44$ ,  $Y=-0.321X_1 - 0.324X_2 + 0.239X_3 + 27.500$ , Y: ET,  $X_1$ : somatization stress,  $X_2$ : depression stress,  $X_3$ : Total VPBA (V: Vocabulary IQ, P: Picture Arrangement IQ, B: Block Design IQ, A: Arithmetic IQ). (B)  $n=20$ ,  $Y=-0.331X_1 + 0.535X_2 + 70.241$ . Y: IQ,  $X_1$ : anger stress,  $X_2$ : emotional application. (C)  $n=22$ ,  $Y=0.664X_1 - 0.382X_2 - 3.755X_3 - 4.447X_4 + 6.403X_5 + 37.297$ . Y: Emotional Thinking,  $X_1$ : IL-10,  $X_2$ : IL-6,  $X_3$ : vocabulary IQ,  $X_4$ : arithmetic IQ,  $X_5$ : vocabulary and arithmetic IQ. EI=emotional intelligence, IQ=intelligence quotient.

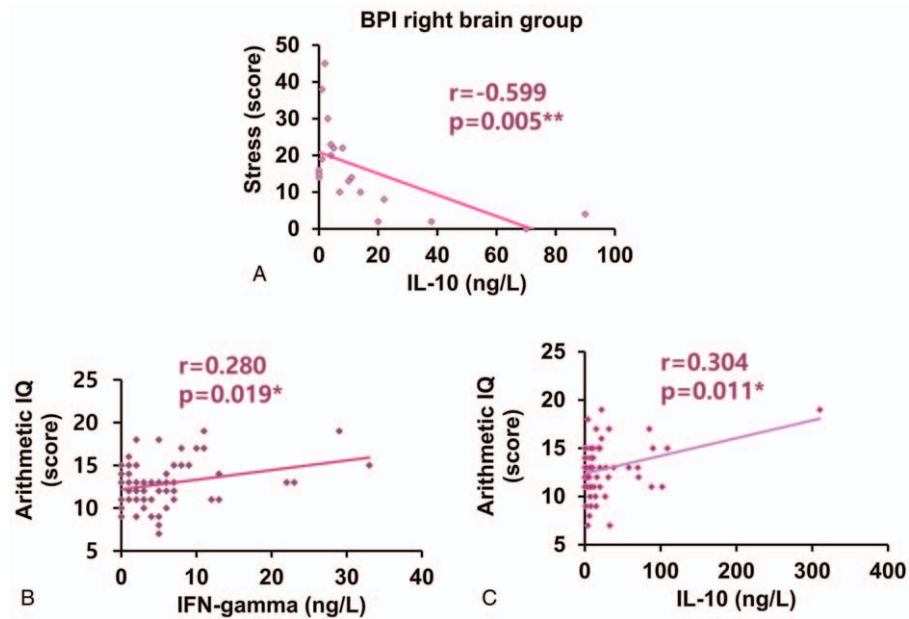


Figure 6. Correlations between cytokines and stress or arithmetic IQ. (A)  $n = 20$ , BPI: brain preference indicator, (B, C)  $n = 70$ . IQ=intelligence quotient.

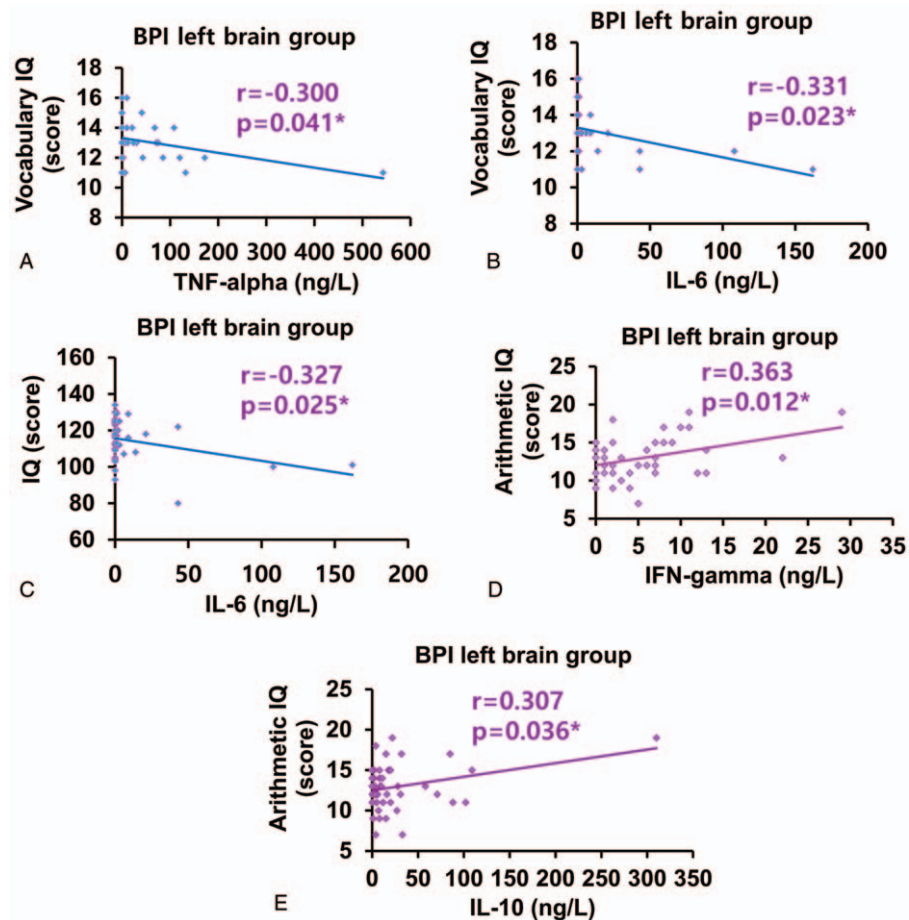
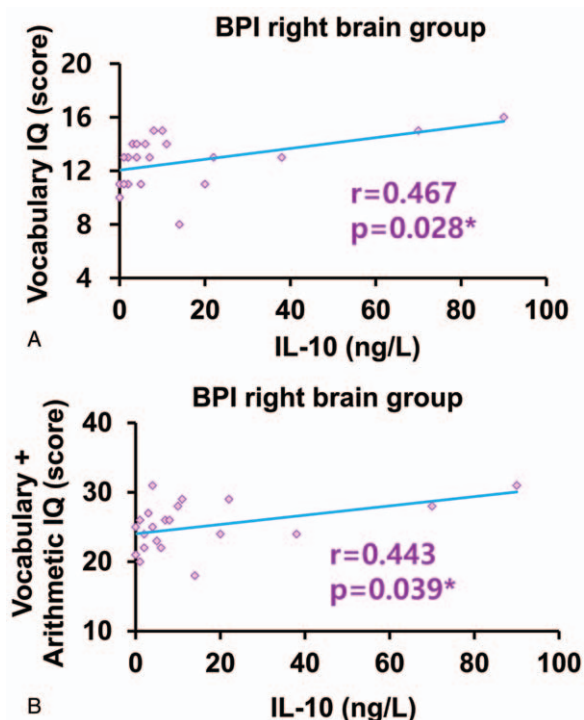


Figure 7. Correlations between cytokines and IQ in the left preference brain group. (A–E)  $n = 47$ , BPI=brain preference indicator, IQ=intelligence quotient.



**Figure 8.** Correlations between cytokines and IQ in the right preference brain group. (A, B)  $n=22$ , BPI: brain preference indicator. IQ=intelligence quotient.

influence of anti-inflammatory cytokine, IL-10 and emotional application, while showing negative influence of pro-inflammatory cytokine, IL-6 in the total subjects. Also, we confirmed complex influence that the sum score of vocabulary and arithmetic IQ positively contributed on EI, while somatization and depression stress and each vocabulary IQ and arithmetic IQ negatively affected on EI. In addition, cytokines were associated with stress and intelligence, and the pro-inflammatory cytokines TNF-alpha and IL-6 negatively affected vocabulary and the full-scale IQ scores, and anti-inflammatory cytokines, such as IL-10 and IFN-gamma, positively affected scores on the vocabulary and arithmetic subtests. On the other hand, the relationships between cytokines and IQ differed according to hemispheric dominance.

High levels of stress were associated with low EI. Interestingly, of the 5 factors comprising EI, high levels of emotional awareness and expression, emotional thinking, and emotional regulation were associated with low levels of stress. On the other hand, empathy and emotional application were not related to stress. Thus, we suggest that high stress may reduce emotional awareness and expression, emotional thinking, and emotional regulation, and that high levels of EI may decrease stress because those with high levels of EI may use proactive and effective coping strategies when dealing with stress.<sup>[4]</sup> These results are consistent with previous reports describing that higher EI is significantly related to lower stress.<sup>[6,7]</sup> Not surprisingly, high levels of anger, one contributor to stress, were related to low levels of emotional regulation. Thus, low levels of emotional regulation may lead to high levels of anger.

EI influences stress level, ability to perform tasks, and effectiveness when working with others,<sup>[8]</sup> and the importance of IQ and EI in cognitive control processes has been established.<sup>[11]</sup> Participants with a higher self-reported EI were

able to perform more cognitive tasks and did so more effectively than those with lower EI.<sup>[34]</sup> Internalized and externalized emotional dysfunction were not related to WAIS-IV full-scale IQ or verbal comprehension, perceptual reasoning, working memory, and processing speed scores; however, fear level, which includes health-related preoccupations and distorted perceptions, was significantly related to WAIS-IV full-scale IQ and verbal comprehension scores.<sup>[35]</sup> General intelligence is also negatively affected by psychopathology.<sup>[36]</sup> Among the 5 subscales comprising EI, only emotional application was associated with increased full-scale IQ scores and increased scores on the vocabulary, picture arrangement, and block design subtests. Emotional application includes abilities related to discriminating among, thinking about, and understanding various emotional states and different kinds of emotion. Future research should investigate why only emotional application was correlated with IQ.

Pro-inflammatory cytokine, IL-6 level has been associated with acute psychosocial stress in humans,<sup>[37]</sup> and decreased IL-10 expression was found in the hippocampus of stressed mice.<sup>[38]</sup> In this study, high levels of IL-10 were associated with low levels of stress. Thus, stress may affect the increase of pro-inflammatory cytokines and, at the same time, anti-inflammatory cytokines, such as IL-10, may contribute to the protection from stress.

Blunted HPA axis reactivity is associated with low intelligence in children with attention-deficit/hyperactivity disorder.<sup>[39]</sup> Circulating levels of TNF-alpha, sTNFRs, and IL-6 were negatively correlated with IQ at age 85.<sup>[40]</sup> In this study, IL-10 and IFN-gamma were related to high scores on the arithmetic subtest. Thus, we can infer that pro-inflammatory cytokines may negatively affect IQ and that anti-inflammatory cytokines may positively affect IQ. Additionally, better cognitive control following an emotional stressor is uniquely associated with less pronounced pro-inflammatory cytokine reactivity to such stress.<sup>[41]</sup> Therefore, cognitive control may decrease stress and pro-inflammatory cytokines but may increase anti-inflammatory cytokines and IQ.

The specific features that may affect IQ include the size and shape of the frontal lobes. Indeed, structural and functional brain-imaging studies have found differences in the brain pathways, especially especially parieto-frontal pathways that contribute to intelligence differences.<sup>[42]</sup> Interestingly, although we found correlations between cytokine levels and IQ scores, these associations differed according to hemispheric dominance. That is, in the left-brain-dominant group, high levels of pro-inflammatory cytokines, such as TNF-alpha and IL-6, were related to low full-scale IQ and vocabulary scores, whereas high levels of anti-inflammatory cytokines, such as IL-10 and IFN-gamma, were associated with high arithmetic scores. On the other hand, in the right-brain-dominant group, high levels of IL-10 were associated with high arithmetic and vocabulary scores. The activities of the HPA axis are related to behavioral lateralization and brain asymmetry, and brain IL-6 may be a mediator of the asymmetrical immunomodulation by the central nervous system.<sup>[43]</sup> The asymmetry of hemispheric volume has been related to verbal IQ minus performance IQ.<sup>[44]</sup> Thus, these hemispheric differences likely reflect differences in the mechanisms underpinning the relationships between the immune system and cognitive intelligence and warrant further exploration in the future.

Higher trait EI which refers to the individual differences in the perception, processing, regulation and utilization of emotional



information were significantly associated with lower reactivity to stress at both psychological and biological levels.<sup>[45]</sup> The emotional–cognitive interaction in stress, which has been established,<sup>[46]</sup> involves relationships among stress, emotion, and cognitive intelligence. The importance of functional connectivity within the limbic–frontal circuitry during emotional regulation has been reported,<sup>[47]</sup> and the structural and functional brain networks related to IQ have been identified.<sup>[48,49]</sup> Thus, the close relationships among stress, emotion, and IQ have been established and proven by research in fields such as psychology and biology and research on structural and functional connectivity in the brain. Interestingly, although significant correlations between stress and EI and between EI and IQ were found, no significant correlation between stress and IQ was observed. We can infer that this result may be related to brain structure. The HPA axis, which is related to stress,<sup>[19,20]</sup> is closely connected to the limbic area, which is associated with emotion<sup>[50]</sup>; moreover, the limbic area is directly connected with the frontal cortex and the brain pathways related to IQ.<sup>[18,42]</sup> That is, it is possible that stress is not significantly correlated with IQ because the HPA axis is not directly structurally connected with the frontal cortex and the brain pathways most strongly implicated in intelligence. Furthermore, higher levels of inflammation are associated with longitudinal changes in brain function in regions important for cognition.<sup>[51]</sup> Therefore, stress, emotion, cognitive intelligence, and the status of the inflammatory system seem to be both structurally and functionally very strongly associated with one another, leading to interactions between psychological and biological functions. Actually, we demonstrated these integrative associations among cytokines, stress, emotional and cognitive intelligence by using linear regression analysis. We confirmed that anti-inflammatory cytokine such as IL-10 has positive influence on emotional and cognitive intelligence, while pro-inflammatory cytokine such as IL-6 shows negative influence on them, supporting bodily healthy immune function is closely associated with emotional and cognitive intelligence. Also, we confirmed negative influence of stress on emotional and cognitive intelligence. Furthermore, we demonstrated different associations among cytokines, stress, emotional, and cognitive intelligence according to right-brain and left-brain dominance, which can demonstrate that right and left hemisphere is differentiated on emotional and cognitive intelligence.

There are a few limitations in this study that should be noted, particularly concerning multiple correlations. Multiple correlations can be accounted for with Bonferroni and other corrections, or by the approach of controlling the false discover rate, but these approaches are not always needed, given that reducing the type I error for null associations increases the type II error for those associations that are not null.<sup>[52,53]</sup> Thus, we used a rather liberal threshold for significance in correlation analysis, although requires a stricter significance threshold for individual comparisons, so as to compensate for the number of inferences being made. We may miss important findings when we stick to corrections for multiple correlations. Thus, our exploratory analyses may be meaningful for the further study. Another limitation is that correlation does not imply causation, but we can also infer causation with regression models we suggest in this study.

In conclusion, we found significant correlations between stress and EI and between EI and IQ. These results can show integrative associations among stress, EI and cognitive intelligence,

supporting complex interactions related to the structure and function of brain. Moreover, the pro-inflammatory cytokines TNF-alpha and IL-6 negatively affected stress and intelligence, and anti-inflammatory cytokines, such as IL-10 and IFN-gamma, positively affected these factors. Additionally, as these relationships between cytokines and IQ differed depending on hemispheric dominance, additional research is needed to explore the interactions and mechanisms that lead to hemispheric differences in stress, inflammation, emotion, and IQ.

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## Author contributions

**Conceptualization:** Ye-Ha Jung.

**Data curation:** Na Young Shin, Do-Hyung Kang.

**Formal analysis:** Ye-Ha Jung.

**Funding acquisition:** Do-Hyung Kang.

**Investigation:** Ye-Ha Jung, Na Young Shin.

**Methodology:** Ye-Ha Jung, Na Young Shin, Yoobin Choi.

**Project administration:** Ye-Ha Jung, Do-Hyung Kang.

**Supervision:** Soo-Hee Choi, Do-Hyung Kang.

**Visualization:** Dasom Lee.

**Writing – original draft:** Ye-Ha Jung.

**Writing – review & editing:** Ye-Ha Jung, Joon Hwan Jang, Won Joon Lee, Soo-Hee Choi, Do-Hyung Kang.

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