Aberrant function of frontoamygdala circuits in adolescents with previous verbal abuse experiences

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ABSTRACT

Previous studies reported an association of depressive disorder and structural alteration of frontolimbic brain regions in subjects with emotional abuse experiences during childhood and adolescence. The results suggest that aberrant function of the frontolimbic circuit and its relation with psychiatric symptoms can be found in adolescents with preclinical status. We investigated functional changes of frontolimbic networks during implicit negative emotional face processing and their relationships with depressive symptoms in adolescents with previous verbal abuse experiences. We designed a gender discrimination task using emotional faces to induce an implicit level of emotional exposure, and was completed by 31 preclinical male adolescents during an fMRI scan. The right amygdala activity and its functional connectivity with the rostral anterior cingulate cortex (ACC) during implicit processing of negative emotional faces showed a significant relationship with previous verbal abuse experiences. The hierarchical regression analyses showed that their current depressive symptoms were associated with aberrant functional interaction between the right amygdala activity and right amygdala-rostral ACC connectivity. Our findings of verbal abuse-related functional changes in the right frontoamygdala circuit may be related to vulnerability to future mood disorder.

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1. Introduction

Among various kinds of childhood maltreatments, emotional abuse has similar harmful effects on mental health to physical and sexual abuse (Teicher et al., 2006), and has been shown to have a higher association with depressive symptoms than other types of abuse. A recent study showed that only emotional abuse is associated with adulthood mood disorder (Martins et al., 2014). Childhood emotional abuse experiences were stronger predictors of depressive disorders than physical or sexual abuse in adult psychiatric outpatients (Gibb et al., 2007). Also, emotional abuse and neglect in childhood were closely related to depressive symptoms after controlling for physical abuse, sexual abuse, and lifetime trauma exposure (Spertus et al., 2003). High association
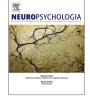
between previous emotional abuse and future depression may suggest that emotional abuse experiences can induce aberrant brain developments, especially in emotion regulation-related areas.

In emotionally abused victims, amygdala hyperreactivity to negative emotional stimuli was one of the most replicated findings in previous neuroimaging studies (Dannlowski et al., 2013, 2012; Maheu et al., 2010; Tottenham et al., 2011; van Harmelen et al., 2013). The amygdala, which plays a role in emotion identification, interacts with prefrontal brain regions for regulating emotion (Phillips et al., 2008). Among various brain regions, the ventro-medial side of the prefrontal cortexes including the rostral anterior cingulate cortex (ACC) functionally interacts with the amygdala for automatic emotion regulation, and these ventro-medial prefrontal cortexes develop relatively earlier than the dorsal and lateral sides of the prefrontal cortexes (Fuster, 2002; Phillips et al., 2008). Both resting functional connectivity (Gabard-Durnam et al., 2014) and reciprocal functional coupling, during fearful faces processing (Gee et al., 2013), between amygdala and medial prefrontal cortex

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(MPFC) mainly develop through adolescence periods. Also, a major white matter tract that connects the ACC and limbic regions, such as the cingulum bundle, matured through childhood and adolescence periods (Lebel and Beaulieu, 2011; Shaw et al., 2008). Given functional, anatomical, and developmental information, emotional abuse during the childhood and adolescence can have effects on the alteration of ventro-medial frontolimbic network development.

Several studies have tried to clarify the consequences of the experiences of emotional abuse on ventro-medial frontolimbic network maturation. In a previous longitudinal study, early life stress by maternal stress disrupted the resting functional connectivity of left amygdala-ventromedial prefrontal cortex (VMPFC) via high childhood cortisol levels, and the connectivity could predict anxiety and depressive symptoms in adolescents (Burghy et al., 2012). Maternal deprivation accelerates the maturation of amygdala-MPFC functional connectivity that can reduce the symptoms of separation anxiety (Gee et al., 2013). In a DTI study, a reduced fractional anisotropy in the cingulum bundle was reported and was related with depressive symptoms in young adults who have parental verbal abuse (VA) experiences (Choi et al., 2009). These results suggest that changes in the ventro-medial frontolimbic network can lead the victims of emotional abuse to a state where they are vulnerable to mood disorders. Identifying preclinical evidences can be important for improving mental health. Adolescents with VA experience, a common form of emotional abuse, can also face difficulties in the development of the ventro-medial side frontolimbic functional network. Aberrant function of this network may be linked to current psychiatric problems. However, to the best of our knowledge, there have been no studies for clarifying the frontolimbic functional changes in the adolescents who were exposed to VA. We speculated that preclinical adolescents would be appropriate subjects to evaluate early functional changes induced by VA experiences.

In this cross-sectional study, the correlations among previous VA experiences, brain functional changes, and current psychiatric symptoms were evaluated in preclinical adolescents. We hypothesized that previous VA experiences can be related to hyper-responsiveness of the amygdala and aberrant functional connection in the ventro-medial frontolimbic brain network in response to implicit emotional, specifically negative, faces. Also, aberrant information processing to implicit negative emotion may be related with current depressive and anxiety symptoms in adolescents. We anticipate that this study will provide the background of early brain changes related to emotional abuse for early intervention and treatment.

2. Methods

2.1. Subjects

We recruited subjects from general high school. To avoid selection bias that might occur if research was publicized as a study concerning verbal abuse, the research was first introduced as an investigation of language use in Korean adolescents. In total, 43 high school male subjects participated in our study and their depressive mood was evaluated by both the Beck Depression Inventory (BDI, self-report questionnaire) (Beck et al., 1961), and Montgomery–Asberg Depression Rating Scale (MADRS, semi-constructed measurements performed by a psychiatrist) (Montgomery and Asberg, 1979). The trait of anxiety was measured using the State-Trait Anxiety Inventory (STAI, self-report questionnaire) (Spielberger and Gorsouh, 1970). To evaluate psychiatric symptoms, all subjects were interviewed using the Kiddie-Schedule for Affective Disorders and Schizophrenia-Present and

Lifetime Version-Korean Version (KSADS-PL-K). We used the Wechsler Intelligence Scale for Children-Revised (WISC-R) to evaluate subjects' intelligence. Exclusion criteria of our study were previous/current psychiatric history or sexual/physical abuse history, full-scale IQ less than 70, significant head trauma or brain disease history, or any contraindication for functional magnetic resonance imaging (fMRI). Within 43 subjects, twelve subjects were excluded though these exclusion criteria: 7 subjects of low IQ (< 70), 2 subjects of history of major depressive disorder, one subject who reported previous traffic accident, one subject of craniopharyngioma (suspicious) in nasal cavity, and one subject who reported severe verbal abuse history (verbal abuse questionnaire score $> 3SD$). Psychologists reported that six among the seven subjects of low IQ (< 70) may have higher cognitive potential than the estimated IQ and the author of this article, who's also a psychiatrist, was unable to find any clinically relevant evidence for mental retardation during clinical evaluation. Thus, we excluded these subjects since low estimated IQ may represent the possibility of uncooperation and the usage of potential IQ can be a bias in further analyses of our study. Finally, 31 subjects (mean age: 16.12; SD: 0.48) were used for statistical analysis. All subjects except two were right handed.

All subjects joined and their parents agreed to this study voluntarily with written consent. The study was approved by the Ethics Committee of Korea Advanced Institute of Technology (KAIST).

2.2. Measurements of verbal abuse history

To measure previous VA history, we used a verbal abuse questionnaire (VAQ) that evaluates 15 kinds of VA, including scolding, yelling, swearing, blaming, threatening, and so on. The Korean version of the VAQ was recently adapted by our group (Jeong et al., 2015), and it showed good reliability in a previous study (Cronbach's alpha=0.9). A score of 40 or above on the verbal abuse questionnaire (VAQ) was defined as substantial exposure for peer VA (Teicher et al., 2010) and high-level exposure for parental VA (Choi et al., 2009) in the previous studies. This cutoff point of 40 was verified in our previous validation study of the Korean version of the VAQ with 5814 young adults (Jeong et al., 2015). Both parental and peer VA are frequent forms of VA, and the problems of mental health and brain development were induced by these VA (Choi et al., 2009; Teicher et al., 2006, 2010). The degree of VA from parents and peers was evaluated separately, and the quantity of VA was calculated by the sum of the VAQ score from parents and peers. The mean score of the total VAQ, peer VAQ, and parental VAQ were 65.94 (SD: 25.27; range 30–118), 37.77 (SD: 18.07; range 15–75), and 28.16 (SD: 10.92; range 15–65), respectively. To evaluate the effects of VA on the brain network, all subjects reported other forms of abuse history including sexual and physical abuse were excluded.

2.3. fMRI experimental design

To induce automatic and implicit emotion response, a gender identification task using emotional faces was designed. Our block design tasks consisted of faces in different emotional state: contempt, sad, happy, and neutral. The number of negative emotional blocks, contempt and sad, was twice as many as the number of positive emotional blocks consisting of happy faces. Contempt faces were included in the negative stimuli since contempt is one of the most representative expressions in abusive relationships (Laurie, 2008). Thus, we tried to consider the effects of both a general negative emotion (sad) and an emotional abuse-related emotion (contempt) in our design. Each 20s block had eight faces (2s face stimuli+0.5s resting) balanced with male and female, and