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Early life adversity induced third ventricular enlargement in young adult male patients suffered from major depressive disorder: a study of brain morphology

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Background: *Early life adversity (ELA) is not uncommon in major depressive disorder (MDD) patients. Childhood trauma has been reported more frequently in adult MDD patients relative to healthy controls. Recent researches have demonstrated that ELA could result in changes in brain morphology which might be an aetiological factor of MDD development.*

Materials and methods: *We recruited 40 young adult patients suffered from MDD and made computed tomography scan. Subjects were divided in two groups: MDD patients with ELA experience (E+D) vs. MDD patients without ELA experience (E–D) according to Chinese version-Childhood Trauma Questionnaire (CTQ). 17-item Hamilton Depression (HAMD) Scale and Neuropsychiatric Inventory (NPI) were also examined. Student's t-test was used to compare the HAMD scores, NPI scores, CTQ subcomponents scores, third ventricular (TV) width and volume of patients from E+D and E–D groups.*

Results: *Findings demonstrated that ELA might result in TV enlargement; furthermore, there was a correlation between physical neglect and TV volume.*

Conclusions: *These findings supported the hypothesis that ELA could induce changes of structure around the TV, which might undermine the aetiology of MDD.* (Folia Morphol 2018; 77, 3: 428–433)

Key words: early life adversity, major depressive disorder, third ventricle, computed tomography scan

INTRODUCTION

Early life adversity (ELA) refers to series of adversities occurring before sexual maturation, including physical, sexual, and emotional abuse, physical and emotional neglect, malnourishment, and loss of a parent [2, 14]. In Western countries, the experience of ELA is a common phenomenon. Up to 30–40% of the adult population report experiences of emotional or physical maltreatment during childhood [21]. In mainland China, the state of childhood maltreatment seems even severe. According to a study launched in 2004, the prevalence of emotional abuse, physical abuse, and sexual abuse were 45.1%, 32.4%, and 25.5%, respectively [29].

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Early life adversity could be an important factor which affects the later lifestyle and personality [18]. For example, maltreatment before the age of 18 is associated with higher cigarette use during adolescence [17]. Adults reporting more adverse childhood experiences have poorer sleep quality compared with those having less or no adverse experiences [5]. In recent years, ELA was considered to be related to adult affective disorders. There is compelling evidence that early adverse experiences, such as parental loss and maltreatment, are associated with a higher risk for developing depression in later life [4, 9]. In a review, Heim et al. [13] revealed that ELA significantly increases the incidence of affective disorders and can have an impact on the development of emotional abilities.

Major depressive disorder (MDD) is a world-wide problem particularly affecting teenagers and young adults [24], and is among the most prevalent and burdensome of all psychiatric diseases [3]. Early life adversity could exert a direct effect on depression via biological systems, such as the hypothalamic pituitary axis, and these effects could be independent of exposure to adulthood adversity [23]. For example, the risk of depression in persons with multiple early-life adverse experiences is four times that of a person who has not experienced early-life trauma [10]. Among the general population, young adults are in particular vulnerable population to the MDD. However, there is still lack of studies focusing on relationship between ELA and depression in the young adults from the perspective of brain morphology.

Until now, whether ELA has influence on brain morphology is still in controversy; a number of studies show ELA-related hippocampal volume reductions in healthy populations [8, 28], whereas others did not reveal this finding [6]. Considering different models (primates vs. non-primates), different trauma occurring ages, as well as different comorbid diseases, the relationship between ELA and brain structure is far from clear conclusion [1, 16, 22]. As a result, we launched a study comparing the cerebral computed tomography (CT) imaging of young adult of MDD with or without ELA, so as to find the role of ELA in the brain structure of young adult suffered from MDD.

MATERIALS AND METHODS

We performed a clinical cross-sectional observational study and recruited 40 young adult male MDD patients from the Department of Psychiatry of No. 261 Hospital, PLA. All patients (aged between 18 and 26 years old) met the DSM-IV criteria for MDD confirmed by a structured interview conducted by two certified psychiatrists, and had a 17-item Hamilton Depression (HAMD) Scale score more than 17 points. All of the subjects were first-episode, treatment-naïve, then they were further divided into two groups according to whether they had an experience of ELA: MDD patients with ELA experience (E+D) vs. MDD patients without ELA experience (E–D). Subjects were excluded from the study if they had a history of alcohol or drug abuse, neurological or serious physical diseases (e.g., gastrointestinal, neurological, endocrine, or cardiovascular disorders).

Neuropsychiatric Inventory (NPI) was developed by Cummings et al. [7] to assess and quantify neurobehavioural disturbances in dementia patients. It has an Apathy subscale, which consists of a general screening item rated on a Yes/No basis. The overall frequency (1–4) and severity (1–3) are then rated. Scores on the NPI depression subscale range from 0 to 12, with higher scores indicating more severe depression.

Early life adversity was quantified with the 28-item Chinese version-Childhood Trauma Questionnaire (CTQ), which assesses five types of adverse childhood experience subcomponents: emotional abuse (EA), physical abuse (PA), sexual abuse (SA), emotional neglect (EN), and physical neglect (PN). Scores ranged from 5 to 25 for each subscale, with high scores indicating strong exposure to the ELA [11]. According to the manual, patients who were positive for a history of childhood maltreatment based on mild to moderate cutoff scores of the total CTQ score (i.e., 41 points) [2]. In detail, cutoff scores according to Walker et al. [25] for each subscomponents were for sexual abuse ≥ 8, physical abuse ≥ 8, emotional abuse ≥ 10, physical neglect ≥ 10, and emotional neglect ≥ 15.

Brain CT examinations were acquired on a 64-slice SIEMENS SOMATOM Definition Flash CT scanner. All CT images were performed with patients in the supine position, untilted, using the anatomical landmarks of the scull base and vertex. Slice thickness was 5 mm. From each collected CT scan, two representative and consecutive images, displaying the third ventricles (TVs) at the level of the thalami in their largest dimensions were chosen. Maximum diameter of the TV and third ventricular volume were measured and calculated according to the methods of Wang's [26] automatically.

Table 1. Overall characteristics of subjects

	All (n = 40)	E+D (n = 21)	E–D (n = 19)	P
Age [years]	21.73 (2.52)	21.85 (2.65)	21.58 (2.53)	NS
Education level	11.73 (2.35)	11.52 (2.27)	11.94 (2.48)	NS
HAMD	22.40 (4.24)	23.42 (4.75)	21.26 (3.36)	NS
NPI-subscale				
Delusions	1.38 (0.68)	1.29 (0.64)	1.47 (0.70)	NS
Hallucinations	1.45 (1.06)	1.47 (1.08)	1.42 (1.07)	NS
Agitation	0.88 (0.82)	1.05 (0.86)	0.68 (0.75)	NS
Depression	4.87 (1.91)	4.67 (1.83)	5.10 (2.02)	NS
Anxiety	3.25 (2.47)	2.62 (1.96)	3.95 (2.81)	NS
Euphoria	1.35 (1.17)	1.62 (1.36)	1.05 (0.85)	NS
Apathy	4.25 (2.34)	4.61 (2.54)	3.84 (2.09)	NS
Disinhibition	1.25 (1.13)	1.42 (1.03)	1.05 (1.22)	NS
Irritability	1.73 (1.22)	1.71 (1.27)	1.74 (1.20)	NS
Aberrant motor behaviour	1.70 (1.26)	1.71 (1.35)	1.68 (1.20)	NS
Nighttime behaviour disturbances	3.10 (2.76)	2.95 (2.50)	3.26 (3.08)	NS
Appetite and eating abnormalities	3.63 (2.52)	3.62 (2.69)	3.63 (2.39)	NS

NS — not statistically significant

Table 2. Childhood Trauma Questionnaire (CTQ) scores of subjects

	All (n = 40)	E+D (n = 21)	E–D (n = 19)	P
CTQ	39.88 (5.98)	43.76 (4.79)	35.58 (3.83)	0.000
EA	8.63 (3.19)	9.38 (3.56)	7.79 (2.57)	0.116
PA	7.30 (1.90)	7.71 (2.28)	6.84 (1.26)	0.140
SA	6.10 (1.13)	6.24 (1.09)	5.95 (1.17)	0.423
EN	8.65 (3.42)	9.57 (4.01)	7.63 (2.31)	0.067
PN	9.78 (4.36)	11.33 (5.33)	8.05 (1.93)	0.014

EA — emotional abuse; PA — physical abuse; SA — sexual abuse; EN — emotional neglect; PN — physical neglect

Statistical analysis

Student's t-test was used to compare the HAMD scores, NPI scores, CTQ subcomponents scores, TV width and volume of patients from E+D and E–D groups. Bivariate correlation analysis was used to find the association of TV width/volume and total CTQ score/CTQ subcomponent scores. The data are expressed as the mean ± standard error. P value less than 0.05 was considered statistically significant. All statistical analyses were carried out using the SPSS, 17.0 statistical software package (IBM Corp., Armonk, New York, USA).

RESULTS

There were no significant differences across groups with regards to age and years of education. There were no significant differences across groups in total depression scores of HAMD and NPI-items ($p > 0.05$). Scoring of total CTQ and PN scores differed between groups ($p < 0.001$ and $p = 0.016$), while other subcomponent scores did not show significant differences (Tables 1, 2).

The mean ± standard deviation (SD) total ventricle width were 0.077 ± 0.122 cm and 0.697.08 ± ± 0.759 cm in E+D and E–D patients ($p = 0.037$), and the mean (± SD) total ventricle volumes were 1.587 ± ± 0.432 cm^3 and 1.193 ± 0.331 cm^3 in E+D and E–D patients ($p = 0.003$), respectively. This finding revealed that TV enlargement was more obvious in E+D compared with E–D. The examples were showed in Figure 1. Bivariate correlation analysis was done

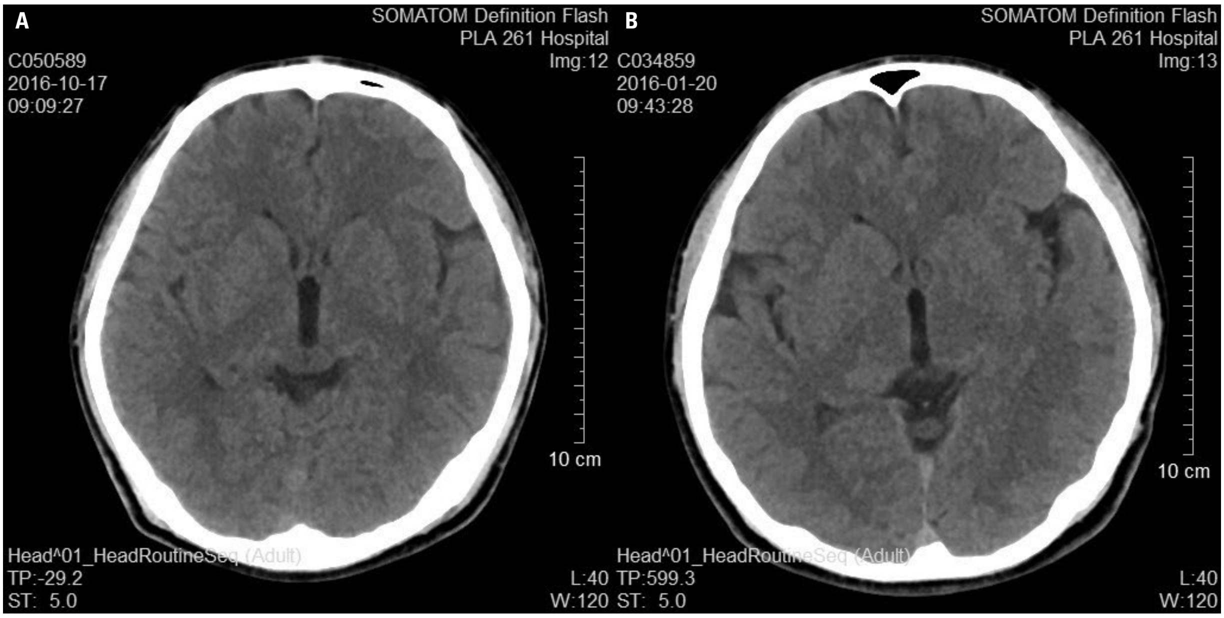

Figure 1. Example of computed tomography scan image from E+D patients (**A**) and E–D patients (**B**).

to find the correlation between CTQ subcomponent scores and TV width/volume. Among all the subcomponents, PN score had a mild correlation width TV volume significantly ($p = 0.02$, $r = 0.36$), while, there is still a trend between PN score and TV width; however, the data did not reach significance ($p = 0.39$).

DISCUSSION

In current study, we found that in adolescents and young adults suffering from MDD, those patients who experienced childhood traumatic events showed more serious TV enlargement; furthermore, TV volume was associated with ELA severity positively more obviously. Furthermore, of Chinese version-CTQ subscales, TV volume, rather than enlargement, showed positive correlation with PN.

Traumatic experiences in childhood can be found in many patients of depression [4]. In a cross-sectional study launched by Negele et al. [19], clinically significant histories of childhood trauma could be reported in as high as 75.6% of chronic depression patients. For those with MDD, a recent study in the United States of America found that nearly 62.5% patients reported more than two traumatic events [27]. In our study, we found 47.5% patients of MDD were ELA positive assessed by Chinese version-CTQ. The discrepancy might lie in two aspects, cultural difference and sample size.

Increased volumetric changes seen in the TV and changes in other closely associated structures are hypothesised as a basic anatomical characteristic of depression [15]. As we have mentioned previously, hypothalamic pituitary axis which was related to ELA and took part in MDD aetiology, also belonged to the structure of TV. In light of the Hendrie's theory, animals as well as human beings have to adapt the potential dangerous situations when they run into attack stimuli. This adaptation is undermined by the anatomical changes of structures around the TV, reflected by the series of clinical symptoms, such as hunched posture, avoidance of eye contact, loss of appetite for food and libido and sleep disruption, etc. [15]. In present study, TV width and volume were significantly larger in MDD patients with ELA experience than those without ELA experience. This finding could be explained by the childhood trauma. We proposed that ELA induced the atrophy of structures around TV causing TV enlargement and MDD vulnerability.

More in detail, bivariate correlation analysis showed that width and volume of TV were positively correlated with CTQ total ($p = 0.037$ vs. $p = 0.003$). For CTQ subcomponent scales, PN score correlated with volume of TV obviously ($p = 0.02$, $r = 0.362$), there is still a trend between PN score and TV width; however, the data did not reach significance ($p = 0.396$).

In 2013, a study from another group from China demonstrated that brain white matter densities in the bilateral inferior parietal lobe negatively correlated with neglect total scores on the CTQ [20]. In their article, authors used PN score (cutoff point = 10) or EN score (cutoff point = 15) or both (cutoff point = 20 for comorbid EN and PN), rather than abuse scores as factors that affected structure and function of specific brain areas related to sensation, perception, cognition, and affective modulation. In our study, our results revealed once again, that PN is an important factor for brain structure of MDD patients. Both results implied that neglect injury (emotional or physical) during childhood might be the most likely element for a child, which could do harm to brain development and result in affective disorders finally. Considering the development style of developing countries, we need to pay more attention to living condition of the left-behind children and orphans in modern society.

Limitations of the study

There are some limitations in our study. First, we only collected a total of 40 patients. The limited number of subjects and data limited a more detailed analysis. Second, we chose to exclude female patients from our study, and one advantage of this is prevention of gender bias. Actually, there are more women than men who suffered from MDD.

CONCLUSIONS

In conclusion, ELA was common in young adult male patients suffering from MDD; those who have a history of childhood trauma show larger TV width and volume. Among CTQ subcomponents, PN correlated significantly with volume of TV. All these findings might serve as a good reference for the aetiology and pathology of ELA in MDD patients.

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