Published in final edited form as:

Neuroimage. 2011 January ; 54S1: S280–S286. doi:10.1016/j.neuroimage.2010.05.027.

Exposure to Parental Verbal Abuse is Associated with Increased Gray Matter Volume in Superior Temporal Gyrus

Akemi Tomoda, MD^{1,2,3}, Yi-Shin Sheu, BS^{2,4}, Keren Rabi, MA², Hanako Suzuki, MA^{2,3}, Carryl P. Navalta, PhD^{1,2}, Ann Polcari, RN, CS, PhD^{1,2}, and Martin H. Teicher, MD, PhD^{1,2}

¹ Department of Psychiatry, Harvard Medical School, Boston, MA, USA

² Developmental Biopsychiatry Research Program, McLean Hospital, Belmont, MA

³ Department of Child Development, Faculty of Life Sciences, Kumamoto University, Kumamoto, Japan

Abstract

Objective—Exposure to parental verbal aggression (PVA) during childhood increases risk for the development of psychopathology, particularly mood and anxiety disorders. Other forms of childhood abuse have been found to be associated with alterations in brain structure. The aim of this study was to ascertain whether exposure to PVA was associated with discernible effects on brain morphology.

Methods—Optimized voxel based morphometry was performed on 21 unmedicated, right-handed subjects (18–25 years) with histories of PVA and 19 psychiatrically healthy controls of comparable age and gender. Group differences in gray matter volume (GMV) – covaried by age, gender, parental education, financial stress, and total GMV – were assessed using high-resolution, T1-weighted, volumetric MRI data sets (Siemens 3T trio scanner).

Results—GMV was increased by 14.1% in the left superior temporal gyrus (STG, BA 22) ($P = 0.004$, corrected cluster level). GMV in this cluster was associated most strongly with levels of maternal ($\beta = 0.544$, $P < 0.0001$) and paternal ($\beta = 0.300$, $P < 0.02$) verbal aggression and inversely associated with parental education ($\beta = -0.577$, $P < 0.0001$).

Conclusion—Previous studies have demonstrated an increase in STG GMV in children with abuse histories, and found a reduction in fractional anisotropy in the arcuate fasciculus connecting Wernicke's and frontal areas in young adults exposed to PVA. These findings and the present results suggest that the development of auditory association cortex involved in language processing may be affected by exposure to early stress and/or emotionally-abusive language.

Correspondence address: Akemi Tomoda, MD, PhD, Department of Child Development, Faculty of Medical and Pharmaceutical Sciences, Kumamoto University, 1-1-1 Honjo, Kumamoto, 860-8566, Japan, tomo@kumamoto-u.ac.jp, Fax: +81-96-373-5200 Tel: +81-96-373-5196.

⁴Current Address: Department of Psychology and Brain Science, The Johns Hopkins University, Baltimore, MD, USA

Financial Disclosures

The authors reported no biomedical financial interests or potential conflicts of interest.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

INTRODUCTION

Brain development is largely guided by genetic factors, but the final form is sculpted by environmental factors and early experience. Exposure to traumatic events such as childhood abuse and neglect, have been associated with alterations in the size or functional activity of a variety of brain regions (e.g., (Andersen et al., 2008; Bremner et al., 1997; De Bellis et al., 1999; De Bellis et al., 2002b; De Bellis and Kuchibhatla, 2006; Richert et al., 2006; Teicher et al., 2004; Teicher et al., 1997; Tomoda et al., 2009a)). We have recently conducted a voxel-based morphometry (VBM) study in young adults with histories of exposure to repeated episodes of childhood sexual abuse (CSA) and found that the most significant differences were bilateral reductions in gray matter volume (GMV) in the visual cortex (Tomoda et al., 2009a). Similarly, our laboratory conducted an analysis of fiber tract integrity in young adults exposed to parental verbal aggression (PVA) using diffusion tensor imaging (DTI) and tract based spatial statistics (TBSS), and observed a reduction in fractional anisotropy in three fiber tracts including the arcuate fasciculus that interconnects Wernicke's and frontal regions (Choi et al., 2009). These findings fit with an emerging hypothesis that exposure to early adversity may be associated with alterations in sensory systems that process and convey the adverse sensory experience (Teicher et al., 2006b).

PVA is a specific form of emotional abuse that some studies suggest may be associated with particularly severe psychiatric consequences (Johnson et al., 2001; Ney, 1987; Ney et al., 1994). However, unlike other forms of abuse, such as CSA, physical abuse (PA) and witnessing domestic violence (WDV), PVA is not considered a traumatic event by DSM-IV A1 and A2 criteria, and is often given little credence by mandated reporters (Manning and Cheers, 1995; Saulsbury and Campbell, 1985). We however, have shown that exposure to PVA was associated in early adulthood with elevated symptoms of depression, anxiety, anger-hostility, dissociation, and 'limbic irritability' (Teicher et al., 2006a). Effect sizes for exposure to PVA were equivalent to those for WDV and non-familial CSA, and exceeded those for parental PA (Teicher et al., 2006a). Delineating the association between exposure to PVA and alterations in brain structure may help to increase awareness regarding the importance of this common but insidious form of childhood abuse.

Hence, the aim of this study was to investigate whether exposure to PVA exerts an enduring effect on GMV. VBM was used to provide an unbiased, even-handed, whole-brain, voxel-by-voxel assessment in a community sample of late adolescents/young adults exposed to VA during childhood. Our sample was screened to exclude extraneous factors that might influence brain development. Further, we sought to assess whether alterations in regional GMV correlated with symptom ratings. We hypothesized that exposure to childhood PVA would be associated with alterations in the developmental trajectory of brain regions involved in processing verbally abusive stimuli, and would also affect brain regions regulating emotion, aggression, attention, and cognition.

MATERIALS AND METHODS

1. Recruitment

The McLean Hospital Institutional Review Board approved all procedures. Participants for the study were recruited from the community through an advertisement entitled "Memories of Childhood." Screenings were conducted on 1,455 volunteers using a detailed online assessment instrument with 2,342 entry fields that provided a vast array of information regarding developmental history and psychiatric symptoms. The questionnaire also included demographic information, such as subjects' and parents' educational levels, annual household income, and race/ethnicity. Subjects provided written informed consent prior to completing the online instrument, and again before interviews and brain imaging.

All potentially eligible subjects from the screenings were invited in for interviews. Those meeting inclusion, exclusion and imaging-safety criteria came in for two additional visits. The goal was to recruit a healthy, unmedicated group of subjects from the community, regardless of psychiatric history (except substance abuse). Selecting subjects with PVA meeting criteria for a specific disorder such as post-traumatic stress disorder would potentially overemphasize the effects of exposure by selecting the most seriously affected subjects. Similarly, selecting subjects without any psychiatric history would potentially underestimate the effects of exposure. The goal was to select a sample that would be representative of subjects exposed to PVA but to no other forms of abuse in order to assess the specific impact of exposure to verbal abuse. About 10% of young adults in the community report exposure to PVA but to no other forms of abuse (Teicher et al., 2006a).

Exclusion criteria included any histories of substance abuse (as this could affect trajectories of brain development), any recent substance use, head trauma with loss of consciousness, significant fetal exposure to alcohol or drugs, perinatal or neonatal complications, neurological disorders, or medical conditions that might adversely affect growth and development. Customary MRI exclusions included pacemakers, cerebral aneurysm clips, a cochlear implant, metal fragments lodged within the eye, dental braces, claustrophobia or pregnancy.

Subjects were enrolled in the PVA group if they had a self-reported history of exposure to PVA – defined by an average (i.e., maternal and paternal) ratings ≥ 40 on the Verbal Aggression Scale (VAS) (Teicher et al., 2006a), or a maximal (maternal or paternal) VAS score ≥ 50 – and if this history was confirmed during interview. Participants who had no significant history of exposure to PVA nor any history of Axis I disorders were grouped into the control group.

2. Subjects

The PVA group consisted of 21 young adults (9 males, 12 females; mean age, 21.2 ± 2.4 years) with substantial exposure to PVA during childhood (Table I). The control group consisted of 19 young adults (7 males, 12 females; mean age, 21.1 ± 1.9 years) with neither a current nor past DSM-IV Axis I disorder. Control subjects had no histories of exposure to abuse, traumatic events, or harsh corporal punishment. All participants were right-handed and unmedicated.

3. Procedures

The first visit was a face-to-face interview to obtain the subject's developmental history and current or lifetime diagnoses of psychiatric disorders using the Structured Clinical Interview for DSM-IV Axis I and II Disorders (SCID-I and SCID-II) (First et al., 1997) supplemented by the ADHD section of the K-SADS-PL (Kaufman et al., 1996). The semi-structured Traumatic Antecedents Interview (TAI) was used to provide detailed information on exposure to varying forms of abuse and discipline. Subjects needed to be consistent on self-report and interview.

During the second visit subjects were assessed using a variety of standardized psychometric tests, including the Wechsler Adult Intelligence Scale III (WAIS-III) (Wechsler, 1997), the Woodcock-Johnson Tests of Achievement-Revised, and the Memory Assessment Scale (Williams, 1991). During the third visit they were escorted to the Brain Imaging Center for neuroimaging on the centers 3T Siemens Trio Scanner. Imaging protocols including T1-volumetrics, DTI and T2-relaxometry scans.

4. Assessment Measures

Exposure to PVA was assessed with the Verbal Aggression Scale (VAS) (Teicher et al., 2006a). The VAS consists of 15 items that cover the key components of verbal abuse—scolding, yelling, swearing, blaming, insulting, threatening, demeaning, ridiculing, criticizing, belittling, etc. In a separate group of college students, the questionnaire showed high internal consistency as applied to both maternal and paternal behaviors (Cronbach alphas, 0.98 and 0.94, respectively). The VAS provides a continuous measure of exposure. A cut off score (average maternal and paternal VAS ≥ 40) or maximal (maternal or paternal) VAS ≥ 50 was used to identify subjects exposed to a substantial degree of verbal aggression (Choi et al., 2009).

Self-report ratings of psychiatric symptoms were obtained using Kellner's Symptom Questionnaire (SQ; (Kellner, 1987)). The SQ is a 92-item yes/no questionnaire used to elicit four symptom scales (depression, anxiety, anger-hostility, somatization) and four well-being subscales (content, relaxed, friendly, somatic well-being). It was developed to readily detect response to psychotropic medications, and, with the well-being items, is very sensitive to subtle differences from normal. (Kellner, 1987). Ratings of dissociation and 'limbic irritability', were obtained using the Dissociative Experience Scale (Bernstein and Putnam, 1986) and limbic system checklist-33 (LSCL-33) (Teicher et al., 1993). Scores on these scales are elevated by exposure to other forms of childhood traumatic stress (Teicher et al., 2006a), and have been found in previous studies to correlate with regional alterations in structure or function associated with maltreatment (Anderson et al., 2002; Choi et al., 2009). Hence, we used these ratings in an exploratory manner to delineate potential functional correlates of regions of altered GMV.

Low income and poverty may be important developmental risk factors for psychopathology. Young adult subjects were often uncertain about parental income while they were growing up. However, they were well aware of the degree of *perceived financial sufficiency*, or stress they experienced during this time. This was rated on a Likert scale ranging from 1 (much less than enough money for our needs) to 5 (much more than enough money for our needs). In all cases, perceived financial sufficiency explained a greater share of the variance in ratings of depression, anxiety, anger-hostility, 'limbic irritability' and dissociation than combined family income. Instead of a composite measure of socioeconomic status we included both the subject's level of perceived financial stress and parental education as studies suggest that these factors may provide more meaningful covariates than a composite score (Duncan and Magnuson, 2003).

5. MRI acquisition and analysis

Image analysis was performed on high-resolution, T1-weighted MRI datasets, which were acquired on a Trio Scanner (3T; Siemens AG, Siemens Medical Solutions, Erlangen, Germany). An inversion prepared 3D MPRAGE sequence was used with an eight-element phased-array RF reception coil (Siemens AG). The GRAPPA acquisition and processing was used to reduce the scan time, with a GRAPPA factor of 2. Scan parameters were: the sagittal plane, TE/TR/TI/flip = 2.74 ms/2.1 s/1.1 s/12 deg; 3D matrix $256 \times 256 \times 128$ on $256 \times 256 \times 170$ mm field of view; bandwidth 48.6 kHz; scan time 4:56.

As a fully automated whole-brain morphometric technique, VBM detects regional structural differences between groups on a voxel-by-voxel basis (Good et al., 2001a; Good et al., 2001b). VBM was performed using SPM5 (Statistical Parametric Mapping 5, developed by The Wellcome Department of Imaging Neuroscience, University College London, London, UK; <http://www.fil.ion.ucl.ac.uk/spm/software/spm5/>) for imaging processing (MATLAB 6.5; The MathWorks Inc., Natick, MA, USA). Images were segmented coarsely into gray

matter, white matter, cerebrospinal fluid, and skull/scalp compartments using tissue probability maps. We used a standard template (Ashburner and Friston, 2000, 2005) which conforms to the space defined by the ICBM, NIH P-20 project. It approximates the space described in the Talairach and Tournoux atlas (Talairach and Tournoux, 1988). The transform for this normalization was used to rewrite the original image into standard space. Volume changes induced by normalization were adjusted via a modulation algorithm. Spatially normalized images were segmented into gray and white matter and then smoothed using a 12-mm full-width half-maximum isotropic Gaussian kernel. Regional differences in GMV between groups were analyzed statistically using the general linear model. Potential confounding effects of age, sex, parental education, perceived financial sufficiency, and whole segment GMV were modeled, and variances attributable to them excluded. The resulting set of voxel values used for comparison generated a statistical parametric map of t -statistic SPM[t] that was transformed to a unit normal distribution (SPM[Z]). Statistical threshold was set at $P < 0.05$ with correction for multiple comparisons at cluster level (height threshold of $Z > 3.09$) because of the increased sensitivity of clusters to detect spatially extended signal changes (Hayasaka et al., 2004; Moorhead et al., 2005). Inference testing was based on the theory of Gaussian fields (Friston et al., 1996). We corrected for potential problems relating to non-isotropic smoothness, which can invalidate cluster level comparisons (Ashburner and Friston, 2000), by adjusting cluster size from the resel per voxel image (Hayasaka et al., 2004; Worsley et al., 1999).

6. Statistical analyses

Because effects of exposure to PVA cannot be studied using a randomized control trial we used a cohort design. A key statistical consideration in cohort studies is whether confounding factors stemming from selection bias significantly influenced the results. A characteristic is a confounder if it meets three criteria. First, it must be an extraneous risk factor for the outcome, second it must be associated with the exposure under study in the source populations, and third it must not be affected by the exposure; in particular, it cannot be an intermediate step in the causal path between exposure and outcome (Rothman et al., 2008). Variables that could potentially act as confounders are presented in Table I. Standardized difference scores (d') > 0.1 were used to identify variables that may be differentially distributed between exposed and non-exposed groups (Mamdani et al., 2005). Associations between these potential confounders and GMV findings were calculated using PASW Statistics 17 (SPSS Inc., Chicago, IL) and displayed in Table III.

Partial and multiple correlation analyses was used to explore the relationship between GMV in the identified cluster, neuropsychiatric measures and symptom ratings while controlling for age, gender, parental education, perceived, financial sufficiency and whole brain GMV. Distribution of STG GMV and paternal VAS values did not depart significantly from being normally distributed based on the Kolmogorov-Smirnov test. We used the false discovery rate method of Benjamini and Hochberg (Hochberg and Benjamini, 1990) to minimize the risk of type I errors in multiple comparisons. This method rank-orders observed p -values and only accepts those above a critical threshold as significant in order to limit the overall False Discovery Rate, which was set as < 0.05 to balance Type-I and Type-II risk in an exploratory analysis.

RESULTS

As seen in Table I, the two groups were well matched in age, parental education and degree of drug use. The most robust difference between groups, aside from their degree of exposure to PVA, was in their degree of perceived financial stress growing up ($d' = -0.96$). PVA subjects indicated that their family's financial resources were on average adequate, while controls indicated that they were more than adequate. There were slight differences between

the groups in gender distribution, years of education, alcohol use, and measures of memory and IQ that could serve as potential confounders based on a $d' > 0.1$ criteria.

As expected, subjects in the PVA group had substantially higher levels of anxiety, depression, somatization and anger-hostility. Altogether, 48% of the subjects in the PVA group had a history of mood disorders, and 24% had a history of anxiety disorders. Almost all were currently in remission.

The most prominent neural finding was a significant increase in GMV in the left superior temporal gyrus (STG) in individuals exposed to VA (BA 22; Talairach's coordinates $x = -61 - 50$, $y = -34 - 18$, $z = -1 - 13$, cluster size = 676, $P = 0.004$, corrected cluster level) (Fig. 1). On average there was a 14.1% increase in GMV in this cluster in the VA subjects. No other areas of increase were found with a corrected cluster probability value that approached significance.

A significant correlation was found between the left STG GMV and PVAS scores at the corrected cluster level ($P = 0.002$), FWE corrected voxel level ($P = 0.001$), and FDR corrected voxel level ($P = 0.002$). GMV of this region correlated significantly with PVAS scores across all subjects ($r = 0.521$, $P = 0.001$). This relationship was particularly strong for the subjects with PVA ($r = 0.55$, $P = 0.01$), but was not apparent in healthy control subjects ($r = 0.238$, $P > 0.3$).

Multiple regression analysis, using the covariates included in the VBM analysis, indicated that GMV in left STG (BA 22) correlated significantly with maternal and paternal VAS scores and parental education. As indicated in Table 2, the overall correlation was high ($r = 0.810$, adjusted $r^2 = 0.573$, $P < 0.0001$) with the major determinants being maternal VAS ($\beta = 0.544$, $P < 0.0001$), paternal VAS ($\beta = 0.300$, $P = 0.018$), and level of parental education ($\beta = -0.577$, $P < 0.0001$) (Fig 2). Interestingly, in the PVAS group maternal VAS ($\beta = 0.763$, $P = 0.006$) and paternal VAS ($\beta = 0.629$, $P = 0.013$) were significant independent variables, but parental education was not. In contrast, parental education ($\beta = -0.705$, $P = 0.013$) was a strong determinant in controls, but maternal and paternal VAS were not (Table II).

Table III indicates the association between potential confounders and left superior temporal gyrus GMV. Overall, none of these potential confounders, either alone or in combination, correlated significantly with the dependent variable ($r^2 = 0.26$, adjusted $r^2 = -0.19$; $F_{13,21} = 0.58$, $p > 0.8$). This suggests that none of these parameters qualified as confounders that could account for the association between exposure to PVA and superior temporal gyrus GMV.

Multiple regression analysis indicated that STG GMV accounted for a modest portion of the variance in the verbal comprehension index ($\beta = 0.25$, $P = 0.05$) in addition to FSIQ ($\beta = 0.67$, $P < 0.0001$) ($r^2 = 0.4988$, adjusted $r^2 = 0.4546$, $P < 0.0001$). There was also a significant correlation between left STG GMV and consumption of hard liquor ($r = 0.497$, $P < 0.002$). There were no other significant corrected correlations between psychiatric symptom ratings and STG GMV.

Using a lower criteria for statistical significance revealed a 10.5% increase in GMV in the left parahippocampal gyrus (BA 36; Talairach's coordinates $x = -38$, $y = -37$, $z = -10$, cluster size = 129, $P < 0.001$, uncorrected voxel level) in PVA subjects. Examination of voxels with reduced GMV in PVA subjects identified no significant corrected voxel level-cluster regions. One tiny region of reduced GMV in PVA subjects was identified. There was a 9.4% reduction in GMV in the right middle frontal gyrus (BA 9, $x = 30$ $y = 32$ $z = 28$, cluster size = 4) that was significant at the uncorrected voxel level ($Z = 3.15$, $P = 0.001$).

DISCUSSION

During the last few decades, researchers have made considerable progress in elucidating the neurobiological consequences of exposure to child abuse or maltreatment. Most studies have focused on individuals exposed to multiple forms of trauma (typically CSA and/or PA) who are highly symptomatic (Bremner et al., 1997; Carrion et al., 2007; De Bellis et al., 1999; De Bellis et al., 2002a; De Bellis et al., 2002b; Jackowski et al., 2008; Richert et al., 2006; Stein et al., 1997; Teicher et al., 2004; Vermetten et al., 2006; Vythilingam et al., 2002). These studies have predominantly identified alterations in corpus callosum, hippocampus and frontal cortex.

We have recently focused on the potential consequences of exposure to specific forms of childhood maltreatment and have included in the analysis both symptomatic and asymptomatic individuals. What we have learned from this approach is that sensory systems involved in processing and relaying the aversive sensory input may be specifically affected. Hence, we observed alterations in GMV in primary and secondary visual cortex in individuals exposed to repeated episodes of CSA (Tomoda et al., 2009a), and reduced FA in a portion of the arcuate fasciculus in individuals exposed to PVA (Choi et al., 2009). We have also collected data indicating that the visual-limbic pathway is affected in individuals who witnessed domestic violence, and cortical pain pathways affected in individuals exposed to harsh corporal punishment (Tomoda et al 2009b).

The present study expands on this body of knowledge by showing that exposure to PVA was associated with alterations in left STG/BA22. This region plays a critical role in processing of language and speech. Lesions in the posterior portion of BA22 typically result in the development of Wernicke's aphasia (Gartus et al., 2009). Hence, it makes sense that exposure to high levels of PVA would potentially stimulate this region during childhood and potentially alter its developmental trajectory. These finding fit, to a significant degree with our previous findings of reduced FA in the left arcuate fasciculus of the left superior temporal gyrus (Choi et al., 2009). The most curious aspect of this finding, however, was that GMV was increased in direct proportion to their degree of exposure. We had predicted that GMV would have been reduced in this region, analogous to the reduction in visual cortex GMV we observed in subjects with CSA. However, in retrospect this present finding makes sense. Recent studies indicate that this region continues to mature into late adolescence/early adulthood with a progressive decline in regional cerebral blood flow, presumably associated with dendritic pruning (Devous et al., 2006). Hence, a relatively low level of GMV in subjects within this age range may be indicative of typically healthy development. This seems plausible given our finding of an inverse relationship between left STG/BA22 GMV and parental education. One potential explanation is that parents with higher levels of education may tend to provide their children with a greater or richer degree of verbal stimulation, and this may be reflected in a developmental trajectory that emphasizes both a high degree of overproduction prior to puberty and by extensive pruning during adolescence, as previously reported to occur in subjects with superior IQs (Shaw et al., 2006). Exposure to PVA may interfere with the development of the left STG/BA22 by delaying its development or attenuating the degree of pruning.

Previous studies on the effects of early abuse did not report results for STG, with one notable exception. Our finding of increased GMV in left STG are commensurate with a previous report from De Bellis *et al.*, (De Bellis et al., 2002a) who conducted a volumetric MRI study of abused female pediatric subjects with PTSD. He found that STG GMV was increased bilaterally, particularly on the right side.

The present finding, along with our previous finding of reduced FA in the left arcuate fasciculus and left cingulum bundle in a subset of subjects with high-level exposure to PVA (Choi et al., 2009) suggest that left temporal lobe structures may be particularly susceptible to exposure to PVA. How these alterations may affect function is unclear. STG GMV explained a portion of the variance in verbal comprehension that was not accounted for by FSIQ or age. We suspect that the potential effects may be much more subtle and may influence the subject's response to emotionally laden content or to highly personal communications.

The main limitation of this study is the relatively small sample size. A large, initial sample of 18- to 25-year-olds from the community were surveyed to identify an ideal healthy sample of subjects exposed only to PVA and to no other forms of trauma or early adversity to provide the most direct test of our hypotheses. Exposure to high levels of PVA but to no other forms of abuse is a relatively common occurrence, reported by about 10% of subjects in this age range. Our findings should generalize well to subjects experiencing PVA but no other forms of abuse, as we selected subjects without regard to psychopathology (except substance abuse). It remains to be seen if the same findings emerge in subjects exposed to PVA along with other forms of maltreatment.

VBM studies provided an unbiased, even-handed, assessment of regional alterations in GMV. However, these studies have a significant number of limitations. Care was taken to make sure that there were no issues with alignment. Subjects in the two groups were of virtually identical age, and selected from a narrow age range to minimize any potential developmental differences in template registration. All subjects were scanned on the same machine over the same time-period. There were no significant differences between groups in gender distribution and degree of drug and alcohol use. There was a slight but highly significant difference in degree of perceived financial stress, which were controlled for statistically. There were also slight differences between groups in a number of other parameters (Table III), but none of these were significantly associated with GMV in the identified region, indicating that they were not meaningful confounders. The primary finding of increased GMV in left STG was observed with a corrected $P = 0.004$ at the cluster level. Additional findings of increase in GMV in left parahippocampal gyrus and reduced GMV in right middle frontal gyrus were only observed at the uncorrected voxel level and mentioned for completeness. They are consistent with previous findings of reduced FA in the cingulum bundle in the left parahippocampal gyrus of subjects with PVA (Choi et al., 2009) and reduced right prefrontal cortex GMV in subjects exposed to harsh corporal punishment (Tomoda et al., 2009b). There is no guarantee that these were not false-positive results or that all relevant brain areas were identified.

Although this study revealed a strong association between a self-reported history of PVA and increased GMV in left STG, it should be emphasized that the finding is correlational and does not prove that PVA caused the increased. A variety of alternative explanations could be advanced, such as the possibility that individuals with increase STG GMV may be prone to over-interpret verbal communications as abusive. Prospective longitudinal studies may help to better establish a causal relationship. Nevertheless, these findings are consistent with a causal relationship and suggest that exposure to PVA may act as a traumatic stressor to alter the development of the superior temporal gyrus. If so, these results underscore efforts to prevent children from experiencing verbal abuse from parents, other adults or peers (Teicher et al., 2006a; Teicher et al., in press).

These findings may also be relevant to the development of therapeutic strategies for treating survivors of childhood maltreatment. Most forms of psychotherapy require patients to verbally process their therapists' feedback and guidance, and patients rely on language to

communicate their experiences and emotional states. However, if speech processing and language comprehension abilities are altered due to past abusive experiences, then novel treatment methodologies may be needed to effectively cope with these neurobiological differences.

Acknowledgments

This study was supported by RO1 awards from the U.S.A. National Institute of Mental Health (MH-53636, MH-66222) and National Institute of Drug Abuse (DA-016934, DA-017846) to MHT, and Grant-in-Aid for Scientific Research to AT from Japan-U.S. Brain Research Cooperation Program. We thank Ms. Cynthia E. McGreenery and Daniel Webster R.N., M.S., C.S., for recruitment and interviewing of subjects.

References

- Andersen SL, Tomoda A, Vincow ES, Valente E, Polcari A, Teicher MH. Preliminary evidence for sensitive periods in the effect of childhood sexual abuse on regional brain development. *J Neuropsychiatry Clin Neurosci* 2008;20:292–301. [PubMed: 18806232]
- Anderson CM, Teicher MH, Polcari A, Renshaw PF. Abnormal T2 relaxation time in the cerebellar vermis of adults sexually abused in childhood: potential role of the vermis in stress-enhanced risk for drug abuse. *Psychoneuroendocrinology* 2002;27:231–244. [PubMed: 11750781]
- Ashburner J, Friston KJ. Voxel-based morphometry--the methods. *Neuroimage* 2000;11:805–821. [PubMed: 10860804]
- Ashburner J, Friston KJ. Unified segmentation. *Neuroimage* 2005;26:839–851. [PubMed: 15955494]
- Bernstein EM, Putnam FW. Development, reliability and validity of a dissociation scale. *J Nerv Ment Dis* 1986;174:727–735. [PubMed: 3783140]
- Bremner JD, Randall P, Vermetten E, Staib L, Bronen RA, Mazure C, Capelli S, McCarthy G, Innis RB, Charney DS. Magnetic resonance imaging-based measurement of hippocampal volume in posttraumatic stress disorder related to childhood physical and sexual abuse--a preliminary report. *Biol Psychiatry* 1997;41:23–32. [PubMed: 8988792]
- Carrion VG, Weems CF, Reiss AL. Stress predicts brain changes in children: a pilot longitudinal study on youth stress, posttraumatic stress disorder, and the hippocampus. *Pediatrics* 2007;119:509–516. [PubMed: 17332204]
- Choi J, Jeong B, Rohan ML, Polcari AM, Teicher MH. Preliminary evidence for white matter tract abnormalities in young adults exposed to parental verbal abuse. *Biol Psychiatry* 2009;65:227–234. [PubMed: 18692174]
- De Bellis MD, Keshavan MS, Clark DB, Casey BJ, Giedd JN, Boring AM, Frustaci K, Ryan ND. Developmental traumatology. Part II: Brain development. *Biol Psychiatry* 1999;45:1271–1284. [PubMed: 10349033]
- De Bellis MD, Keshavan MS, Frustaci K, Shifflett H, Iyengar S, Beers SR, Hall J. Superior temporal gyrus volumes in maltreated children and adolescents with PTSD. *Biol Psychiatry* 2002a;51:544–552. [PubMed: 11950456]
- De Bellis MD, Keshavan MS, Shifflett H, Iyengar S, Beers SR, Hall J, Moritz G. Brain structures in pediatric maltreatment-related posttraumatic stress disorder: a sociodemographically matched study. *Biol Psychiatry* 2002b;52:1066–1078. [PubMed: 12460690]
- De Bellis MD, Kuchibhatla M. Cerebellar volumes in pediatric maltreatment-related posttraumatic stress disorder. *Biol Psychiatry* 2006;60:697–703. [PubMed: 16934769]
- Devous MD Sr, Altuna D, Furl N, Cooper W, Gabbert G, Ngai WT, Chiu S, Scott JM 3rd, Harris TS, Payne JK, Tobey EA. Maturation of speech and language functional neuroanatomy in pediatric normal controls. *J Speech Lang Hear Res* 2006;49:856–866. [PubMed: 16908880]
- Duncan, GL.; Magnuson, KA. Off With Hollingshead: Socioeconomic Resources, Parenting, and Child Development. In: Bornstein, MH.; Bradley, RH., editors. *Socioeconomic Status, Parenting, and Child Development*. Lawrence Erlbaum; Mahwah, New Jersey: 2003. p. 83-106.
- First, MB.; Spitzer, RL.; Gibbon, M.; Williams, JBW. Structured clinical interview for DSM-IV axis I disorders - clinician version (SCID-CV). American Psychiatric Press; Washington, DC: 1997.

- Friston KJ, Holmes A, Poline JB, Price CJ, Frith CD. Detecting activations in PET and fMRI: levels of inference and power. *Neuroimage* 1996;4:223–235. [PubMed: 9345513]
- Gartus A, Foki T, Geissler A, Beisteiner R. Improvement of clinical language localization with an overt semantic and syntactic language functional MR imaging paradigm. *AJNR Am J Neuroradiol* 2009;30:1977–1985. [PubMed: 19643917]
- Good CD, Johnsrude I, Ashburner J, Henson RN, Friston KJ, Frackowiak RS. Cerebral asymmetry and the effects of sex and handedness on brain structure: a voxel-based morphometric analysis of 465 normal adult human brains. *Neuroimage* 2001a;14:685–700. [PubMed: 11506541]
- Good CD, Johnsrude IS, Ashburner J, Henson RN, Friston KJ, Frackowiak RS. A voxel-based morphometric study of ageing in 465 normal adult human brains. *Neuroimage* 2001b;14:21–36. [PubMed: 11525331]
- Hayasaka S, Phan KL, Liberzon I, Worsley KJ, Nichols TE. Nonstationary cluster-size inference with random field and permutation methods. *Neuroimage* 2004;22:676–687. [PubMed: 15193596]
- Hochberg Y, Benjamini Y. More powerful procedures for multiple significance testing. *Stat Med* 1990;9:811–818. [PubMed: 2218183]
- Jackowski AP, Douglas-Palumberi H, Jackowski M, Win L, Schultz RT, Staib LW, Krystal JH, Kaufman J. Corpus callosum in maltreated children with posttraumatic stress disorder: a diffusion tensor imaging study. *Psychiatry Res* 2008;162:256–261. [PubMed: 18296031]
- Johnson JG, Cohen P, Smailes EM, Skodol AE, Brown J, Oldham JM. Childhood verbal abuse and risk for personality disorders during adolescence and early adulthood. *Compr Psychiatry* 2001;42:16–23. [PubMed: 11154711]
- Kaufman, J.; Birmaher, B.; Brent, D.; Rao, U.; Ryan, ND. *Kiddie-SADS PL*. Western Psychiatric Institute and Clinic. University of Pittsburgh Medical Centre; 1996.
- Kellner R. A symptom questionnaire. *Journal of Clinical Psychiatry* 1987;48:268–273. [PubMed: 3597327]
- Mamdani M, Sykora K, Li P, Normand SL, Streiner DL, Austin PC, Rochon PA, Anderson GM. Reader's guide to critical appraisal of cohort studies: 2. Assessing potential for confounding. *Bmj* 2005;330:960–962. [PubMed: 15845982]
- Manning C, Cheers B. Child abuse notification in a country town. *Child Abuse Negl* 1995;19:387–397. [PubMed: 7606518]
- Moorhead TW, Job DE, Spencer MD, Whalley HC, Johnstone EC, Lawrie SM. Empirical comparison of maximal voxel and non-isotropic adjusted cluster extent results in a voxel-based morphometry study of comorbid learning disability with schizophrenia. *Neuroimage* 2005;28:544–552. [PubMed: 16085427]
- Ney PG. Does verbal abuse leave deeper scars: a study of children and parents. *Can J Psychiatry* 1987;32:371–378. [PubMed: 3651980]
- Ney PG, Fung T, Wickett AR. The worst combinations of child abuse and neglect. *Child Abuse Negl* 1994;18:705–714. [PubMed: 8000901]
- Richert KA, Carrion VG, Karchemskiy A, Reiss AL. Regional differences of the prefrontal cortex in pediatric PTSD: an MRI study. *Depress Anxiety* 2006;23:17–25. [PubMed: 16247760]
- Rothman, KJ.; Greenland, S.; Lash, TL. *Modern Epidemiology*. 3. Lippincott, Williams, & Wilkins; Philadelphia, PA: 2008.
- Saulsbury FT, Campbell RE. Evaluation of child abuse reporting by physicians. *Am J Dis Child* 1985;139:393–395. [PubMed: 3976630]
- Shaw P, Greenstein D, Lerch J, Clasen L, Lenroot R, Gogtay N, Evans A, Rapoport J, Giedd J. Intellectual ability and cortical development in children and adolescents. *Nature* 2006;440:676–679. [PubMed: 16572172]
- Stein MB, Koverola C, Hanna C, Torchia MG, McClarty B. Hippocampal volume in women victimized by childhood sexual abuse. *Psychol Med* 1997;27:951–959. [PubMed: 9234472]
- Talairach, J.; Tournoux, P. *Co-planar stereotaxic atlas of the human brain*. Thieme; New York: 188.
- Teicher MH, Dumont NL, Ito Y, Vaituzis C, Giedd JN, Andersen SL. Childhood neglect is associated with reduced corpus callosum area. *Biol Psychiatry* 2004;56:80–85. [PubMed: 15231439]

- Teicher MH, Glod CA, Surrey J, Swett C Jr. Early childhood abuse and limbic system ratings in adult psychiatric outpatients. *Journal of Neuropsychiatry & Clinical Neurosciences* 1993;5:301–306. [PubMed: 8369640]
- Teicher MH, Ito Y, Glod CA, Andersen SL, Dumont N, Ackerman E. Preliminary evidence for abnormal cortical development in physically and sexually abused children using EEG coherence and MRI. *Annals of the New York Academy of Sciences* 1997;821:160–175. [PubMed: 9238202]
- Teicher MH, Samson JA, Polcari A, McGreenery CE. Sticks, stones, and hurtful words: relative effects of various forms of childhood maltreatment. *Am J Psychiatry* 2006a;163:993–1000. [PubMed: 16741199]
- Teicher MH, Samson JA, Sheu Y-S, Polcari A, McGreenery CE. Hurtful words: Exposure to peer verbal aggression is associated with elevated psychiatric symptom scores and corpus callosum abnormalities. *Am J Psychiatry*. in press.
- Teicher MH, Tomoda A, Andersen SL. Neurobiological consequences of early stress and childhood maltreatment: are results from human and animal studies comparable? *Ann N Y Acad Sci* 2006b; 1071:313–323. [PubMed: 16891580]
- Tomoda A, Navalta CP, Polcari A, Sadato N, Teicher MH. Childhood sexual abuse is associated with reduced gray matter volume in visual cortex of young women. *Biol Psychiatry* 2009a;66:642–648. [PubMed: 19560122]
- Tomoda A, Suzuki H, Rabi K, Sheu YS, Polcari A, Teicher MH. Reduced prefrontal cortical gray matter volume in young adults exposed to harsh corporal punishment. *Neuroimage* 2009b; 47(Suppl 2):T66–71. [PubMed: 19285558]
- Vermetten E, Schmahl C, Lindner S, Loewenstein RJ, Bremner JD. Hippocampal and amygdalar volumes in dissociative identity disorder. *Am J Psychiatry* 2006;163:630–636. [PubMed: 16585437]
- Vythilingam M, Heim C, Newport J, Miller AH, Anderson E, Bronen R, Brummer M, Staib L, Vermetten E, Charney DS, Nemeroff CB, Bremner JD. Childhood trauma associated with smaller hippocampal volume in women with major depression. *Am J Psychiatry* 2002;159:2072–2080. [PubMed: 12450959]
- Wechsler, D. Wechsler Adult Intelligence Scale-III Administration and Scoring Manual. The Psychological Corporation; San Antonio: TX: 1997.
- Williams, JM. Memory Assessment Scales: Professional Manual. Psychological Assessment Resources; Odessa, FL: 1991.
- Worsley KJ, Andermann M, Koulis T, MacDonald D, Evans AC. Detecting changes in nonisotropic images. *Hum Brain Mapp* 1999;8:98–101. [PubMed: 10524599]

Figure 1.

Figure 2.

Table 1

Demographic characteristics and ratings of control and parental verbal abuse groups

Characteristics	Controls mean [95% conf int]	Parental Verbal Abuse mean [95% conf int]	Statistics (Anova, other)	p-value	Standardized Difference
Gender (Males/Females)	7M/12F	9M/12F	Fisher	0.76	0.12
Age (years)	21.1 [20.2 – 22.0]	21.2 [20.1 – 22.3]	0.02	0.90	0.04
Parental Education (years)	15.8 [14.7 – 16.9]	15.7 [14.4 – 17.0]	0.00	0.98	-0.01
Perceived Financial Sufficiency	3.9 [3.6 – 4.2]	3.0 [2.6 – 3.4]	11.77	0.001	-0.96
Parental Verbal Abuse Score	12.7 [9.2 – 16.3]	45.0 [33.4 – 56.5]			1.63
Maternal Verbal Abuse	13.4 [9.0 – 17.8]	54.2 [43.9 – 64.5]			1.50
Paternal Verbal Abuse	11.7 [8.2 – 15.2]	34.6 [23.0 – 46.2]			1.03
Subject Education (years) ^a	14.3 [13.6 – 15.0]	14.0 [13.3 – 14.7]	0.87	0.36	-0.17
Drug use (days/month) ^{a,b}	0	0			
Alcohol use (drinks/month) ^{a,b}	3.1 [0.8 – 5.4]	5.6 [1.2 – 10.0]	0.95	0.34	0.33
<i>Memory Assessment Scale</i>					
Short-term memory ^{a,b}	107.2 [99.8 – 114.6]	104.1 [96.7 – 111.5]	0.34	0.57	-0.20
Verbal memory ^{a,b}	112.3 [105.8 – 118.8]	112.2 [106.7 – 117.7]	0.00	0.99	-0.01
Visual memory ^{a,b}	111.7 [107.4 – 116.0]	108.1 [101.7 – 114.5]	0.78	0.39	-0.30
Global memory ^{a,b}	113.7 [109.2 – 118.2]	112.1 [106.4 – 117.8]	0.19	0.66	-0.15
<i>Wechsler Adult Intelligence Scale</i>					
Verbal IQ ^{a,b}	125.2 [119.5 – 130.9]	121.4 [116.0 – 126.8]	0.85	0.36	-0.30
Performance IQ ^{a,b}	117.5 [112.8 – 122.2]	115.0 [110.0 – 120.0]	0.52	0.48	-0.23
Full Scale IQ ^{a,b}	122.8 [117.7 – 127.9]	119.9 [114.8 – 125.0]	0.59	0.45	-0.25
Verbal Comprehension Index ^{a,b}	124.5 [119.1 – 129.9]	123.4 [117.9 – 128.9]	0.08	0.77	-0.09
Perceptual Organization ^{a,b}	119.8 [115.2 – 124.4]	116.2 [110.6 – 121.8]	0.93	0.34	-0.32
Working Memory Index ^{a,b}	115.1 [107.9 – 122.3]	112.9 [106.8 – 119.0]	0.21	0.65	-0.16
Processing Speed Index ^{a,b}	116.4 [110.1 – 122.7]	111.1 [104.8 – 117.4]	1.27	0.27	-0.38
<i>Kellner Symptom Questionnaire</i>					
Anxiety ^{a,b}	3.9 [2.5 – 5.3]	8.3 [5.6 – 11.0]	8.74	0.005	0.86

Characteristics	Controls mean [95% conf int]	Parental Verbal Abuse mean [95% conf int]	Statistics		Standardized Difference
			(Anova, other)	p-value	
Depression ^{a,b}	3.4 [1.7 – 5.1]	8.0 [5.4 – 10.6]	8.94	0.005	0.89
Somatization ^{a,b}	3.4 [2.0 – 4.8]	6.5 [4.5 – 8.5]	5.86	0.02	0.74
Anger-hostility ^{a,b}	2.9 [2.0 – 3.8]	5.6 [3.4 – 7.8]	5.82	0.02	0.74

Adjusted for

^a age,

^b gender

Multiple Regression Analysis Indicating Relationship between Gray Matter Volume in Superior Temporal Gyrus and Exposure to Verbal Aggression

Table II

Measures	All Subjects		Parental Verbal Abuse		Control Subjects	
	Beta	p-value	Beta	p-value	Beta	p-value
Maternal Verbal Abuse	0.544	<0.0001	0.763	0.006	0.331	0.21
Paternal Verbal Abuse	0.300	0.018	0.629	0.013	0.086	0.78
Age	0.073	0.53	-0.015	0.94	0.306	0.20
Gender	0.265	0.13	0.135	0.59	0.353	0.39
Parental Education (yrs)	-0.577	<0.0001	-0.378	0.08	-0.705	0.013
Perceived Financial Sufficiency	0.222	0.11	0.087	0.66	0.055	0.85
Total Gray Matter Volume	0.378	0.028	0.359	0.13	0.473	0.21
Overall Correlation	0.810	<0.0001	0.847	0.02	0.845	0.03

Table III

Association between potential confounders and superior temporal gyrus GMV

Characteristics	Estimate	Std Error	t-value	Probability
Age (years)	−0.007	0.011	−0.66	0.5
Gender (Males/Females)	−0.046	0.035	−1.32	0.2
Subject Education (years)	0.010	0.017	0.61	0.5
Perceived Financial Sufficiency	−0.018	0.025	−0.72	0.5
Alcohol use (drinks/month)	0.001	0.002	0.59	0.6
Short-term memory	0.001	0.002	0.82	0.4
Visual memory	−0.001	0.003	−0.41	0.7
Global memory	0.002	0.002	0.90	0.4
Verbal IQ	0.001	0.003	0.54	0.6
Performance IQ	−0.002	0.005	−0.33	0.7
Perceptual Organization	0.001	0.004	0.32	0.7
Working Memory Index	−0.003	0.003	−1.01	0.3
Processing Speed Index	0.000	0.002	−0.19	0.8