Published in final edited form as:

J Child Neurol. 2011 June ; 26(6): 738–742. doi:10.1177/0883073810391904.

Consequence of Preterm Birth in Early Adolescence: The Role of Language on Auditory Short-term Memory

David Fraello, BA^a, Jill Maller-Kesselman, MS^a, Betty Vohr, MD^b, Karol H. Katz, MS^a, Shelli Kesler, PhD^c, Karen Schneider, MPH^a, Allan Reiss, MD^c, Laura Ment, MD^a, and Marisa N. Spann, PhD, MPH^d

^aYale University School of Medicine, Department of Pediatrics, New Haven, Connecticut ^bThe Warren Alpert Medical School of Brown University, Providence, Rhode Island ^cStanford University School of Medicine, Psychiatry & Behavioral Science, Center for Interdisciplinary Brain Science Research, Palo Alto, California ^dColumbia University Medical Center & the New York Psychiatric Institute, New York, New York

Abstract

This study tested the hypothesis that preterm early adolescents' short-term memory is compromised when presented with increasingly complex verbal information, and associated neuroanatomical volumes would differ between preterm and term groups. Forty-nine preterm and 20 term subjects were evaluated at age 12 with neuropsychological measures and MRI. There were no differences between groups in simple short-term and working memory. Preterms performed lower on learning and short-term memory tests that included increased verbal complexity. They had reduced right parietal, left temporal, and right temporal white matter volumes, and greater bilateral frontal gray and right frontal white matter volumes. There was a positive association between complex working memory and the left hippocampus and frontal white matter, in terms. While not correlated, memory scores and volumes of cortical regions known to subserve language and memory were reduced in preterms. This study provides evidence of possible mechanisms for learning problems in former preterm infants.

Keywords

Preterm; MRI; Language; Working Memory; Short-term Memory

Corresponding Author: Marisa Spann, PhD, MPH, Columbia University Medical Center, New York State Psychiatric Institute, 1051 Riverside Drive, Unit 74, New York, NY 10032, spannMa@childpsych.columbia.edu, Phone: (212) 543-6702, Fax: (212) 543-6660.

Author Contribution (Roles)

Mr. Fraello and Dr. Spann contributed to conception and design, analysis and interpretation, drafting the article, and article revision. Mrs. Maller-Kesselman contributed to conception and design, interpretation of data, and article revision. Karol Katz contributed to analysis and interpretation of data and article revision. Dr. Vohr contributed to acquisition of data, analysis and interpretation and article revision. Mrs. Schneider contributed to conception, acquisition of data, and article revision. Drs. Kesler and Reiss contributed to data analysis and interpretation of data, and article revision. Dr. Ment contributed to conception and design, analysis and interpretation of data, and article revision. All authors contributed to manuscript revision and approval.

Conflict of Interest

The authors have indicated they have no relevant financial relationships to disclose.

Ethical Approval

The Multicenter Randomized Indomethacin Intraventricular Hemorrhage Prevention Trial was approved by Yale University School of Medicine IRB.

Introduction

Preterm children often exhibit learning problems that may compromise school achievement [1–6]. A recent study reported reduced left hippocampus volume in preterm adolescents, associated with poorer performance on measures of verbal learning and recognition [7]. Using a subsample of our previously described cohort [8–10], the current investigation sought to better understand the role of language, a demonstrated weakness in preterm children [2, 7], in learning new verbal information (as measured by verbal short-term/working memory tasks). Differences between preterm and term early adolescents' short-term memory proficiency were evaluated using increasingly complex verbal information.

Language plays a key role in early theories of short-term and working memory [11]. Both concepts are viewed as temporary storage systems; while short-term memory briefly stores information, working memory also manipulates information. Performance on nonword repetition tasks requiring short-term memory recall have a positive association with vocabulary development in children with specific language disability and normal controls [12, 13], indicating a likely relationship between verbal learning/memory and language deficits.

The goal of the current study is to examine the association of verbal complexity with learning and short-term memory in a cohort of preterm and term early adolescents. It was hypothesized that both groups would demonstrate similar short-term recall of simple verbal information, but as information increased in length and complexity, differences would be identified. Differences in regional brain volume in areas that have been associated with memory in typically developing children: bilateral frontal, parietal, and temporal white matter; bilateral frontal gray matter; bilateral hippocampi [7, 14–16] were compared between the two groups. Exploratory analyses investigating the association between regional brain volumes and verbal memory were also performed.

Methods

Subjects

The current sample of 49 preterm and 20 term controls is a subset of individuals from the Multicenter Indomethacin IVH Prevention Trial. This clinical trial evaluating the efficacy of early administration of low-dose Indomethacin enrolled 505 preterm infants between September 5, 1989 and August 31, 1992. All preterm subjects, enrolled following parental consent, weighed between 600 to 1250 grams at birth, and were admitted by 6-hours of age to Women and Infants' Hospital (Providence, Rhode Island), Maine Medical Center (Portland, Maine), and/or Yale New Haven Hospital (New Haven, Connecticut). Unlike preterm subjects, who were enrolled at 6 hours of life, term controls were enrolled at age 8 years, therefore neonatal data is not available. Calculations at that time suggested that an imbalance in study groups would provide adequate power ($\alpha = 0.80$) to determine a significant difference in cognitive testing scores between the preterm and term study groups.

All preterm subjects enrolled in the follow-up component of the Multicenter Randomized Indomethacin Intraventricular Hemorrhage Prevention Trial NCT00033917[17] were recruited sequentially for the MRI study when they reached 12 years of age. These children were representative of the cohort of subjects with no evidence of neonatal brain injury from which they were selected, with respect to gender, handedness, full-scale IQ scores, minority status, and maternal education. Twenty-two healthy term children, 12 years of age, were recruited from the local community and group-matched with the preterm group according to age, gender, and minority status. Additional details of the newborn protocol are described in previous publications [9, 10].

Procedure

The institutional review boards of the three participating centers approved all protocols related to the Multicenter Randomized Indomethacin IVH Prevention Trial. Informed consent was obtained from parents at the 12-year visits.

Materials

Simple short-term and working memory was assessed using the Digit Span subtest from the Wechsler Intelligence Scale for Children – Third Edition [18] and Non-Word Repetition subtest from The Comprehensive Test of Phonological Processing [19]. During Digit Span Forward, the subject repeats a dictated series of numbers verbatim, and in Digit Span Backward the subject repeats the numbers in reverse order. In Non-Word Repetition, the subject repeats pronounceable nonsense words.

Short-term memory tasks of increasing language complexity were measured by two subsets from the Clinical Evaluation of Language Fundamentals – Third Edition [20]. With graduated information complexity, Recalling Sentences requires the subject to repeat them verbatim, and Concepts and Directions require the subject to follow multistep oral directions.

Image Acquisition

Imaging was performed on a General Electric-Signa 1.5-T scanner or, after this magnet was decommissioned, a Siemens-Sonata 1.5-T scanner. For the General Electric scanner, images were acquired with a three-dimensional volumetric radio frequency spoiled gradient echo pulse sequence using the following parameters: repetition time, 24 milliseconds; echo time, 5 milliseconds; flip angle, 45°; number of excitations 1; matrix size, 256 × 192; field of view, 30 cm; slice thickness, 1.2 mm; 124 contiguous slices. The Siemens-Sonata scanner parameters were equivalent with the exception of a repetition echo time of 2.9 milliseconds and Number of excitations of 2.

Volumetric Imaging Analysis

Subject scans were analyzed using volumetric image processing software BrainImage (cibsr.stanford.edu/tools) and FSL (www.fmrib.ox.ac.uk/fsl). Data preprocessing are described elsewhere [21–23]. Intrarater reliabilities for volumes described in this study were all .95.

Statistical Analysis

Analyses were conducted with SAS 9.1 [24]. Demographic and neuropsychological data were analyzed using Fisher's Exact test for categorical data and Mann-Whitney test for continuous data to account for non-normal data distribution.

General linear models were used to evaluate group differences in gray and white matter volumes. Prior to modeling, a previously described statistical method was used to convert frontal, parietal, and temporal brain volumes acquired on the Siemens scanner to "General Electric compatible" data to account for scanner specific differences in gray-white tissue segmentation [17, 25]. (Because no gray-white tissue segmentation was required for determination of hippocampal boundaries, data were covaried by scanner only). Total brain volume, age at time of scan, and gender were included as covariates to assess regional brain volume differences between preterm and term controls. To determine whether ethnicity, Verbal IQ, or special education services confounded the effect of prematurity on outcomes, separate analyses were performed that included these variables as covariates. To further

ensure the consistency of findings, primary analyses were rerun excluding preterm subjects with a positive history of intraventricular hemorrhage.

Exploratory analyses were performed to better understand neuroanatomical structures' association with verbal memory performance. Due to the non-normal data distribution, Spearman-rank partial correlations were used. Age at scan and total brain volume were included as partial variables. Short-term memory variables that yielded significant differences between groups were included in the analyses with regional brain volumes: bilateral frontal, parietal, and temporal white matter; bilateral frontal gray matter; bilateral hippocampi. Correlations were performed for each subject group, and the combined group.

Data are presented as mean (M) $\pm$ standard deviation (SD), least square mean (LSMean) $\pm$ standard error of measurement (SEM), r (Spearman correlation), and a significance level of $p = 0.05$.

Results

Neonatal and demographic data for the study subjects are shown in Table 1. No gender differences were found for neuropsychological variables or regional brain volumes and there was no significant difference in maternal education between the two groups. Eleven of 49 (23%) preterm subjects were diagnosed with intraventricular hemorrhage, study findings remained consistent when these subjects were excluded from the analyses; therefore they remained in the preterm sample for hypotheses testing. More preterm subjects received special education services and performed significantly lower on IQ measures, although neither of these contributed to the targeted outcomes (see Table 1 and 2).

When considering memory subtests, there were no significant differences in the Digit Span Forward and Backward or Non-Word Repetition between the study groups (see Table 2). In contrast, term subjects obtained significantly higher scores on both Recalling Sentences and Concepts and Directions.

Volumetric analyses were performed to determine brain volume differences between preterm and terms (see Table 3). Preterm subjects had significantly larger volumes of bilateral frontal gray and right frontal white matter compared to term subjects. In addition, preterm subjects had significantly smaller regional volumes in right parietal and bilateral temporal white matter. There were no significant differences in the following regions: left frontal and parietal white and bilateral hippocampus.

Spearman-rank partial correlations revealed a positive association between Concepts and Directions and the left hippocampus ($r = 0.54$, $p = 0.02$) and left frontal white matter volumes ($r = 0.46$, $p = 0.05$), in the term group. Analyses combining both groups' revealed significant relationships between right temporal white matter and Recalling Sentences ($r = 0.28$, $p = 0.02$) and Concepts and Directions ($r = 0.26$, $p = 0.04$). There were no independent significant results for the preterm group.

Discussion

The learning problems of the prematurely-born have been well described, but the specific functional-learning domains and neural systems subserving these deficits are just beginning to be explored. In seeking to better understand the interrelationship of language and short-term/working memory in early adolescents born prematurely, this study demonstrated that as the complexity of novel verbal information increased, problems in short-term recall emerged. This complex verbal processing in short-term memory may later impact information's ability to move into long-term storage [12, 25]. Therefore, as efficient short-

term memory is necessary for long-term retention, this has broad implications for initial recall of new contextual-verbal information and possibly learning.

These data support longstanding research indicating that language processing may be secondary to preterm birth [2, 3], and provide greater insight into previous research that demonstrates verbal learning deficits in preterm adolescents [7, 26].

Differential size in regional brain volumes between term and preterms provide further support that the consequence of preterm extends beyond childhood. Frontal lobe development is a primary brain region undergoing refinement in adolescence through adulthood. Bilateral frontal lobe (gray) increases in preterms relative to controls may suggest that this refinement is delayed [25–27]. Increased size of bilateral frontal gray matter may also lead to compensatory over-refinement of other regions, such as the bilateral temporal and right parietal lobe white matter volumes, which were significantly smaller in preterms. This leads to the question of whether significantly differing volumes (in tandem larger and smaller) highlight continued challenge in differentiating language- and nonverbal-specific pathways in preterms.

Although our exploratory analyses between memory performance and structural brain volumes demonstrated significant findings for the term subjects, they were not independently significant for the preterm group. Structure-function correlates are difficult to elucidate, likely due to the complexity of cognitive function. Studies from other investigators have shown promising associations in preterm adolescents with voxel-based morphometry and functional MRI [7, 14–16, 27].

The lack of association in the preterm group may also suggest an alternate functional network [30], as other researchers have found. For example, while term pre-adolescents are utilizing networks involving left frontal white matter and hippocampus, preterms may call upon right hemisphere resources in their attempt to retain meaningful strings and complex verbal information in short-term memory [30–31]. Thus, performance deficits at increased levels of complexity in the preterms may reflect neural inefficiency associated with alternative neural circuits.

A major limitation of the study was the sample size, which likely decreased the power of study findings. Although the regions we examined in our correlational analysis are known to subserve language and memory systems, the specific structure-function relationships examined here may involve other aspects of neurobiologic status such as microstructural or neurofunctional changes.

Considering the current results in conjunction with previous findings, a logical next step is to expand on learning and language as interrelated constructs that involve overlapping neuroanatomical regions. Functional MRI, diffusion tensor imaging, MR spectroscopy and/or voxel-based morphometry data provide a means to study possible changes and enhance current understanding of the associations between neurodevelopment, and language and memory outcome in prematurely born adolescents. Structural connectivity methods, used in tandem with functional connectivity, may provide a means to model the course of short-term memory and verbal processing efficiency as well as the likely intersections in their developing networks. This will not only contribute to existing knowledge regarding the developmental trajectory of short-term and working memory, but will also further elucidate the mediating effect of language [17, 28, 29].

Acknowledgments

We thank Ms. Marjorene Ainley and Ms. Victoria Watson.

Funding

This work was supported in part by National Institute of Health grants NS 27116, MO1-RR06022, and MO1-RR00125.

References

1. Saigal S, Doyle LW. An overview of mortality and sequelae of preterm birth from infancy to adulthood. *Lancet*. 2008; 371(9608):261–269. [PubMed: 18207020]
2. Saigal S, Stoskopf B, Streiner D, Boyle M, Pinelli J, Paneth N, Goddeeris J. Transition of Extremely Low-Birth-Weight Infants From Adolescence to Young Adulthood. *JAMA*. 2006; 295(6):667–675. [PubMed: 16467235]
3. Taylor H, Minich NM, Klein N, Hack M. Longitudinal outcomes of very low birth weight: Neuropsychological findings. *Journal of International Neuropsychological Society*. 2004; 10(2): 149–163.
4. Saigal S. Follow-up of very low birthweight babies to adolescence. *Semin Neonatol*. 2000; 5(2): 107–118. [PubMed: 10859705]
5. Saigal S, Hoult LA, Streinier DL, Stoskopf BL, Rosenbaum PL. School difficulties at adolescence in a regional cohort of children who were extremely low birth weight. *Pediatrics*. 2000; 105(12): 305–331.
6. Doyle L, Casalaz D. Outcome at 14 years of extremely low birthweight infants: a regional study. *Arch Dis Child Fetal Neonatal Ed*. 2001; 85(3):F159–F164. [PubMed: 11668155]
7. Giménez M, Junqué C, Narberhaus A, Caldú X, Salgado-Pineda P, Bargalló N, Segarra D, Botet F. Hippocampal gray matter reduction associates with memory deficits in adolescents with history of prematurity. *Neuro Image*. 2004; 23(3):869–877. [PubMed: 15528087]
8. Luu T, Ment LR, Schneider KC, Katz K, Allan WC, Vohr BR. Lasting effects of preterm birth and neonatal brain hemorrhage at 12 years of age. *Pediatrics*. 2009; 123(3):1037–1044. [PubMed: 19255037]
9. Ment L, Peterson BS, Vohr B, Allan W, Schneider KC, Lacadie C, Katz KH, Maller-Kesselman J, Pugh K, Duncan C, Makuch RW, Constable RT. Cortical recruitment patterns in children born prematurely compared with control subjects during a passive listening functional magnetic resonance imaging task. *Journal of Pediatrics*. 2006; 149(4):490–498. [PubMed: 17011320]
10. Ment L, Oh W, Ehrenkranz RA, Phillip AG, Vohr B, Allan W, Makuch RW, Taylor KJ, Schneider KC, Katz KH, et al. Low-dose indomethacin therapy and extension of intraventricular hemorrhage: a multicenter randomized trial. *J Pediatrics*. 1994; 124(6):951–955.
11. Pascual-Leone J. A mathematical model for the transition rule in Piaget's developmental stages. *Acta Psychologica*. 1970; 32:301–345.
12. Baddeley A. Working memory and language: An overview. *Journal of Communication Disorders*. 2003; 36(3):189–208. [PubMed: 12742667]
13. Baddeley, A.; Hitch, GJ. Working memory. In: Bower, GH., editor. *The psychology of learning and motivation*. Academic Press; New York: 1974. p. 28–61.
14. Narberhaus A, Lawrence E, Allin MP, Walshe M, McGuire P, Rifkin L, Murray R, Nosarti C. Neural substrates of visual paired associates in young adults with a history of very preterm birth: Alterations in fronto-parieto-occipital networks and caudate nucleus. *Neuro Image*. 2009; 147(4): 1884–1893. [PubMed: 19376244]
15. Nosarti C, Giouroukou E, Healy E, Rifkin L, Walshe M, Reichenberg A, Chitnis X, Williams S, Murray R. Grey and white matter distribution in very preterm adolescents mediates neurodevelopmental outcome. *Brain*. 2008; 131(1):205–217. [PubMed: 18056158]
16. Klingberg T. Development of a superior frontal-intraparietal network for visuo-spatial working memory. *Neuropsychologia*. 2006; 44(11):2171–2177. [PubMed: 16405923]
17. Constable R, Ment LR, Vohr BR, Kesler SR, Fulbright RK, Lacadie C, Delancy S, Katz KH, Schneider KC, Schafer RJ, Makuch RW, Reiss AR. Prematurely born children demonstrate white matter microstructural differences at 12 years of age, relative to term control subjects: An investigation of group and gender effects. *Pediatrics*. 2008; 121(2):306–316. [PubMed: 18245422]

18. Wechsler, D. Wechsler Scale of Intelligence for Children. Vol. 3. New York, NY: Psychological Corp; 1991.
19. Wagner, R.; Torgesen, JK.; Rashotte, CA. Comprehensive Test of Phonological Processing. Austin, TX: PRO-ED; 1999.
20. Semel, E.; Wiig, EH.; Secord, WA. Clinical Evaluation of Language Fundamentals. Vol. 3. San Antonio, TX: Corporation Harcourt Brace Co; 1995.
21. Kates W, Warsofsky IS, Patwardhan A, Abrams MT, Liu A, Naidu S. Automated Talairach atlas-based parcellation and measurement of cerebral lobes in children. *Psychiatry Res.* 1999; 91(1):11–30. [PubMed: 10496689]
22. Talairach, J.; Tournoux, P. Co-planar Stereotaxic Atlas of the Human Brain. New York, NY: Thieme Medical Publishers; 1998.
23. Reiss A, Hennessey JG, Rubin M, Beach L, Abrams MT, Warsofsky IS, Liu AMC, Links JM. Reliability and validity of an algorithm for fuzzy tissue segmentation of MRI. *Journal of Computer Assisted Tomography.* 1998; 22(3):471–479. [PubMed: 9606391]
24. SAS, 9.1.2. SAS Institute, Inc; Cary, North Carolina: 2002–2008.
25. Ment L, Kesler S, Vohr B, Katz KH, Baumgartner H, Schneider KC, Delancy S, Silbereis J, Duncan CC, Constable RT, Makuch RW, Reiss AL. Longitudinal brain volume changes in preterm and term control subjects during late childhood and adolescence. *Pediatrics.* 2009; 123(2): 503–511. [PubMed: 19171615]
26. Taylor H, Klein N, Minich NM, Hack M. Verbal memory deficits in children with less than 750 g birth weight. *Child Neuropsychology.* 2000; 6(1):49–63.
27. Giménez M, Carrea Junqué, Narberhaus A, Botet F, Bargalló N, Mercader J. Correlations of thalamic reductions with verbal fluency impairment in those born prematurely. *Neuro Report.* 2006; 17(5):463–466.
28. Gozzo Y, Vohr B, Lacadie C, Hampson M, Katz KH, Maller-Kesselman J, Schneider KC, Peterson BS, Rajeevan N, Makuch RW, Constable RT, Ment LR. Alterations in neural connectivity in preterm children at school age. *Neuro Image.* 2009; 48 (2):458–463. [PubMed: 19560547]
29. Schafer R, Lacadie C, Vohr B, Kesler S, Katz K, Schneider K, Pugh K, Makuch R, Reiss A, Constable T, Ment L. Alterations in functional connectivity for language in prematurely born adolescents. *Brain.* 2009; 132(3):661–670. [PubMed: 19158105]

Table 1

Neonatal and Demographic Characteristics for the Study Children

Variable	Group		P-value
	Preterm	Term	
N	49	20	---
Neonatal Characteristics			
Birth weight, mean $\pm$ SD, g	972.7 $\pm$ 151.4	---	---
Gestational age, mean $\pm$ SD, wk	28.4 $\pm$ 1.8	---	---
IVH, n (%)	11 (22.5%)	---	---
PVL, n (%)	0 (0.0%)	---	---
VM, n (%)	0 (0.0%)	---	---
Demographic Characteristics			
Age at scan, mean $\pm$ SD, y	12.3 $\pm$ 0.4	12.1 $\pm$ 0.6	0.145
Male, n (%)	29 (59.2%)	9 (45.0%)	0.301
Nonwhite, n (%)	27 (55.1%)	4 (20.0%)	0.009
Height, mean $\pm$ SD, cm	149.3 $\pm$ 10.7	150.3 $\pm$ 6.7	0.668
Weight, mean $\pm$ SD, kg	48.3 $\pm$ 15.3	51.9 $\pm$ 13.4	0.285
Right-handed, n (%)	41 (89.1%)	19 (95.0%)	0.659
Any special education services, n (%)	19 (38.8%)	2 (10.0%)	0.022
Maternal education, n (%)	---	---	0.108
Less than high school	6 (12.2%)	0 (0.0%)	---
High school graduate	14 (28.6%)	6 (30.0%)	---
Some college/college graduate	29 (59.2%)	14 (70.0%)	---

Note: Neonatal variables were not available for term controls.

Abbreviations:

IVH: Intraventricular Hemorrhage

PVL: Periventricular Hemorrhage

VM: Ventriculomegaly

Table 2

Mean Comparison between Preterm and Term on Cognitive and Memory Variables.

Variable	Group		P-value
	Preterm	Term	
	Mean $\pm$ SD	Mean $\pm$ SD	
Intelligence Scores			
Verbal IQ (WISC-III composite score)	92.4 $\pm$ 16.3	102.6 $\pm$ 16.1	0.024
Performance IQ (WISC-III composite score)	86.8 $\pm$ 15.0	103.8 $\pm$ 20.1	0.002
Full Scale IQ (WISC-III composite score)	88.7 $\pm$ 15.4	103.4 $\pm$ 18.1	0.005
Short-term and Working Memory Scores			
Digit Span Forward (WISC-III raw score)	8.7 $\pm$ 1.9	8.8 $\pm$ 1.6 ^a	0.658
NonWord Repetition (CTOPP scaled score)	9.5 $\pm$ 2.0 ^b	9.8 $\pm$ 2.3	0.860
Digit Span Backward (WISC-III raw score)	5.0 $\pm$ 1.9	5.5 $\pm$ 1.9 ^a	0.399
Concepts and Directions (CELF-3 scaled score)	7.4 $\pm$ 2.7	10.4 $\pm$ 3.1	0.001
Recalling Sentences (CELF-3 scaled score)	8.5 $\pm$ 3.2	11.1 $\pm$ 2.8	0.004

^aN = 19^bN = 48

Abbreviations:

WISC-III: Wechsler Intelligence Scale for Children – Third Edition

CTOPP: The Comprehensive Test of Phonological Processing

CELF-3: The Clinical Evaluation of Language Fundamentals – Third Edition

Table 3

General Linear Model comparing Preterm and Term Regional Brain Volumes.

Variable	Group		P-value
	Preterm	Term	
	LSMean $\pm$ SEM	LSMean $\pm$ SEM	
Gray Matter			
Left Frontal	110.7 $\pm$ 1.8	95.2 $\pm$ 2.9	<0.0001
Right Frontal	111.6 $\pm$ 1.7	98.7 $\pm$ 2.6	0.0002
White Matter			
Left Frontal	71.4 $\pm$ 1.0	71.3 $\pm$ 1.6	0.939
Right Frontal	70.0 $\pm$ 1.8	59.5 $\pm$ 2.9	0.005
Left Parietal	54.6 $\pm$ 1.0	53.6 $\pm$ 1.6	0.609
Right Parietal	56.2 $\pm$ 0.8	61.6 $\pm$ 1.3	0.0009
Left Temporal	31.3 $\pm$ 0.8	34.9 $\pm$ 1.3	0.029
Right Temporal	32.6 $\pm$ 1.0	41.4 $\pm$ 1.6	<0.0001
Hippocampal Matter			
Left Hippocampus	3.0 $\pm$ 0.1	3.1 $\pm$ 0.1	0.745
Right Hippocampus	3.2 $\pm$ 0.1	3.3 $\pm$ 0.1	0.470

All volumes are reported as LSMean $\pm$ SEM, covaried for total brain volume, age at time of scan, and gender (and scanner for hippocampal volumes).