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Neuropsychological Lateralization of Brain Dysfunction in Children With Mesial Temporal Sclerosis: A Presurgical Evaluation

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Abstract

Presurgical evaluation of children with mesial temporal sclerosis has shown severe neurocognitive impairments. There is debate about lateralized material specific deficits in memory in children with mesial temporal sclerosis. The authors examined lateralization of brain dysfunction and age appropriate development of cognitive functions in 17 children (7-15 years) with mesial temporal sclerosis who have histories of uncontrolled epilepsy. The National Institute of Mental Health and Neurosciences (NIMHANS) neuropsychological battery for children was employed and each participant's performance was compared with the norms. Results showed that the battery was sensitive to deficits in learning and memory associated with mesial temporal sclerosis. However, a lack of clearly lateralized material specific memory deficits in children with left/right mesial temporal sclerosis was also observed. Performance on tests that assess learning, attention, working memory, and visuospatial functions was found to be below the age appropriate level. Children with mesial temporal sclerosis showed widely distributed neuropsychological deficits.

Keywords

mesial temporal sclerosis, intractable epilepsy, seizure, neuropsychological tests, lateralization, presurgical evaluation, children

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Complex partial seizures that originate from the temporal lobe are common in children and adults. Mesial temporal sclerosis is the most common pathology underlying temporal lobe seizures in adults. Hippocampal sclerosis is common in children with intractable temporal lobe epilepsy, and can be detected reliably and accurately through magnetic resonance imaging (MRI).[1] It is characterized by therapy-resistant temporal lobe seizures associated with hippocampal sclerosis that arise in the first decade of life.[2] Mesial temporal sclerosis is associated with intractable seizures and neuropsychological impairment. A general cognitive decline, material specific learning, and memory deficits have all been observed in epilepsy patients. There has been an increase in the interest in surgical management of mesial temporal sclerosis in children over the last decade. Although neurosurgery has been considered the best therapeutic option to control seizures and reduce long-term medications, it may have an adverse effect on cognition.[3]

Plasticity of the developing brain, and the effects of uncontrolled seizures on the brain, make early surgery a possible therapy. All patients with uncontrolled partial seizures are potential candidates for surgery and merit a detailed presurgical evaluation. This consists of a detailed neurological evaluation, electroencephalography (EEG), a high resolution MRI scan, single photon emission computed tomography (SPECT), and a neuropsychological assessment. Presurgical evaluation in children requires a careful assessment of structural and functional deficits based on anatomical and functional neuroimaging as well as the neurological and neuropsychological examination. Extensive hemispheric abnormalities have been

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found in children with mesial temporal sclerosis.[4] It is essential to find the anatomical substrates responsible for the seizures prior to the surgery by using techniques like EEG and MRI. It is also essential to examine the cognitive deficits prior to the surgery to assess the functional status of the brain and to be able to predict the surgical outcome.

Several neuropsychological impairments have been defined as associated with mesial temporal sclerosis. Children with mesial temporal sclerosis show deficits when measuring learning and memory. Material specific memory deficits are reliable indicators of the laterality of seizure focus as indicated by lesion studies. While patients with left-sided mesial temporal sclerosis show material specific verbal memory deficit, those with right mesial temporal sclerosis exhibit visual memory deficit.[5] Functional neuroimaging studies have also shown that verbal encoding primarily engages the left medial temporal lobe, and nonverbal encoding engages the right medial temporal cortex. Decisions regarding the medial temporal resection depend on the evidence on the side of seizure onset, which is determined by clinical investigations, and also functional impairments as observed on neuropsychological assessment.

Presurgical evaluation in children with mesial temporal sclerosis has shown severe memory impairments. Postoperative improvement in memory in terms of reorganization of memory to the contra lateral region has also been reported. Neuropsychological assessment is a noninvasive method to measure brain functioning. It would be able to delineate the pattern of brain dysfunction. The National Institute of Mental Health and Neurosciences (NIMHANS) neuropsychological battery for children has been standardized on Indian populations with norms based on the empirical validation of age trends of neuropsychological functions.[6]

The relationship between performance on neuropsychological measures and lateralization of an epileptic focus is not clear in children. Many studies have reported equally impaired verbal and visual memory,[7] whereas some studies have also reported a material specific memory deficit concordant with the side of an epileptic focus.[8]

Intractable epilepsy may also affect the ongoing maturation of cognitive functions. Consequently, a developmentally sensitive tool should be used to examine the adverse effect of uncontrolled seizures on cognitive development in children with mesial temporal sclerosis. Many studies on epilepsy surgery in these children have recommended an early surgery. Yet, these studies have not made an objective assessment of the effect of intractable epilepsy on the ongoing development of cognitive functions, particularly learning and memory, which are crucial functions in terms of the lateralized deficits characterizing epilepsy.

The present study was carried out with the following 3 objectives: (1) to validate the NIMHANS neuropsychological battery for children in terms of its sensitivity for lateralization of brain dysfunction; (2) to determine whether children with mesial temporal sclerosis show material specific deficits in learning and memory with respect to the lateralization of an epileptic focus; and (3) to study the effect of mesial temporal sclerosis on the development of cognitive functions, particularly verbal and visual learning and memory. It was hypothesized that the NIMHANS neuropsychological battery for children would be able to lateralize brain dysfunction in concordance with a MRI scan. It was also expected that as seen in adults, children would also show material specific deficits with respect to the lateralization of an epileptic focus. Developmental delay in functions of learning and memory in particular, and overall cognitive functions in general, would be found in children with mesial temporal sclerosis.

Methods

Participants

A total of 17 children in the age range of 5 to 15 years, who were diagnosed with mesial temporal sclerosis, were recruited from the inpatient and outpatient services at the department of neurology and neurosurgery at NIMHANS in Bangalore, India. There were 9 girls and 7 boys. The children's mean years of education were 7.2 years. Children with more than a 2-year history of epilepsy were included in the study. The protocol for epilepsy surgery at NIMHANS requires a thorough clinical evaluation, a MRI scan, a surface and video EEG, and a neuropsychological evaluation. Mesial temporal sclerosis was diagnosed on the basis of the MRI scan by the neurology/neurosurgery consultant. Mesial temporal sclerosis was the only pathology in the patients who were included in the study. Etiology for mesial temporal sclerosis was the uncontrolled seizures. Hence, all the children included in the study were advised surgery. All of the participants had a history of uncontrolled seizures. SCN1A was not checked for any of the participants. Out of the 17 total participants, a MRI report of 1 child could not be traced; however, the child was assessed as this child was referred to us from their physician for further consultation. Profiles of this child were not included in further analysis. Out of the remaining 16 participants, 6 children had left mesial temporal sclerosis, 7 children had right mesial temporal sclerosis, and the remaining 3 children were bilateral. All of the participants were right-handed to ensure homogeneity in terms of cerebral dominance. The Edinburgh Handedness Inventory was administered to test handedness.[9] All of the participants had normal or corrected-to-normal vision. All of the children were assessed on colored progressive matrices[10] (for ages 5-11 years) and standard progressive matrices[11] (for ages 12-15 years) to examine their levels of intellectual functioning. The Binet Kamat test of intelligence[12] was administered for 5 children (who were between the ages of 12-15 years) out of 17, as they found the standard progressive matrices very difficult. All of the participants were found to be in the range of average/below average intellectual functions. Written informed consent was obtained from the parents of each participant. The study was approved by the Ethics Committee in Behavioral Sciences at NIMHANS in Bangalore, India.

Measures

NIMHANS Neuropsychological Battery for Children.[6] The NIMHANS neuropsychological battery for children has been developed as a psychometric instrument. It has been standardized on a normative sample of 400 Indian children who were in the age range of 5 to 15 years. The battery consists of tests of motor speed, sustained and focused attention, fluency, verbal and visuospatial working memory, planning, visuoperceptual ability, visuoconceptual and visuoconstructive

Table 1. NIMHANS Neuropsychological Test Battery for Children

Functions	Tests	Test Scores
Motor speed	Finger tapping test[13]	Average number of taps: right hand Average number of taps: left hand
Sustained attention	Color cancellation (Kapur, 1974)	Time in seconds
Focused attention	Trail making test, color trails A and B[16]	Time in seconds
Executive functions		
Design fluency	Design fluency[20]	Novel output score
Verbal working memory	N back test-verbal[22]	Hits (number correct)
Visuospatial working memory	N back test-visual[22]	Hits (number correct)
Planning	Porteus maze[21]	Test age
Visual perceptual ability	Motor-free visual perception test[25]	Number correct
Visual conceptual reasoning	Picture completion[26]	Number correct
Verbal comprehension	Token test[27]	Number correct
Verbal learning and memory	Rey's auditory verbal learning test[28]	Total learning score Delayed recall score
Visual learning and memory	Memory for designs[31]	Total learning score Delayed recall score

ability, verbal comprehension, and verbal and visual learning and memory (Table 1). The battery also provides norms for each test and age level. The norms are based on the empirical validation of age related differences in performance. These norms have been derived on the basis of the growth curve modeling approach. Scores that are $\leq$ the fifth percentile indicate a deficit for accuracy measures, and scores that are $\geq$ the 95th percentile indicate a deficit for time measures. The test–retest reliability of all of the tests falls in the range of 0.53 to 0.83.[6] The battery has been validated on children with focal (cortical tumors) and diffuse brain damage (head injury).

The NIMHANS neuropsychological test battery for children was administered on 17 children with intractable epilepsy to assess neuropsychological functions. A comprehensive battery of neuropsychological tests was employed as children with mesial temporal sclerosis had also shown deficits in their executive functions, excluding language related and material specific deficits in memory. This battery also provides information about the spared functions as well as the influence of the functional deficits on neuropsychological performance.

Motor Speed

Finger tapping test.[13] This test is a measure of motor speed. On this test, performance tends to be worse in the hand contralateral to the lesion. The test has shown stronger effects related to age, as compared to education in children, and it has been standardized on children in the west.[14] The subject is asked to tap the mounting key on a finger tapping instrument as rapidly as possible using the index finger of the preferred hand. A comparable set of measurements is then obtained with the nonpreferred hand. A total of 5 trials are given for each hand. Each trial lasts for 10 seconds. The average number of taps for each hand comprised the score. The finger tapping test has shown improvement in performance up to 9 years.[15]

Attention

Color trails test.[16] This test is a measure of focused attention and conceptual tracking. Children between the ages of 5 to 16 years show a steady age progression on this test. It is sensitive to the effects of frontal lobe damage.[17] Children between the ages of 8 to 16 years show a steady age progression on this test as well.[18] In trail 1, the participants were given numbers 1 to 25 printed in 2 colors and were asked to serially connect the numbers irrespective of color. In trail 2, they were shown a set of numbers 1 to 25 printed in pink and yellow circles. The participant was instructed to serially connect numbers, but alternate colors disregarding the number in the same color. [0]They scored by the length of time required to complete each trail.

Color cancellation test. This test is a measure of visual scanning/ sustained attention. It consists of 150 circles in red, blue, yellow, black, and gray. The participants were required to cross out only the yellow and red circles as fast as they could. Time in seconds comprised the score. (Kapur, unpublished thesis, 1974.)

Executive Functions

Design fluency test.[19] This test is a measure of design fluency, cognitive flexibility, and imaginative capacity. It is a visual analogue of verbal fluency task. Patients with right frontal or central damage have difficulty on this test.[20] The participants are required to generate and draw as many abstract designs as possible in 5 minutes. The participants obtain a novel output score and a perseverative score. Children show improvement in scores on design fluency test until 12 years.[15]

Porteus maze test.[21] This test is a measure of planning and foresight (ie, choosing, trying, rejecting, and adopting alternative courses of conduct or thought). It consists of 12 mazes increasing in complexity across age levels. The participant was required to trace the maze from the starting point to the goal and follow certain rules. Two trials were allowed for specified mazes, which followed the administration and scoring pattern originally given by Porteus. Test age was calculated on the basis of the credits earned.

N back test (verbal). This test is a measure of verbal working memory based on the concept proposed by Smith and Jonides.[22] It consists of a list of phonemes for 2 separate conditions: 1 back and 2 back. One back requires the participant to say yes for a consecutively similar phoneme that is being read aloud at the rate of 1 per second. Two back requires the participants to say yes for every alternatively similar phoneme. Number of correct responses in each part of the test comprises the score.

N back task (visual). This test is a measure of visuospatial working memory and aims to assess executive control and active maintenance of spatial information. It consists of 36 cards each in the 1 back and 2 back tasks. Each card has a dot on a specific location. The subject has to decide whether the location of the dot in the present card matches the location of the dot in the card that appeared just before the present card. For the 2 back task, the subject has to decide whether or not the location of the dot in the present card matches with the location of the dot that appeared 2 cards before the present card. Number of correct responses in each part of the test comprises the score. A gradual improvement in working memory from childhood until adolescence has been reported.[23] A developmental study on Indian population showed a steady developmental trend between 5 to 8 years with respect to the maintenance and manipulation components of visuospatial working memory.[24]

Visuospatial Functions

Motor-free visual perception test.[25] This test is a measure of visuoperceptual ability and it uses 36 items to determine visual discrimination, visual closure, figure-ground, perceptual matching, and visual memory. Since this test has been originally developed for children between 5 to 8 years, it was modified and items in increasing difficulty level were added by the authors to make it applicable for the children above 8 years. Number of correct responses comprises the score.

Picture completion test.[26] This test is a measure of visuoconceptual ability, visual organization, and visuoconceptual reasoning. It consists of 20 cards with pictures of different objects with a missing feature. The participants are required to name or point out the missing feature. Number of correct responses comprises the score.

Comprehension, Learning, and Memory

Token test.[27] This test is a measure of verbal comprehension of commands of increasing complexity. It is a sensitive test of receptive aphasia and also developmental aphasia. Its sensitivity has been reported by demonstrating problems of speech comprehension by patients who showed no difficulty in understanding a normal conversation. It consists of tokens in 2 shapes (circle and square), 2 sizes (large and small), and 5 colors (red, blue, yellow, green, and white). There are 36 commands read aloud one by one by the examiner. As the examiner gives the command, the subject has to carry it out by manipulating the tokens accordingly. One point is given for each correctly performed command. A correct response after 1 repetition earns a score of 0.5. Two repetitions are deemed as failure.

Rey's auditory verbal learning test.[28] This test is a measure of verbal learning and memory. It is a measure of immediate memory, acquisition or new learning, retention, primacy/recency effect, and susceptibility to proactive and retroactive interference. Delayed verbal recall on this test has been found to be a sensitive parameter of the cognitive deficits in adults with left and bilateral temporal lobe epilepsy.[29] Nonlinear age effects on this test have been reported in children with greater improvement in performance during middle childhood than during early adolescence.[30] Age related improvement has been reported in verbal learning and memory on this test up until 9 years.[15]

Rey's auditory verbal learning test consists of a list of 15 words presented 5 times with an immediate recall after each of the 5 trials. A delayed recall is taken after a 30-minute time period that is filled with other nonverbal tests. It has been used with adults and children to examine the lateralized effects in focal epilepsy, including mesial temporal sclerosis.

Memory for designs test.[31] This test is a measure of visual learning and memory. The role of right temporal lobe in memory for visual patterns is well documented. Bilateral damage to the medial temporal lobe structures results in a profound, global and anterograde amnesia.[32] This test consists of 18 abstract designs each printed on a separate card. The number of designs presented to the children varies across age groups. 5 learning trials are given with a delayed recall after a 1-hour time period that is filled with verbal tests. Number of correct designs on each of the 5 trials gives the learning rate. Number of correctly recalled designs on delayed recall is the other score. Figural memory has been extensively used with children to examine material specific memory deficit for visual material and has been found sensitive to show lateralized deficits in right mesial temporal sclerosis.

Procedure

Children with a diagnosis of mesial temporal sclerosis were referred by the neurology consultants at the inpatient and outpatient services at NIMHANS in Bangalore, India. Lateralization of brain dysfunction in children with intractable epilepsy was determined by the concordance between the lateralized deficits on neuropsychological assessment and MRI findings. This is particularly important with reference to the presurgical evaluation of the epileptic focus in children with mesial temporal sclerosis. In each case, the investigator was blind to the findings of the MRI scan, EEG, and clinical investigations, while administering the neuropsychological tests. Children with mesial temporal sclerosis were subjected to a presurgical neuropsychological assessment. Each child was individually assessed and the entire assessment was conducted in 3 to 4 sessions with adequate rest pauses.

Analysis

The data was first analyzed by comparing the performance of children with mesial temporal sclerosis with the age appropriate norms of the NIMHANS neuropsychological battery for children, which have been presented as neuropsychological profiles in Table 2. The table shows the tests in which performance was found to be deficient with reference to the norms. Children with left and right mesial temporal sclerosis were further compared in their performance on neuropsychological tests using a *t* test. While comparing the children with left and right mesial temporal sclerosis, children across ages were grouped together. The neuropsychological performance of both groups was compared to find out if the differences in the lateralization of mesial temporal sclerosis, as per the MRI scan, also resulted in a difference in neuropsychological performance and if this was consistent with the side of the epileptic focus.

Results

The mean age of children with mesial temporal sclerosis (in the range of 7-15 years) was 11.6 years (SD = 2.49), and the mean

Table 2. Neuropsychological Profiles of Children with Mesial Temporal Sclerosis

	Children with Mesial Temporal Sclerosis																
Variables	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Age (years)	15	12	9	13	15	10	13	14	14	7	8	10	10	9	14	12	11
Lateralization[a]	3	3	2	1	1	2	1	2	3	1	1	2	2	2	2	1	–
CPM/SPM	–	22	24	–	–	20	–	–	–	17	14	–	16	28	–	–	22
IQ on BKT	73	–	–	–	–	–	95	–	106	–	–	–	–	–	77	85	–
FTTRT	28.4[b]	27.4[b]	34.2	34.4	48.4	33.8	40.8	36	45.2	23.2[b]	24.6[b]	25.8[b]	33.2	37.4	37	33.2	35.2
FTTLT	26.6[b]	25[b]	25.4[b]	29.4[b]	44.8	35.2	36.8	34.4	35.6	23.6[b]	24[b]	19.8[b]	28.2	35.6	26.2[b]	30.6	30.4
CCTIME[c]	193[b]	89[b]	90	54	66[a]	180[b]	94[b]	75[b]	44	135	178[b]	94	80[b]	53	180[b]	75	96[b]
TMTA[c]	345[b]	134[b]	89	59	86	240[b]	67	66	87	–	205[b]	174[b]	174[b]	125	193[b]	190[b]	127[b]
TMTB[c]	440[b]	406[b]	185	139	227[b]	435[b]	165	162	142	–	268	245	306[b]	189	336[b]	247[b]	216[b]
DFNOS	7[b]	7	20	7	2[b]	6	8	9	17	7	7	7	5	8	6[b]	9	3[b]
PMTTA	7.6[b]	9[b]	10	13.6	12	7[b]	13	13	13.6	–	6[b]	9.6	9.6	13.6	9[b]	11.6	9.6
VSWMA	2[b]	6[b]	8	10	9	6[b]	8	9	10	3[b]	2[b]	9	7	8	7[b]	8	6[b]
VSWMB	0[b]	1[b]	2	3	2[b]	0[b]	2[b]	2[b]	4	0[b]	3	4	3	2	3	0[b]	2[b]
VWMA	5[b]	7[b]	9	8[b]	8[b]	9	7[b]	9	9	7[b]	5[b]	6[b]	9	9	6[b]	9	7[b]
VWMB	8[b]	6[b]	20	16	9[b]	5[b]	10[b]	14	16	11	7[b]	9[b]	16	15	11[b]	16	11[b]
MVPT	15[b]	27	28	32	27[b]	12[b]	24[b]	34	32	26	25	24[b]	25[b]	32	28[b]	27	28
PC	5[b]	9	11	12	6[b]	8	11	9	11	5[b]	8	6[b]	9	11	8[b]	10	9
TT	23[b]	31	31	32	32	16[b]	35	30	33	22[b]	25[b]	27[b]	27[b]	33	30	33	28[b]
AVLTDR	5[b]	10[b]	11	13	8[b]	3[b]	13	7[b]	12	7[b]	9	5[b]	10	4[b]	8[b]	10	4[b]
AVLTSUM	27[b]	46	52	54	42[b]	35[b]	56	45	42[b]	38	39	32[b]	45	34[b]	42[b]	54	35[b]
MFDTDR	2[b]	8[b]	9	14	12[b]	4[b]	11[b]	17	16	6[b]	8[b]	4[b]	10	8[b]	7[b]	11	7[b]
MFDTSUM	14[b]	50	44	52	47	20[b]	59	55	59	28	30	23[b]	36[b]	40	32[b]	44	36[b]

Abbreviations: CPM/SPM, colored progressive matrices/standard progressive matrices; IQ, intelligence quotient; BKT, Binet Kamath test of intelligence; FTTRT, finger tapping test right hand; FTTLT, finger tapping test left hand; CCTIME, color cancellation test, time in seconds; TMTA, trail making test A; TMTB, trail making test B; DFNOS, design fluency novel output score; PMTTA, Porteus maze test, test age; VSWMA, visuospatial working memory 1 back; VSWMB, visuospatial working memory 2 back; VWMA, verbal working memory 1 back; VWMB, verbal working memory 2 back; MVPT, motor free visual perception test; PC, picture completion test; TT, token test; AVLTDR, auditory verbal learning test-delayed recall; AVLTSUM, auditory verbal learning test-total learning; MFDTDR, memory for designs test- delayed recall; MFDTSUM, memory for designs test-total learning.

[a] Scores that fall below the cut off with reference to the norms indicating deficit.

[b] Lateralization: 1 = left, 2 = right, 3 = bilateral.

[c] Measures for which cut-off scores were kept as equal to or greater than 95th percentile.

years of education for these children (in the range of 3-11 years) was 7.44 (SD = 2.74). According to the MRI scans, the epileptic focus was lateralized to the left hemisphere for 6 out of the 15 children and to the right hemisphere for 7 children. These children, with left and right mesial temporal sclerosis, were matched by age (mean age for left mesial temporal sclerosis group = 11.3 years, and mean age for right mesial temporal sclerosis group = 10.8 years; $t = .321$, $P > .05$), and years of education (mean years of education for left mesial temporal sclerosis group = 7, and mean years of education for right mesial temporal sclerosis group = 6.1; $t = .591$, $P > .05$). Performance on neuropsychological tests was examined with reference to the norms of the tests. The neuropsychological profiles of each child with mesial temporal sclerosis were evaluated with reference to the cut-off scores for the respective age level for each test score (Table 2). The normal cut-offs are different for each age, and the scores presented in Table 2 were compared with the norms of the respective age of each child when performance on each test was evaluated. Certain values in Table 2 indicate a score equal to or less than the fifth percentile for accuracy scores and a score equal to or more than the 95th percentile for time measures as per the age norms qualifying for a deficit. The cut-off scores for each test score for each age from 5 to 15 years have been provided in the NIMHANS neuropsychological battery for children. Cut-offs denote if the performance on a particular test was deficient, ie, less than the fifth percentile, which is much below the normal level of functioning (50th percentile). The neuropsychological profiles of 16 children with mesial temporal sclerosis were examined on the basis of a case-by-case analysis. Additionally, the neuropsychological profiles of children with left mesial temporal sclerosis versus right mesial temporal sclerosis were also compared.

Results showed that the tests of learning and memory for verbal and visual material could pick up lateralized deficits related to the epileptic focus, as depicted by the MRI scans. Children with left mesial temporal sclerosis and those with right mesial temporal sclerosis showed deficits in verbal and visual learning as depicted by the total learning score (see Figure 1). The total learning score is the total number of words/designs learned across all of the 5 trials. Verbal and visual memory was measured by the delayed recall score in terms of the number of words/designs recalled after a delay period. Children with left-sided mesial temporal sclerosis

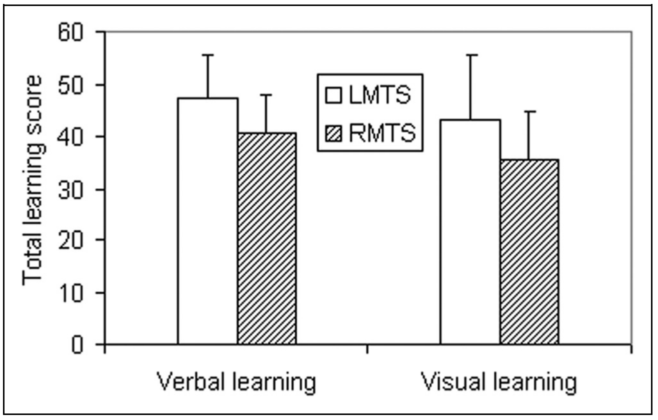

Figure 1. Verbal and visual learning in children with left and right mesial temporal sclerosis. LMTS, left mesial temporal sclerosis; RMTS, right mesial temporal sclerosis.

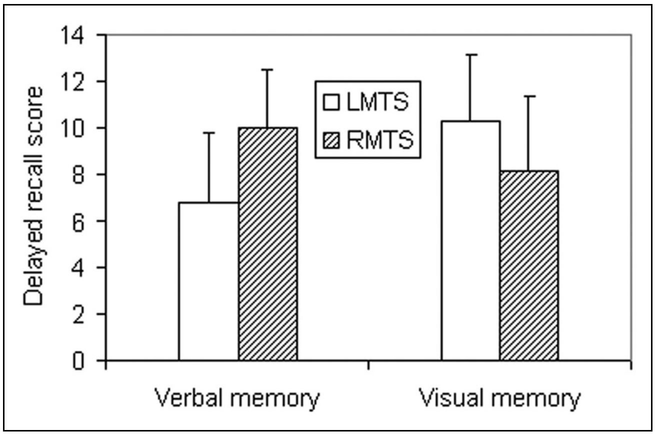

Figure 2. Verbal and visual memory in children with left and right mesial temporal sclerosis. LMTS, left mesial temporal sclerosis; RMTS, right mesial temporal sclerosis.

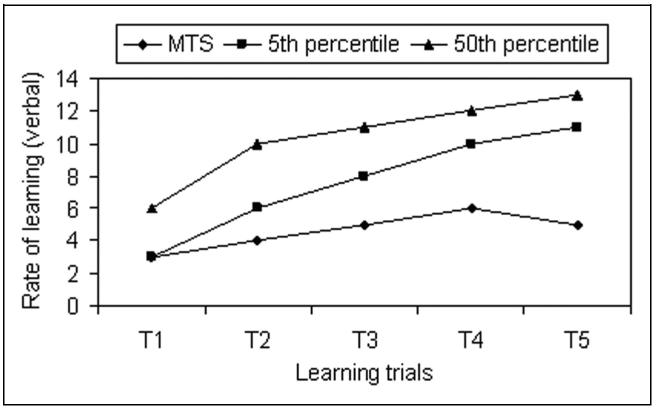

Figure 3. Rate of learning (verbal) of a 14-year-old child with left mesial temporal sclerosis. MTS, mesial temporal sclerosis.

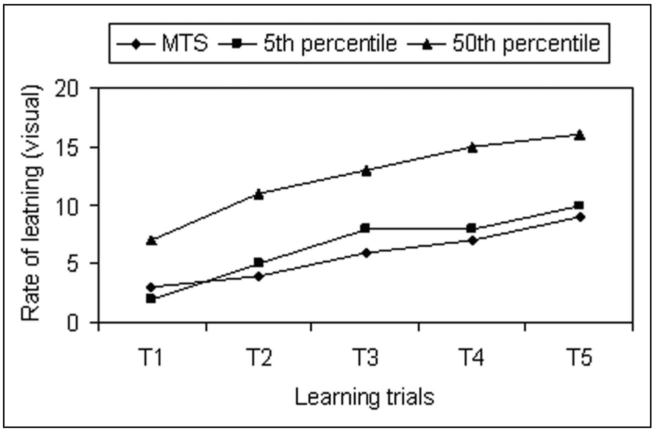

Figure 4. Rate of learning (visual) of a 14-year-old child with right mesial temporal sclerosis. MTS, mesial temporal sclerosis.

showed greater deficits in verbal memory, whereas children with right-sided mesial temporal sclerosis showed greater deficits in visual memory (see Figure 2).

Although the neuropsychological tests on learning and memory could provide data on material specific learning and memory deficits, the test comparing the 2 groups showed that the performance of the children with left mesial temporal sclerosis (mean = 47.16 $\pm$ 8.3) and right mesial temporal sclerosis (mean = 40.71 $\pm$ 7.29; $t = 1.48$, $P > .05$) was not significantly different on verbal or visual learning (left mesial temporal sclerosis: mean = 43.33 $\pm$ 12.22; right mesial temporal sclerosis: mean = 35.71 $\pm$ 12.12; $t = 1.12$, $P > .05$). Children with left mesial temporal sclerosis (mean = 10.0 $\pm$ 2.5) were not found to be significantly different from those with right mesial temporal sclerosis (mean = 6.8 $\pm$ 3.0; $t = 2.01$, $P > .05$) on verbal memory as well as visual memory (left mesial temporal sclerosis: mean = 10.33 $\pm$ 2.8; right mesial temporal sclerosis: mean = 8.42 $\pm$ 4.2; $t = .90$, $P > .05$) (see Figures 1 and 2). These results indicate that the deficits were not specific to the side of the epileptic focus as indicated by the MRI scans. Though the norms of the tests provided in the battery were sensitive enough to pick up deficits when compared to the age appropriate normative data, the deficits showed more of bilateral functional deficits in both groups (see Table 2). These findings suggest that children may not show clearly lateralized deficits as seen in adults. There could be an absence of asymmetry in functional deficits in children with mesial temporal sclerosis as most of the children (53.3%) showed bilateral deficits in learning and memory.

Deficits observed in the learning rate and delayed recall score on the Rey's auditory verbal learning test and the memory for designs test of visual learning and memory also showed slower age appropriate improvement across trials. These deficits showed the effect of mesial temporal sclerosis on the rate of learning and memory (acquisition and maintenance of verbal/visual material) (see Figures 3 and 4). Learning curves of each child with mesial temporal sclerosis were plotted against the learning curves that represented the normative data on the fifth and 50th percentile functions. The Rey's auditory verbal learning test and the memory for designs test provided scores that depicted the rate of learning across the 5 learning trials.

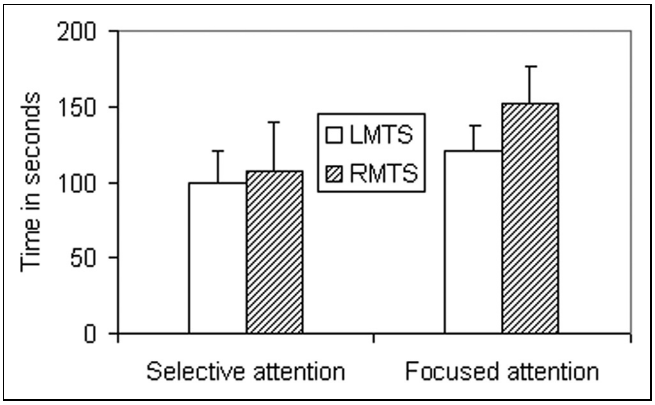

Figure 5. Selective and focused attention in children with left and right mesial temporal sclerosis. LMTS, left mesial temporal sclerosis; RMTS, right mesial temporal sclerosis.

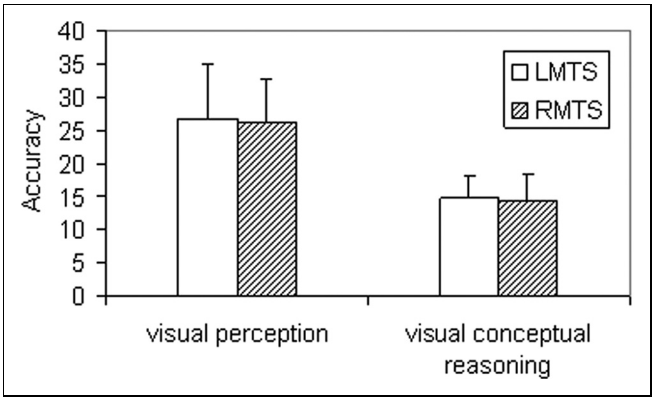

Figure 6. Visual perception and visual conceptual reasoning in children with left and right mesial temporal sclerosis. LMTS, left mesial temporal sclerosis; RMTS, right mesial temporal sclerosis.

We present the data of 2 children to demonstrate the effect of mesial temporal sclerosis on the development of learning and memory (see Figures 3 and 4). Such a comparison was not possible with the entire data because this is an age-related comparison with reference to norms and we had very few children in each of the age levels. Figures 3 and 4 present the comparisons for the rate of learning of verbal and visual material across the 5 learning trials for a child with mesial temporal sclerosis against the 50th and fifth percentiles. The learning curve of case 1 for verbal material falls below the fifth percentile and is indicative of a deficit in the rate of learning with reference to the age norms. The learning curve of case 1 for visual material is also close to the fifth percentile, which indicates a poor learning rate. Both the tests also provide the delayed recall score, which is a measure of long-term retention.

Children with mesial temporal sclerosis also showed deficits in working memory, attention, and visuospatial relations with reference to the age appropriate norms (see Table 2). Most of these children showed deficits in visuospatial working memory (80%), focused attention (73.3%), selective attention, visual and verbal memory (60%-66%), and finally deficits in visuospatial functions (40%-46.6%). Verbal and visual learning, in terms of the total learning score, were less severely affected, but the rate of learning across trials was severely affected in both groups.

Mean comparisons between the children with left mesial temporal sclerosis and right mesial temporal sclerosis with respect to those cognitive functions showed a deficit with reference to norms. The *t* test was computed and the 2 groups did not show a significant difference in performance on any of the cognitive functions. These results further strengthen the finding with respect to the lack of clearly lateralized deficits in children with mesial temporal sclerosis. Children with mesial temporal sclerosis showed deficits in attention and visuospatial functions (see Figures 5 and 6). According to the neuropsychological profiles, when the performance of these children on various neuropsychological tests was compared with the norms (see Table 2), 2 out of 6 children with left mesial temporal sclerosis showed primarily left sided deficits and the other 4 showed bilateral deficits. Among children with right mesial temporal sclerosis, only 1 child showed deficits primarily lateralized to the right, which was concordant with the MRI scan, 2 of them showed left sided deficits, and 4 were bilateral. Mostly participants had bilateral frontal deficits along with bilateral temporal, right or left temporal deficits, and a few of them also showed right parietal deficit.

Discussion

Neuropsychological assessment is an integral part of the presurgical evaluation of mesial temporal sclerosis. Neuropsychological profiles provide support for lateralization as well as information on the functional status of cognitive functions other than learning and memory in individuals with mesial temporal sclerosis.[33] Very few studies have been carried out on the cognitive effects of mesial temporal sclerosis in children, and these studies have reported stable intelligence quotients (IQs) but impaired memory functions.[34] Lesion studies indicate that left and right medial temporal structures are essential for verbal and visual memory respectively.[35,36]

Material specific memory deficits have been reported mostly in adults and also in children. Few of the recent studies on children with mesial temporal sclerosis have questioned the status of functional deficits as being specifically lateralized to left or right medial temporal region. These studies have shown bilateral deficits in terms of memory impairments for verbal and visual material, irrespective of the side of the epileptic focus.[37] We have observed deficits in verbal and visual learning and memory, but not with a clear-cut lateralization of these deficits in children with mesial temporal sclerosis. Most of the studies on adults report that left medial temporal region is more important than the right for the functions of learning and the retention of verbal material. We have observed deficits in verbal learning and memory on an auditory verbal learning test in children with right mesial temporal sclerosis. Five out of 7 children with right mesial temporal sclerosis showed deficits in verbal memory along with deficits in memory for visual material. However, the severity of the verbal memory deficits was less when compared to visual memory in children with right mesial temporal sclerosis. One of the recent studies on 22 children with mesial temporal sclerosis also reported that the right mesial temporal sclerosis group has lower delayed recall score on the auditory verbal learning test.[2] In the present study, we observed that it is difficult to find clearly lateralized material specific deficits in children with mesial temporal sclerosis as reported in adults. Left-sided deficits in learning and memory for verbal material were not only observed in children with left mesial temporal sclerosis, but were also observed in children with right mesial temporal sclerosis as well. A similar trend was observed in the case of deficits in learning and memory for visual material.

Most of the children with mesial temporal sclerosis had hippocampal sclerosis that impairs the ability to learn and retain information over a delay period. Although children with mesial temporal sclerosis showed deficits on tests of learning and memory, these findings did not correspond with the left-sided/right-sided epileptic focus depicted by the MRI scan and EEG. These findings indicate that the decision for surgery in children with intractable epilepsy caused by mesial temporal sclerosis may be critical with respect to the more generalized picture of functional deficits. Neuropsychological measures provide data for functional impairments that are mediated by the structural abnormalities that result from mesial temporal sclerosis, and these measures also help to monitor and predict surgical outcome and ongoing recovery of cognitive deficits.

The NIMHANS neuropsychological battery for children was found to be sensitive to deficits, particularly with respect to functions of learning and memory in children with mesial temporal sclerosis. Identification of structural abnormalities alone is not an adequate means of assessing the functional status; however, direct relationships between structural and functional measures are modest.[38]

Studies on the application and adaptation of neuropsychological tests in children with

mesial temporal sclerosis are very few in the literature. Apart from showing concordance in terms of lateralized deficits with clinical investigations, neuropsychological tests could be sensitive indicators for the child's ongoing learning and memory maturation as well as other cognitive functions. These tests could also be sensitive indicators to track the effects of structural pathology and antiepileptic medication.

The NIMHANS neuropsychological battery for children has been found to be sensitive to focal as well as diffuse brain damage. The battery is also sensitive to the developmental changes in cognitive functions for children in the age range of 5 to 15 years, and it is standardized on the Indian population. This battery is a comprehensive tool to be used on Indian children and is sensitive for localization and lateralization of brain dysfunction. It can provide clinically valuable data regarding the disease process and plasticity in terms of spontaneous functional recovery.[39] The norms of the battery are based on empirically validated age trends of cognitive functions. Such a battery can provide profiles of neuropsychological impairments in Indian children with brain damage. The sensitivity of the test battery in localizing and lateralizing brain dysfunction highlights the significance of the test battery in presurgical evaluation and the ongoing monitoring of the functional status of brain in children with focal lesions and mesial temporal sclerosis. Very few test batteries offer a comprehensive neuropsychological assessment for children, particularly test batteries with norms that are based on empirically validated age trends of cognitive functions.

Mesial temporal sclerosis is also associated with impairment in executive functions as observed in the present study.[40] Cognitive deficits were also observed on tests of attention, working memory, verbal comprehension, and visual perception other than learning and memory in children with mesial temporal sclerosis. However, statistically significant differences were not observed between children with left mesial temporal sclerosis and right mesial temporal sclerosis on these cognitive deficits. Although these findings are consistent with studies that reported cognitive deficits in attention, language comprehension, and visuoconstructive abilities, they have also found poorer language comprehension (token test) in children with left mesial temporal sclerosis.

We examined the effect of pathology that resulted from mesial temporal sclerosis on the ongoing maturation of learning and memory. So far, studies have looked at age-related recovery of cognitive functions and compared preoperative and postoperative neuropsychological performance. However, these studies have not tested the effect of mesial temporal sclerosis on the development of learning and memory in children. This assessment would help to know the effect of mesial temporal sclerosis on cognitive development and would have implications for the strategies for cognitive rehabilitation.

Normal age appropriate development of learning and memory has shown a gradual improvement in delayed recall scores across the age range of 5 to 15 years with faster improvement in the middle childhood years. Another study has reported similar age trend with a steep rise in scores on tests like auditory verbal learning test with children between 8 to 10 years.[15] We observed a decline in the rate of learning for verbal and visual material in children with mesial temporal sclerosis. The neuropsychological performance of children with mesial temporal sclerosis was found much below (< the fifth percentile) the age appropriate level of functioning. These findings suggest a delay in the development of attention, working memory, visuospatial ability, and most severely, learning and memory in children with mesial temporal sclerosis. Here also the 2 groups with left and right mesial temporal sclerosis were equally affected. The interesting findings of this study related to functional lateralization and cognitive development need to be tested with a larger sample and in a longitudinal study.

Conclusion

Neuropsychological assessment explains the functional status of the brain with respect to an epileptic focus, lateralized cognitive deficits, and the development of cognitive functions in children with mesial temporal sclerosis. It is difficult to find clearly lateralized or material specific deficits in children with mesial temporal sclerosis compared to adults. Deficits pertaining to cognitive functions such as rate of learning, verbal and visual memory, attention, working memory, and visuospatial functions are also associated with mesial temporal sclerosis.

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