

Auditory verbal memory and psychosocial symptoms are related in children with idiopathic epilepsy

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ABSTRACT

Objective: Idiopathic epilepsies are considered to have relatively good prognoses and normal or near normal developmental outcomes. Nevertheless, accumulating studies demonstrate memory and psychosocial deficits in this population, and the prevalence, severity and relationships between these domains are still not well defined. We aimed to assess memory, psychosocial function, and the relationships between these two domains among children with idiopathic epilepsy syndromes using an extended neuropsychological battery and psychosocial questionnaires.

Methods: Cognitive abilities, neuropsychological performance, and socioemotional behavior of 33 early adolescent children, diagnosed with idiopathic epilepsy, ages 9–14 years, were assessed and compared with 27 age- and education-matched healthy controls.

Results: Compared to controls, patients with stabilized idiopathic epilepsy exhibited higher risks for short-term memory deficits (auditory verbal and visual) ($p < 0.0001$), working memory deficits ($p < 0.003$), auditory verbal long-term memory deficits ($p < 0.0021$), and more frequent psychosocial symptoms ($p < 0.0001$). The severity of auditory verbal memory deficits was related to severity of psychosocial symptoms among the children with epilepsy but not in the healthy controls.

Significance: Results suggest that deficient auditory verbal memory may be compromising psychosocial functioning in children with idiopathic epilepsy, possibly underscoring that cognitive variables, such as auditory verbal memory, should be assessed and treated in this population to prevent secondary symptoms.

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1. Introduction

Idiopathic epilepsy (IE) denotes a group of disorders in which seizures occur in the absence of structural brain damage with no abnormal

neurological signs and for which no etiology can be found other than a genetic predisposition. Idiopathic epilepsy constitutes almost one-third of all epilepsies [1]. The majority of affected children are thought to follow a normal developmental course, and the prognosis with respect to seizure control is generally favorable as opposed to the more severe epilepsies such as temporal lobe epilepsy (TLE) [2] and Lennox–Gastaut syndrome [3,4].

However, since children with IE experience only rare seizures, and because of the good medical prognosis, the cognitive impact of idiopathic epilepsies is often underestimated and is still debated. Research shows that school difficulties [5,6], attention difficulties [7–9], and linguistic deficits [10–12] are common among children with IE. In addition, the neuropsychological mechanism accounting for these deficits is not yet understood. According to recent studies, memory deficits are frequent among children with generalized or partial IE [13–16] and play a significant role in school performance [17]. For this reason, understanding the specific characterization of memory deficits in children with IE may serve to improve their developmental outcome.

Abbreviations: IE, Idiopathic epilepsy; TLE, Temporal lobe epilepsy; STM, Short-term memory; LTM, Long-term memory; WM, Working memory; AEDs, Antiepileptic drugs; ILAE, International League against Epilepsy; ADHD, Attention deficit hyperactivity disorder; LD, Learning difficulty; BRE, Benign rolandic epilepsy; IGE, Idiopathic generalized epilepsy; ABE, Absence epilepsy; ESIQ, Estimated IQ; WISC-IV, Wechsler intelligence scale for children edition IV; TOMAL, Test of memory and learning; RAVLT, Rey auditory verbal learning test; RCFT, Rey complex figure test; CBCL, Child behavior checklist, parent's form; YSR, Youth self-report from the Achenbach assessment, child's form; MFS, Memory for stories; DF, Digits forward; DB, Digits backwards; MFSD, Memory for stories delayed.

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1.1. Memory systems in IE

Memory is a multidimensional construct, with different types of memory systems affected to varying degrees in childhood epilepsy [13–16]. Our approach was based on a theoretical framework that differentiates between two types of time-dependent memory systems: short-term memory [STM; 18,19] and long-term memory [LTM; 20–24]. Working memory [WM; 25–28] is another type of memory that was examined in this study. According to several studies, STM is affected very little by childhood idiopathic epilepsy [14,16], whereas LTM and WM are usually affected by childhood IE [29–33]. More specifically, these studies highlight the following memory deficits: recognition, immediate and delayed recall, proactive interference, and working memory. These deficits may also be consistent with a larger set of data about memory disorders in other types of epilepsy, namely with rolandic epilepsy [for instance; 34–38] and other forms of benign epilepsy such as Panayiotopoulos epilepsy [for instance; 39,40].

Although the causes of memory impairments in patients with epilepsy have not been completely elucidated, three factors are considered to be involved. The first factor is the underlying etiology of epilepsy. Secondly, the effects of seizures/epileptiform EEG discharges themselves or as a consequence of the chronic repetitive spikes inhibiting/disrupting activity in the same cortical area for many years [5]. The last factor concerns the effects of antiepileptic drugs (AEDs) on the central nervous system. It appears that all commonly used AEDs have some effect on cognitive function, and the effect may be substantial when crucial functions are involved and affect learning in children [41]. Nevertheless, not all AEDs induce memory problems; only a few AEDs such as topiramate and phenobarbital have been found to increase memory problems in children [41].

By integrating these data, it seems that children with IE tend to suffer more from memory deficits than do healthy controls. Little is known, however, of the particular characteristics of this deficit; for example, if it involves auditory verbal memory or visual memory as well; or the relationships between the severity of patients' memory difficulties and daily and socioemotional functioning in children with IE.

1.2. Socioemotional functioning in IE

In addition to memory deficits, children with epilepsy were found to have a four times greater risk of developing behavioral and emotional problems than the general childhood population [42]. Several studies indicate that childhood epilepsy is a significant risk factor for poor psychosocial outcomes, including depression, anxiety, psychosis, and behavioral problems [43–47]. In addition, children with IE often demonstrate lower self-esteem than children with other chronic illnesses such as diabetes or asthma [43,45,48–51]. These data highlight the lower socioemotional functioning in children with IE in addition to their reported memory difficulties.

We postulated that memory and socioemotional symptoms may be related in children with IE. This relationship has been the focus of extensive research in the last decade in other risk cohorts [52]. The relationship may arise from a shared neural network that supports both functions. There is growing evidence for the activation of similar neuroanatomical loci in tasks that involve the retrieval of memorable events and for processing socially loaded stimuli, such as activating autobiographical memories (i.e., recalling personally experienced events), inferring the mental states of others (i.e., mentalization or theory of mind) [53–56], and others [55,57–59]. This integration indicates that some of the differences in social behavior may relate to how we use memory in a social context [52].

In addition, cognitive operations may be mediated by emotion [60–63]. In view of this notion, it seems important to study the relationships between memory performance and emotional status in children with IE. More specifically, we examined the extent to which the type of memory (i.e., STM, LTM and WM), modality type (auditory verbal

versus visual), and the severity of memory deficits relate to socioemotional functioning and to socioemotional symptoms in children with IE. For this aim, the present study intended to (1) assess memory abilities and socioemotional status in children with IE compared to age-matched controls and (2) examine the relationship between memory performance and psychosocial status as reported by the children themselves and their parents.

2. Methods

2.1. Participants

The study's cohort consisted of 33 young adolescent children (51% girls) diagnosed with IE and 27 healthy control participants (52% girls), aged 9–14 years, fluent in their native language, Hebrew, with an estimated intelligence within normal limits (based on the block design subtest from the WISC-IV [64]; estimated intelligence quotient, ESIQ > 79).

Children with IE were recruited through the neurology department at Sheba Medical Center and at the Department of Pediatric Neurology at Schneider Children's Medical Center in Israel. Medical history, electroencephalography, and imaging data were reviewed by the treating neurologists according to the International League against Epilepsy (ILAE) criteria for IE [65]. Inclusion criteria consisted of at least one unprovoked nonfebrile seizure or status epilepticus in the past but no current seizures (balanced condition) at present, idiopathic etiology: benign rolandic epilepsy ($n = 18$), absence epilepsy ($n = 4$), and generalized epilepsy ($n = 11$), an age range of 9–14 years, intelligence within the normal range, and attendance in mainstream educational schools. Exclusion criteria included temporal lobe epilepsy, structural epilepsy, metabolic epilepsy, comorbid neurological disorders other than ADHD [66], comorbid chronic illness (e.g., diabetes and asthma), major depression [66] and psychosis, and prescribed use of topiramate and phenobarbital AEDs. Overall, 39 were children referred by neurologists, but six of them were excluded – two due to low intelligence and four due to the presence of more severe epilepsy (temporal lobe epilepsy (TLE) or Lennox–Gastaut syndrome).

The control participants were comprised of 27 children (14 females, 13 males) who were matched for age and sex to the group with epilepsy but showed no evidence of any neurological or other disorder. Children were randomly recruited from mainstream public schools in the same (central) district of Israel via word of mouth (snowball recruitment) and were exposed to the same educational curriculum. Their past medical history, as reported by their parents, was unremarkable. The inclusion criteria used for the patient group was used for this group as well with regard to age, intelligence, reported head injuries, schooling, psychiatric involvement, and/or medication. All children who participated in the study were reported to be average academic achievers by their parents based on their last school report card.

The demographics, seizure characteristics, and medication profiles of the participants are summarized in Table 1.

Overall, the participants with IE were diagnosed at a mean age of 9.5 ± 0.7 years and had experienced epilepsy for an average of 4.34 ± 2.2 years. Most patients with IE used antiepileptic drugs (AEDs): 25 were treated with monotherapy, eight with polytherapy, and none of the participants were medication free. Ten participants received psychotherapy. The group with IE and control group did not differ in age or sex distribution, but there was an expected difference in the frequency of ADHD and/or learning difficulties diagnoses (see Table 1) and psychotherapy. The mean ESIQ of the group with IE was significantly lower than that of the control group, but both groups were within the normal range.

2.2. Neuropsychological tests

An extensive, age appropriate assessment battery of STM, LTM, and WM was used. Auditory memory using heard verbal material and visual

Table 1

Participant demographics, seizure characteristics, and medication profile.

	IE mean \pm SD	Controls mean \pm SD	Test of significance	p Value
N	33	27		
Age	10.88 \pm 1.52	10.18 \pm 1.4	$T_{58} = 1.83$	>0.072 NS
Age at diagnosis	9.5 \pm 0.7	10.18 \pm 1.4	$T_{58} = 1.68$	0.1 NS
Sex (F/M)	17/16	14/13	$\chi^2_{58} = 0.01$	>0.974 NS
ESIQ	−0.85 \pm 0.84	0.16 \pm 0.93	$T_{58} = -3.87$	<0.01
Vocabulary	−1.3 \pm 0.88	0.14 \pm 0.94	$T_{58} = -6.29$	<0.01
Comorbid ADHD/LD	6/4	0/0	$\chi^2_{58} = 9.9$	<0.02
Medication profile (monotherapy/polytherapy)	25/8	0/0		
Epilepsy type (BRE/IGE/AB)	19/11/3	0/0/0		
Psychotherapy	10	0	$\chi^2_{58} = 16.63$	<0.01

Legend: IE, idiopathic epilepsy; ESIQ, estimated IQ (average of block design from the WISC-IV [1]); ADHD, attention deficit hyperactivity disorder; LD, learning difficulty; BRE, benign rolandic epilepsy; IGE, idiopathic generalized epilepsy; ABE, absence epilepsy.

Table 2

Neuropsychological assessment tools as a function of memory system and sensory modality.

Domain	Test (subtest)	
	Auditory verbal	Visual
Intelligence		WISC-IV: block design
Short-term memory	TOMAL: paired recall, digit forward, immediate memory for stories RAVLT: immediate (1)	TOMAL: facial memory, abstract visual memory, visual sequential memory, memory for location RCFT: immediate and delayed visual memory
Long-term memory	TOMAL: delayed memory for stories, object recall. RAVLT: delayed (8) recognition	
Working memory and attention	TOMAL: digits backwards CBCL (parents): attention YSR (child): attention	WISC-IV: cancellation

Legend: WISC-IV, Wechsler intelligence scale for children edition IV [64]; TOMAL, test of memory and learning [67]; RAVLT, Rey auditory verbal learning test [68]; RCFT, Rey complex figure test [69]; CBCL, Child behavior checklist, parent's form [70]; YSR, Youth self-report from the Achenbach assessment, child's form [70].

memory using nonverbal material were evaluated to obtain an in-depth characterization of memory. In addition, age appropriate attention tools were used to evaluate attention. The clinical neuropsychological battery instruments are presented in Table 2.

2.3. Psychosocial measures

To estimate emotional and social problems among children with IE, child and parent self-reported questionnaires were used. These questionnaires are detailed in Table 3.

2.4. Procedure

The study was approved by the Institutional Review Boards of the participating medical centers: Sheba Medical Center, Tel Hashomer; Schneider Children's Hospital, Rabin's Medical Center, Petach Tikva; and Bar Ilan University, Israel.

Written informed consent was obtained from the parents of all participants, and oral consent was obtained from the participants during

routine medical visits, at which time they were invited for a testing day on campus at their convenience. Testing was conducted individually at the Developmental Neuropsychological lab over one 120-minute session that included breaks for refreshment, as required. Developmental histories and information regarding relevant epilepsy home care variables were gathered via parental interviews. Neurological and psychiatric information concerning patients with epilepsy was verified by the treating pediatric neurologists.

2.5. Statistical analysis

To estimate the relative risk for a specific memory deficit in our sample, odds ratios were computed in the experimental and control groups. Because each memory domain was measured by using different tests, all scores were standardized. A memory deficit in a domain was defined when a participant showed a Z-score < −1 on at least two tests, in accordance with other studies in this field [71,72]. A psychosocial deficit was defined in all cases where at least one T-score was greater than 65 [73]. In the next step, we examined the relationships between memory domains and psychosocial status by computing Pearson correlations. Finally, differences in correlation strengths between the group with IE and control group were explored using the Fisher's Z-coefficient [74,75].

3. Results

3.1. Risk for memory deficits

Odds ratios were computed to assess the hypothesis that children with IE were at a higher risk for STM, WM, and LTM deficits. For absolute rates of memory deficits and group differences in rates of memory deficits, see Fig. 1. It was found that children with IE were at a higher risk for auditory verbal STM (odds ratio: 0.137, 95% confidence interval:

Table 3

Psychosocial assessment tools.

Domain	Test (subtest)
Introvert	CBCL (parents): depression, anxiety, somatic complaints YSR (child): depression, anxiety, somatic complaints
Extrovert	CBCL (parents): delinquent behavior, aggressive behavior YSR (child): delinquent behavior, aggressive behavior
Social problems	CBCL (parents): social problems YSR (child): social problems
Cognitive distractions	CBCL (parents): thought problems YSR (child): thought problems

Legend: CBCL, Child behavior checklist, parent's form [70]; YSR, Youth self-report from the Achenbach assessment, child's form [70].

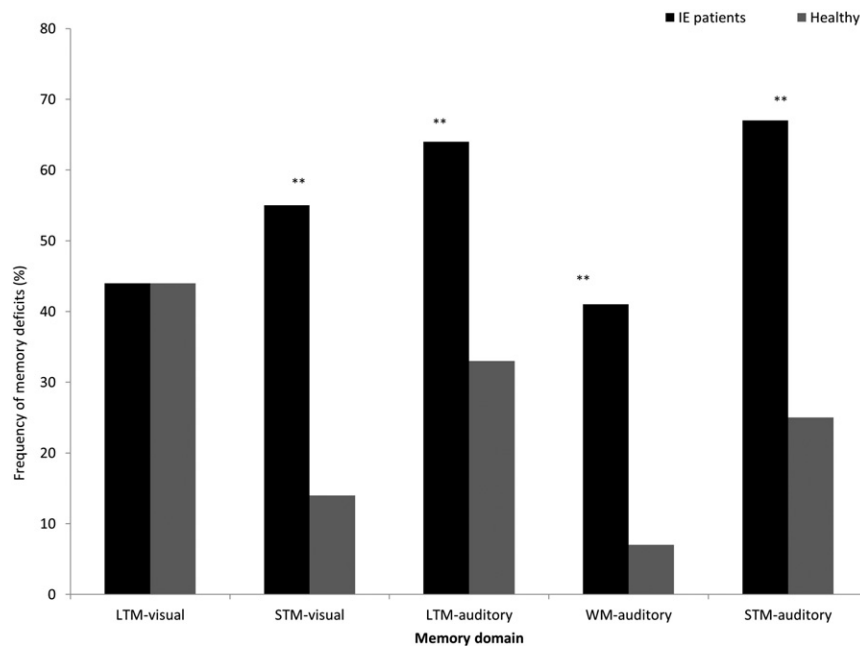


Fig. 1. Frequencies of memory deficits in each group (% deficits). Legend: ** $p < 0.01$.

0.03–0.48, $p < 0.001$) and visual STM deficits (odds ratio: 0.167, 95% confidence interval: 0.05–0.514, $p < 0.002$). In addition, a risk for WM deficits (odds ratio: 0.11, 95% confidence interval: 0.02–0.563, $p < 0.003$) was found. Moreover, a higher risk for auditory verbal LTM deficits (odds ratio: 0.273, 95% confidence interval: 0.094–0.791, $p < 0.021$) but not visual LTM deficits (odds ratio: 1.013, 95% confidence interval: 0.366–2.8024.2, $p = 1$) was detected. Thus, in our sample, children with IE were at higher risk than controls for STM (auditory verbal and visual), WM, and auditory verbal LTM deficits, indicating a pervasive auditory verbal memory deficit.

In order to examine if these differences resulted from the type of medication used (mono- versus polytherapy), psychotherapy, or the presence of ADHD, odds ratio were computed. Results indicated no difference in memory performance between the patients who used monotherapy and patients who used polytherapy ($\chi^2_{(1, N=33)} = 0.434$, $p = 0.510$,

NS), between patients receiving psychotherapy and patients not receiving psychotherapy ($\chi^2_{(1, N=33)} = 0.209$, $p = 0.647$, NS), and between patients with ADHD and patients without ADHD ($\chi^2_{(1, N=33)} = 0.1$, $p = 0.752$, NS).

3.2. Risk for psychosocial problems

Odds ratios were computed to assess the hypothesis that children with IE are at a higher risk for social and emotional problems. For absolute rates of social and emotional problems and group differences, see Fig. 2. It was found that the children with IE were at a higher risk for socioemotional symptoms (odds ratio: 0.077, 95% confidence interval: 0.01–0.3, $p < 0.001$). More specifically, relative to the controls, the children with IE were at a higher risk for social problems (odds ratio: 0.111, 95% confidence interval: 0.02–0.44, $p < 0.001$), externalization problems

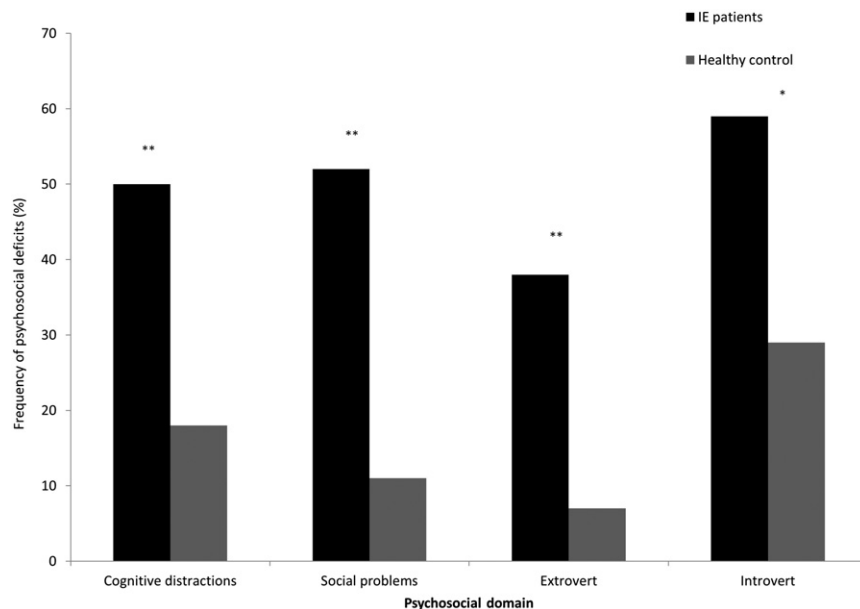


Fig. 2. Frequencies of psychosocial symptoms in each group (% deficits). Legend: * $p < 0.05$, ** $p < 0.01$.

(odds ratio: 0.129, 95% confidence interval: 0.026–0.63, $p < 0.007$), internalization problems (odds ratio: 0.295, 95% confidence interval: 0.1–0.86, $p < 0.03$), and distractibility (odds ratio: 0.227, 95% confidence interval: 0.07–0.74, $p < 0.01$).

In order to examine if these differences resulted from the type of medication used (mono- versus polytherapy), psychotherapy, or the presence of ADHD, odds ratio were computed. Results indicated no difference in psychosocial status domains between the patients who used monotherapy and patients who used polytherapy ($\chi^2_{(1, N=33)} = 0.83$, $p = 0.362$, NS), and between patients with ADHD and patients without ADHD ($\chi^2_{(1, N=33)} = 1.595$, $p = 0.207$, NS). In addition, significant differences were found in externalization problems ($\chi^2_{(1, N=33)} = 4.609$, $p < 0.05$), social problems ($\chi^2_{(1, N=33)} = 6.556$, $p < 0.01$), and distractibility ($\chi^2_{(1, N=33)} = 12.6$, $p < 0.01$) indicating that children receiving psychotherapy had more symptoms than children not receiving psychotherapy.

3.3. Relationships between memory functions and psychosocial outcome problems

A correlation matrix was constructed to assess the hypothesis that memory deficits were associated with poorer socioemotional status

(Table 4). The table first shows that there were significant correlations in both groups between auditory verbal STM and total psychosocial functioning ($r = -0.458$, $p < 0.021$ for the group with IE and $r = -0.417$, $p < 0.05$ for the control group) and between auditory verbal LTM and total psychosocial functioning ($r = -0.553$, $p < 0.03$ for the group with IE and $r = -0.501$, $p < 0.018$ for the control group).

In addition, a significant set of correlations was found only in the group with IE. This set, comprised of relations between auditory verbal STM, visual STM, auditory verbal LTM, WM, and diverse psychosocial domains, was found for the group with IE but not for the healthy control group. These relationships indicated interrelations between memory difficulty severity and psychosocial problems among children with IE that do not necessarily operate in the general population. Specifically, unlike the findings for the control group, the severity of internalizing problems, in particular, the severity of anxiety and depression, were related to the efficacy of auditory verbal STM and auditory verbal LTM in the children with IE. Similarly, the degree of severity of externalizing problems, delinquency, and aggressive behavior were related to the efficacy of auditory verbal STM in children with IE but not in the controls such that overall, the severity of social problems was related to auditory verbal STM and LTM in the group with IE but not in the controls. Finally, the results of Fisher's Z-coefficients showed that the difference between

Table 4
Correlations between psychosocial outcome problems and memory functions.

Psychosocial domain	Psychosocial symptoms	Dependent measures	Pearson's r in IE group (p<)	Pearson's r in healthy control group	Fisher's Z	p *1-tailed **2-tailed	
<i>Auditory verbal STM</i>							
Introvert	Anxiety	MFS	− 0.57 (0.006)	− 0.137 (0.54)	− 1.64	0.05* 0.1** NS	
		DF	− 0.44 (0.027)	− 0.226 (0.312)	− 0.8	0.4 NS	
	Depression	MFS	− 0.5 (0.008)	− 0.03 (0.8)	− 1.7	0.04* 0.08 NS**	
Extrovert	Delinquent behavior	MFS	− 0.387 (0.03)	− 0.007 0.(71)	− 1.39	0.16 NS	
	Aggressive behavior	MFS	− 0.406 (0.04)	0.04 (0.85)	− 1.52	0.12 NS	
Social problems	Social problems	MFS	− 0.48 (0.01)	− 0.09 (0.66)	− 1.43	0.15 NS	
		DF	− 0.425 (0.021)	0.135 (0.5)	− 1.98	0.0239* 0.0477**	
Cognitive deficits	Thought problems	MFS	− 0.533 (0.005)	− 0.18 (0.4)	− 1.33	0.18 NS	
		DF	− 0.47 (0.018)	− 0.345 (0.115)	− 0.48	0.6 NS	
	Attention	MFS	− 0.556 (0.002)	− 0.12 (0.58)	− 1.63	0.05* 0.1 NS**	
		DF	− 0.417 (0.024)	0.258 (0.2)	− 2.38	0.0087* 0.017**	
Total psychosocial functioning	Total YSR	MFS	− 0.64 (0.0000)	− 2.22 (0.3)	− 1.72	0.04* 0.08 NS**	
		DF	− 0.458 (0.021)	− 0.417 (0.05)	− 0.16	0.8 NS	
<i>WM</i>							
Extrovert	Delinquent behavior	DB	− 0.415 (0.025)	0.145 (0.51)	− 1.97	0.024* 0.0488**	
<i>Auditory verbal LTM</i>							
Introvert	Anxiety	MFSD	− 0.52 (0.006)	− 0.407 (0.06)	− 0.47	0.6 NS	
		RAVL78	− 0.429 (0.046)	− 0.017 (0.945)	− 1.32	0.1868 NS	
	Depression	MFSD	− 0.408 (0.038)	− 0.27 (0.213)	− 0.5	0.61 NS	
	General	MFSD	− 0.49 (0.009)	− 0.58 (0.004)	0.41	0.68 NS	
		RAVL78	− 0.43 (0.041)	− 0.17 (0.47)	− 1.23	0.218 NS	
Extrovert	Delinquent behavior	MFSD	− 0.58 (0.003)	− 0.118 (0.58)	− 1.87	0.03* 0.06**NS	
			RAVL79	− 0.564 (0.006)	− 0.003 (0.9)	− 1.9	0.0287* 0.057**
Social problems	Social problems	RAVL78	− 0.441 (0.04)	− 0.062 (0.79)	− 1.29	0.1971 NS	
		MFSD	− 0.247 (0.03)	− 0.358 (0.1)	− 0.34	0.773 NS	
		RAVL78	− 0.447 (0.037)	0.043 (0.856)	− 1.57	0.058* 0.116** NS	
Cognitive distractions	Thinking problems	MFSD	− 0.516 (0.007)	− 0.36 (0.1)	− 0.62	0.5353 NS	
	Attention	MFSD	− 0.468 (0.016)	− 0.162 (0.473)	− 1.11	0.267 NS	
Total psychosocial functioning	Total YSR	RAVL78	− 0.441 (0.04)	− 0.143 (0.547)	− 0.99	0.322 NS	
		MFSD/total YSR	− 0.553 (0.03)	− 0.501 (0.018)	− 0.23	0.818 NS	

Legend: MFS, memory for stories (from TOMAL); DF, digits forward (from TOMAL); DB, digits backwards (from TOMAL); MFSD, memory for stories delayed (from TOMAL); RAVLT8, Rey auditory learning verbal test recognition; RAVLT9, Rey auditory learning verbal test delayed memory; YSR, Youth self-report from the Achenbach assessment, child's form.

the relationships found in the group with IE and the controls were significant, indicating that the pattern of relationships between memory and social problems was specific to IE.

4. Discussion

The main goal of this study was to assess memory abilities and socioemotional functioning in children with idiopathic epilepsy and explore the relationships between memory functions and socioemotional competence in this specific population.

In accordance with previous reports, the results of the present study provide evidence of a higher risk for STM (auditory verbal and visual), WM, and auditory verbal LTM deficits among children with IE relative to healthy age-matched controls. Importantly, current findings also show that in addition to having memory deficits, the children in the group with IE were at higher risk for socioemotional problems and showed a higher prevalence of social problems and externalizing, internalizing, and distractibility issues compared to controls. These findings, with regard to memory and socioemotional problems, place children with IE at risk for poor well-being and maladjustment.

The extensive battery used was useful in underscoring the specific memory deficits frequently present in children with IE and highlights significant differences between children with IE and controls in the pattern of relationships between memory functions and socioemotional profile. Current data demonstrate strong and significant relationships between anxiety, depression, delinquent and aggressive behavior, and memory skills, in particular, the ability to retrieve verbal materials from the STM, WM, and the LTM system, demonstrating a specific relationship between auditory verbal memory and psychosocial problems among children with IE. In contrast, in healthy controls, in whom such issues were less frequent, the correlations between auditory verbal memory and psychosocial functioning were more general, i.e., related to total social functioning and personality traits, such as an introverted character, and were not related to socioemotional symptoms. These findings may imply that, in the general population, memory functioning seems to be related to the general level of social functioning but not to behavioral symptoms, while in IE patients, memory functioning (with emphasis on auditory verbal memory) is related to socioemotional functioning and to socioemotional symptoms (introverting issues: e.g., anxiety and depression; extroverting issues: e.g., delinquency and aggression).

Hence, the current project suggests two classes of correlations between memory and socioemotional issues — those that characterize all children and those that seem to be specific to children with IE. Regarding the relationship operating in the general population, the term “memory self-efficacy” may apply in depicting the general relations between affect, motivation, and cognition [76,77]. It refers to a dynamic, self-evaluative system of beliefs and judgments regarding one's memory competence and confidence [77] and their relationship to cognitive performance including memory, which has been studied in aging populations [78] as well as younger populations [79]. This trend was shown in the current study with children in the control group as well as in children with IE.

An additional different pattern emerged only for the children with IE, indicating a relationship between memory deficits and social symptoms. This set of relationships may underscore two potential processes that operate in IE: 1) the influence of auditory verbal memory deficits on social behavior and 2) the influence of socioemotional aspects on memory performance.

4.1. Role of memory in social skills

As mentioned previously, during the last decade, several researchers have examined the role that memory plays in social behavior and interpersonal sensitivity [52]. It was suggested that memory systems are vital not only to recall the past, but also to form and update models of

our experiences and use these models to navigate the world. This integration may provide a means for personal experiences to become integrated and consolidated into coherent social conceptual knowledge that, in turn, informs strategic social behavior. The relationships between memory functioning and social issues as an outcome have been documented in several clinical populations. For example, it was suggested that memory deficits found in individuals with autism may explain some of the clinical symptoms exhibited. More specifically, failure to encode all of the information, especially its social aspects, may contribute to dysfunction in the social, communication, and reasoning domains [80]. In another clinical population, ADHD, it has been suggested that social problems are a major source of functional impairment [81] and that WM impairments significantly predict these pervasive difficulties [82]. The converging evidence presented from autism and ADHD indicates the role of memory deficits in social functioning among clinical populations. The current data extend this notion to children with IE and further strengthen the importance of memory functions and, in particular, auditory verbal memory, in socioemotional regulation of pediatric clinical populations.

4.2. Role of emotion regulation on memory

In contemplating the relationship between memory and socioemotional performance, it is important to also consider the potential effect of mood on memory. It has been suggested that negative affect and avoidance can inhibit or disrupt implementation of the more purely cognitive problem-solving skills [83–85]. In this study, in addition to finding higher rates of depression and anxiety in children with IE, many of the parents of the group with IE anecdotally reported impulsive behavior and high rates of anxiety in response to memory lapses or failing in school. This trend amounted to a significant difference in the group with IE in both domains as compared with carefully matched controls. These findings call for specific interventions focusing on limiting anxiety and avoidance reactions and on strategies to facilitate memory operations among children with epilepsy to prevent the vicious circle of memory deficit–emotional reaction–avoidance–memory deterioration in this population.

4.3. Neuropsychology, memory, and social cognition

To consider the direction of the relationship between memory and social functioning in children with IE, one may benefit from referring to the neuropsychological framework. Genizi et al. [46] have raised the possibility that rolandic epilepsy may affect neural networks, affecting cognition and mediating social cognition essential for social behavior. Social cognition is considered to be processed in both the right and left hemispheres and includes an extended network involving the medial temporal lobe (which is relevant for auditory verbal memory processing), medial parietal regions, temporoparietal junction, occipital lobe, lateral prefrontal cortex, and medial prefrontal and lateral temporal regions [54]. Considering this evidence, it seems that temporal regions are involved in both memory and social functioning. Nevertheless, unlike temporal lobe epilepsy, in which recurrent, unprovoked epileptic seizures that originate in the temporal lobe cause severe memory loss [86,87], it is possible that in the case of IE, the socioneuronal network does not necessarily suffer from a specific primary deficit but that the involvement of this circuitry emerges as a secondary deficit, in a manner that is tightly linked to the primary deficit.

In this context, it is important to note that most of the children in our sample suffer from idiopathic generalized epilepsy or benign rolandic epilepsy. Among neurologists, such forms of epilepsy are considered to have the best prognosis of all epilepsies [3,88]. Indeed, most children with IE attend mainstream educational schools and are considered as functioning within the normal range. Current findings highlight the notion that this group merits professional evaluation and care, as they are at increased risk for auditory verbal

memory deficits that are quite debilitating on their own and are also related to socioemotional symptoms in this group.

Moreover, current findings may have therapeutic implications. First, the use of a battery that addresses auditory verbal memory and other cognitive domains in addition to psychosocial functioning is recommended to yield a more accurate clinical representation of the patients' neuropsychological and psychoeducational profile and enable identification of neuropsychological risk factors at the time of diagnosis of IE. Second, the significant relationships between auditory verbal memory and socioemotional symptoms may guide new intervention protocols focusing on auditory verbal memory in addition to psychosocial interventions that focus on social skills to prevent secondary IE-related social deficits. Therefore, providing emotional support through psychotherapy, while ignoring memory issues or reliance on verbal communication, may be less effective for treating children with IE.

In considering the implications of the current study, it may be imperative to consider its limitations, in addition to a desired larger sample size. First, the current results underscore the role of auditory verbal memory in this population. It is plausible that attention plays important roles in this finding. In addition, previous studies have demonstrated a linkage between attention and memory problems in patients with IE [7–9,33,89]. In this study, we evaluated attention using the canceling subtest from the WISC-IV [64] and the attention scale from the CBCL [70]. No correlation between the cancelation subtest and social problems was found, yet a correlation between the attention scale and the social problems scale from the CBCL was observed. Future work may focus further on this issue. Children in the group with IE were found to show an auditory verbal memory deficit, and, in comparison with the average language abilities of healthy children, they had low average language abilities as measured in vocabulary test [WAIS-IV; 64]. Future studies may evaluate language performance more extensively to understand the role of language in memory functioning and social skills in this population. In addition, it may be preferable to employ nonverbal interventions or interventions aimed directly at improving auditory verbal memory functioning. Lastly, in view of the potential similarity suggested by current findings between memory abilities of children with IE and children with other types of epilepsy, in addition to a healthy control group, it may be useful to compare the relationships between memory and psychosocial performance with nonidiopathic and nonbenign epilepsy syndromes such as TLE, to get a more comprehensive understanding of the specificity and sensitivity of memory and socioemotional dysfunction in IE, and to examine specific remedial and iatrogenic medication effects on these two domains.

In conclusion, this study provides support for the notion that children with IE are at higher risk for STM, WM, and LTM deficits, mostly of auditory verbal information and higher psychosocial susceptibility. The data underscore the relationships between pervasiveness of memory deficits and severity of psychosocial symptoms among children with IE. These findings may call for interventions that are designed as memory rehabilitation and socioemotional therapy for children with IE to help these children cope with and improve their prognosis in the long run.

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Disclosures

The authors declare no conflicts of interest.

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