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Pediatric epilepsy and comorbid reading disorders, math disorders, or autism spectrum disorders: Impact of epilepsy on cognitive patterns

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ABSTRACT

Introduction: In pediatric epilepsy, comorbidities are reported to be frequent. The present study focusedon the cognitive patterns of children with isolated epilepsy, children with isolated neurodevelopmental disorders (reading disorders, math disorders, autism spectrum disorders), and children with epilepsy and these neurodevelopmental disorders as comorbidities.

Methods: Based on two samples of referred children, one with epilepsy, reading disorders, math disorders, or ASDs occurring in "*isolation*" ($n = 117$) and one with reading disorders, math disorders, and ASDs occurring *comorbid* with epilepsy ($n = 171$), cognitive patterns were compared. The patterns displayed by verbal and nonverbal abilities from the WISC series were studied with repeated measures ANOVA. Thereafter, an exploratory $2 * 3 * 2$ factorial analysis was done to study the independent contribution of the type of comorbidity and of the presence or absence of epilepsy to the VIQ–PIQ pattern.

Results: In isolated epilepsy, a VIQ > PIQ pattern was found, which was not seen in the other disorders. When epilepsy and another disorder co-occurred, patterns were altered. They resembled partly the pattern seen in isolated epilepsy and partly the pattern seen in the isolated neurodevelopmental disorder. In comorbid reading disorders, the VIQ > PIQ pattern was mitigated; in comorbid math disorders, it was exacerbated. In comorbid ASDs, no clear pattern emerged. In the presence of epilepsy, patterns characteristic of isolated disorders appeared systematically shifted toward relatively lowered performance abilities or relatively spared verbal abilities. The similar "impact" exerted by epilepsy on the patterns of the various conditions suggested shared mechanisms.

1. Introduction

Seizure conditions in children are heterogeneous disorders in terms of age at onset, severity, type of seizures, response to medication, duration, and cognitive outcomes [1,2]. They are often accompanied by general cognitive problems as a somewhat lowered IQ [2–6]. Besides this general impact on cognition, studies have also suggested differential effects on cognitive patterns. A number of studies on the Wechsler Intelligence Scales for Children (WISC series) in mixed samples of children with epilepsy referred for neuropsychological evaluation suggest that verbal abilities (verbal IQ, VIQ, or the factor verbal comprehension index, VCI) are relatively spared while performance abilities (performance IQ, PIQ, or the factor perceptual organization index (POI)) are lowered. This differential "impact" of epilepsy on the verbal and performance scales, suggesting a VIQ > PIQ pattern, seems independent of epilepsy variables such as the side of seizure onset, seizure type, number of antiepileptic drugs (AEDs), or presence of MRI abnormalities [7,8]. In addition, while the level of IQ was lower in children in special education as well as in children with parents with lower education, the pattern displayed by VIQ and PIQ was not related to the type of education or to the level of parental education [8]. Neuropsychological studies on epilepsy generally include data on verbal and performance abilities as descriptives of the samples even when VIQ–PIQ patterns are not the focus of the study. Based on this information, the VIQ > PIQ pattern (or, similarly, a VCI > POI pattern) is also observed in children with epilepsy in association with mixed samples, frontal lobe epilepsies, Panayiotopoulos syndrome, benign epilepsy with centrotemporal spikes (BECTS) and daytime seizures, the use of polytherapy, and interictal discharges [9–13]. However, in other studies, the opposite pattern is observed. Specifically, VIQ < PIQ patterns have been reported in mixed samples with learning problems and in association with BECTS and nighttime seizures and older age at testing [11, 14–18]. Also, some studies have presented data suggestive of similar VIQ and PIQ, such as studies on lateralized seizures, studies on mixed samples, as well as studies on samples with epilepsy which were either referred or not referred for psychological evaluation [12,15,16,19–22]. Overall, although there is evidence of VIQ > PIQ patterns in epilepsy, results across studies vary even within a single epilepsy syndrome (as in BECTS). These inconsistencies in the literature may be associated with

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differences across samples in terms of the duration of epilepsy: the VIQ > PIQ pattern is mostly seen in the early stages of epilepsy [8]. These differences, however, could also be related to differences associated with comorbidities in epilepsy.

The plea to study comorbidities in epilepsy is sounding increasingly louder [23,24]. Studies have highlighted the relevance of comorbidities in epilepsy, indicating their high frequency of occurrence [25–27]. In particular, learning, psychiatric, social, or behavioral comorbidities have been frequently reported in children with seizures [26,28–30]. Learning problems are common [26,31,32], and in an epidemiological study, Russ et al. [26] indicated that the adjusted relative risk ratio for various kinds of school problems in epilepsy was 6.7. The rate of children with epilepsy with reading scores below the seventh percentile has been reported to be 20.1%; specific reading problems (i.e., based on IQ–achievement discrepancy) comorbid with epilepsy have been reported in 12.8% of children [27]. For math problems, the percentage of children with epilepsy scoring below the seventh percentile was found to be 26.8%, and 20.1% had specific math problems based on IQ–achievement discrepancy [27]. Autism spectrum disorders (ASDs) are also a major comorbidity in epilepsy. Russ et al. [26] reported a relative risk ratio of 15.5. Rates of co-occurrence of epilepsy and autism tend to vary from 15% [26] to 30% [33]. Autism spectrum disorders in epilepsy are most often seen in the presence of intellectual disabilities; it remains unsettled whether rates of ASDs are elevated in children with epilepsy with average IQs [34]. Importantly, although some comorbidities have been reported to occur mostly in association with specific epileptic syndromes [35,36], overall, comorbidities have been found to occur across epilepsy syndromes [25,27,29].

Children with epilepsy present with neuropsychological disorders of all kinds [16,19,37]. These disorders, however, need not lead to the diagnosis of comorbidities. The disorders may be considered the neuropsychological counterpart of the epileptic condition reflecting the interference of the seizure condition with performance on cognitive tasks, not necessarily clustering into a specific second diagnosis. Such children will be referred to, in the present paper, as children with "isolated" epilepsy. Some authors suggest that the focus on the medical condition (epilepsy) and its treatment may be leading to underdiagnosis and underreporting of the comorbidity [23,38]. Available studies have suggested that the combined presence of epilepsy and learning or behavioral disorders is associated with overall lowered IQ [5]. Not much is known as to whether the neurocognitive *pattern* (like the pattern displayed by the verbal and performance abilities) seen in children with epilepsy and a second diagnosis (a comorbidity) resembles the pattern seen in the neurodevelopmental diagnosis when it occurs as a single diagnosis without epilepsy, that is, when it occurs as an "isolated" condition.

Henceforth, the term "isolated" will also be used to denote children with a single diagnosis of a developmental disorder (reading disorders, math disorders, autism spectrum disorders or epilepsy) in contrast to the child with a comorbidity. Similar to epilepsy, children with other developmental disorders may also have other neuropsychological weaknesses which do not qualify for a second diagnosis. Both isolated epilepsy as well as other neurodevelopmental conditions occurring in isolation may be characterized by patterns of cognitive strengths and weaknesses. As said, although the results of the literature remain inconclusive, for mixed samples of children with epilepsy referred for neuropsychological evaluation, a VIQ > PIQ pattern has been found. For language-based neurodevelopmental disorders, like reading and spelling disorders, patterns of relatively spared performance abilities and relatively depressed verbal abilities have been found. Pelletier et al.[39] reported that 61% to 78% of their samples with reading disabilities showed a VIQ < PIQ discrepancy of at least 10 points. For children with math problems, large discrepancies were seen, favoring either the verbal or performance scale [40], but sometimes predominantly the verbal scale [39]. In ASDs, high rates of children (41%–50%) have been reported to have VIQ–PIQ discrepancies of 12 or more IQ points in either direction [41,42]. Relatively high scores on the performance scale and strengths on specific performance subtests have been found in mixed ASD samples [41,43,44], and relatively high scores on the verbal scale have been observed particularly in Asperger syndrome [44,45]. Thus, in ASDs, both verbal strengths and performance strengths can be seen, possibly with a predominance for a VIQ < PIQ pattern.

It has been suggested that the manifestations of neurodevelopmental disorders in epilepsy (comorbidities) may have both commonalities as well as differences to their manifestation as isolated conditions [29]. As in isolated reading disorders, reading problems comorbid with epilepsy have been associated with lower verbal abilities and difficulties with verbal memory and learning [46,47]. The epilepsy syndrome most consistently associated with reading disorders is BECTS [36]. Studies on BECTS have provided some evidence for lowered verbal abilities, but these results have been reported as being associated with older age and the presence of nighttime seizures [11,12,14–16]. For math disorders in epilepsy, no specific patterns have been described. Problems with processing speed, younger age at epilepsy onset, symptomatic epilepsies, generalized seizures, and frequent interictal discharges have been identified as risk factors for math disorders [27,47–49]. Given that both PIQ weaknesses [8] and math problems [49,50] have been reported early in the course of epilepsy, a VIQ > PIQ pattern would be more likely to be seen in math problems in epilepsy than a VIQ < PIQ pattern. For ASDs and epilepsy, associations between language disorders have been described [33], but literature on patterns of verbal and nonverbal abilities in epilepsy and ASDs is still scarce. Some features of a disorder may be masked and others may be emphasized in light of epilepsy [29], and more work has to be done to understand cognitive patterns seen in children with epilepsy with or without a comorbid condition.

One aim of the current study was to compare the cognitive patterns of children across conditions, both *isolated* conditions (that is, without an additional comorbid diagnosis) as well as conditions *comorbid* with epilepsy. Two main research questions were addressed. The first research question focused on the pattern of verbal and nonverbal abilities in children with isolated epilepsy contrasted (a) to control children and (b) to children with other isolated neurodevelopmental disorders, in particular reading disorders, math disorders, and autism spectrum disorders. The first hypothesis was that children with isolated epilepsy would show a VIQ > PIQ (or VCI > POI) pattern and that this pattern would be different from that in control children or other isolated developmental disorders (reading disorders, math disorders, or ASDs).

The second research question addressed VIQ–PIQ discrepancies for children with isolated epilepsy versus epilepsy with comorbid disorders. We aimed at studying (a) to what extent isolated epilepsy and epilepsy with comorbid conditions differ in VIQ–PIQ and (b) whether VIQ–PIQ patterns in epilepsy depend on the type of comorbid disorder. Do children with epilepsy show a different cognitive pattern in light of comorbidities like reading disorders, math disorders, or autism spectrum disorders? Do developmental disorders present with different patterns when accompanied by epilepsy? The second hypothesis was that in light of comorbidities, cognitive patterns will appear altered. If this is the case, it will provide better understanding of the inconsistent results reported on the literature. That is, if cognitive patterns in isolated epilepsy are different from patterns seen in epilepsy with comorbidities, the variation in findings on VIQ–PIQ patterns could be due to variation in the type and proportion of comorbid disorders across samples reported in the literature. If patterns in comorbidities appear altered, the finding will also have implications for the clinical diagnosis of the comorbidity and for its remediation. The present study was based on two samples: one with isolated conditions and one with comorbid conditions.

2. Methods

2.1. Participants

Except for the control children, all participating children had been referred for special services including psychological assessment

because of developmental concerns. The children with epilepsy came from a tertiary center for epilepsy and from an associated school which provided special services to children with epilepsy and heterogeneous epileptic conditions. The children with specific learning disorders and ASDs came from schools providing special educational services to children with learning disorders and to children with psychiatric and behavioral disorders, respectively. The Wechsler IQ data for the current study were gathered from the files of the schools and the epilepsy center; over time, two different test versions of the Wechsler were used. For each version, there were insufficient numbers of children to fill each disorder (reading, math, and autism spectrum disorders) by comorbidity (with or without comorbid epilepsy) condition. Therefore, for this study, two separate samples were used. Sample 1 was tested with the Dutch version of the WISC-R (to be called WISC-R^{NL}) and consisted of four groups of children matched for age: 39 with isolated epilepsy, 29 with a reading disorder, 25 with a math disorder, and 24 with an autism spectrum disorder. A portion of the first sample has been described earlier [51].

Sample 2, tested with the Dutch WISC-III (WISC-III^{NL}), included 171 children with epilepsy and 81 nonreferred control children. The control children came from regular schools and were included only if no disabilities were suspected by parents or teachers and if their FS-IQ was between 76 and 130. The sample of 171 children with epilepsy consisted of four groups of children: 100 with epilepsy without a comorbid disorder, 31 with a comorbid reading disorder, 19 with a comorbid math disorder, and 21 with comorbid ASDs. The majority of children were not included in samples reported upon in earlier publications. However, in order to maintain adequate sample sizes of children with comorbidities, 9 children (5.3% of the present sample) were included, which overlapped with an earlier study [8].

Children were included only if they had taken the complete Wechsler Intelligence Scales for Children and had a FS-IQ above 75. It should be noted that while FS-IQ was a criterion for eligibility for special services for children with specific learning disorders and for children with ASDs, patterns displayed by the scales (e.g., VIQ–PIQ discrepancy) were not.

Children with epilepsy had a confirmed diagnosis of epilepsy by a neurologist or child epileptologist. Information on epilepsy was obtained from medical reports and related to seizure type (focal or generalized seizures), side of seizure onset, localization, presence of abnormalities on neuroimaging (MRI+), epilepsy syndrome, age at onset of epilepsy (AOE), and number of AEDs used. Epilepsy syndrome severity was rated on a 10-point scale [52], where 10 was the most severe. Duration of epilepsy was calculated as the difference between AOE and age at testing.

For inclusion in a sample with learning disorders, an expert in special education verified the presence of significant and persistent achievement problems on the domains of reading/spelling or math or a qualified psychologist provided a diagnosis of specific reading or math disorder. Children with both reading and math disorders were excluded. Inclusion in the sample with specific learning disorders was based on three criteria, for reading and math alike: (a) severity, defined as achievement scores below the 7th percentile on reading, spelling, or both reading and spelling for a specific reading disorder and on mathematics for a specific math disorder; (b) insufficient response to intervention, i.e., persistence over time in spite of special remediation measures; and (c) achievement not explained by a low IQ, for which FS-IQ > 75 was required. These criteria have been maintained over time in the Netherlands in order to qualify for diagnoses of specific learning disabilities [53–55].

Children were included in the sample of children with ASDs if they had a diagnosis by a psychiatrist or by a qualified mental health psychologist according to DSM-IV criteria. Diagnoses of autism, pervasive developmental disorders (PDD-NOS), or Asperger syndrome as well as broad diagnoses of ASDs were pooled into the diagnosis of ASDs. Three (14.3%) children in Sample 2 had been diagnosed with Asperger syndrome and all others with ASDs or PDD-NOS. Children with ASDs and another behavioral comorbidity (e.g., ADHD) were excluded. Table 1 shows data on age and sex of the two samples. Table 2 displays data on the epilepsy characteristics of the groups with epilepsy.

2.2. Wechsler test versions

Sample 1 was tested with the Dutch adaptation of the WISC-R (to be called WISC-R^{NL}, [56]), in use up to 2005. Sample 2 and the sample of control children were tested with the most recent WISC version in the Netherlands, the Dutch WISC-III (WISC-III^{NL}, [57]). The test versions share the same two-scale structure, the verbal and performance scales, and are composed of 5 verbal and 5 performance core subtests with the same names. Both test versions also share two-factor indexes, verbal comprehension index (VCI) and perceptual organization index (POI), which consist of the same subtests [57–60]. The third factor, however, differs between the two samples: freedom from distractibility (FD) is included in the WISC-R^{NL} and processing speed (PSI) in the WISC-III^{NL}. While the focus in the present paper was on VIQ and PIQ and VCI and POI will be reported as well, the role of PSI on the pattern will be considered only briefly. The subtest substitution was converted to a deviation quotient in order to provide an indication of speed for all children (Table 3).

2.3. Analyses

The analyses for the two samples were run in parallel. For both samples, ANOVAs with repeated measures were conducted with IQ scale (VIQ or PIQ and VCI or POI, respectively) as the within-subjects variable and type of disorder (epilepsy, reading disorder, math disorder, and ASD) as the between-subjects variable. Simple contrasts followed to compare epilepsy with the other disorders. Thereafter, using ANOVA with planned contrasts, post hoc analyses were conducted directly on the discrepancy scores (VIQ–PIQ, VCI–POI) to contrast isolated epilepsy to each of the other disorders. The analyses were repeated with age and sex as covariates. Similarly, an ANOVA with repeated measures was done on the factor triad VCI–POI–PSI to study the effect of processing speed on isolated epilepsy in the second sample only. In addition, in the second sample, verbal and nonverbal abilities of children with isolated epilepsy were contrasted with those of the nonreferred control sample.

3. Results

This section starts with preliminary comparisons on age, sex, epilepsy variables, and IQ of the various groups. Then, results of repeated measures ANOVA are presented in which VIQ–PIQ and VCI–POI patterns across groups were examined. The means and standard deviation on the

Table 1
Characteristics of the samples: sample sizes, number of boys, and age.

	N	Male	Age
		N (%)	Mean (SD)
Sample 1: WISC-R^{NL}			
Isolated epilepsy	39	22 (56.4)	12.3 (1.9)
Isolated reading disorder	29	19 (65.5)	12.6 (0.8)
Isolated math disorder	25	17 (68.8)	12.8 (1.2)
Isolated ASD	24	23 (95.8)	12.2 (1.3)
Sample 2: WISC-III^{NL}			
Isolated epilepsy	100	48 (48.0)	10.0 (2.6)
Epilepsy + reading disorder	31	20 (64.5)	9.6 (2.7)
Epilepsy + math disorder	19	5 (26.3)	9.2 (1.9)
Epilepsy + ASD	21	18 (85.7)	9.4 (3.2)
Control	81	40 (49.4)	9.4 (1.7)

Note: ASD = autism spectrum disorder. Sample 1 consists of children with epilepsy or reading, math, or autism spectrum disorders "in isolation". Sample 2 consists of children with epilepsy in isolation and children with reading, math, or autism spectrum disorders comorbid with epilepsy.

Table 2
Seizure characteristics of the samples with epilepsy.

	Sample 1		Sample 2							
	Isolated epilepsy		Isolated epilepsy		Epilepsy + reading		Epilepsy + math		Epilepsy + ASDs	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
N	39		100		31		19		21	
Test version	WISC-R^{NL}		WISC-III^{NL}		WISC-III^{NL}		WISC-III^{NL}		WISC-III^{NL}	
Age at onset of epilepsy	6.7	4.6	6.0	3.0	6.2	3.2	5.3	2.4	5.7	3.7
Duration of epilepsy upon testing	5.7	3.7	4.1	3.2	3.4	2.4	3.9	3.0	3.6	2.1
AEDs tried	2.4	1.5	2.2	1.3	2.0	1.8	1.9	1.3	2.3	1.9
Epilepsy syndrome severity	5.1	1.4	5.4	1.7	5.2	1.7	5.6	1.7	5.1	0.8
	Sample 1		Sample 2							
	Isolated epilepsy		Isolated epilepsy		Epilepsy + reading		Epilepsy + math		Epilepsy + ASDs	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
Seizure types										
Generalized seizures	6	15.4	24	24.0	10	32.3	6	31.6	4	19.0
Absences/atypical absences	2/1	5.1/2.6	11/3	11.0/3.0	3/0	9.7/0.0	3/0	15.8/0.0	0/0	0.0/0.0
Tonic–clonic seizures/myoclonic seizures	0/0	0.0/0.0	2/1	2.0/1.0	1/2	3.2/6.5	1/0	5.3/0.0	2/0	9.5/0.0
Several generalized seizure types	1	2.6	5	5.0	3	9.7	1	5.3	2	9.5
Generalized, not specified	2	5.1	2	2.0	1	3.2	1	5.3	0	0.0
Focal (all focal)	25	64.1	56	56.0	15	48.4	11	57.9	15	71.4
(Also) temporal/(also) frontal	6/11	15.4/28.2	22/13	22.0/13.0	5/11	16.1/35.5	1/8	5.3/42.1	3/5	14.3/23.8
(Also) parietal/(also) central	2/5	5.1/12.8	10/16	10.0/16.0	1/4	3.2/12.9	0/1	0.0/5.3	1/1	4.8/4.8
(Also) occipital	7	17.9	9	9.0	4	12.9	1	5.3	1	4.8
Focal: LH/RH	7/5	17.9/12.8	22/13	22.0/13.0	4/7	12.9/22.6	4/1	21.1/5.3	6/2	28.6/9.5
Bilateral or multifocal	13	33.3	21	21.0	4	12.9	6	31.6	7	33.3
Uncertain/unknown	3/5	7.7/12.8	19/1	19.1/1.0	5/1	16.1/3.2	1/1	5.3/5.3	2/0	9.5/0
MRI−/MRI+	32/7	82.1/17.9	83/17	83.0/17.0	27/4	87.1/12.9	16/3	84.2/15.8	18/3	85.7/14.3
Epilepsy syndromes										
Focal idiopathic										
BECTS/rolandic epilepsy (2)[a]	3	7.7	5	5.0	2	6.5				
BEOP/Panayiotopoulos (3)	1	2.6	1	1.0	1	3.2			1	4.8
Focal symptomatic										
By virtue of: etiology (5)/localization (7)	5/13	12.8/33.3	11/36	11.0/26.0	3/10	9.7/32.3	1/5	5.3/26.3	2/8	9.5/38.1
Cryptogenic localization related (6.5)	6	15.4	5	5.0			4	21.1	1	4.8
Generalized epilepsy										
Generalized idiopathic epilepsy										
CAE (3)/JME (5)	1/0	2.6/0.0	12/2	12.0/2.0	5/1	16.1/3.2	3/0	15.8/0.0	0/1	0.0/4.8
Other generalized idiopathic epilepsy not defined above (5)	3	7.7	11	11.0	3	9.7			4	19.5
Cryptogenic and/or symptomatic										
West syndr. (9.5)/nonspecific etiology (8)			1/0	1.0/0.0	0/1	0.0/3.2	1/2	5.3/10.3		
Epilepsy syndromes undetermined (focal/generalized)										
Epilepsy with CSWS (8)			8	8.0	2	6.5				
LKS, atypicalrolandic, pseudo-Lennox (8)			7	7.0	1	3.2	1	5.3		
Others (1–9)	3	7.7	3	3.0						
Unknown	4	10.3	8	8.0	2	6.5	2	10.3	4	19.0

Isolated epilepsy = epilepsy and cognitive concerns but no comorbid diagnosis of reading, math, or autism spectrum disorders;epilepsy + reading = epilepsy and comorbid reading disorders; epilepsy + math = epilepsy and comorbid math disorders; epilepsy + ASDs = epilepsy and comorbid ASDs; AEDs tried = number of antiepileptic drugs tried; several generalized seizure types = e.g., myoclonic seizures and absences; (also) temporal = temporal seizures reported possibly in addition to seizures from another localization, e.g., temporal and occipital; LH/RH = left hemisphere or right hemisphere seizure onset; MRI−: no abnormalities on neuroimaging or no neuroimaging available; MRI+: abnormalities reported on neuroimaging; BECTS: benign epilepsy with centrotemporal spikes; BEOP = benign epilepsy with occipital paroxysm; CAE = childhood absence epilepsy; JME = juvenile myoclonic epilepsy; CSWS = continuous spikes and waves during slow sleep; LKS = Landau–Kleffner syndrome. Note that rates presented under the heading of seizure types and under epilepsy syndromes may sometimes appear incongruent (e.g., atypical absence seizures may be classified as belonging to a focal syndrome and focal seizures may be seen in CSWS).

[a] Epilepsy syndrome severity score in brackets according to Dunn et al.[52].

various IQ scales for the various disorders and for the control groups are presented in Table 3. The results of the statistical analyses are reported in Table 4.

The results on the cross-group differences in the VIQ–PIQ difference will be presented in four sections: (1) differences in the VIQ–PIQ pattern between the nonreferred control group and the group with isolated epilepsy (Sample 2); (2) differences in the VIQ–PIQ pattern in the group with isolated epilepsy versus the group with isolated reading disorders, isolated math disorders, and isolated ASDs (Sample 1); (3) differences in the VIQ–PIQ pattern in the group with isolated epilepsy versus the group with epilepsy with comorbid reading disorders, comorbid math disorders, and comorbid ASDs (Sample 2); and (4) differences in the VCI–POI–PSI pattern in the group with isolated epilepsy (Sample 2) to determine the role of processing speed in epilepsy, and (5) an exploratory overall analysis of both samples that examines the independent contributions of the type of disorder (reading, math, or autism spectrum disorders) and comorbid epilepsy status (absent or present) to the difference between VIQ and PIQ. Results on VCI and POI are reported in Table 4 but will only be described if the results differ from those for VIQ–PIQ.

3.1. Preliminary analyses

Comparison of isolated epilepsy between Samples 1 and 2 with *t*-tests or chi-square tests showed that the first sample was older at the age of testing ($t = 5.64$, $p < .001$, $d = 1.16$) and the duration of epilepsy was also longer ($t = 2.45$, $p = .015$, $d = .43$). Otherwise, statistically significant differences were not seen for sex, any epilepsy variable, or any of the Wechsler scales or factor indexes. Multivariate analysis of covariance, adjusting for age and duration of epilepsy, revealed that the two samples with isolated epilepsy showed highly similar patterns of verbal and performance abilities (for VIQ–PIQ, $F(1,$

Table 3
Means and SDs on the WISC-R^{NL} and the WISC-III^{NL}.

		Sample 1				Sample 2				Control
		"Isolated disorder"				Disorder comorbid with epilepsy				
		Epilepsy	Reading disorder	Math disorder	ASD	Epilepsy	Reading disorder	Math disorder	ASD	
FS-IQ	Mean	93.0	93.1	93.5	92.5	90.5	94.0	85.9	94.3	103.0
	SD	11.0	11.5	9.1	10.0	11.4	10.1	9.6	13.6	10.7
VIQ	Mean	96.4	90.5	93.9	91.6	93.8	94.6	91.6	96.1	102.5
	SD	10.9	11.9	8.6	10.1	12.1	10.3	8.5	13.8	11.0
PIQ	Mean	90.8	97.8	95.6	94.4	88.4	95.0	82.9	93.6	103.1
	SD	13.5	13.1	11.1	14.6	12.4	10.8	11.9	12.9	12.4
VIQ–PIQ	Mean	5.6	−7.3	−1.6	−2.8	5.3	−0.5	8.7	2.5	−0.6
	SD	13.9	13.8	11.5	16.6	13.5	11.1	11.4	11.7	13.7
VCI	Mean	98.0	89.7	92.8	92.5	94.8	95.3	95.6	96.8	102.7
	SD	12.0	11.9	10.0	10.3	11.5	11.0	9.7	13.0	11.7
POI	Mean	92.9	96.1	92.4	95.6	90.0	95.9	83.1	96.1	103.3
	SD	13.3	12.4	12.3	17.1	12.4	10.4	12.4	12.8	12.5
VCI–POI	Mean	5.1	−6.4	0.3	−3.0	4.8	−0.6	12.6	0.7	−0.6
	SD	15.5	12.7	15.3	19.4	13.6	12.6	11.4	12.1	13.4
SU	Mean	89.0	97.1	94.0	90.0	90.4	96.1	91.1	89.0	103.0
	SD	11.4	15.8	12.4	12.9	14.5	13.2	10.9	13.3	15.3
PSI	Mean					91.1	96.8	89.0	87.9	104.1
	SD					14.6	13.2	12.8	13.8	14.8
VCI–PSI	Mean					3.7	−1.6	6.6	8.8	−1.4
	SD					17.1	14.3	16.5	13.2	18.2
POI–PSI	Mean					−1.1	−0.9	−5.9	8.1	−0.86
	SD					15.7	15.2	16.1	15.6	18.3

Note: VCI = verbal comprehension index, POI = perceptual organization index, PSI = processing speed index (WISC-III^{NL} only), and SU = subtest substitution converted into a deviation quotient.

132) = 0.035, $p = .852$ and for VCI–POI, $F(1,132) = 0.003$, $p = .958$). Similar results were found when the square root of the duration of epilepsy [8] was entered in the MANCOVA instead of the duration of epilepsy.

Within each sample, there were no age differences across groups with disorder. For Sample 2, ANOVA and chi-square tests did not reveal statistically significant differences across the four groups with epilepsy for any of the epilepsy variables. Chi-square tests showed that boys were overrepresented in ASDs in Sample 1 (χ^2 (3) = 11.2, $p = .011$) and Sample 2 (χ^2 (3) = 17.1, $p = .001$). Comparison for each disorder between Samples 1 and 2 showed similar sex ratios for reading disorders and ASDs. However, girls were overrepresented in comorbid math (Sample 2) relative to isolated math (Sample 1; χ^2 (1) = 7.50, $p = .006$) disorders. There were no differences in FS-IQ between Samples 1 and 2 before or after adjusting for differences in age and sex as revealed by ANOVA and ANCOVA.

3.2. Children with isolated epilepsy versus nonreferred controls

Repeated measures ANOVA (Table 4, lower part) showed a significant main effect of group ($F(1,179) = 62.27$, $p < .001$, $\eta_p^2 = 0.26$). The control children outperformed the children with isolated epilepsy. A main effect was seen for the IQ scales, indicating that VIQ was higher than PIQ ($F(1,179) = 5.38$, $p = .022$, $\eta_p^2 = 0.03$). In addition, the interaction of VIQ and PIQ by group was significant ($F(1,179) = 8.64$, $p = .004$, $\eta_p^2 = 0.05$; for VCI and POI,$F(1,179) = 7.03$, $p = .009$, $\eta_p^2 = 0.04$). The group with epilepsy had higher verbal than performance abilities, while the control sample had a flat pattern of verbal and performance abilities. Thus, the results indicated that the control children had higher overall scores on the Wechsler test and that the children with epilepsy had a VIQ > PIQ pattern not seen in the controls. There were no age and sex differences between samples.

3.3. Verbal and performance abilities in isolated conditions: epilepsy, reading disorders, math disorders, and ASDs

Repeated measures ANOVA showed that the main effect of disorder groups was not significant (see Table 4, Sample 1), indicating that overall IQ scores were highly similar across groups. Also, the overall difference between VIQ and PIQ was not significant,but as expected, there was a significant effect of disorder by IQ–scale (VIQ–PIQ) interaction, indicating that the discrepancy between VIQ and PIQ differed across disorder groups. Planned contrasts revealed a significant difference in the VIQ–PIQ pattern between epilepsy and each of the disorders (reading disorder, math disorder, and ASD). In epilepsy, VIQ was higher than PIQ, whereas in the other disorders, the VIQ–PIQ pattern was opposite or flat. These results did not change when the analyses were redone with age and sex as covariates.

3.4. Verbal and performance abilities in epilepsy: isolated epilepsy and epilepsy comorbid with reading disorders, math disorders, and ASDs

Repeated measures ANOVA revealed a significant main effect of disorder groups, suggesting differences in overall IQ across groups (see Table 4, Sample 2). Post hoc tests revealed no IQ differences when the comorbid conditions (epilepsy with reading disorder, math disorder, or ASD) were compared to isolated epilepsy. Children with a comorbid reading disorder, however, outperformed children with a comorbid math disorder (FS-IQ of 94.0 versus 85.9).

The interaction effect of disorder by IQ scale (VIQ–PIQ) fell short of statistical significance ($p = .056$). However, the interaction of disorder by factor index (VCI–POI) was significant, indicating that the VCI–POI difference varied across groups. Using planned contrasts, isolated epilepsy was compared to each comorbid condition. A significant difference in the VCI–POI pattern was found between the group with isolated epilepsy and the group with epilepsy with comorbid reading disorders (similar to the results for VIQ–PIQ). The higher VCI than POI pattern found in the group with isolated epilepsy was not seen in the group with an additional reading disorder. Comparison of isolated epilepsy and epilepsy with a comorbid math disorder showed that the VCI–POI difference was significantly higher in the group with a comorbid math disorder (but not for the VIQ–PIQ discrepancy). No differences were found in the VCI–POI pattern between isolated epilepsy and epilepsy with comorbid ASDs. Overall, the results of these analyses suggest that in the sample with epilepsy, verbal abilities were higher than performance abilities. However, this pattern is qualified by a

Table 4
Results of repeated measures ANOVA.

Repeated measures ANOVA							Post hoc analyses													
Sample 1: isolated disorders		df1	df2	*F*	*p*	η_p^2	Epilepsy vs reading					Epilepsy vs math					Epilepsy vs ASDs				
							Contrast	SE	*p*	95% CI		Contrast	SE	*p*	95% CI		Contrast	SE	*p*	95% CI	
										UL	LL				UL	LL				UL	LL
VIQ PIQ																					
Within-subjects	VIQ vs PIQ	1	116	1.35	.247	0.01															
Between-subjects	Disorder	3	113	0.15	.930	0.00	0.53	2.49	.833	−4.4	5.5	1.11	2.47	.654	−3.8	6.0	−0.63	2.63	.812	−5.8	4.6
Interaction	VIQ vs PIQ * disorder	3	113	4.99	.003	0.12	−12.89	3.43	<.001	−19.7	−6.1	−7.26	3.59	.046	−14.4	−0.1	−8.45	3.63	.022	−15.6	−1.3
VCI POI																					
Within-subjects	VCI vs POI	1	116	0.48	.491	0.00															
Between-subjects	Disorder	3	113	0.58	.632	0.02	−2.56	2.50	.310	−7.5	2.4	−2.84	2.51	.260	−7.8	2.1	−1.37	2.65	.605	−6.6	3.9
Interaction	VCI vs POI * disorder	3	113	3.25	.025	0.08	−11.53	3.84	.003	−19.1	−3.9	−4.76	4.03	.240	−12.7	3.2	−8.12	4.07	.048	−16.2	−0.1

Repeated measures ANOVA							Post hoc analyses													
Sample 2: comorbidities		df1	df2	*F*	*p*	η_p^2	Isolated epilepsy vs epilepsy + reading					Isolated epilepsy vs epilepsy + math					Isolated epilepsy vs epilepsy + ASDs				
							Contrast	SE	*p*	95% CI		Contrast	SE	*p*	95% CI		Contrast	SE	*p*	95% CI	
										UL	LL				UL	LL				UL	LL
VIQ PIQ																					
Within-subjects	VIQ vs PIQ	1	170	11.32	.001	0.06															
Between-subjects	Disorder	3	168	3.00	.032	0.05	3.70	2.08	.078	−0.4	7.8	−3.82	2.52	.132	−8.8	1.2	3.77	2.43	.123	−1.0	8.6
Interaction	VIQ vs PIQ * disorder	3	168	2.57	.056	0.04	−5.79	2.61	.028	−11.0	−0.6	3.34	3.17	.293	−2.9	9.6	−2.82	3.05	.358	−8.8	3.2
VCI POI																					
Within-subjects	VCI vs POI	1	170	12.56	.001	0.07															
Between-subjects	Disorder	3	168	2.56	.057	0.04	3.19	2.03	.118	−0.8	7.2	−3.05	2.45	.215	−7.9	1.8	4.01	2.37	.092	−0.7	8.7
Interaction	VCI vs POI * disorder	3	168	4.61	.004	0.08	−5.46	2.69	.044	−10.8	−0.1	7.77	3.27	.018	1.3	14.2	−4.10	3.14	.194	−10.3	2.1

Repeated measures ANOVA						Post hoc analyses				
Sample 2: isolated epilepsy vs controls		df1	df2	*F*	*p*	η_p^2	Isolated epilepsy vs controls			
							Contrast	SE	*p*	95% CI
										UL / LL
VIQ PIQ										
Within-subjects	VIQ vs PIQ	1	179	5.38	.022	0.03				
Between-subjects	Group	1	179	62.27	<.001	0.26	11.71	1.48	<.001	8.8 / 14.6
Interaction	VIQ vs PIQ * group	1	179	8.64	.004	0.05	−5.97	2.03	.004	−10.0 / −2.0
VCI POI										
Within-subjects	VCI vs POI	1	179	4.42	.037	0.02				
Between-subjects	Group	1	179	50.90	<.001	0.22	10.59	1.48	<.001	7.7 / 13.5
Interaction	VCI vs POI * group	1	179	7.03	.009	0.04	−5.37	2.02	.009	−9.4 / −1.4

Note: Reading/math = reading disorders/math disorders. The right side of the table presents the results of post hoc analyses: simple contrasts from repeated measures for the between-subjects effects and planned contrasts from ANOVA (on the discrepancy) for the interaction effects. LL/UL: lower and upper limits of the 95% confidence interval.

comorbid reading or math disorder. In comorbid reading disorders, the VIQ > PIQ pattern is not found, while in math disorders, the VIQ > PIQ pattern seems exacerbated. Comorbid ASDs did not affect the pattern of verbal and performance abilities. The results did not change when the analyses were redone with age and sex as covariates.

3.5. The role of processing speed

Repeated measures ANOVA with polynomial contrasts was conducted on the factor triad VCI–POI–PSI in isolated epilepsy. It was hypothesized that if lowered performance abilities would be mainly due to lowered speed of processing, the factor PSI, with its high reliance on speed, should be the lowest in the pattern and a linear downward pattern should emerge. The analysis revealed a pattern best described as quadratic ($F(1,99) = 6.11$, $p = .015$, $\eta_p^2 = 0.58$); a linear pattern was also supported ($F(1,99) = 4.74$, $p = .032$, $\eta_p^2 = 0.46$). That is, VCI was highest and POI as well as PSI were lowered, but PSI was relatively less lowered. Pairwise contrasts indicated that VCI was higher than both POI ($t = 3.53$, $p = .001$, $d = 0.43$) and PSI ($t = 2.18$, $p = .032$, $d = 0.28$). No significant difference was seen for POI–PSI ($t = -0.69$, $p = .492$).

3.6. The impact of epilepsy and of diagnostic condition on verbal–performance patterns

Results from Sample 1 and Sample 2 indicate that in isolated epilepsy, PIQ is lower than VIQ. In the other disorders (Sample 1), such pattern is not seen. In reading disorders, VIQ is relatively lower than PIQ, and in math disorders and ASDs, VIQ is approximately equal to PIQ. In comorbid disorders (Sample 2), however, the VIQ–PIQ patterns are different from the VIQ > PIQ pattern that characterizes isolated epilepsy. In comorbid reading disorders, the pattern is relatively flat, and in comorbid math disorders, an even greater VIQ > PIQ discrepancy emerges. In ASDs, no major changes are seen.

In a final exploratory analysis, we examined whether these VIQ–PIQ differences across disorders (reading disorders, math disorders, and ASDs) were similarly affected by the status of epilepsy (presence or absence). For this analysis, the disorder groups of the two samples were taken together. The control children (Sample 2) and the children with isolated epilepsy (Samples 1 and 2) were excluded. Sample 1 and Sample 2 differed in the type of Wechsler test that was administered. In taking together groups from both samples, it is assumed that different types of Wechsler tests do not affect the VIQ–PIQ discrepancies, although they may have an impact on mean IQ differences. This assumption appears warranted given that VIQ–PIQ discrepancies were highly similar across Samples 1 and 2. The assumption will be further considered in the Discussion section. A 2 * 3 * 2 factorial analysis was done, which included two IQ scales (VIQ and PIQ) by three disorders (reading disorder, math disorder, and ASD) by two values of status of epilepsy (present or absent). Thereafter, the results were redone including age and sex as covariates, and no major changes were seen on the main effects.

There was no significant difference in overall IQ between the isolated and comorbid disorder ($F(1,143) = 1.05$, $p = .308$), which indicated there was no overall effect of epilepsy status on IQ. There was also no significant difference in the overall IQ level across disorders ($F(2,143) = 1.76$, $p = .175$). However, the disorder by epilepsy interaction was significant ($F(2,143) = 3.11$, $p = .047$, $\eta_p^2 = 0.04$) because of a lower overall IQ for math disorder comorbid with epilepsy.

Overall, the difference between VIQ and PIQ was not significant ($F(1,143) = .024$, $p = .877$). More interestingly, significant interactions were found with epilepsy and with the type of disorder. The interaction of VIQ–PIQ with epilepsy status ($F(1,143) = 12.35$, $p = .001$, $\eta_p^2 = 0.08$) was due to a VIQ < PIQ pattern in the isolated disorders and a VIQ > PIQ pattern in the comorbid disorders. The interaction between VIQ–PIQ and disorder ($F(2,143) = 4.19$, $p = .017$, $\eta_p^2 = 0.06$) indicated differences in VIQ–PIQ patterns across disorders, irrespective of epilepsy status. Most importantly, the IQ scales by disorder by epilepsy interaction was not significant ($F(2,143) = 0.44$, $p = .647$), indicating that the VIQ–PIQ discrepancies across the disorders were similar for the isolated and comorbid disorders given the VIQ > PIQ pattern seen in epilepsy. Put differently, the VIQ–PIQ discrepancy in each of the disorders is affected in a similar way by the comorbid presence of epilepsy. This can also be seen in Fig. 1, where the lines are largely parallel, suggesting a systematic shift in the difference between VIQ and PIQ due to comorbid epilepsy. A similar shift is visible in Fig. 1 between the control group and the group with isolated epilepsy.

4. Discussion

The present study further supported the finding that the cognitive pattern of referred children with isolated epilepsy – that is, epilepsy without an additional diagnosis – is characterized by relatively spared verbal abilities and relatively depressed performance abilities (VIQ > PIQ). This pattern is not seen in children with isolated neurodevelopmental disorders – reading disorders, math disorders, or ASDs – of similar overall IQ. In children who had two conditions diagnosed jointly — epilepsy and either reading disorders, math disorders, or autism spectrum disorders, patterns are different. The VIQ > PIQ

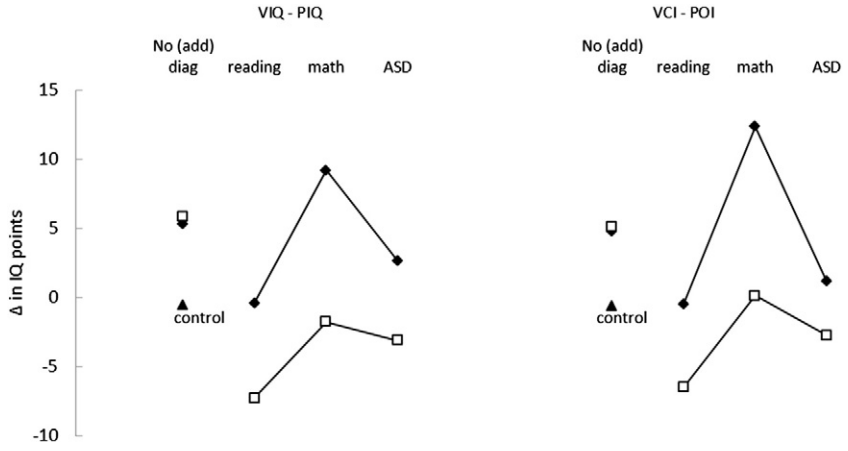

Fig. 1. Means after adjusting for age and sex with MANCOVA for VIQ–PIQ discrepancies (left) and VCI–POI (right) for the data of the two studies. No (add) diag = no (additional) diagnoses, denotes "isolated" epilepsy and controls. Open squares = children with isolated epilepsy (=no additional diagnosis), reading disorders (=reading), math disorders (=math), and ASDs. Filled triangles = nonreferred control sample (WISC-III^{NL}). Filled diamonds: children with epilepsy: isolated epilepsy or epilepsy comorbid with reading disorders, math disorders, and ASDs. Note that positive values – values in the upper part of the figure – denote lowered performance/perceptual abilities and negative values – in the lower part of the figure – denote lowered verbal abilities, while overall FS-IQs do not differ.

pattern appears mitigated in reading disorders and exacerbated in math disorders.

Alternatively, from the perspective of the learning or behavioral condition, the results suggest that in the presence of epilepsy, the cognitive patterns of neurodevelopmental disorders are altered. This change is the direction of *relatively* lowered performance abilities or relatively spared verbal abilities. A strength in the performance abilities seen in isolated reading disorders appears leveled off; a flat pattern seen in isolated math disorders is changed into a VIQ > PIQ pattern in comorbid math disorders. Supplementary exploratory analyses further suggested that the impact of *epilepsy* on VIQ–PIQ discrepancies is similar across the various disorders. These results might suggest a common mechanism from the seizure condition impinging on the comorbid neurodevelopmental disorder.

The study shed new light on the previous equivocal findings on the VIQ–PIQ pattern in children with epilepsy, suggesting that patterns vary according to the presence of children with comorbidities. By carefully checking for comorbid disorders, the present study found higher verbal than performance/perceptual abilities in isolated epilepsy. However, VIQ > PIQ patterns in isolated epilepsy were altered when epilepsy appeared with a comorbidity. These results illustrate that VIQ–PIQ differences across samples of children with epilepsy can differ if comorbidity with other disorders is not taken into account.

The VIQ > PIQ pattern in isolated epilepsy was different from the pattern observed in other isolated disorders. Depressed VIQ was seen in reading disorders, and relatively flat VIQ–PIQ patterns were seen in math disorders and ASDs, overall in accordance with previous studies [39,40,44,57]. Earlier studies comparing children with epilepsy with other referred children have reported similar differences in cognitive patterns between the referred children with and without epilepsy [48,51,61].

A VIQ > PIQ pattern was also found in an earlier study on pediatric epilepsy [8], particularly in early-onset epilepsy and in the early years of the epilepsy and fading away over time. The lowered scores on PIQ subtests might be caused by impairments in visual perceptual abilities, perceptual reasoning, or constructional and motor abilities, which are all involved in the subtests constituting PIQ (and POI). Also, several of these subtests are timed, which means that quicker speed leads to better scores. Earlier studies have, indeed, pointed toward lowered speed and executive abilities in children with epilepsy [62], impaired visual perceptual reasoning, visual attention, sustained attention, motor abilities, and motor speed [19,63]. Lowered scores on speed, executive, and visual tasks have also been reported in new-onset epilepsy before the start of medication [49,64,65] and persisting over time [49]. Lowered scores on processing speed were also seen in the present work. The most depressed scores were seen, however, on the performance/perceptual abilities, suggesting that the more complex constructional abilities tapped by the scales may be most vulnerable to the epileptic condition where speed may be one of the constituents leading to low scores.

Compromised performance abilities have also been seen in children born prematurely [66], children with traumatic brain injury [67], and children with lateralized perinatal brain damage, regardless of the side of the lesion [68]. These results suggest that the performance scale appears particularly vulnerable to neurological risks, including epilepsy.

An interesting finding of the present study is that comorbid epilepsy in various disorders appeared to be associated with a similar "systematic" shift in the difference between VIQ and PIQ compared to these disorders in isolated form. Though potentially important, this finding should be considered with some caution. First, it should be acknowledged that the sample sizes were probably too small to detect small interaction effects. Second, the finding is based on the combination of samples tested with two different versions of the Wechsler scales and with an age difference of 3.1 years. In merging the data into a final analysis, it was assumed that differences in test version and age would not influence the results. Changes in test version can potentially be associated with changes in verbal–performance patterns given that Flynn effects may affect the subtests differentially [69]. In a previous study on epilepsy, however, which explicitly modeled for effects of test version (Dutch WPPSI-R, WISC-R, and WISC-III) on VIQ–PIQ patterns, no effect of test version was seen [8].

With regard to age differences, earlier studies on children with isolated reading disorders, math disorders, and autistic spectrum disorders with wider age ranges were congruent with the present results [39,40,44,57]. Also, studies on serial testing of referred children reported negligible mean differences [70] in VIQ–PIQ discrepancy over time. A follow-up study on nonreferred children reported moderate to high correlations for the VIQ–PIQ discrepancy across ages and a higher stability over time for VIQ < PIQ discrepancies than for VIQ > PIQ discrepancies [71]. Therefore, although results should be treated with caution, there are also arguments suggesting that differences in age and test version did not unduly affect the results. Notably, the samples with isolated epilepsy – regardless of age and test version – showed conspicuous similarities in cognitive patterns.

In line with the current knowledge, both epilepsy as well as the comorbidities are understood as complex, multidimensional conditions in terms of etiology and presentation [72–74]. Epilepsy and the comorbidity may be independent conditions, or they may be related conditions partly sharing underlying risk factors [30]. Several models on the causes of comorbidities have been proposed [75], which may all be valid in particular cases. According to one model, the seizure condition could be understood as the cause of the comorbid disorder. The epileptic networks could be interfering with cognitive networks involved in reading (for example), causing a reading disorder [75]. In this model, the VIQ–PIQ pattern in a particular isolated disorder would be similar to the pattern of this disorder comorbid with epilepsy — a finding not supported by the current study. A second model suggests that there may be one or more causes leading to epilepsy as well as the comorbidity, which may present alone or in combination. According to the third model [75], epilepsy and the comorbidity may or may not share a common cause, but epilepsy might impact on the comorbidity, for example, by aggravating it. The current study was not designed to test these models and does not permit conclusions about their validity. However, the present study may contribute to the understanding of comorbidities in epilepsy, suggesting that in familiarly unrelated cases, isolated neurodevelopmental disorders show different cognitive patterns from patterns in isolated epilepsy and when neurodevelopmental disorders present together with epilepsy, an altered cognitive pattern is seen relative to the isolated condition. Cognitive patterns seen in isolated disorders appear systematically shifted toward relatively lowered performance abilities (or relatively spared verbal abilities) when they co-occur with epilepsy.

A limitation of the study is the inclusion of two samples. Although efforts were done to select children with developmental problems according to objective criteria, new insights and new assessment tools develop over time and sharpen the diagnostic criteria for classification [54,55], leading to differences. Some criteria remained stable over time, as the 7th percentile criterion to determine a true weakness in learning disorders, even if subtyping of disorders has progressed. In the diagnosis of ASDs, the earlier reliance on subtypes as PDD-NOS and Asperger syndrome is leading to a broad categorization of "ASD", possibly with the advent of DSM-V. Despite these unavoidable differences, cognitive patterns found for the isolated disorders resembled those described in the literature.

Overall, the present study suggests that in isolated epilepsy, the cognitive pattern is characterized by VIQ > PIQ. In other developmental disorders, such a pattern was not seen. When these disorders appear as comorbidities in epilepsy, the patterns are altered: partly resembling the isolated condition and partly differing from the isolated condition. In clinical evaluations of children with epilepsy and independent of epilepsy syndrome, the possibility of comorbidities should be considered. The most relevant clinical implication of the present study is that the cognitive pattern seen in the disorder comorbid with epilepsy is likely

to differ from the pattern seen in the isolated condition. One possibility is that the difficulties encountered by the child with epilepsy may be associated with specific "subtypes" of the disorder. It may be speculated that in children with epilepsy and reading disorders, problems with rapid naming may be more prominent than phonological disorders. Regardless of whether the starting point is epilepsy or another developmental disorder, if the disorder is accompanied by epilepsy, the clinician should take into consideration that the cognitive pattern may be unlike the pattern seen in the isolated condition. Remediation measures should, therefore, be tailored to fit the individual profile of the child with epilepsy and a comorbid diagnosis.

Ethical statement

The authors confirm having read the position of the Journal in issues involved in ethical publication and affirm that this paper is consistent with those guidelines.

Conflict of interest statement

The authors disclose no conflicts of interest. The authors did not receive financial support for the study.

References

[1] Schmidt D, Sillanpää M. Evidence-based review on the natural history of the epilepsies. Curr Opin Neurol 2012;25(2):159–63.
[2] Berg AT, Langfitt JT, Testa FM, Levy SR, DiMario F, Westerveld M, et al. Global cognitive function in children with epilepsy: a community-based study. Epilepsia 2008; 49:608–14.
[3] Ellenberg JH, Hirtz DG, Nelson KB. Do seizures in children cause intellectual deterioration? N Engl J Med 1986;314:1085–8.
[4] Nolan MA, Redoblado MA, Sabaz M, Cunningham AM, Bleasel AF, Bye AM. Memory function in childhood epilepsy syndromes. J Paediatr Child Health 2014;40:20–7.
[5] Hermann B, Jones J, Seth R, Koehn M, Becker T, Fine J, et al. Growing up with epilepsy: a two-year investigation of cognitive development in children with new onset epilepsy. Epilepsia 2008;49:1847–58.
[6] Elger CE, Helmstaedter C, Kurthen M. Chronic epilepsy and cognition. Lancet Neurol 2004;3:663–72.
[7] van Iterson L, Augustijn PB. Unilateral hemisphere involvement associated predominantly to VIQ > PIQ discrepancies in children with (refractory) epilepsy. Epilepsia 2006;47:158–9.
[8] van Iterson L, Zijlstra BL, Augustijn PB, Fvan der Leij A, de Jong PF. Duration of epilepsy and cognitive development in children: a longitudinal study. Neuropsychology 2014;28:212–21.
[9] Lopes R, Simoes MR, Leal AJ. Neuropsychological abnormalities in children with the Panayiotopoulos syndrome point to parietal lobe dysfunction. Epilepsy Behav 2014; 31:50–5.
[10] O'Leary SD, Burns TG, Borden KA. Performance of children with epilepsy and normal age-matched controls on the WISC-III. Child Neuropsychol 2006;12:173–80.
[11] Overvliet GM, Besseling RMH, Vles JSH, Hofman PAM, van Hall MHJA, Backes W, et al. Association between frequency of nocturnal epilepsy and language disturbances in children. Pediatr Neurol 2011;44:333–9.
[12] Tedrus GMAS, Fonseca LC, Melo EMV, Ximenes VL. Educational problems related to quantitative EEG changes in benign childhood epilepsy with centrotemporal spikes. Epilepsy Behav 2009;15:486–90.
[13] Smith ML, Elliott IM, Lach L. Cognitive skills in children with intractable epilepsy: comparison of surgical and nonsurgical candidates. Epilepsia 2002;43:631–7.
[14] Verrotti A, D'Egidio C, Agostinelli S, Parisi P, Chiarelli F, Coppola G. Cognitive and linguistic abnormalities in benign childhood epilepsy with centrotemporal spikes. Acta Paediatr 2011;100:768–72.
[15] Vago C, Bulgheroni S, Franceschetti S, Usilla A, Riva D. Memory performance on the California Verbal Learning Test of children with benign childhood epilepsy with centrotemporal spikes. Epilepsy Behav 2008;13:600–6.
[16] Northcott E, Connolly AM, Berroya A, McIntyre J, Christie J, Taylor A, et al. Memory and phonological awareness in children with Benign Rolandic Epilepsy compared to a matched control group. Epilepsy Res 2007;75:57–62.
[17] Miranda C, Smith ML. Predictors of intelligence after temporal lobectomy in children with epilepsy. Epilepsy Behav 2001;2:13–9.
[18] Aldenkamp AP, Alpherts WCJ, De Bruine-Seeder D, Dekker MJA. Test–retest variability in children with epilepsy — a comparison of WISC-R profiles. Epilepsy Res 1990; 7:165–72.
[19] Braakman HM, Ijff DM, Vaessen MJ, Debeij-van Hall MH, Hofman PA, Backes WH, et al. Cognitive and behavioural findings in children with frontal lobe epilepsy. Eur J Paediatr Neurol 2012;16:707–15.
[20] van Mil SGM, Reijs RP, Van Hall MHJA, Snoeijen SM, de la Parra NM, Aldenkamp AP, et al. Behavioral status of children with cryptogenic localization-related epilepsy. J Child Neurol 2009;24:449–53.
[21] Westerveld M, Sass KJ, Chelune GJ, Hermann BP, Barr WB, Loring DW, et al. Temporal lobectomy in children: cognitive outcome. J Neurosurg 2000;92:24–30.
[22] Jones JE, Siddarth P, Gurbani S, Shields WD, Caplan R. Cognition, academic achievement, language, and psychopathology in pediatric chronic epilepsy: short-term outcomes. Epilepsy Behav 2010;18:211–7.
[23] Helmstaedter C, Aldenkamp AP, Baker GA, Mazarati A, Ryvlin P, Sankar R. Disentangling the relationship between epilepsy and its behavioral comorbidities — the need for prospective studies in new-onset epilepsies. Epilepsy Behav 2014;31C: 43–7.
[24] Asato MR, Caplan R, Hermann BP. Epilepsy and comorbidities — what are we waiting for? Epilepsy Behav 2014;31C:127–8.
[25] Berg AT, Caplan R, Hesdorffer DC. Psychiatric and neurodevelopmental disorders in childhood-onset epilepsy. Epilepsy Behav 2011;20:550–5.
[26] Russ SA, Larson K, Halfon N. A national profile of childhood epilepsy and seizure disorder. Pediatrics 2012;129:256–64.
[27] Fastenau PS, Shen J, Dunn DW, Austin JK. Academic underachievement among children with epilepsy: proportion exceeding psychometric criteria for learning disability and associated risk factors. J Learn Disabil 2008;41:195–207.
[28] Austin JK, Fastenau PS. Are seizure variables related to cognitive and behavior problems? Dev Med Child Neurol 2010;52:4–9.
[29] Lin JJ, Mula M, Hermann BP. Uncovering the neurobehavioural comorbidities of epilepsy over the lifespan. Lancet 2012;380:1180–92.
[30] Brooks-Kayal AR, Bath KG, Berg AT, Galanopoulou AS, Holmes GL, Jensen FE, et al. Issues related to symptomatic and disease-modifying treatments affecting cognitive and neuropsychiatric comorbidities of epilepsy. Epilepsia 2013;54(Suppl. 4):44–60.
[31] Reilly C, Neville BG. Academic achievement in children with epilepsy: a review. Epilepsy Res 2011;97:112–23.
[32] Austin JK, Huberty TJ, Huster GA, Dunn DW. Does academic achievement in children with epilepsy change over time? Dev Med Child Neurol 1999;41:473–9.
[33] Tuchman R, Alessandri M, Cuccaro M. Autism spectrum disorders and epilepsy: moving towards a comprehensive approach to treatment. Brain Dev 2010;32: 719–30.
[34] Berg AT, Plioplys S. Epilepsy and autism: is there as special relationship? Epilepsy Behav 2012;23:193–8.
[35] Besag FMC. The relationship between epilepsy and autism: a continuing debate. Acta Paediatr 2009;98:618–20.
[36] Clarke T, Strug L, Murphy P, Bali B, Carvalho J, Foster S, et al. High risk of reading disability and speech sound disorder in rolandic epilepsy families: case–control study. Epilepsia 2007;48:2258–65.
[37] Hoie B, Mykletun A, Waaler PE, Skeidsvoll H, Sommerfelt K. Executive functions and seizure-related factors in children with epilepsy in Western Norway. Dev Med Child Neurol 2006;48:519–25.
[38] Matsuo M, Maeda T, Sasaki K, Ishii K, Hamasaki Y. Frequent association of autism spectrum disorder in patients with childhood onset epilepsy. Brain Dev 2010;32: 759–63.
[39] Pelletier PM, Ahmad SA, Rourke BP. Classification rules for basic phonological processing disabilities and nonverbal learning disabilities: formulation and external validity. Child Neuropsychol 2001;7:84–98.
[40] Desoete A. Co-morbidity in mathematical learning disabilities: rule or exception? Open Rehabil J 2008;1:15–26.
[41] Charman T, Pickles A, Chandler S, Loucas T, Baird G. IQ in children with autism spectrum disorders: data from the Special Needs and Autism Project (SNAP). Psychol Med 2011:619–27.
[42] Black DO, Wallace GL, Sokoloff JL, Kenworthy L. Brief report: IQ split predicts social symptoms and communication abilities in high-functioning children with autism spectrum disorders. J Autism Dev Disord 2009;39:1613–9.
[43] Scheirs JGM, Timmers EA. Differentiating among children with PDD-NOS, ADHD and those with a combined diagnosis on the basis of WISC-III profiles. J Autism Dev Disord 2009;39:549–56.
[44] de Bruin EI, Verheij F, Ferdinand RF. WISC-R subtest but no overall VIQ-PIQ difference in Dutch children with PDD-NOS. J Abnorm Child Psychol 2006;34:263–71.
[45] Cederlund M. One hundred males with Asperger syndrome: a clinical study of background and associated factors. Dev Med Child Neurol 2004;46:652–60.
[46] Vermeulen J, Kortstee SWAT, Alpherts WCJ, Aldenkamp AP. Cognitive performance in learning disabled children with and without epilepsy. Seizure 1994;3:13–21.
[47] Dunn DW, Johnson CS, Perkins SM, Fastenau PS, Byars AW, deGrauw TJ, et al. Academic problems in children with seizures: relationships with neuropsychological functioning and family variables during the 3 years after onset. Epilepsy Behav 2010;19:455–61.
[48] Nicolai J, Ebus S, Biemans DP, Arends J, Hendriksen J, Vles JS, et al. The cognitive effects of interictal epileptiform EEG discharges and short nonconvulsive epileptic seizures. Epilepsia 2012;53:1051–9.
[49] Rathouz PJ, Zhao Q, Jones JE, Jackson DC, Hsu DA, Stafstrom CE, et al. Cognitive development in children with new onset epilepsy. Dev Med Child Neurol 2014;56: 635–41.
[50] Masur D, Shinnar S, Cnaan A, Shinnar RC, Clark P, Wang J, et al. Pretreatment cognitive deficits and treatment effects on attention in childhood absence epilepsy. Neurology 2013;81:1572–80.
[51] van Iterson L, Kaufman AS. Intraindividual subtest variability on the Dutch Wechsler Intelligence Scales for Children — Revised (WISC-RNL) for children with learning disabilities, psychiatric disorders, and epilepsy. Psychol Rep 2009;105:995–1008.
[52] Dunn DW, Buelow JM, Austin JK, Shinnar S, Perkins SM. Development of syndrome severity scores for pediatric epilepsy. Epilepsia 2004;45:661–6.
[53] van Luit JEH, Bloemert J, Ganzinga EG, Mönch ME. Protocol Dyscalculie: Diagnostiek voor gedragsdeskundigen. (Dyscalculia protocol for psychologists). Doetichem, The Netherlands: Graviant Educatieve Uitgaven; 2012 223.

[54] Resing WCM, Evers A, Koomen HMY, Pameijer NK, Bleichrodt N, van Boxtel H. Indicatiestelling: condities en instrumentarium in het kader van de leerlinggebonden financiering. Amsterdam: Boom; 2002.
[55] Pijl IJ, Pijl SJ. Are pupils in special education too "special" for regular education? Int Rev Educ 1998;44:5–20.
[56] van Haasen P, et al. WISC-R. Wechsler Intelligence Scale for Children Revised. Nederlandstalige uitgave. Lisse, The Netherlands: Swets Test Services; 1986.
[57] Wechsler D. WISC-III^{NL}. Wechsler Intelligence Scale for Children. Derde editie NL. Handleiding en Verantwoording. London/Amsterdam: The Psychological Corporation/Nederlands Dienstencentrum NIP; 2005.
[58] Sattler JM. Assessment of children. 3rd ed. San Diego: author; 1990.
[59] Sattler JM. Assessment of children. Cognitive applications. 4th ed. San Diego: author; 2001.
[60] de Bruyn EEJ, Vandersteene G, van Haasen PP. WISC-R. Wechsler Intelligence Scale for Children-Revised. Nederlandstalige uitgave. Verantwoording. Lisse, The Netherlands: Swets Test Services; 1986.
[61] Vermeulen J, Aldenkamp AP. Cognitive side effects of chronic antiepileptic drug treatment: a review of 25 years of research. Epilepsy Res 1995;21:65–95.
[62] Gottlieb L, Zelko FA, Kim DS, Nordli DR. Cognitive proficiency in pediatric epilepsy. Epilepsy Behav 2012;23:146–51.
[63] Bhise VV, Burack GD, Mandelbaum DE. Baseline cognition, behavior and motor skills in children with new-onset, idiopathic epilepsy. Dev Med Child Neurol 2010;52: 22–6.
[64] Hermann B, Jones J, Sheth R, Dow C, Koehn M, Seidenberg M. Children with new-onset epilepsy: neuropsychological status and brain structure. Brain 2006;129: 2609–19.
[65] Oostrom KJ, van Teeseling H, Smeets-Schouten A, Peters AC, Jennekens-Schinkel A. Three to four years after diagnosis: cognition and behaviour in children with 'epilepsy only'. A prospective, controlled study. Brain 2005;128(Pt 7):1546–55.
[66] Lee ES, Yeatman JD, Luna B, Feldman HM. Specific language and reading skills in school-aged children and adolescents are associated with prematurity after controlling for IQ. Neuropsychologia 2011;49:906–13.
[67] Babikian T, Asarnow R. Neurocognitive outcomes and recovery after pediatric TBI: meta-analytic review of the literature. Neuropsychology 2009;23:283–96.
[68] Ballantyne AO, Spilkin AM, Hesselink J, Trauner DA. Plasticity in the developing brain: intellectual, language and academic functions in children with ischaemic perinatal stroke. Brain 2008;131:2975–85.
[69] Kaufman AS. In what way are apples and oranges alike?: A critique of Flynn's interpretation of the Flynn effect. J Psychoeduc Assess 2010;28:382–98.
[70] Canivez GL, Watkins MW. Long-term stability of the Wechsler Intelligence Scale for Children — Third edition. Psychol Assess 1998;10:285–91.
[71] Moffitt TE, Silva PA. WISC-R verbal and performance IQ discrepancy in an unselected cohort: clinical significance and longitudinal stability. J Consult Clin Psychol 1987; 55:768–74.
[72] Walsh P, Elsabbagh M, Bolton P, Singh I. In search of biomarkers for autism: scientific, social and ethical challenges. Nat Rev Neurosci 2011;12:603–12.
[73] Pennington BF. From single to multiple deficit models of developmental disorders. Cognition 2006;101:385–413.
[74] Berg AT, Berkovic SF, Brodie MJ, Buchhalter J, Cross JH, van Emde Boas W, et al. Revised terminology and concepts for organization of seizures and epilepsies: report of the ILAE Commission on Classification and Terminology, 2005–2009. Epilepsia 2010;51:676–85.
[75] Pal DK. Epilepsy and neurodevelopmental disorders of language. Curr Opin Neurol 2011;24:126–31.