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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