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Panayiotopoulos syndrome and Gastaut syndrome are distinct entities in terms of neuropsychological findings

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ABSTRACT

Background: Although the courses of self-limited focal epilepsies of childhood are considered as benign, a handful of studies suggested that these children may suffer from cognitive problems. Implementing tailor-made educational strategies would aid these children to reach their full potentials. Therefore, it is crucial to understand and differentiate the complete neuropsychological and behavioral profiles of these rather common syndromes. We aimed to examine the distinct cognitive and behavioral profiles of the Panayiotopoulos syndrome (PS) and the Gastaut syndrome (GS), comparatively.

Method: Twenty patients with PS, 20 patients with GS, and 20 healthy controls have been recruited. The testing protocol included Wechsler Intelligence Scale for Children-Revised, Conner's Continuous Performance Test, Verbal Fluency Test, Stroop Color and Word Test, Color Trails Test, Tower of London Test, Symbol Digit Modalities Test, California Verbal Learning Test-Children's Version, Rey Complex Figure Test, Benton Face Recognition Test, Benton Judgment of Line Orientation, Peabody Picture Vocabulary Test, Reading and Writing Test, Child Behavior Checklist, Conner's Parent Rating Scale-48, and Behavior Rating Inventory of Executive Function. Demographical, clinical, electrophysiological data, and imaging findings have also been evaluated.

Results: With regard to intelligence, the patients with PS scored less in all scales compared to the healthy controls. However, only the performance IQ (intelligence quotient) scores differed significantly between the patient groups, with the patients with PS scoring lower than the patients with GS. Verbal memory problems were eminent in both of the patient groups; whereas, visual memory was impaired only in the group with PS. Psychomotor speed was affected in both groups. Reading problems were prominent only in the patients with PS. Writing and arithmetic skills were defective in both patient groups. There were no noteworthy behavioral problems in comparison to healthy subjects.

Conclusion: Using neuropsychological profiles, this study demonstrated that the GS and the PS are two distinct entities. Cognitive dysfunction is a more prominent and widespread feature of the patients with PS; whereas, the patients with GS suffer only from milder and isolated cognitive problems.

1. Introduction

Self-limited occipital lobe epilepsies of childhood are pharmacosensitive epileptic syndromes and are among the most common types of focal epilepsies in the pediatric population [1,2]. They are customarily divided into two groups. The early onset type (Panayiotopoulos syndrome [PS]) and late onset type (Gastaut syndrome [GS]) have well-known, clinically distinctive features [2–4]. Estimated prevalence among children 1 to 15 years of age with afebrile seizures is 6% for PS and 1–2% for GS [2]. However, there is not enough evidence about the differences between the cognitive and neuropsychiatric profiles of these syndromes. The former studies either included both groups together or evaluated only the cases with PS [4–15]. One study recruiting patients with PS revealed normal intelligence and only minor problems in arithmetic, comprehension, and picture arrangement in comparison with controls [4]. Another study showed that 17% of the cases with typical PS had neurobehavioral disorders, 9% had borderline to mild mental retardation, and another 9% had a significant discrepancy in verbal vs. performance IQ (intelligence quotient) scores [12]. Hodges studied three cases with PS and reported prominent impairments on visual

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memory tasks and visual processing speed which were not due to inattention since tests evaluating attention indicated normal performance [7]. De Rose et al. also studied visual and visual–perceptual functions in the cases with PS only to reveal unexpectedly low rates of abnormalities in these domains in the face of EEG (electroencephalographic) abnormalities involving the occipital regions [13]. However, Bedoin et al. has shown that children with PS have a reduced ability to diffuse inhibition outside the focus of visual–spatial attention, which is most likely reflecting the frontal disturbance in these children, possibly due to posteroanterior spike propagation [14,15]. In another study, all cases with PS showed normal IQ scores but had subtle anomalies in visual–perceptual abilities and in semantic processing, pointing out to an additional involvement of the parietal lobe [6]. The neuropsychological data on the GS are very scarce, and to the best of our knowledge, there is only a case study and a case series with a limited number of patients [16,17]. These case reports suggested us problems in attention and visual-motor coordination in GS.

In this study, we aimed to examine whether the PS and the GS are two distinct syndromes or not in terms of intelligence, cognitive functions, and behavioral problems, and to highlight their differences in their cognitive profiles.

2. Materials and methods

2.1. Patients

Twenty patients with PS and 20 patients with GS, diagnosed according to the relevant literature [18] by experienced pediatric neurologists based on clinical, semiological, and electrophysiological findings, and 20 healthy controls with matched age, gender, socioeconomic, and parental status participated the research. Patients are recruited from four tertiary epilepsy centers. Children diagnosed as having the PS or the GS, who were between the ages of 6 to 16 years, and had at least one sleep EEG showing characteristic findings and normal cranial magnetic resonance (MR) imaging are selected for the research. Patients with current seizures (within the last month) are excluded in order to avoid the possible effects of seizure on cognitive performance. Other exclusion criteria were clinical and electrophysiological remissions for three years, parenteral consanguinity, overt neurological or mental abnormalities before the onset of the seizures, lack of proper skills, and noncompatibility with the tests due to sociocultural status. The control group is selected from healthy volunteers, who were not related to the patient group (PG), and had no self or family history of epilepsy or psychiatric disorders.

2.2. Data collection tools

Demographical data, disease history (age of onset, seizure semiology, seizure frequency, treatment modalities, etc.), EEG, and MRI (magnetic resonance imaging) findings have been noted. For the evaluation of the cognitive profile, the following tests were used: Wechsler Intelligence Scale for Children-Revised (WISC-R) for intelligence; California Verbal Learning Test-Children's Version (CVLT-CV) and Rey Complex Figure Test (RCFT) for verbal and visual memory; Conner's Continuous Performance Test-II (CCPT-II), Verbal Fluency Test (VFT), Stroop Color and Word Test (SCWT), Color Trails Test (CTT), and Tower of London Test (TLT) for attention and executive functions; Symbol Digit Modalities Test (SDMT) for motor ability; Benton Face Recognition (BFR) Test and Benton Judgment of Line Orientation (BJLO) for visual–spatial functions; Peabody Picture Vocabulary Test (PPVT) and Reading and Writing Test (RWT) for language; and Child Behavior Checklist (CBCL), Conner's Parent Rating Scale-48 (CPRS-48), and Behavior Rating Inventory of Executive Function (BRIEF) for behavior [19]. All tests were previously validated and used in Turkish language. These tests were applied in two separate sessions, in a room suitable for testing by the first author who is experienced in neuropsychological studies with children, as a part of her doctorate thesis research. Parental inventories were answered by the volunteered parents. The study protocol was approved by the Ethics Committee (2017-7), and all parents gave signed informed consent.

2.3. Statistical analysis

Nonparametric tests were used for comparison of values not distributed normally. Kruskal-Wallis test was used to compare the group with PS, group with GS, and control group. Mann–Whitney *U* test was utilized for the post hoc analysis of the differences between two groups. P values below 0.05 were considered significant. Spearman's rho correlation analysis was used to determine the relationship between seizure characteristics and neuropsychological and behavioral findings. Bonferroni correction was applied to correlation analyses, and significance value was set to 0.005.

3. Results

The demographic findings of the included patients are summarized in Table 1.

3.1. Results of intelligence tests

3.1.1. Panayiotopoulos syndrome and intelligence

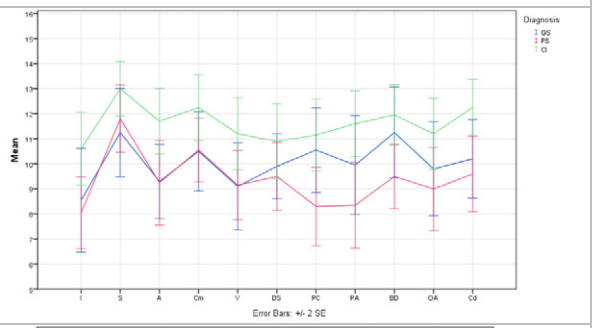
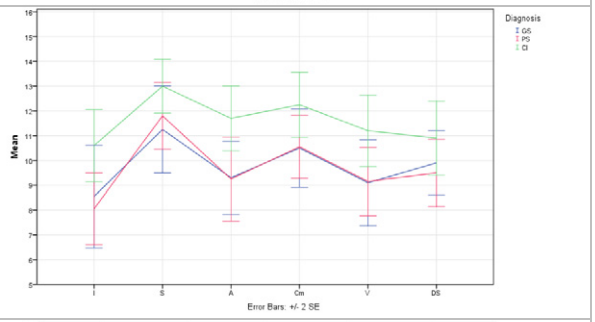
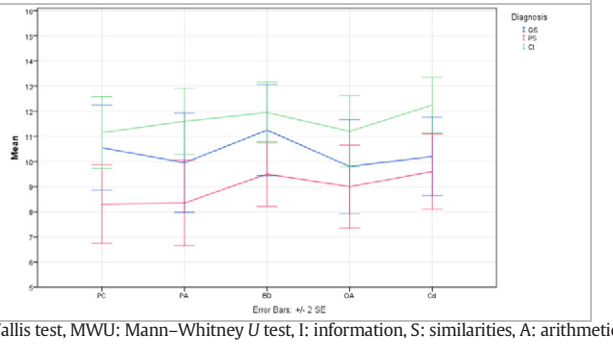
General IQ, verbal IQ, and performance IQ scores were significantly lower in the patients with PS compared to the healthy controls (Table 2). The deficits in performance IQ tests were more pronounced compared with the deficits in verbal IQ tests; however, this finding was not statistically significant. Of the patients with PS, 35% (N = 7) had a general IQ score below 90 (range: 65–87). Among them, 30% (N = 6) had a verbal IQ score below normal (range: 79–85), whereas only 20% (N = 4) had a performance IQ score below normal (range: 55–81), one of which had a very low score (55).

Table 1
Demographic characteristics of the groups with Panayiotopoulos and Gastaut syndromes.

Diagnostic group	Gender	N	Age (SD)	Disease duration (months) N: mean (SD)	Treatment duration (months) N: mean (SD)	Time lag between tests and last seizure (months) N: mean (SD)
GS	Female	12	10.21 (2.71)	20: 29.47 (16.91)	17: 31.00 (19.34)	20: 13.50 (10.88)
	Male	8	11.97 (2.64)			
	Total	20	10.92 (2.76)			
PS	Female	12	10.12 (1.72)	20: 38.40 (30.72)	15: 41.95 (27.04)	20: 21.75 (13.45)
	Male	8	11.06 (1.81)			
	Total	20	10.50 (1.77)			
Control	Female	12	9.68 (2.19)			
	Male	8	9.96 (1.05)			
	Total	20	9.79 (1.79)			
P value (MWU)		NS	NS	0.215	0.732	0.057

GS: Gastaut syndrome, PS: Panayiotopoulos syndrome, MWU: Mann–Whitney *U* test, NS: not significant.

Table 2
The results of the WISC-R test.

	Groups	Mean (SD)	P value	
WISC-R General	GS	100.85 (23.12)	***0.010*** *(KWT)* PS vs Cl= ***0.001*** *(MWU)*	
	PS	95.35 (16.69)		
	Cl	112.65 (15.41)		
WISC-R Verbal	GS	99.45 (22.38)	***0.049*** *(KWT)* PS vs Cl= ***0.022*** *(MWU)*	
	PS	99.10 (16.66)		
	Cl	111.85 (16.03)		
WISC-R Performance	GS	102.55 (23.45)	***0.003*** *(KWT)* PS vs Cl= ***0.001*** *(MWU)*	
	PS	92.05 (17.42)		
	Cl	111.45 (13.93)		

GS: Gastaut syndrome, PS: Panayiotopoulos syndrome, Cl: control, KWT: Kruskal–Wallis test, MWU: Mann–Whitney *U* test, I: information, S: similarities, A: arithmetic, Cm: comprehension, V: vocabulary, DS: digit span, PC: picture completion, PA: picture arrangement, BD: block design, OA: object assembly, Cd: coding.
p values below 0.05 were considered significant.

3.1.2. Gastaut syndrome and intelligence

General IQ, verbal IQ, and performance IQ scores did not significantly differ between the patients with GS and the healthy controls (Table 2). Of the group with GS, 25% (N = 5) scored lower than normal (range: 67–86) in general IQ tests. Only 5% (N = 1) of the patients with GS were classified as having moderate mental retardation, and 20% (N = 4) were classified as mild mental retardation according to the verbal IQ scores. Performance IQ scores were lower than normal in 15% (N = 3) of the patients with GS.

3.1.3. PS versus GS

Compared to the patients with PS, the patients with GS performed markedly better in general IQ and performance IQ tests. Verbal scores did not significantly differ between the patient groups.

In WISC-R verbal test subscales, both the patients with GS and PS received lower scores in arithmetic (p = 0.026 and 0.035) and vocabulary subscales (p = 0.037 and 0.026) compared to the control group. In these subscales, there was no significant difference between patients with GS and PS (p = 0.754 and 0.956). Performance in the remaining subscales of the WISC-R verbal test was similar across all groups.

In WISC-R performance test subscales, the patients with PS received lower scores in picture completion subscale compared to the controls and the patients with GS (p = 0.012 and 0.046), and in picture arrangement and block design compared to the controls (p = 0.007 and 0.012). Both the patients with GS and PS received lower scores in coding compared to the controls (p = 0.044 and 0.013). In the remaining subscale, object assembly, performance was similar across all groups.

3.2. Verbal and visual memory

California Verbal Learning Test-Children's Version revealed a recognition deficiency in the patient groups. The patients with PS and GS received significantly higher scores compared to the control group in the false positive responses (p = 0.024 and 0.030) and intrusion scores (p = 0.049 and 0.004). Discriminability scores were significantly lower only in the patients with PS (p = 0.007). The rest of the subscores were similar across all groups (Fig. 1a).

Rey Complex Figure Test revealed an immediate recall problem in the patients with PS (p = 0.017). In the rest of the tests, all groups received scores within the normal range revealing a visual attention deficit rather than a memory problem (Fig. 1b).

3.3. Attention and executive functions

Out of multiple tests used to evaluate attention and executive functions, only two of the subscales revealed problems in the patients with

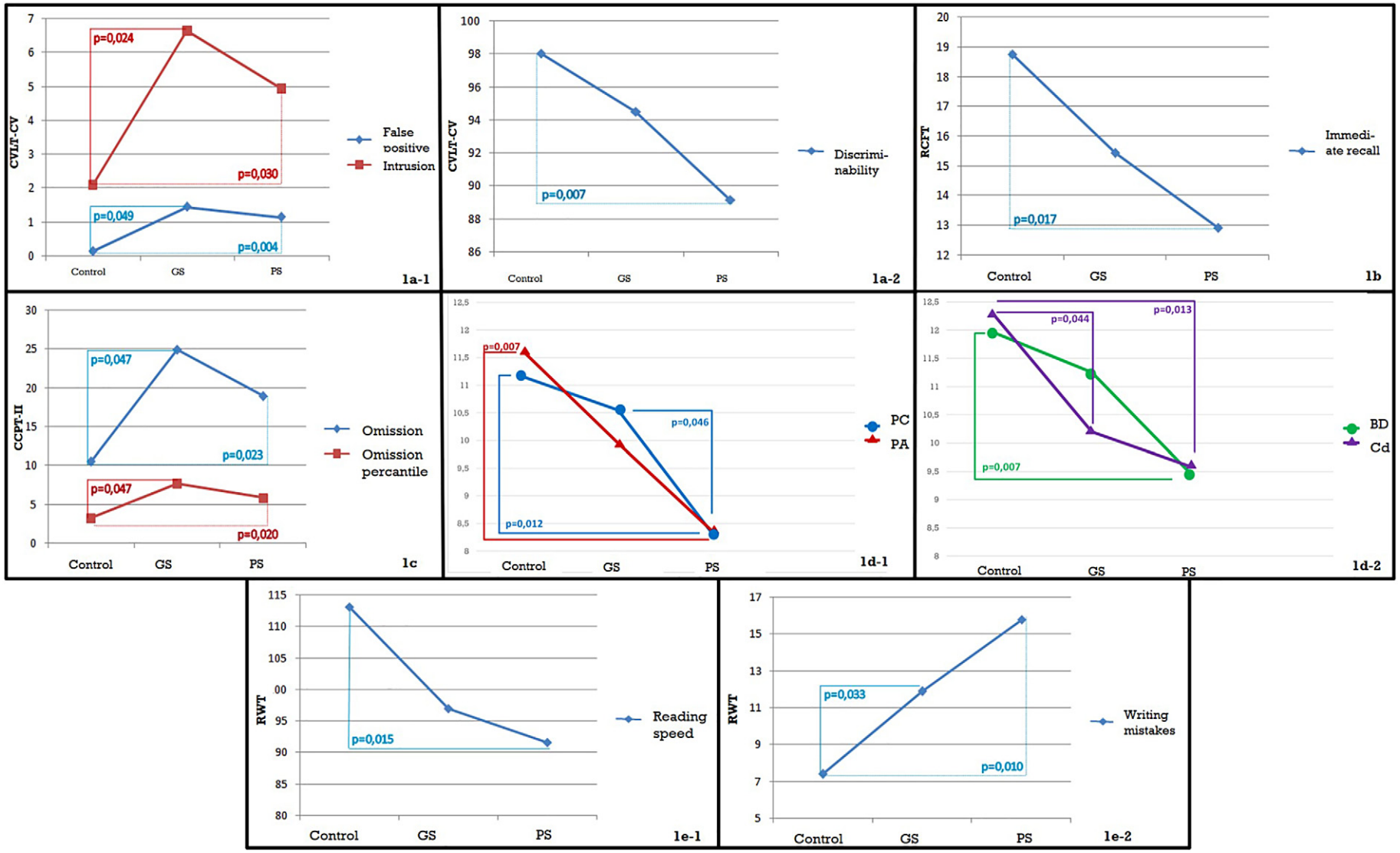


Fig. 1. a-1: CVLT-CV: California Verbal Learning Test-Children's Version; false positive responses and intrusion scores were significantly higher in patients compared to controls. 1a-2: Discriminability scores were significantly lower only in patients with PS. 1b: RCFT: Rey Complex Figure Test; immediate recall is problematic in patients with PS. 1c: CCPT-II: Conner's Continuous Performance Test-II; omission and omission percentile scores are lower in patients with PS and GS compared to healthy controls. 1d-1: Subscales in WISC-R; picture arrangement (PA) scores are lower in both patients with PS and GS compared to controls and patients with PS performed worse in picture completion (PC) subscale compared to the controls and patients with GS. 1d-2: Coding (Cd) scores are lower in both patients with PS and GS compared to controls and patients with PS performed worse in block design (BD). 1e-1: RWT: Reading and Writing Test; reading speed is lower in patients with PS compared to controls. 1e-2: Writing errors are higher in both patients with GS and PS compared to controls.

PS. Both omission and omission percentile scores were lower in the patients with PS and GS compared to the healthy controls ($p = 0.047$, 0.023 and 0.047, 0.020) (Fig. 1c). The rest of the tests revealed similar profiles across all groups. Some subscales in WISC-R also reflected problems in attention and executive functions: coding and picture arrangement scores were lower in both the patients with PS and GS compared to the controls and the patients with PS performed poorer in picture completion subscale compared to the controls and the patients with GS (Fig. 1d).

3.4. Motor ability

Symbol Digit Modalities Test was used to evaluate motor abilities. The scores and subscores were similar across all groups.

3.5. Visual–spatial functions

Benton Face Recognition Test and BJLO test scores were similar across all groups. Other WISC-R subscales evaluating visual–spatial dysfunctions are shown in Fig. 1d. As seen in the figure, block design scores were lower in the group with PS although all groups received similar scores in the RCFT.

3.6. Language

Peabody Picture Vocabulary Test scores were similar across all groups. Reading and Writing Test revealed lower reading speed in the patients with PS compared to the controls ($p = 0.015$) and more writing errors in both the patients with GS and PS compared to the controls ($p = 0.033$ and 0.010) (Fig. 1e). Both patient groups scored lower in vocabulary tests compared to controls ($p = 0.037$ and 0.026).

3.7. Behavior

Child Behavior Checklist, CPRS-48, and BRIEF tests were used in order to evaluate the behavioral profile of the patients. None of the tests significantly differed between the patient groups and the control subjects.

3.8. Patient characteristics, EEG findings, and medication history

The correlations between the neuropsychological test findings and the patient characteristics such as age at the time of neuropsychological testing, disease duration (time since the first seizure onset), duration of antiepileptic drug (AED) treatment, and time since the last seizure are given in the Supplementary Table 1.

The number of the patients with PS and GS with normal and abnormal EEG findings and the localization of the abnormalities were statistically similar ($p = 1.000$ and 0.496). Electroencephalographic findings did not show a consistent correlation with any of the neuropsychological scales used in our study.

Patients were grouped into following 3 categories: drug-free, on monotherapy (carbamazepine (CBZ) or valproic acid (VPA)), and on polytherapy. The distribution of cases for each of 3 categories were similar in both patient groups ($p = 0.341$). The only difference between these categories was observed in higher rule breaking behavior score in the CBCL test, which was associated with polytherapy usage.

4. Discussion

Using their neuropsychological profiles, this study demonstrates that the GS and the PS are distinct entities. Neuropsychological dysfunction is a more noticeable and common feature of the patients with PS, whereas the patients with GS suffer more from milder and isolated cognitive problems. With regard to intelligence, the patients with PS scored less in all scales compared to the healthy controls. Performance IQ scores differed significantly between the patient groups where the patients with PS scored lower than the patients with GS, supporting a distinctive pattern of cognitive dysfunction. On the other hand, behavioral aspects of these two self-limited syndromes, investigated for the first time in relevant literature, did not highlight any problems in comparison to the matched control subjects and were similar in both the groups with PS and GS.

4.1. Intelligence

There are contradictory findings on mental retardation in the patients with PS, probably due to the methodology. Some studies report cohorts of the patients with PS with no mental problems, while others report 16 to 40% of the cases to have mental retardation [4,9,10], and some studies use mental retardation as an exclusion criterion altogether [6]. Our cohort ranked in the higher end of this spectrum since 35% of the study group had general IQ scores below 90. Similar to the previous studies, our group with PS also performed poorer in WISC-R [4,9,17]. Intriguingly, however, the verbal scores of the cohorts of Germanò were lower compared to their performance scores [9]. The opposite is the case in our findings, since our patients scored less in the performance tests. When individual IQ scores are taken into account, there were no cases with mental retardation in Germanò's cohort. Therefore, lower scores in the performance tests might be due to the rather high percentage of mental retardation in our group. On the other hand, a study by Lopes et al., performed in a cohort of 19 patients with PS, showed that the verbal scores were higher than the performance scores as in our findings, but the lack of a control group in their study makes it difficult to interpret [6]. Chilosi also reported a better verbal profile compared to performance; however, the number of included patients is too few to make a firm inference [10].

To the best of our knowledge, our study is the first to examine the cognitive profile of the GS with a sufficient number of patients. Our findings show that the general, verbal, and performance IQ test scores of patients with GS do not significantly differ from those of the healthy controls, although the mean scores for each of these items are lower in the patients with GS as seen in figures. There is just one study which evaluates only the intelligence level of the patients with GS and compares them with the patients with PS. This study is conducted on 7 patients with GS and 10 patients with PS and used only 4 subscales (not all the 5 required subscales) of WISC-R performance section without any reasons stated. Although they reported that the patients with GS have lower IQ scores compared to the healthy controls, we believe that these results do not reflect the actual state because of the scarcity of their cohort and the lack of a proper WISC-R testing [17].

The most important factors known to affect intelligence in patients with epilepsy are the seizure frequency, disease duration, age of seizure onset, treatment regimens, and sociocultural differences [20–22]. Since the seizures are rare, polypharmacy is uncommon, drugs impairing cognition (such as topiramate and phenobarbital) are avoided, and sociocultural backgrounds are similar in our study group, we believe that age is the most important factor. This important effect of age is further supported by the results of the correlation analysis. Pathological process starts at an earlier age in PS compared to GS. A critical hit during the peak of the maturation course in the patients with PS may be the root of these defects in intelligence. Since appearance of seizures and EEG pathologies starts rather later in GS, possibly after, this pivotal time window of maturation is exceeded. Therefore, the physiological basis of the intelligence is already established when the disease develops in the patients with GS and the detrimental effect on memory is less apparent.

4.2. Memory

We think that the relative preservation of memory is due to the low seizure frequency of the cohort, in relation with the natural course of

these epileptic syndromes, which markedly spare the limbic structures. Relatively high mean age of our cohort coincides with clinical remission, further contributing to the preservation or perhaps recovery of the memory. It can also be assumed that the lower verbal skills, as reflected by the low verbal IQ, is the main reason for the scant number of cases with a deteriorated verbal score in verbal memory tests rather than a primary memory problem itself. Lopes et al. also found similar results in a cohort of patients with PS but speculated a dysfunction of association areas in left parietal lobe [6]. Although our cohort is capable of retrieving the same amount of verbal data as the healthy controls, the scores for false positive responses and intrusion were high for both patient groups, and discriminability scores were low for the patients with PS; indicating a dysfunction in the recognition process and a tendency for confabulation.

Regarding the visual memory, the only noteworthy finding was an immediate recall problem in the patients with PS, which was also supported by the performance IQ subtests. Copying and delayed recall scores were similar to the scores of the healthy controls, possibly reflecting a visual attention deficit rather than a memory problem [14]. Furthermore, the scores of the patients with GS were also similar to the scores of the healthy controls.

4.3. Attention and executive functions

Given that attention and executive functions have been evaluated thoroughly using various tests in our study, it is safe to think that these functions are relatively preserved in both patients with GS and PS in contrast to most of the other cohorts with epilepsy up to now. Most noticeable finding was the omission mistakes, suggesting problems in visual attention and prolonged reaction time [14]. The psychomotor speed evaluated by the coding test was also significantly slower in both patient groups. Another finding consistent with attention deficiency (or atypical attentional skills) was found in the performance of the patients with PS in WISC-R picture concept and picture completion subtests. These findings were consistent with other studies [4,5,9].

Picture completion test was the only subscale differentiating between the patients with PS and GS, with patients with PS performing significantly poorer. Compared to GS, which is known to be more localized, PS has a more widespread dispersion of multiple epileptic foci, therefore, it is possible that expansive pathology is more likely to affect parietal and frontal areas partaking in neural networks of attention [15, 23–25]. Another possible explanation is the interference of the rather early onset of PS with the maturational process of the prefrontal lobe, which is heavily associated with attention and executive functions, and also the last area to mature in association with the chronological age.

4.4. Visual–spatial functions

Our results supported a normal visual–spatial function profile in both patient groups [4,13]. Previously, only one study has reported problems in the ventral pathway in children with idiopathic occipital epilepsy, but the low number of cases (only 5 children) and the lack of distinction between the PS and GS render their results unreliable [10].

For the constructive abilities, it is noteworthy that RCFT scores were similar across all groups while the block design subscale of the WISC-R revealed a poorer performance in the group with PS. As mentioned above, Lopes et al. reported abnormalities in the RCFT results in the patients with PS compared to the control group. However, they did not perform the WISC-R to the healthy controls, therefore did not have normative data for the block design subtest in their cohort [6]. Block design test provides a reliable assessment of visual perception and visual–perceptive organization. We believe that the deterioration in constructive abilities is due to attention, psychomotor speed, and conceptualization problems in the patients with PS, rather than to the influence of the pathological process in the parietal lobe as suggested by Lopes et al.

4.5. Language

Difficulties regarding vocabulary were the most notable finding in both patient groups, consistent with the existing literature [5,9,11]. The dysfunction was more noticeable in the expressive component of the language skills. Since perirolandic spikes are common findings in GS and PS, this dysfunction is probably due to problems in the networks employed in speech production.

4.6. Academic success

Both patient groups performed poorer in arithmetic test in WISC-R, compared to the normal controls, a finding consistent with the previous studies [4,5,7,9,11]. The arithmetic test requires a proper processing speed, auditory attention skills, intact complex attention, and visual mental imagery in addition to sound mathematical skills [4,9]. These properties have been elaborately tested in our study, and although the patient groups performed poorer in these tests, the differences were not statistically significant except for block design test, reflecting the visual perceptive abilities. Therefore, more focused and extensive batteries are necessary to understand the role of visual perceptive ability dysfunction in arithmetic skill problems in this population, and to clarify whether arithmetic skills are indeed problematic or a specific learning disorder, namely dyscalculia, exists in these patients.

Reading is affected greatly by age, gender, sociocultural status, and education factors [26]. In our study, age, gender, and sociocultural status variables were similar across the group with PS, group with GS, and control group. However, there was a significant difference regarding the grades of these children in their schools (14 of the children in the PS, 8 in the GS, and 12 in the control group were students in the first four grades of primary school), so the findings related to reading and writing in our study should be interpreted with great caution.

Assessment of the reading and writing skills showed that patients with PS were slower in reading tests, and that both the patients with GS and PS made more writing mistakes compared to the healthy controls as mentioned in other studies [9,27]. Since our cohort has findings indicating attention deficit problems, psychomotor speed problems as shown by the coding test, and vocabulary problems, it is not possible to discriminate whether the problems in writing are primary or secondary to other dysfunctions.

4.7. Behavior

Epilepsy is well-known for causing various psychiatric comorbidities and behavioral problems [28]. The normal behavioral profile of these children may relate to the benign course of the epileptic syndrome, rarity of the seizures, avoidance of polytherapy, and mood stabilizing effect of valproic acid and carbamazepine, which are frequently used AEDs in our cohort.

4.8. Patient characteristics and medication history

As regards the treatment, polytherapy was associated with “higher rule breaking behavior”. Since none of the patients were using AEDs which are associated with negative effects on cognitive performance, these findings probably originate from active disease processes.

The correlation analysis in Supplementary Table 1 shows that longer AED therapy and longer disease duration are associated with behavioral abnormalities, therefore, this group should be followed up for possible behavioral problems in the long run.

4.9. Academic accommodations

Academic accommodations and management strategies would play a critical role in these children's education planning. Implementing a tailor-made curriculum based on the child's neuropsychological profile would aid these children to reach their full potentials.

Since verbal memory problems are eminent in both patient groups, limiting the amount of information communicated in each session, providing "cheat sheets", and written directions can enhance the learning process, whereas employing examination formats requiring recognition (such as multiple choice questions) and allowing open book tests may provide a fairer evaluation of the child. Since the group with PS also suffered from visual memory problems, employing multiple modalities (writing, speaking, listening, drawing, etc.) during the learning process can reap lasting benefits.

As for psychomotor speed deficiencies in both groups, allowing the child to have some extra time to complete the mentioned task, focusing on the work's quality rather than the speed, dividing long tasks into shorter ones, and shortening repetitive tasks can be helpful.

Reading problems in the patients with PS and writing problems in both groups can be resolved by means of using different modalities for learning and examination. Audiobooks, charts, and drawings can be used for studying and oral examinations instead of written ones which may be a better way for the children to express their knowledge. A reading buddy can contribute greatly not only to the academic success, but also to the motivation and social development of the child. Age appropriate literature consistent with the child's interest can be used in order to allure the child into reading more.

Using a step-by-step approach and avoiding mixing problems (such as subtraction and addition within the same problem) until the child masters each step, allowing the use of calculators and cheat sheets, using graphs, diagrams, and real life examples can help the children with arithmetic skill deficits.

4.10. Strengths and limitations of the study

This is the first study that reports the neuropsychological profile of a GS sample with a statistically enough number of patients and that documents the distinctive neuropsychological features of the patients with PS and GS matched by current age, sex, and sociocultural status using an extensive neuropsychological battery. The healthy control group provides a purer clinical picture and supports the reliability of our results. The main limitations of our study have been the lack of uniformity in the AED regimen and the lack of psychiatric examination prior to inclusion. A simultaneous EEG recording during testing procedure, which would allow for the correlation analysis of clinical with the pathophysiological, could have been very informative in order to make a clinical and pathophysiological correlation.

5. Conclusion

This study demonstrates that GS and PS are distinct entities in terms of neuropsychological profiles. The patients with PS suffer from a more widespread dysfunction compared to the patients with GS, mostly but not solely related to early age at onset. Our report highlights for the first time that behavioral problems are not expected in these syndromes except in selected older cases. Further prospective research is necessary to determine the temporal picture of the neuropsychological abnormalities, as well as the perseveration or regression of them after seizure remission. We also want to emphasize that the neuropsychological testing will be helpful to elucidate some specific unnoticed cognitive defects which may benefit from management strategies other than waiting for remission in order to avoid losing time during a critical period for academic development.

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Declaration of Competing Interest

On behalf of all authors, the corresponding author states that there is no conflict of interest. SAK, ADE, VD, OO, ZY, SS, AG, AD, and BB declare no relevant financial or nonfinancial relationships to disclose.

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