Psychiatric evaluation of children with CSWS (continuous spikes and waves during slow sleep) and BRE (benign childhood epilepsy with centrotemporal spikes/rolandic epilepsy) compared to children with absence epilepsy and healthy controls

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SUMMARY: Taner Y, Erdoğan-Bakar E, Turanlı G, Topçu M. Psychiatric evaluation of children with CSWS (continuous spikes and waves during slow sleep) and BRE (benign childhood epilepsy with centrotemporal spikes/rolandic epilepsy) compared to children with absence epilepsy and healthy controls. Turk J Pediatr 2007; 49: 397-403.

This investigation examined psychopathology and IQ levels in 30 children with CSWS and 42 children with BRE and compared them with 40 healthy controls and 23 children with absence epilepsy by using the Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS) and Wechsler Intelligence Test for Children (WISC-R). The CSWS and BRE groups had the highest rate of psychiatric diagnoses and lowest IQ scores. The BRE group had higher rates of psychopathology and lower IQ scores compared to the healthy controls. While BRE and absence groups did not differ with regard to presence of psychopathology, IQ levels and types of psychopathologies, children with CSWS had more psychiatric disorders and lower IQ scores compared to the patient group with absence epilepsy. These findings suggest that CSWS and BRE are two epileptic syndromes that lead to psychiatric disorders and lower IQ scores. Hence, psychiatric consultation should be a part of the treatment while managing these children.

Key words: psychiatric evaluation, continuous spikes and waves during slow sleep (CSWS), benign childhood epilepsy with centrotemporal spikes/rolandic epilepsy (BRE).

Epilepsy in children and adolescents is a neurological condition that is associated with psychiatric pathologies. Children with epilepsy can have learning or other psychological difficulties related to either brain pathology or medication effects, with age of onset, type, frequency and severity of seizures, and type of medication being important variables[1]. Among the variables, seizure control is found to be the most powerful predictor of behavioral disturbances[2]. Pediatric epilepsy patients represent a 3-6 times increased risk for psychopathology, as compared with the general population[3], and they also have a higher rate of psychopathology compared to children with other medical conditions. Common psychiatric diagnoses include attention, behavior, anxiety and depressive disorders[1].

In a community-based study, Rutter and colleagues[4] found psychopathology in 29% of 63 children with uncomplicated epilepsy, and the rate of psychopathology was four times higher than the general population and twice as much as in children with chronic, nonneurological illnesses. More recent studies conducted using different instruments including the Child Behavior Checklist (CBCL), the Rutter Scale and the Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS) found psychopathology at a rate ranging from 21% to 60% in pediatric epileptic patients[5-9].

Seizure type is one of the most important variables for which its association with psychopathology is extensively studied. Historically, children with complex partial

seizures were defined as aggressive, whereas absence epilepsy patients were called neurotic[3]. In more recent studies investigating psychopathology in epileptic children and adolescents, no differences in terms of psychopathology rates and types were found between complex partial seizures and primary generalized seizures[8,9].

Benign childhood epilepsy with centrotemporal spikes/rolandic epilepsy (BRE) and continuous spikes and waves during slow sleep (CSWS) are two epileptic syndromes which are activated by sleep[10].

Continuous spikes and waves during slow sleep (CSWS) is a rare epileptic syndrome characterized by pathological slow wave paroxysm during sleep. Although in most of the patients, neuropsychological and motor development is in normal limits before the emergence of the syndrome, as disease progresses, spatial orientation deficits and orientation deficit related to time, attention problems, hyperactivity, short-term memory difficulties, decline in verbal and performance intelligence quotients (IQs) as well as in fine motor skills, apraxia, worsening of speech functions, autism, psychosis, aggressiveness, apathy and social functioning difficulties become recognizable[11,12]. Some patients with CSWS refer to the physicians not because of seizures but because of nervousness, attention deficits, learning difficulties, low school success, behavioral disturbances and speech disturbances.

Benign childhood epilepsy with centrotemporal spikes/rolandic epilepsy (BRE) is another epileptic syndrome that activates during sleep and it is characterized by epileptic activity in the rolandic – also called the centrotemporal – area of the brain. Attention deficit/hyperactivity disorder (ADHD), dyslexia and difficulties with reading, language or with drawing and visuospatial skills may accompany this syndrome, although serious cognitive impairment is not an expected finding[13,14]. Fluctuations in the IQ levels may be seen in BRE due to the severity of epileptic discharges, age of onset of the syndrome and the effects of the medication used as well as the presence of ADHD[15-17].

This study examined psychopathology and IQ levels in a large group of pediatric patients who were diagnosed as CSWS or BRE for the first time, using the Wechsler Intelligence Test for Children (WISC-R)[18] and the K-SADS-PL (Present and Life-time Version)[19] and compared those children with absence epilepsy patients and nonepileptic children. We hypothesized that as it is a devasting epileptic syndrome, children with CSWS would have more psychopathologies and lower IQ scores than the other epileptic groups as well as the controls and BRE would lead to psychiatric diagnosis to the extent seen in absence epilepsy, in which psychiatric disorders are seen more frequently than in the general population[9,20].

Material and Methods

Subjects and Procedure

Thirty children with CSWS and 42 children with BRE who were diagnosed for the first time and who were drug-free participated in this study. Twenty-three children with absence epilepsy and 40 nonepileptic children without any history of chronic medical illness were taken as the control groups.

To be included in the study, a child had to have a diagnosis of CSWS, BRE or absence type of epilepsy. The type of epilepsy was identified by an experienced child neurologist (M.T.) who made the neurologic examination and interpreted the EEG of each child. After the neurological diagnosis was made, the patients and their parents who accepted to join the study were referred to the child and adolescent psychiatrist (Y.T.), and psychiatric disorders were screened clinically according to DSM-IV-TR (APA 2000)[21] criteria and Schedule for Affective Disorders and Schizophrenia for School-Age Children: Present and Lifetime Version (K-SADS-PL)[19], which is a semi-structured interview used to further verify the diagnosis. Informed consent process was verbal as is customary given the literacy level of the parents. All epilepsy cases were screened for psychosis, mood disorders, ADHD, conduct disorder (CD) and oppositional defiant disorder (ODD), anxiety disorders, elimination disorders, tic disorders, eating disorders and substance use disorders with corresponding K-SADS-PL modules. Autism and other pervasive developmental disorders were evaluated by clinical observation. Each participant's IQ level was evaluated by a clinical psychologist (E.E.B.) using the WISC-R[18]. The study was conducted from January 2005 to December 2006.

Children with a mixed seizure disorder, underlying neurological disorder, metabolic disorder, hearing disorder as well as with a prior history of treatment for epileptic disorder were excluded from the study.

Age-matched healthy control subjects were mainly recruited from the community by local means. These subjects without a history of known neurological disorder or other chronic medical illnesses were also screened for epileptic disorders by the child neurologist and psychopathology was screened with clinical interviews and K-SADS-PL. All of the control subjects also underwent WISC-R to determine their IQ levels.

Materials

Schedule for Affective Disorders and Schizophrenia for School-Age Children: Present and Lifetime Version

Schedule for Affective Disorders and Schizophrenia for School-Age Children: Present and Lifetime Version (K-SADS-PL) is a semistructured instrument developed by Kaufman and colleagues[19] to screen psychopathology in children and adolescents between ages 6-18 by gathering information from both parents and the offsprings. Mood disorders, psychotic disorders, anxiety disorders, disruptive behavioral disorders, elimination disorders, eating disorders, tic disorders and alcohol and other substance use disorders are the psychiatric conditions included in this instrument. Reliability and validity of K-SADS-PL were determined in Turkey in 2004[22].

Wechsler Intelligence Scale for Children-Revised Form

Wechsler Intelligence Scale for Children-Revised Form (WISC-R)[18] consists of 12 subtests which assess verbal and performance abilities. WISC-R subtests are Information, Similarities, Arithmetic, Comprehension, Digit Span, Picture Completion, Picture Arrangement, Block Design, Object Assembly, and Digit Symbol. The reliability and validity studies of the Turkish form were conducted in 1978[23].

Data Analysis and Statistics

Comparisons related to categorical measures were performed by using chi-square tests or by Fisher's exact tests if there were cells with expected frequencies of less than five. Comparison of the numerical variables between epileptic groups and control group was performed by Mann-Whitney U test. Intergroup differences were measured by MANOVA and post hoc analysis was performed by Tukey test. Test results were considered significant at values of $p<0.05$ level. All statistics were reported two-tailed; standard deviations were reported throughout. Data was evaluated by SPSS-13.0.

Results

Demographic variables of epilepsy subgroups and control group are presented in Table I. Absence ($z=1.264$, $p>0.05$), CSWS ($z=1.448$, $p>0.05$) and BRE ($z=0.895$, $p>0.05$) groups were matched with the control group in terms of age.

Rates of subjects with psychopathology and distribution of psychiatric diagnosis (mean scores and percentage of subjects with score in the clinical range) in whole sample and also the $\chi 2$ and p values are presented in Table II. Groups differed from each other in terms of ADHD, ODD, CD, mental retardation (MR), pervasive developmental disorders (PDD) and total number of psychopathologies ($p<0.05$). To determine the group(s) which generated the difference, paired groups were compared. Subjects in CSWS, BRE and absence groups

Table I. Demographic Characteristics of Patients

		Absence epilepsy	CSWS	BRE	Control
Age (in mos±SD)		115.21±36.15	114.36±28.68	118.16±27.73	120.95±27.16
Sex (N)					
	Girls	14 (60.9%)	7 (23.3%)	12 (28.6%)	20 (50%)
	Boys	9 (39.1%)	23 (76.7%)	30 (71.4%)	20 (50%)

CSWS: Continuous spikes and waves during slow sleep.
BRE: Benign childhood epilepsy with centrotemporal spikes/rolandic epilepsy.

Table II. Type of Psychopathologies in Epilepsy Patients and Group Comparison with Regard to Presence of Psychopathology

	Absence (n=23) N (%)	CSWS (n=30) N (%)	BRE (n=42) N (%)	Control (n=40) N (%)	Test χ^2 (p)
ADHD	10 (43.5)	16 (53.3)	20 (47.6)	2 (5)	23.73 (0.001)
Depression	4 (17.2)	1 (3.3)	2 (4.8)	1 (2.5)	6.72 (NS)
ODD	1 (4.35)	9 (30)	6 (14.3)	1 (2.5)	13.49 (0.004)
MR	1 (4.35)	10 (33.3)	5 (11.9)	0	19.86 (0.001)
EN	3 (13.0)	3 (10)	9 (21.4)	2 (5)	5.26 (NS)
PDD	10 (43.5)	21 (70)	23 (54.8)	3 (7.5)	31.97 (0.001)
CD	0	8 (26.7)	4 (9.5)	0	17.82 (0.001)
Anxiety Disorders	1 (4.3)	9 (30)	5 (11.9)	2 (5)	11.79 (NS)
Number of subjects with any psychopathology	14 (60.9)	28 (93.3)	34 (81)	7 (17.5)	52.25 (0.001)

CSWS: Continuous spikes and waves during slow sleep. BRE: Benign childhood epilepsy with centrotemporal spikes/rolandic epilepsy. NS: Not significant. ADHD: Attention deficit/hyperactivity disorder. ODD: Oppositional defiant disorder. MR: Mental retardation. EN: Enuresis nocturna. PDD: Pervasive developmental disorder. CD: Conduct disorder.

had statistically higher rates of ADHD and PDD compared to control group ($p<0.05$). Subjects in CSWS group had higher ODD, CD and MR compared to control ($p<0.05$), whereas BRE and absence groups were not different from the control group in terms of ODD, CD and MR ($p>0.05$). Furthermore, the subjects in CSWS group had significantly higher rates of ODD, CD and MR compared to subjects in absence group ($p<0.05$). Any type of psychopathology was observed more in CSWS, BRE and absence groups compared to controls, and total psychopathology was statistically higher in CSWS than in absence group ($p<0.05$). Test results including $\chi 2$ and p values of paired comparisons are presented in Table III.

Comparison of the epileptic groups and the control group in terms of intelligence scores yielded a difference among groups ($p<0.05$). The mean and standard deviations of intelligence scores of subjects with regard to groups are presented in Table IV. Post hoc analysis was used to determine the group or groups which generated this difference. Analysis of the difference in intelligence scores between groups yielded all epileptic groups to have less intelligence scores compared to controls

Table III. Comparison of Groups in Pairs in Terms of Presence of Psychopathology

	CSWS vs Control	BRE vs Control	Absence vs Control	Absence vs CSWS	Absence vs BRE	CSWS vs BRE
Psychopathology	χ^2 (p)	χ^2 (p)	χ^2 (p)	χ^2 (p)	χ^2 (p)	χ^2 (p)
ADHD	20.96 (0.001)	18.95 (0.001)	14.02 (0.001)	0.50 (NS)	0.11 (NS)	0.22 (NS)
ODD	10.58 (0.002)	3.64 (NS)	0.16 (NS)	5.59 (0.039)	1.52 (NS)	2.62 (NS)
MR	15.55 (0.001)	5.07 (NS)	1.76 (NS)	6.65 (0.015)	1.01 (NS)	4.87 (0.027)
PDD	29.72 (0.001)	21.13 (0.001)	11.54 (0.001)	3.72 (NS)	0.75 (NS)	1.71 (NS)
CD	12.04 (0.001)	4.00 (NS)	–	7.22 (0.007)	2.33 (NS)	3.70 (NS)
Subjects with any psychopathology	39.43 (0.001)	32.99 (0.001)	12.36 (0.001)	8.34 (0.004)	3.1 (NS)	2.24 (NS)

CSWS: Continuous spikes and waves during slow sleep. BRE: Benign childhood epilepsy with centrotemporal spikes/rolandic epilepsy. NS: Not significant. ADHD: Attention deficit/hyperactivity disorder. ODD: Oppositional defiant disorder. MR: Mental retardation. PDD: Pervasive developmental disorder. CD: Conduct disorder.

Table IV. Mean and Standard Deviations of Intelligence Scores of Subjects with Regard to Groups

IQ	Absence (n=23) mean±SD	CSWS (n=30) mean±SD	BRE (n=42) mean±SD	Control (n=40) mean±SD	Total (n=40) mean±SD
VIQ	84.04±20.97	67.83±22.77	93.61±15.68	111.12±8.31	91.44±23.04
PIQ	85.30±20.66	71.06±26.35	90.78±14.99	118.40±10.93	93.65±25.20
TIQ	83.86±20.80	68.80±24.42	91.52±14.69	116.07±10.05	92.44±24.50

CSWS: Continuous spikes and waves during slow sleep. BRE: Benign childhood epilepsy with centrotemporal spikes/ rolandic epilepsy. IQ: Intelligence quotient. VIQ: Verbal intelligence quotient. PIQ: Performance intelligence quotient. TIQ: Total intelligence quotient.

($p<0.05$). However, one epileptic group of patients, CSWS, had not only lower intelligence scores compared to healthy controls but also had lower intelligence scores compared to the two other epileptic groups ($p<0.05$) (Table V).

Discussion

To our knowledge, this is the first study which demonstrates psychopathology specifically in CSWS and BRE, two epileptic syndromes activated by sleep, comparing them with absence epilepsy as well as with a group of healthy controls.

In the current study, the rates of psychopathology observed in children with CSWS and BRE were comparable with other studies that investigated psychopathology rates in pediatric cases with different types of epilepsies[5-9]. Compared with the healthy control group, epileptic children had significantly more psychiatric diagnoses. For patients with a newly diagnosed seizure disorder, the time needed by the family and the child to accept this diagnosis may delay psychiatric interventions, which may be necessary at the early stages of the seizure disorder[5,6]. Findings of this study support the higher rates of psychiatric diagnoses in these children and points out the need to investigate these patients in terms of psychopathology.

Within the epilepsy group, although CSWS and BRE patients as well as the absence patients had more psychiatric diagnoses than the healthy controls, CSWS patients had the highest rate of psychopathology and the psychiatric diagnosis rates of these patients were significantly higher than in the absence patients. In addition to this finding, although the IQ scores of epileptic children were lower than of healthy controls, IQ scores of CSWS patients were significantly lower than in the absence epilepsy patients.

Table V. MANCOVA Results for WISC-R IQ and Related Post Hoc (Tukey) Analysis

IQ	Sum of Squares	df	Mean Square	f	sig	Post hoc analysis (Turkey) ($p<0.05$)
VIQ	40834.67	3	13611.56	45.00	.000	CSWS<Absence CSWS< BRE Absence<Control CSWS<Control BRE<Control
PIQ	33657.93	3	11225.31	39.20	.000	CSWS<Absence CSWS< BRE Absence<Control CSWS<Control BRE<Control
TIQ	41749.23	3	13916.41	41.10	.000	CSWS<Absence CSWS< BRE Absence<Control CSWS<Control BRE<Control

CSWS: Continuous spikes and waves during slow sleep. BRE: Benign childhood epilepsy with centrotemporal spikes/ rolandic epilepsy. IQ: Intelligence quotient. VIQ: Verbal intelligence quotient. PIQ: Performance intelligence quotient. TIQ: Total intelligence quotient.

CSWS is known to be a progressing epileptic syndrome leading to cognitive deficits and psychiatric problems[11,12]. Lower IQ in subjects with CSWS compared to controls and subjects with absence epilepsy may be a reflection of the cognitive deterioration observed in these patients. Therefore, all patients with CSWS should be screened for cognitive impairment. Screening for the psychiatric diagnosis, which may lead to early intervention, might decrease not only the deterioration but also the psychiatric morbidity, and will probably increase the life quality and school success of these children.

There were no differences in terms of IQ scores and psychopathology rates between BRE patients and children with absence type of epilepsy. Absence epilepsy has been extensively studied in terms of cognitive measures and psychiatric diagnosis[9,20]. The results of our study suggest that BRE is an epileptic syndrome that leads to psychopathology and cognitive deficits to the same extent as seen in absence epilepsy.

When psychiatric diagnoses were evaluated separately, ADHD was significantly higher in patients with CSWS and BRE than the healthy controls and this result supports the findings that attention problems and hyperactivity may be present in children with these two types of sleep-related epilepsies[11-14]. Even for some of the parents, symptoms related to ADHD may be the presenting complaints that resulted in their seeking help. Therefore, child and adolescent psychiatrists should also be aware of the epileptic syndromes not only for the correct diagnosis of the patients but also for participating in the multidisciplinary approach to these patients. In terms of ADHD, no difference was found between CSWS and BRE patients and the absence epilepsy group. As absence epilepsy has a devastating effect on attention and ADHD is seen more frequently in children with this kind of seizure disorder[24], statistical nonsignificance between the three epilepsy groups in terms of ADHD may be conceptualized as an expected finding.

Conduct disorder (CD) and ODD, which are two disruptive disorders, were significantly higher in CSWS patients than the healthy controls as well as the absence epilepsy group. Aggressiveness, social functioning difficulties and behavioral problems are known to exist in children with CSWS[11,12]. Central nervous system insults of various types can result in higher rates of CD and ODD[25], and as CSWS is the most devastating seizure disorder in our study, it is an expected finding to determine CD and ODD at higher rates in children with CSWS. Another reason for the significantly higher rates of these disorders than in the absence epilepsy patients as well as the controls may result from lower IQ and higher level of cognitive deficits in children with CSWS. Noncompliance and disobedience are known to be common in children with mental retardation and because of the cognitive inability to understand rules, difficulty in comprehending expectations and varying intent and motives might further aggravate or cause these disruptive disorders[26].

Pervasive developmental disorders (PDD) were significantly higher in children with CSWS and BRE than in healthy controls. Epilepsy and PDD comorbidity has been recognized for a long time and autism is stated to be higher in patients with CSWS[11,12]. The present study reveals that both CSWS and BRE may be seen in children with PDD as comorbid seizure disorders.

Although it is known that depression and anxiety disorders were seen more frequently in epileptic children[20], the findings of our study revealed no difference in terms of depression and anxiety disorders between epileptic patients and the healthy controls. It is known that behavioral disturbances may be present before the onset of seizures[5] and our study supports the higher incidence of behavioral disturbances in newly diagnosed patients. Environmental stressors and traumatic experiences as well as the biologic concomitants and genetic predisposition are known to have an etiologic association with depression and anxiety disorders. Especially the onset of depressive disorders often appears associated with adverse or problematic environmental factors[27,28]. The seizure disorder may act as a stressor for the child and lead to the development of depression and anxiety disorders during the disease process, so these children who were diagnosed for the first time should be carefully monitored for depression and anxiety disorders during the follow-up visits.

The higher incidence of psychopathology and cognitive deficits in epileptic patients, especially in those with CSWS, necessitates the

requirement for a multidisciplinary approach to these patients including child neurologist and child and adolescent psychiatrist for the management of the treatment plan. It is clear that those children should be assessed for behavioral problems at the time of the first seizure.

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