Psychopathology in Children with Epilepsy: A Meta-Analysis

Roos Rodenburg,[1] MA, Geert Jan Stams,[1] PhD, Anne Marie Meijer,[1] PhD, Albert P. Aldenkamp,[2,3] PhD, and Maja Deković,[4] PhD

[1]University of Amsterdam, [2]University Hospital Maastricht, [3]Department of Behavioral Sciences, Epilepsy Center Kempenhaeghe, and [4]Utrecht University

Objective To examine the types and severity of psychopathology in children with epilepsy. **Methods** A series of meta-analyses were conducted to review 46 studies, including 2,434 children with epilepsy. **Results** Effect sizes were medium to large for comparisons with children from the general population, which indicates that children with epilepsy are at increased risk for psychopathology, including internalizing and externalizing behavior problems. Comparisons with children with another chronic illness revealed small to medium effect sizes, indicating that psychopathology in children with epilepsy may partly be attributed to chronicity of the disease. Attention problems, thought problems, and social problems proved to be relatively specific to epilepsy. Comparisons with siblings suggested that psychopathology in children with epilepsy may be associated with family factors, especially where behavioral disorders appear to be more generic. **Conclusions** Clinicians should consider both neurological and psychosocial factors, including the family system, when treating psychopathology in children with epilepsy.

Key words behavior problems; childhood epilepsy; family factors; meta-analysis; psychopathology.

Epilepsy is a chronic disorder, characterized by recurrent seizures (Aldenkamp & Mulder, 1998). It is considered to be a heterogeneous condition, resulting from various causes and consisting of different syndromes and different seizure types. The unpredictability and distressing nature of the seizures and social stigma associated with epilepsy are assumed to influence psychosocial development (Aldenkamp & Mulder, 1998; Austin, Shafer, & Deering, 2002; MacLeod & Austin, 2003) and to have a negative impact on quality of life, causing psychopathology (Austin et al., 2002; Ronen, Streiner, & Rosenbaum, 2003). Even adults who had seizures during a limited period in childhood may still experience adverse long-term effects (Sillanpää, Jalava, Kaleva, & Shinnar, 1998).

There is indeed empirical evidence showing that children with epilepsy exhibit more psychopathology than children from the general population. For example, the epidemiological Isle of Wight studies that evaluated a broad range of educational, psychiatric, and physical disorders in school children in relation to behavioral and educational outcomes revealed that 28.6% of the children with uncomplicated epilepsy had psychiatric disturbances compared with 6.6% of the children from the general population (Rutter, Tizard, & Whitmore, 1970; Rutter, Tizard, Yule, Graham, & Whitmore, 1976). Factors common to chronic illnesses — that is, generic factors such as medication regimen, frequent hospitalization, disruption of family life, and limitation of activities (Hamlett, Pellegrini, & Katz, 1992; Kazak, Segal-Andrews, & Johnson, 1995) — rather than epilepsy itself may impede normal developmental processes in children with epilepsy. Other generic features of chronic illness, such as invisibility and unstableness could have

All correspondence concerning this article should be addressed to H.R. Rodenburg, Faculty of Social and Behavioral Sciences, Department of Educational Studies, University of Amsterdam, Wibautstraat 4, 1090 GE Amsterdam, The Netherlands. E-mail: H.R.Rodenburg@uva.nl.

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negative social and psychological consequences for both the child and its family (Jessop & Stein, 1985).

Furthermore, available evidence suggests that children with epilepsy show more psychopathology than children with other chronic illnesses, such as diabetes and asthma (Austin, Smith, Risinger, & McNelis, 1994; Hoare, 1984a). Therefore, the researchers of the present study suggest that psychopathology in children with epilepsy should not be attributed solely to the chronicity of the disease, but that specific epilepsy-related factors, including the underlying brain dysfunction, could also play a role. This is in line with the general finding that children with neurological disorders are at higher risk for psychopathology than children with nonneurological diseases (Breslau, & Marshall, 1985; Lavigne & Faier-Routman, 1992; Rutter, Graham, & Yule, 1970).

The development or maintenance of psychopathology in children with epilepsy may also be influenced by family factors, such as increased parenting stress (Austin, Dunn, Johnson, & Perkins, 2004). Sibling research has shown that children with epilepsy exhibit more psychopathology than their siblings, although siblings themselves are also at increased risk for the development of psychopathology compared to children from the general population (Austin et al., 2002; Austin et al., 2001; Hoare, 1984b). This may be due to unequal attention to the child's needs, differential treatment of siblings or parenting stress (Mims, 1997; Williams, Williams et al., 2002). Hoare (1984b) suggested that chronicity of epilepsy might exert negative effects on family functioning, as he found that siblings of children with chronic epilepsy were at higher risk for psychopathology than siblings of children with newly onset epilepsy.

The burden of epilepsy as a chronic disease may thus generate negative effects on the family, for example, by increasing parenting stress, which may affect parent–child interactive behavior (Kazak et al., 1995). Recent research shows that poor parent–child relationship quality contributes to child behavior problems in families with a child with epilepsy. For instance, parental criticism has been shown to be related to behavioral disturbances and antisocial behavior in children with epilepsy (Hodes, Garralda, Rose, & Schwartz, 1999), whereas Sbarra, Rimm-Kaufman, and Pianta (2002) showed that parental acceptance was associated with lower levels of externalizing behavior problems. Other studies found that psychological control, another dimension of parenting, significantly contributed to internalizing and externalizing behavior problems (Carlton-Ford, Miller, Nealeigh, & Sanchez, 1997; Sbarra et al., 2002). Haber, Austin, Huster, Lane, and Perkins (2003) found that family functioning was associated with depression in children with epilepsy, while Pianta and Lothman (1994), as well as Austin, Risinger, and Beckett (1992) found that family stress contributed to child behavior problems.

Thus, several studies provide evidence for increased levels of psychopathology in children with epilepsy when compared with children from the general population, children with a chronic illness and sibling controls. Although narrative reviews have confirmed the high prevalence of psychopathology in children with epilepsy (Besag, 2002; Dunn, 2003; Kim, 1991; Leonard & George, 1999) and have reported specific psychopathology as being present in children with epilepsy, such as depression (Plioplys, 2003), it is difficult to ascertain which particular problems are most common and how severe these problems are among children with epilepsy. Furthermore, although results from empirical studies indicate that children with epilepsy are at higher risk for psychopathology in comparison with control groups, including children with another chronic illness, or siblings, it remains unclear in which specific domains these differences are largest.

Although global conclusions about psychopathology in children with epilepsy are available, these conclusions tend to be constrained by inconsistent research findings at the level of specific symptomatology. Meta-analysis is a method for combining the numerical results of studies with different research methods and findings. It enables researchers to discover the consistencies in a set of seemingly inconsistent findings, and to draw conclusions that are more accurate than those presented in any of the separate studies (Durlak & Lipsey, 1991). As small effects can be taken into account, due to increased statistical power, and because subjective bias in the interpretation of results is systematically reduced, a more reliable quantitative estimation of behavior problems in children with epilepsy can be achieved.

To date, no meta-analyses of psychopathology in children with epilepsy have been undertaken. Using meta-analysis it becomes possible to examine the following questions. Which types of psychopathology predominate in children with epilepsy? Which types of psychopathology predominate when children with epilepsy are compared to children with another chronic illness? Which types of psychopathology predominate when children with epilepsy are compared to siblings? This study consists of several meta-analyses, comparing children with epilepsy to four different control groups (normative groups, healthy study controls, children with a chronic illness, and siblings) from a multi-informant perspective (parent report, teacher report, and self-report).

The goal of the current meta-analytic study is threefold:

1. To examine the types and severity of psychopathology in children with epilepsy, by comparing children with epilepsy to children from the general population, that is, normative groups and healthy study controls.
2. To examine differences in specific symptomatology between children with epilepsy and children with another chronic illness, by comparing children with epilepsy to children with other chronic diseases, such as asthma and diabetes. If effect sizes (i.e., the magnitude of differences between groups) for comparisons with children with a chronic illness are considerably smaller than effect sizes for comparisons with normative and healthy controls, this could indicate that psychopathology in children with epilepsy is at least partly inherent to epilepsy as a chronic disease.
3. To examine differences in specific symptomatology between children with epilepsy and their siblings. If effect sizes for differences with siblings are small compared to effect sizes for differences with normative and healthy controls, this could indicate that siblings are also at increased risk for psychopathology (Austin et al., 2001; Austin et al., 2002; Hoare, 1984b), and that family factors may be associated with psychopathology in children with epilepsy (Hoare, 1984b).

Method

Selection of Studies

A literature search was carried out, inspecting the childhood epilepsy literature that was published between 1970 (since The Isle of Wight study) and 2003. First, the researchers searched for studies with computerized databases including PsycINFO, MEDLINE, ERIC, and the Social Sciences Citation Index (SSCI). The databases were explored with a wide range of keywords given in different combinations: behavior, behavior problems, internalizing problems, externalizing problems, psychopathology, adjustment, epilepsy, children, adolescents, behav*, epilep*, child*, and problem*. (An asterisk indicates that the search was not limited to the particular word or fragment.)

Second, the ancestry method was used to find more studies on psychopathology in reviews and articles reporting on empirical studies, that is, reference sections of articles were inspected for relevant studies that had not yet been detected. When there was doubt about the relevance of these articles, they were visually inspected. The criteria for inclusion in the meta-analyses studies were

1. Studies had to include children with epilepsy between 4 and 21 years of age without severe mental retardation. Empirical research on epilepsy in children with mental retardation from an epidemiological point of view is sparse (Caplan & Austin, 2000; Steffenburg, Gillberg, & Steffenburg, 1996), probably because it is too difficult to find adequate comparison groups. Inclusion of children with mental retardation in the study would hamper the interpretations of results, as it is not possible to separate the effects of mental retardation from the effects of epilepsy if no adequate comparison groups or normative data are available.
2. Studies had to measure broadband behavior problems (e.g., internalizing and externalizing problems), narrowband behavior problems (e.g., depression or aggressive behavior), or both (Achenbach & Edelbrock, 1983).
3. Effect sizes were calculated based on ratings of the primary caregivers, teachers, or children themselves.
4. Studies had to include information enabling the calculation of effect sizes through comparison with a normative control group, healthy study controls, children with a chronic illness, or siblings.
5. Samples had to be statistically independent. When studies were identified as being statistically dependent, the oldest, original study was included in the analysis.

Authors were contacted if their data did not provide enough statistical information for the calculation of effect sizes, or if there were doubts about dependent samples from multiple studies that were conducted by the same research groups.

The literature search resulted in 46 studies (Table I) that met the inclusion criteria. Initially, 62 studies were identified that addressed psychopathology in children with epilepsy. However, 16 studies were excluded as samples were statistically dependent, or because it was not possible to derive statistical data relevant for the calculation of effect sizes (the authors could not be reached or they did not have access to their original data sets). Effect sizes were calculated for parent report, teacher

Table I. Study Characteristics of the Studies Included in the Meta-Analyses

Study	Year	Number of epilepsy	Number of control group	% Male	Age	Instrument used for analyses	Type of control group
Austin	1988	54	57	43	10.7	CBCL/TRF	Asthma
Austin et al.	1992	127	—	50	10.5	CBCL	—
Austin and Huberty	1993	136	133	52	10.4	CBCL	Asthma
Austin et al.	1994	136	134	52	10.5	CBCL/TRF	Asthma
Austin et al.	1996	117	111	52	14.5	CBCL/TRF/PH	Asthma
Austin et al.	2001	224	135	49	8.8	CBCL	Siblings
Apter et al.	1991	26	90/26	54	14.9	CBCL	Healthy/asthma
Bailet and Turk	2000	74	23/13	46	9.6	CBCL/TRF	Siblings/migraine
Brent et al.	1987	39	—	—	11.8	CBCL/CDI	—
Buelow et al.	2003	164	—	51	11.8	CBCL/CDI	—
Dorenbaum et al.	1985	38	—	47	10.3	CBCL	—
Dunn et al.	1997	42	—	45	8.4	CBCL	—
Dunn et al.	1999	115	—	52	14.4	YSR	—
Dunn et al.	2002	192	65	47	8.4	TRF	Asthma
Epir et al.	1984	15	15/12	—	10.0	CTRS	Healthy/siblings
Ettinger et al.	1998	44	—	55	12.4	CDI	—
Hermann et al.	1981	56	—	52	6–16	CBCL	—
Hernandez et al.	2003	32	—	63	11.6	CBCL	—
Hoare	1984a	58	58/65	48	9.1	RS-P/T	Healthy/diabetes
Hoare	1984b	58	46	48	9.1	RS-P/T	Siblings
Hoare and Kerley	1991	108	78	55	10.4	RS-P/T/PH	Siblings
Hoare and Mann	1994	62	91	62	11.8	CBCL	Diabetes
Hodes et al.	1999	22	16	59	11.9	RS-P/T/BS	Siblings
Huberty et al.	2000	121	—	51	14.4	CBCL	—
Kölfen et al.	2001	76	37	—	6–15	CBCL	Healthy
Korneluk et al.	2003	13	—	53	11.0	CBCL	—
Lendt et al.	2000	28	—	50	11.5	CBCL	—
Long and Moore	1979	19	19	47	8.6	RS-P/T	Siblings
Matthews and Barabas	1982	15	15	47	9.8	PH	Healthy/diabetes
McCusker et al.	2002	48	—	65	7.1	CBCL	—
McDermott et al.	1995	121	3,950/285	—	11.9	BPI	Healthy/cardiac
Mitchell et al.	1994	88	—	43	7.7	CBCL	—
Nicholas and Pianta	1994	59	—	51	9.7	CBCL	—
Oğuz et al.	2002	35	35	—	12.9	CDI	Healthy
Oostrom et al.	2003	69	66	—	9.2	CBCL/TRF	Healthy
Ott et al.	2001	88	59	44	5–16	CBCL	Healthy
Pulsifer et al.	2001	65	—	55	5.4	CBCL	—
Sabaz et al.	2001	94	—	49	11.4	CBCL	—
Sbarra et al.	2002	29	—	45	16.9	CBCL/YSR	—
Schoenfeld et al.	1999	57	27	33	10.8	CBCL	Siblings
Stores et al.	1978	71	35	50	11.0	TRIS	Healthy
Weglage et al.	1997	40	40	58	8.4	CBCL	Healthy
Williams and Sharp	1996	84	—	50	10.1	CBCL	—
Williams et al.	1998	37	26	59	10.9	CBCL	Diabetes
Williams et al.	2002	42	—	48	10.4	ADDES-HV	—
Williams et al.	2003	101	—	53	11.3	RCMAS	—

ADDES-HV, Attention Deficit Disorders Evaluation Scale-Home Version (McCarney, 1995); BPI, Behavior Profile Inventory (Adams & Hardy, 1988); BS, Birleson Depression Scale (Birleson, 1981); CBCL, Child Behavior Checklist (Achenbach & Edelbrock, 1983; Achenbach, 1991a); CDI, Child Depression Inventory (Kovacs, 1981); CTRS, Conners Teacher Rating Scale (Conners, 1969); PH, Piers Harris Self-Concept Scale (Piers, 1984); RCMAS, Revised Children's Manifest Anxiety Scale (Reynolds & Richmond, 1985); RS-P/T, Rutter Behavioural Scales, Parent/Teacher Form (Rutter et al., 1970); TRF, Teacher Report Form (Achenbach, 1991b); TRIS, Teacher's Rating of Inattentiveness at School (Stores et al., 1978); and YSR, Youth Self-Report (Achenbach, 1991c).

report, and self-report. Children with epilepsy were compared with:

1. normative controls, which means that the calculation of effect sizes was based on available published normative data [for instance, norms of the Child Behavior Checklist (CBCL)],
2. healthy study controls, who are children included in the studies resembling children from the general population,
3. children with a chronic illness (asthma, diabetes, cardiac disease, and migraine), and
4. siblings.

None of the studies relying on self-report examined comparisons with healthy study controls, children with a chronic illness, or sibling controls (except for self-report of depression). When multiple effect sizes were calculated for subsamples within the same study (e.g., different age groups or boys and girls) average effect sizes were computed and subsequently reported.

Measurements of Psychopathology

Most studies reported findings obtained with the CBCL, the Teacher Report Form (TRF), or the Youth Self-Report (YSR) (Achenbach, 1991a, 1991b, 1991c; Achenbach & Edelbrock, 1983). These instruments assess total behavior problems, internalizing problems and externalizing problems (broadband scales). The CBCL, TRF, and YSR also contain eight narrowband scales: anxiety/depression, withdrawal, somatic complaints, aggression, delinquent behavior, attention problems, thought problems, and social problems. Some studies reported on psychopathology using the Parental and Teacher Rutter Behavioral Scales (Rutter et al., 1970), the Piers-Harris Self-Concept Scale (Piers, 1984), the Child Depression Inventory (CDI) (Kovacs, 1981), the Birleson Depression Scale (BS) (Birleson, 1981), the Revised Children's Manifest Anxiety Scale (RCMAS) (Reynolds & Richmond, 1985), the Conners Teacher Rating Scale (CTRS) (Conners, 1969), the Behavior Profile Inventory (BPI) (Adams & Hardy, 1988), and the Teacher's Rating of Inattentiveness at School (TRIS) (Stores, Hart, & Piran, 1978).

Calculation and Analysis of Effect Sizes

The calculation of effect sizes for comparisons with normative controls was based on the means and standard deviations (continuous data) provided by the individual studies. These means and standard deviations were mostly reported as t-scores, that is, standardized scores on the CBCL, TRF, and YSR, which are transformations of continuous data to scores corrected for age and gender (Verhulst, van der Ende, & Koot, 1996, 1997). The reported t-scores (CBCL, TRF, and YSR) were compared to the normative T-score of 50 (SD = 10) using one-sample t tests. If only percentages of children scoring above the clinical cutoff were reported, z values were calculated (categorical results). The percentages of children scoring above the clinical cutoff criterion were then compared with percentages found in the normative population: 10% for the broadband scales and 2% for the narrowband scales (Verhulst et al., 1996, 1997). The calculated z values and t values were transformed into the effect size statistic Cohen's d. Combined mean effect sizes were calculated for continuous and categorical results together.

The calculation of effect sizes for studies using *control* groups — healthy study controls, children with a chronic illness, and siblings — was based on reported test statistics (p, t, or χ^2 values), which were transformed into Cohen's d, or on the basis of reported means and standard deviations of behavior problems. If studies reported t-scores (CBCL, TRF, and YSR), the t-scores of both groups (children with epilepsy and the control group) were used for the calculation of t values by means of the two-sample t test. In case of reported means and standard deviations, t values were also calculated with the two-sample t test. The calculated t values were subsequently transformed into Cohen's d. Effect sizes were only calculated for reports of pretest data; posttest data were not taken into account. For studies reporting nonsignificant findings, effect sizes of $d = 0.00$ were inserted, based on a one-tailed p of .50 ($z = 0.00$). Although this is a conservative procedure, leading to an underestimation of effect sizes, excluding nonsignificant results from the meta-analyses leads to an overestimation of effect sizes (Rosenthal, 1995).

The computation of effect sizes for normative control children resulted in 32 combined mean effect sizes based on 276 calculated effect sizes across all studies (broadband behavior problems and narrowband behavior problems for parent report, teacher report, and self-report). The calculation of effect sizes for healthy study controls resulted in 14 combined mean effect sizes, based on 36 calculated effect sizes across all studies (parent report only). For comparisons with children with a chronic illness, 23 combined mean effect sizes were calculated, based on 68 calculated effect sizes across all studies. Sibling comparisons resulted in 15 combined mean effect sizes that were based on 36 calculated effect sizes across all studies. Combined mean effect sizes were computed with Mullen's (1989) Advanced BASIC

Meta-Analysis computer program. Additionally, 95% confidence intervals were computed for each combined mean effect size. According to generally accepted conventions, effect sizes of $d = 0.20$, $d = 0.50$, and $d = 0.80$ were considered as indices of small, medium, and large group differences (Cohen, 1988), whereas effect sizes of $d = 0.00$ indicated that there was no difference between the groups. A positive effect size would indicate that children with epilepsy experience more psychopathology, whereas a negative effect size would indicate that controls have higher levels of psychopathology.

In the statistical analyses, Durlak and Lipsey's (1991) recommendation of sample size weighting was followed; resulting in weighted standardized mean effect sizes. By sample size weighting, studies with large sample sizes exert a greater influence on the combined mean effect size, which is appropriate because studies with large sample sizes are assumed to be statistically more reliable than studies with small sample sizes. This is an adequate procedure in case effect sizes are homogeneous, that is, when effect sizes only differ because of sampling error. One of the disadvantages of sample size weighting is that when sample sizes are characterized by great disparity, studies with extreme large sample sizes will predominate in the weighted analysis (Lipsey & Wilson, 2001, p. 314). Studies with large sample sizes often rely on epidemiological survey methods and may, as a result, have less rigorous medical inclusion criteria. In the meta-analyses, one epidemiological study had an extremely large sample of healthy control children ($N = 3{,}950$) (McDermott, Mani, & Krishnaswami, 1995). To correct for this disproportionate large sample size, analyses for this particular study were based on the windsorized number ($N = 285$), that is, the next highest sample size in the meta-analysis (Hampel, Ronchetti, Rousseeuw, & Stahel, 1986).

Outlying effect sizes were identified on the basis of z values larger than 3.3 or smaller than –3.3 (Tabachnick, & Fidell, 2001). Homogeneity analyses were conducted at $p < .05$ to examine whether samples of studies were homogeneous, that is, to what extent effect sizes were constant across studies. In case of heterogeneity there are differences among effect sizes that have some source other than subject-level sampling error. These differences may be associated with different study characteristics (Lipsey & Wilson, 2001, pp. 115–119).

Disjoint cluster analysis was used to explain heterogeneity of combined mean effect sizes. By way of disjoint cluster analysis, it is possible to examine similarities within clusters, and differences between clusters of effect sizes by identifying clusters that are significantly different from each other (Mullen, 1989). The next step is then to understand the source of these differences and commonalities. For example, if a cluster with relatively large effect size is identified, this may be attributed to particular seizure types.

File Drawer Analysis

A common problem in meta-analysis is that unpublished studies often lie unused in file drawers because of nonsignificant findings, whereas published studies are more likely to have achieved statistical significance (Rosenthal, 1995). Thus, the studies included in any meta-analysis do not form a random sample of all studies carried out on the subject. To inspect whether such possible publication bias exists, one can calculate the fail-safe number that indicates the minimum number of additional studies with nonsignificant results that is needed to decrease significant meta-analytic results to nonsignificance (Durlak & Lipsey, 1991). Meta-analytic findings are considered to be robust if the fail-safe number exceeds the critical value obtained with Rosenthal's (1995) formula of $5 \times k + 10$; k is the number of studies included in the meta-analysis.

Results

The 46 studies included in the meta-analyses reported data on 2,434 children with epilepsy, ranging from 13 from Korneluk, Kuehn, Keene, and Ventureyra (2003) to 224 from Austin et al. (2001), 1,180 healthy children, 762 children with a chronic illness, and 356 sibling controls. The average sample size for children with epilepsy was 65. The mean age of the children included in the meta-analyses was 10 years of age, ranging from 4 to 21 years of age. In 22 out of 46 studies, boys were over represented (50% or more). A detailed list of studies is provided in Table I.

Preliminary Analyses

The researchers conducted homogeneity analyses ($p < .05$) of combined mean effect sizes for parent report, teacher report, and self-report. Almost all samples of studies comparing children with epilepsy with study controls (healthy controls, children with a chronic illness, and siblings) proved to be homogeneous. Homogeneity analysis of combined mean effect sizes for comparisons with normative controls revealed heterogeneity for parent report, but not for teacher report and self-report. In case of parent report, disjoint cluster analyses ($p < .05$) for normative comparisons showed that studies containing high percentages of children with intractable epilepsy

had relatively large effect sizes for attention problems and thought problems (McCusker, Kennedy, Anderson, Hicks, & Hanrahan, 2002; Sabaz, Cairns, Lawson, Bleasel, & Bye, 2001). For example, the combined mean effect size was large for children with intractable epilepsy in the study that was carried out by McCusker et al. (d = 9.64). The researchers also found relatively large effect sizes for social problems, withdrawn behavior, and somatic complaints in the study by McCusker et al. Deletion of that study from the meta-analyses resulted in slightly smaller combined mean effect sizes (e.g., attention problems decreased from d = 2.49 to d = 2.31), but did not result in homogeneity. As heterogeneity remained after deletion of those studies that had been identified with disjoint cluster analysis, and because the magnitude of combined mean effect sizes was only slightly affected by removal of these studies, the researchers chose to report on the full set of studies.

For normative comparisons of broadband and narrowband behavior problems (parent report and teacher report), externalizing problems and somatic complaints (parent report), and total problems and attention problems (teacher report), the calculated fail-safe numbers exceeded Rosenthal's (1995) critical value ($k \times 5 + 10$), which indicated that the number of studies with nonsignificant results (tucked away in file drawers) that would be required to reduce significant results to nonsignificance was sufficient, indicating no publication bias. Most fail-safe numbers were extremely large. For instance, in case of normative controls, parent report of internalizing problems revealed a fail-safe number of 2,458 (k = 17), which exceeds Rosenthal's critical value of $17 \times 5 + 10 = 95$.

The researchers did, however, encounter possible publication bias for self-report, with the exception of depression. Fail-safe numbers calculated for study control groups (parent report) indicated possible publication bias for the whole range of problems, except for total behavior problems and attention problems. For example, in case of healthy control children, parent report of internalizing problems revealed a fail-safe number of 3.39 (k = 3). The critical value was $3 \times 5 + 10 = 25$, which indicates that the fail-safe number falls below the critical value. In case of teacher report and self-report, fail-safe numbers indicated possible publication bias for all scales, and with respect to all study control groups.

The Type and Severity of Psychopathology: Comparisons with Normative Controls

Data were available for parent report, teacher report, and self-report (Table II). Effect sizes were not calculated for total behavior problems on the basis of self-report, as data could not be obtained. Effect sizes for differences between children with epilepsy and normative controls were consistently large for the whole range of psychopathology. Meta-analyses of total behavior problems revealed large effect sizes for both parent report and teacher report: d = 1.39 ($p < .001$) and d = 0.75 ($p < .001$).

The researchers found larger effect sizes for comparisons between children with epilepsy and normative controls on internalizing problems than on externalizing problems. Effect sizes for internalizing problems were d = 1.27 ($p < .001$) for parent report, d = 1.38 ($p < .001$) for teacher report, and d = 0.83 ($p < .001$) for self-report. Effect sizes for externalizing problems were d = 0.81 ($p < .001$) for parent report, d = 0.80 ($p < .001$) for teacher report, and d = 0.35 ($p < .05$) for self-report.

Meta-analyses of the narrowband scales revealed that attention problems and somatic complaints were

Table II. Effect Sizes For Children with Epilepsy Compared with Normative Controls: Parent Report, Teacher Report, and Self-Report

	Parent report				Teacher report				Self-report			
Psychopathology	*k*	*n*	*d*	95% CI	*k*	*n*	*d*	95% CI	*k*	*n*	*d*	95% CI
Total problems	15	1,248	1.39***	1.02–1.76	2	258	0.75***	–0.25–1.75	—	—	—	—
Internalizing	17	1,294	1.27***	0.92–1.62	4	410	1.38***	0.67–2.09	2	149	0.83***	–0.69–2.35
Externalizing	17	1,294	0.81***	0.46–1.16	4	410	0.80***	0.10–1.50	2	149	0.35*	–0.67–2.37
Withdrawn	14	1,025	1.83***	1.35–2.31	3	213	1.71***	0.85–2.57	2	149	1.58***	0.49–2.67
Somatic complaints	15	1,113	2.38***	1.86–2.90	3	213	1.51***	0.65–2.37	2	149	2.33***	0.24–4.42
Anxious/depressed	15	1,098	1.90***	1.54–2.26	3	213	1.67***	0.82–2.52	8	569	0.82***	0.05–1.59
Social problems	15	1,066	2.10***	1.66–2.55	4	330	1.84***	1.09–2.59	1	120	1.51***	0.08–2.94
Thought problems	16	1,095	1.93***	1.44–2.42	4	330	1.30***	0.58–2.02	2	149	1.67***	0.61–2.73
Attention problems	16	1,109	2.49***	1.51–3.47	4	330	1.82***	1.08–2.56	2	149	1.61***	–0.19–3.41
Delinquency	14	1,025	1.44***	1.05–1.83	3	213	1.55***	0.69–2.41	2	149	1.51***	0.34–2.68
Aggression	15	1,081	1.70***	1.32–2.08	3	213	1.55***	0.69–2.41	2	149	1.38***	0.35–2.41

*$p < .05$. ***$p < .001$. (Self-report, for externalizing behavior problems a d of .35* is reported.)

rated largest by parents, namely, $d = 2.49$ ($p < .001$) and $d = 2.38$ ($p < .001$), which is about 0.40 larger than the combined mean effect size for the narrowband scales ($d = 1.97$). Somatic complaints were rated largest by children with epilepsy themselves, $d = 2.33$ ($p < .001$), which is 0.80 larger than the combined mean effect size for the narrowband scales ($d = 1.55$). Notably, depression (self-report) was rated relatively small, $d = 0.82$ ($p < .001$), which is 0.73 smaller than the mean effect size for the narrowband scales. For teacher report, the differences between effect sizes were less pronounced, that is, more uniform across problem domains.

The Type and Severity of Psychopathology: Comparisons with Healthy Study Controls

Meta-analyses of total behavior problems (Table III) showed that effect sizes for differences between children with epilepsy and healthy study controls were medium, $d = 0.57$ ($p < .001$) for parent report and $d = 0.61$ ($p < .001$) for teacher report. Effect sizes for comparisons with healthy controls (parent report only) were small, $d = 0.23$ ($p < .01$) for internalizing problems and medium, $d = 0.45$ ($p < .001$) for externalizing problems.

Meta-analyses of the narrowband scales (parent report only) revealed that attention problems had the largest effect size: $d = 0.72$ ($p < .001$), which is about 0.30 larger than the mean effect size for the narrowband scales ($d = 0.43$).

The Type and Severity of Psychopathology: Comparisons with Children with a Chronic Illness

The researchers examined which types of psychopathology were most prevalent when children with epilepsy were compared to children with another chronic illness, which may be an indication whether psychopathology is more generic to chronic illness or specific to epilepsy. Effect sizes for differences between children with epilepsy and children from the general population (normative groups and healthy study controls) were compared to children with a chronic illness (see Table III). Effect sizes for differences between children with epilepsy and children with a chronic illness were available for parent report, teacher report and self-report (depression only).

Inspection of effect sizes showed that the magnitude of effect sizes decreased from large effect sizes for comparisons with normative controls, and small to medium effect sizes for comparisons with healthy study controls to small effect sizes for comparisons with children with a chronic illness. Thus, effect sizes for comparisons with children with a chronic illness were generally considerably smaller when compared with children from the general population, indicating that psychopathology in children with epilepsy is at least partially a consequence of the generic effects of a chronic disease, rather than specific to epilepsy. A deviation from this pattern was found for social problems, thought problems, and attention problems. Attention problems ($d = 0.46$, $p < .001$),

Table III. Effect Sizes for Children with Epilepsy Compared with Healthy Controls, Children with a Chronic Illness and Siblings: Parent Report and Teacher Report

	Healthy study controls[a]				Children with a chronic illness[b]								Siblings[c]			
	Parent report				Parent report				Teacher report				Parent report			
Psychopathology	*k*	*n*	*d*	95% CI	*k*	*n*	*d*	95% CI	*k*	*n*	*d*	95% CI	*k*	*n*	*d*	95% CI
Total problems	8	1,604	0.57***	0.45–0.69	6	1,114	0.31***	0.16–0.46	3	323	0.20	–0.21–0.61	7	799	0.49***	0.17–0.81
Internalizing	3	472	0.23**	–0.16–0.62	5	625	0.17**	–0.06–0.43	3	563	0.17*	–0.23–0.57	3	534	0.42***	0.10–0.74
Externalizing	3	472	0.45***	0.23–0.67	5	625	0.20**	–0.01–0.41	3	563	0.12	–0.21–0.45	3	534	0.08	–0.04–0.60
Withdrawn	3	196	0.32*	–0.21–0.85	3	268	0.14	–0.35–0.63	1	206	–0.01	–0.27–0.31	2	443	0.04	–0.53–0.61
Somatic complaints	3	196	0.38**	–0.28–1.04	3	268	0.19	–0.39–0.77	1	206	–0.05	–0.35–0.25	2	443	0.46***	0.18–0.74
Anxious/depressed	3	855	0.42***	0.14–0.70	6	1,025	0.19**	0.06–0.26	1	206	–0.02	–0.32–0.28	3	467	–0.06	–0.62–0.50
Social problems	1	80	0.37*	–0.08–0.82	3	444	0.40***	0.21–0.59	2	434	0.23**	–0.36–0.80	2	443	0.34**	0.03–0.65
Thought problems	3	196	0.47***	0.15–0.79	4	496	0.37***	0.19–0.55	2	434	0.13	–0.15–0.40	2	443	0.38***	0.00–0.76
Attention problems	3	1,016	0.72***	0.25–1.19	5	902	0.46***	0.32–0.50	2	434	0.26**	–0.25–0.77	3	457	0.49***	0.08–0.90
Delinquency	3	196	0.38**	0.07–0.69	3	268	0.11	–0.22–0.43	1	206	–0.05	–0.35–0.25	2	443	–0.06	–0.14–0.02
Aggression	3	1,016	0.38***	0.06–0.70	4	674	0.20***	–0.13–0.53	1	206	–0.20	–0.50–0.10	3	461	–0.01	–0.58–0.56

[a]Effect sizes could not be calculated for teacher report, except for total behavior problems ($d = 0.61$, $p < .001$) and attention problems ($d = 0.28$, $p < .001$); and self-report, except for depression ($d = 0.87$, $p < .001$).

[b]Effect sizes could not be calculated for self-report, except for depression ($d = 0.27$, $p < .05$).

[c]Effect sizes could not be calculated for teacher report, except for total behavior problems ($d = 0.35$, $p < .01$), internalizing problems ($d = 0.43$, $p < .05$), and externalizing problems ($d = 0.48$, $p < .01$); and self-report, except for depression ($d = 0.36$, *ns*).

*$p < .05$. **$p < .01$. ***$p < .001$

thought problems (d = 0.37, p < .001), and social problems (d = 0.40, p < .001) had larger effect sizes than withdrawal (d = 0.14, *ns*), somatic complaints (d = 0.19, *ns*), depression (d = 0.19, p < .01), delinquency (d = 0.11, *ns*), and aggression (d = 0.20, p < .01), which indicates that attention problems, thought problems, and social problems could be considered to be relatively specific to epilepsy. For teacher report, results were less clear, as all effect sizes proved to be small or nonsignificant. The only significant effect sizes were found for attention problems (d = 0.26, p < .01) and social problems (d = 0.23, p < .01).

The Type and Severity of Psychopathology: Comparisons with Siblings

The researchers investigated in which areas of psychopathology children with epilepsy differed from siblings. Effect sizes for differences between children with epilepsy and children from the general population (normative groups and healthy study controls) were compared with effect sizes for differences between children with epilepsy and their siblings (see Table III). Effect sizes were available for parent report, teacher report (broadband scales only), and self-report (depression only).

The meta-analyses revealed that effect sizes for comparisons with siblings were considerably smaller than effect sizes for comparisons with children from normative groups (both parent report and teacher report). Differences in the magnitude of effect sizes may point to the influence of family factors. The substantial decrease in effect sizes was less evident for comparisons involving healthy study controls (parent report only). The largest decrease in effect sizes was found for externalizing problems (aggressive and delinquent behavior), withdrawal, and depression. Meta-analyses of comparisons with siblings (parent report only) revealed that withdrawal (d = 0.04, *ns*), depression (d = −.06, *ns*), delinquency (d = -.06, *ns*), and aggression (d = −.01, *ns*) had extremely small effect sizes, which may indicate relatively strong involvement of family factors. Only few syndromes revealed small to medium and significant effect sizes: attention problems (d = 0.49, p < .001), thought problems (d = 0.38, p < .001), social problems (d = 0.34, p < .01), and somatic complaints (d = 0.46, p < .001). These larger effect sizes may indicate that attention problems, thought problems, social problems, and somatic complaints are less strongly associated with family factors.

Discussion

The aim of this study was to conduct meta-analyses of studies that reported on psychopathology in children with epilepsy in comparison with children from the general population (normative groups and healthy study controls), children with a chronic illness, and siblings to achieve quantitative evidence for the different types and severity of psychopathology in children with epilepsy. In addition, the researchers analyzed whether psychopathology should be considered generic, that is, common to chronic diseases, or specific to epilepsy. Moreover, the researchers examined whether family factors (for instance, family stress or inadequate child rearing practices) could be associated with psychopathology.

The first goal of the study was to examine the severity of psychopathology in children with epilepsy. Meta-analyses of studies comparing children with epilepsy with children from the general population revealed medium to large effect sizes for parent report, teacher report, and self-report, which confirms that children with epilepsy are at high risk for developing psychopathology. This conclusion holds for the whole range of psychopathology, including attention problems, thought problems, and social problems, as well as internalizing and externalizing behavior. When compared with children from normative groups, effect sizes were larger for internalizing than for externalizing behavior problems. This was true for parent report, teacher report, and self-report. A similar pattern has been found for children with other chronic diseases, such as asthma (McQuaid, Kopel, & Nassau, 2001), chronic arthritis (LeBovidge, Lavigne, Donenberg, & Miller, 2003), and for children with a chronic illness in general (Lavigne & Faier-Routman, 1992).

Internalizing problems have been investigated frequently in children with epilepsy, with a special focus on depression and anxiety (Alwash, Hussein, & Matloub, 2000; Dunn, Austin, & Huster, 1999; Oğuz, Kurul, & Dirik, 2002; Williams et al., 2003). Although effect sizes for internalizing problems were larger than for externalizing problems, effect sizes for externalizing problems were still large for parent report and teacher report, indicating that externalizing problems are also frequently present in children with epilepsy. Self-report data, however, showed a small to medium effect size (d = 0.35), which could indicate that children with epilepsy are more accurate reporters of internalizing problems than of externalizing problems (Card, 2001).

Problems that had extremely large effect sizes were attention problems and somatic complaints (parent report and self-report). Especially children with newly diagnosed epilepsy have been shown to be at increased risk for inattentiveness and hyperactivity (Williams, Lange et al., 2002). Davies, Heyman, and Goodman (2003) found that 12% of the children with uncomplicated epilepsy

had attention-deficit/hyperactivity disorder (AD/HD) according to the DSM-IV (Diagnostic and Statistical Manual of Mental Disorders–fourth edition). Dunn, Austin, Harezlak, and Ambrosius (2003) found that 25% of the adolescents with epilepsy and 37% of the children with epilepsy had scores above the clinical cutoff on the attention scale of the CBCL. Research on somatic complaints appears to be underrepresented in the literature. One study showed that 10% of the children with epilepsy had additional health complaints other than neurological impairments (Kurtz, Tookey, & Ross, 1998).

Effect sizes for comparisons with healthy study controls were found to be small to medium, whereas effect sizes for comparisons with normative controls proved to be consistently large (parent report only). A possible explanation is that healthy study controls form a rather heterogeneous group drawn from the general population, consisting of children with psychopathology, not seldom clinically referred, and without psychopathology. In contrast, normative controls constitute homogeneous groups of children who have not been clinically referred for psychopathology (Achenbach, 1991a). An even more compelling explanation for small-to-medium effect sizes for comparisons with "healthy" study controls could be that these effect sizes are less reliable, as they are based on relatively small sample sizes and less adequate recruitment of control groups (e.g., Bailet & Turk, 2000).

To summarize, children with epilepsy are at increased risk for the whole range of psychopathology, with somatic complaints and attention problems being the most salient symptoms. This general finding should be qualified to the extent that children with epilepsy appear to experience more internalizing than externalizing behavior problems.

The second goal of this study was to examine in which areas of psychopathology children with epilepsy differed from children with another chronic illness, indicating whether psychopathology in children with epilepsy should be considered as more generic to chronic illness or specific to epilepsy. The meta-analyses showed that effect sizes for differences with children with a chronic illness were considerably smaller than effect sizes for comparisons with children from the general population. From this, it can be derived that psychopathology in children with epilepsy may partly be interpreted to be associated with generic factors associated with children with chronic illnesses. Withdrawn behavior, somatic complaints, depression, delinquent behavior, and aggressive behavior may be considered as relatively generic, as effect sizes for these problems proved to be small and/or nonsignificant. Attention problems, social problems and thought problems were shown to have the largest effect sizes, which indicates that these kinds of problems may be relatively specific to children with epilepsy in contrast to children with other chronic illnesses.

Thus, psychopathology in children with epilepsy seems partly attributable to epilepsy having an effect as a chronic condition. Findings that children with recurrent seizures have higher levels of behavior problems than children with newly onset seizures support this conclusion (Austin et al., 2001; Nicholas & Pianta, 1994). The analyses, however, do not reveal which particular generic factors may be associated with psychopathology in children with epilepsy. A limitation of the current meta-analytic study is that children with epilepsy could only be compared to children that were not neurologically impaired, that is, children with asthma and diabetes. As such, the researchers have not been able to identify unique aspects of epilepsy relative to other neurologically impairing chronic illnesses.

The third goal of this study was to compare children with epilepsy with their siblings. The analyses revealed that effect sizes were considerably smaller for comparisons with siblings than for comparisons with children from the general population. This could indicate that family factors are associated with psychopathology in children with epilepsy. Several studies found that siblings of children with epilepsy, but also siblings of children with other chronic illnesses, were at higher risk for psychopathology (Austin et al., 2001; Hoare, 1984b; Sharpe & Rossiter, 2002). It is possible that family factors directly cause psychopathology in children with epilepsy, or contribute to the maintenance of problems once they have occurred. Childhood chronic illness, such as epilepsy, may also cause disturbances in family processes that, in turn, could affect the adjustment of siblings. It should be admitted that the analyses provide indirect support for the role of family factors. Given the correlational nature of the evidence, it is impossible to derive the exact direction of effects. Moreover, parents may be biased towards reporting similar behaviors across siblings so as not to emphasize behavioral difficulties in any one particular child.

Except for somatic complaints, relatively smaller effect sizes for comparisons with siblings were most prominent in behavior problems that were identified as generic to chronic illness, namely, externalizing behavior, withdrawal, and depression. Therefore, the researchers suggest that family factors may be related more strongly to behavior problems that are relatively common to chronic diseases. In contrast, the results

suggested that family factors may play a minor role in the contribution to behavior problems that are more specific to epilepsy, namely, attention problems, thought problems, and social problems.

A number of studies examined children with previously unrecognized seizures and found higher levels of psychopathology (Austin et al., 2001; Dunn, Austin, & Huster, 1997; Dunn, Harezlak, Ambrosius, Austin, & Hale, 2002). It was concluded that neurological dysfunction causes both behavior problems and seizures. This does not exclude the possibility, however, that additional risk factors contribute to behavior problems in children with enduring epilepsy. The study findings suggest that especially children with uncontrollable seizures are at risk for the development of behavior problems, since the researchers found relatively large effect sizes for studies that included children with intractable epilepsy. Problems inherent to chronic diseases — such as unpredictability, distress, medication regimen, social stigma, and family stress — may arise in children with longer lasting epilepsy apart from neurological dysfunction.

The current series of meta-analyses have been conducted on the basis of parent report, teacher report and self-report. In general, effect sizes were slightly smaller for teacher report and self-report than for parent report. Relatively large effect sizes for parent report in comparison with teacher report might indicate that children with epilepsy show more psychopathology at home. As such, this could provide additional evidence for the involvement of family factors, such as increased family stress. These larger effect sizes could also indicate that parents are relatively sensitive to their children's behavior problems (Huberty, Austin, Harezlak, Dunn, & Ambrosius, 2000). Smaller effect sizes for self-report may indicate that children with epilepsy underestimate their behavior problems, especially with respect to externalizing behavior, presenting themselves as healthy functioning individuals (Huberty et al., 2000; Sbarra et al., 2002).

Three limitations of this study should be mentioned. A first limitation is that meta-analyses for comparisons with healthy study controls, children with a chronic illness, and siblings were based on a small number of studies per analysis. Fail-safe numbers calculated for comparisons with these control groups often did not exceed Rosenthal's (1995) critical value, indicating the existence of possible publication bias. Rosenthal (1991), however, found a small effect size of only 0.07 for differences between meta-analytic reviews using published studies and meta-analytic reviews using unpublished studies, such as unpublished dissertations, papers and research reports. The researchers conclude that most confidence in research findings can be obtained from comparisons with normative controls by means of parent report, as these comparisons were based on a relatively large number of studies, finding no publication bias.

A second limitation is that most reports of psychopathology were assessed with the CBCL, the TRF, or the YSR. Although these questionnaires are common in the assessment of behavior problems in the realm of pediatrics, it should be noted that the CBCL, TRF, and YSR were not developed to measure behavior problems in children with chronic illnesses (Perrin, Stein, & Drotar, 1991). In children with epilepsy, items may rather measure seizure features than behavior problems *per se* (Oostrom, Schouten, Kruitwagen, Peters, & Jennekens-Schinkel, 2001). However, even if parents were asked not to include behaviors that might be related to seizures, children with epilepsy had higher levels of psychopathology than children from the general population (Austin et al., 2001).

A final limitation is that this study does not report on current and past medication usage of the children with epilepsy included in the meta-analyses. It is well known that children with epilepsy who take antiepileptic drugs experience a wide range of side effects that may have a negative impact on behavioral adaptation independent of actual disease processes (Besag, 2004; Bootsma et al., 2004; Handler & DuPaul, 1999).

This meta-analytic study is unique to the extent that it combines comparisons between children with epilepsy and different control groups into one study from a multi-informant perspective. The researchers found elevated levels of psychopathology in children with epilepsy in comparison with children from the general population. Although children with epilepsy appear to have more internalizing problems than externalizing problems, the presence of externalizing problems remains consistently high. Results suggest that psychopathology is partly attributable to epilepsy as a chronic disorder. Attention problems, thought problems, and social problems were found to be relatively specific to epilepsy. Children with intractable epilepsy were found to be highly at risk for attention and thought problems (McCusker et al., 2002; Sabaz et al., 2001), but also for social problems, withdrawn behavior, and somatic complaints (McCusker et al., 2002). Finally, the researchers found interesting, but indirect evidence for the association of family factors with psychopathology in children with epilepsy.

Future research on psychopathology in children with epilepsy should focus on a multifactorial framework,

considering both neurological and psychosocial factors (including family processes) that may contribute to psychopathology (Hermann & Whitman, 1992, 1984; Seidenberg & Berent, 1992). This also includes broadening the research to include siblings of children with epilepsy. Clinicians should be aware that children with epilepsy are at increased risk for the development of internalizing and externalizing behavior problems. Moreover, they should take into account that some problems may be common to children with a chronic disease, whereas other problems tend to be relatively specific to epilepsy. This may have implications for treatment. As a final point, clinicians should incorporate family factors in their diagnosis and treatment of psychopathology in children with epilepsy.

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