



In the eye of the beholder: Using a multiple-informant approach to examine the mediating effect of cognitive functioning on emotional and behavioral problems in children with an active epilepsy

Tamar Silberg^{a,b,*,1}, Jaana Ahoniska-Assa^{b,c,1}, Ayelet Bord^d, Miram Levav^e, Orli Polack^d, Michal Tzadok^{d,f}, Gali Heimer^{d,f}, Omer Bar-Yosef^{d,f}, Ronny Geva^a, Bruria Ben-Zeev^{d,f}

^a Department of Psychology, Bar-Ilan University, Ramat-Gan, Israel

^b Pediatric Rehabilitation Department, Edmond and Lily Safra Children's Hospital, Sheba Medical Center, Ramat-Gan, Israel

^c School of Behavioral Sciences, Tel Aviv-Yaffo Academic College, Tel-Aviv, Israel

^d Pediatric Neurology Department, Edmond and Lily Safra Children's Hospital, Sheba Medical Center, Ramat-Gan, Israel

^e Child Development Center, Kupat Holim Leumit, Jerusalem, Israel

^f The Sackler School of Medicine, Tel-Aviv University, Tel Aviv, Israel

ARTICLE INFO

Keywords:

Pediatric neurology

Neuropsychology

Multiple informants: CBCL

TRF

Emotional and behavioral problems

ABSTRACT

Purpose: Childhood epilepsy is often associated with cognitive impairments and psychosocial problems. However, it is not clear which factors mediate symptom severity and child's resilience. Emotional and behavioral problems have been associated with various home and school environments, suggesting that information collected may vary depending on both context and informant. In this study we examined the mediating effect of child's cognitive functions on the association between child and epilepsy-related factors and psychosocial problems. Additionally, the differences in psychosocial problems reported by various informants (parents, teachers) in different school settings were explored.

Methods: Participants were 155 children with epilepsy (50 % girls), age range 5–18 years who completed a brief neuropsychological battery. Parents completed the Child Behavior Checklist (CBCL) and teachers completed the corresponding Teacher's Rating Form (TRF), to assess a child's emotional and behavior problems.

Results: The cognitive profile of the sample was within average to low-average range. Parents and teachers both reported high levels of emotional and behavioral problems, and teachers reported relatively higher levels of symptoms. A mediation effect of cognition on the association between child and epilepsy-related factors (i.e., number of antiepileptic medications and illness duration) and child's emotional and behavioral problems was evident only for teachers' reports.

Conclusions: The results emphasize that the complex interactions between epilepsy, cognition and psychosocial outcomes are perceived differently in diverse contexts by different informants.

The incongruities in informants' perceptions regarding the role of cognition in child's psychological state should be acknowledged and incorporated when planning effective educational and rehabilitation interventions for children with epilepsy.

1. Background

1.1. Emotional and behavioral problems among children with epilepsy

Epilepsy is a variety of neurological disorders characterized predominantly by seizures and by the neurobiological, cognitive and

psychosocial consequences associated with the condition [1]. Children and adolescents with epilepsy (CAWE) are at risk of having a psychiatric disorder up to five times that of healthy controls [2]. Increased rates of anxiety and depression have been reported in both clinic-based and population-based studies [3–5]. Even children with self-limited epilepsies and average intelligence, or children who are seizure-free and off

* Corresponding author at: Department of Psychology, Bar-Ilan University, Ramat-Gan, 5290002, Israel.

E-mail address: Tamar.Silberg@biu.ac.il (T. Silberg).

¹ These authors are shared first co-authors.

<https://doi.org/10.1016/j.seizure.2020.09.002>

Received 25 March 2020; Received in revised form 21 August 2020; Accepted 2 September 2020

Available online 14 September 2020

1059-1311/© 2020 British Epilepsy Association.

Published by Elsevier Ltd.

This article is made available under the Elsevier license

(<http://www.elsevier.com/open-access/userlicense/1.0/>).

antiseizure medications (ASMs) have been reported to experience high rates of emotional and behavioral problems (EBPs) [6]. These difficulties often pose a significant burden on CAWE and their families, emphasizing the need for a comprehensive understanding of the relationship between epilepsy and psychosocial difficulties [7,8].

The findings from studies exploring relations between EBPs and a variety of child-related factors (e.g., age, gender) are inconsistent, with some studies reporting younger age and female gender to be associated with poorer psychosocial outcomes [7,9–11] while others fail to provide such association [12]. Studies of the associations between epilepsy-related factors and a child's EBPs have indicated that polytherapy is one of the most significant risk factors for poor psychosocial outcome [13]. Early onset of seizures and extended illness duration were also associated with an increased risk for EBPs [13], with each additional year of epilepsy diagnosis, a child was reported to have a 1.35 times greater chance (95 % CI: 1.05–1.73) of having a psychiatric diagnosis [14]. However, type of seizures (focal vs generalized) or type of epileptic syndrome were less consistent in predicting EBPs [7]. These inconsistencies call for further examination of the relationship between epilepsy-related factors and a child's psychological state, as well as the factors affecting such association.

1.2. Cognition and emotional and behavioral problems in childhood epilepsy

Although normative levels of cognitive functioning have been reported among CAWE [15], specific cognitive impairments leading to difficulties in day-to-day functioning have also been described [16]. For example, memory impairments affect academic achievements and social interactions among CAWE [17], and impairments in executive function (EF) are associated with poorer quality of life [18]. Attention deficits put CAWE at high risk for negative outcomes in the home, school and community [19]. While the cause of cognitive impairments in epilepsy appears to be multifactorial, epilepsy-related factors such as type of epilepsy, age at onset, duration of epilepsy, and number of ASMs have been associated with child's cognitive functioning [20–22].

With regard to the association between cognitive functioning and EBPs among CAWE, absence epilepsy and epilepsy of unknown etiology have been associated with more social and emotional difficulties, if IQ scores are also low [2,14]. Furthermore, lower IQ has been associated with increased risk for EBPs in various neurodevelopmental disorders [23,24]. Additionally, specific epilepsy-related factors have been linked with school placement, with polytherapy (ASMs > 3), longer epilepsy duration and early age at onset associated with a child's placement in special education (SE) settings [13]. Considering that children diagnosed with cognitive deficits report more positive social and emotional functioning when in more inclusive educational placements [25,26], it is important to address the role of the school placement on cognitive functioning and EBPs among CAWE.

1.3. Using multiple perspectives when assessing a child's emotional and behavioral problems

Assessing behavioral and emotional symptoms among children is challenging, as the signs may be highly situational [27]. Accordingly, a multiple-informant approach is considered the 'gold standard' for evaluating psychological problems in CAWE [28–30]. Multiple-informants' paradigm has been used to assess EBPs among children both without [27,30,31] and with neurological disorders [32–35]. Altogether, parents and teachers both tend to perceive CAWE as having more (about 25 %) EBPs than their healthy classmates (about 3–5%) [36]. Furthermore, mothers' ratings of EBPs were reported to be the highest and youths' ratings tended to be the lowest among different informants (mother, father, teacher, youth) across the different Achenbach scales [37]. These findings imply that different informants have different perceptions of specific behavioral expressions and call for the

use of a multiple-informant approach when assessing EBPs among CAWE [38].

Accordingly, in the current study we aimed to examine the associations between child and epilepsy-related factors and a child's EBPs according to parents' and teachers' reports. Further, we aimed to examine whether these associations are mediated by the child's cognitive functioning, using a brief neuropsychological battery. We hypothesized that increase in epilepsy-related factors (defined by the number of ASMs and illness duration), would be positively related to emotional and behavioral difficulties according to both informants, and that cognitive impairments would predict more EBPs.

2. Methods

2.1. Participants

The study followed a retrospective design of N = 185 CAWE (53.5 % girls) diagnosed with an active epilepsy, admitted to a Pediatric Neurology Department at the Sheba Medical Center, Israel, between the years 2005–2015 for a short neuropsychological evaluation.

Participants were included in the analysis if the following criteria were met: (1) a history of an active epilepsy (i.e., seizures occurring within the last year [39], with epilepsy defined by any of the following conditions: (a) at least two unprovoked seizures occurring >24 h apart; (b) one unprovoked seizure and a probability of further seizures similar to the general recurrence risk (at least 60 %) after two unprovoked seizures; (c) diagnosis of an epilepsy syndrome [40]; (2) age at assessment > 5yrs; (3) completion of parent and teacher EBPs questionnaires; and (4) Hebrew as a native language for completion of the neuropsychological battery. Non-inclusion criteria consisted of evidence of surgical intervention for the epilepsy between diagnosis and assessment, or significant neurological co-morbidities (i.e., acquired brain injury, intellectual disability, autism). The study was approved by the Hospital's Ethical Review Board.

Out of the N = 185 participants the following N = 30 were excluded due to: absence of either a parent or a teacher questionnaire (N = 14), acquired brain injury (N = 9), surgical intervention (N = 3), developmental delay (N = 4). Thus, a total of N = 155 participants (50.3 % girls) were included in the final analyses.

Children's mean age at diagnosis was 6.5 ± 3.4 years and mean age at the time of assessment was 9.3 ± 3.1 years (range 5.2–18 years) with N = 116 (75 %) below 11 years at the time of assessment. Mean illness duration ranged from 0.8–14.2 years, with an average of 2.8 ± 3 years (see Table 1 for a detailed description of the sample's characteristics).

2.2. Measures

2.2.1. Emotional and behavioral problems

Parents completed the Child Behavior Checklist (CBCL), and teachers completed the corresponding Teacher's Rating Form (TRF) for the assessment of a child's EBP [41,42]. The CBCL and TRF are 113-item caregiver/teacher reports describing child's behaviors, rated on a 3-point scale (0 = not true, 1 = somewhat or sometimes true, and 2 = very true or often true for the past 6 months). According to the CBCL/TRF scoring system, raw scores are converted to T-scores and generate a Total Problems scale, broad-band Internalizing and Externalizing Symptoms scales, and eight narrow-band Syndrome scales. Scores for the narrow-band Syndrome scales range between *Normal* (T < 65), *Clinical Band* (T = 65–70) and *Clinical* (T > 70). Scores for the broad-band scales range between *Normal* (T < 60), *Clinical Band* (T = 60–64) and *Clinical* (T > 65). The reliability and validity of the CBCL and TRF, as well as norms based on age and gender, were established previously [41,42]. The CBCL and TRF have been translated into a variety of languages, including Hebrew [43], and have been used for assessing emotional and behavioral problems among children with different neurological conditions within the Israeli population [34,35].

Table 1
Detailed description of child and epilepsy-related factors (N = 155):

		N (%)
Child-related factors		
Sex:	Male	77 (49.7)
	Female	78 (50.3)
School placement:	Mainstream	128 (83.1)
	Special Education	27 (16.9)
Additional psychiatric diagnosis:	ADHD	10 (6.5)
	Anxiety Disorder	5 (3.2)
	Mood Disorder	3 (2)
	OCD	1 (0.6)
	Tourett's syndrome	1 (0.6)
Epilepsy-related factors		
Illness duration:	< 1 year	60 (38)
	1–5 years	65 (42)
	>5 years	30 (20)
Number of ASMs:	1	96 (61.9)
	2	40 (25.8)
	>3	19 (12.2)
Epilepsy type:	Generalized	47 (30.3)
	Focal	72 (46.3)
	Combined [†]	8 (5)
	Unknown	8 (5)
	Unclassified ^{††}	20 (13)
Epilepsy etiology*:	Structural	31 (20.4)
	Infectious	1 (0.6)
	Genetic	109 (71.7)
	Unknown	11 (7.3)

ADHD = attention deficit hyperactivity disorder; OCD = obsessive compulsive disorder; ASM = antiseizure medications.

[†] Generalized and focal.

^{††} According to Berg et al. [73] seizures that cannot be classified into one of the preceding categories should be considered as *unclassified* (such as CAWE with Electrical status epilepticus during slow-wave sleep; ESES).

* N = 152.

2.2.2. Cognitive profile

All participants completed a brief neuropsychological assessment addressing four major cognitive domains: visuomotor, EF, memory, and attention (see appendix A for a list of the cognitive tests used in the neuropsychological battery). An index score for each cognitive domain was composed in accordance with the literature on well-established neuropsychological tests representing specific cognitive domains [44, 45]. All scaled scores were converted into Z scores to allow comparison between the different tests, and only tests with correlations of a p value <0.001 were included in each specific index.

2.2.3. Data analysis

Zero-order correlations were conducted between child and epilepsy-related factors (illness duration and number of ASMs), cognitive functions (according to the four cognitive domains) and EBPs (as reported by teachers and parents). Independent *t*-tests were conducted to examine differences in cognitive functions and in EBPs between participants in SE and mainstream schools and between girls and boys.

Path analysis was used to test the full mediation model (Fig. 1). A major benefit of path analysis is that it enables testing for mediation without risking capitalization on chance and provides estimates of the magnitude, significance, and direction of hypothesized causal connections between sets of variables, as the model suggests [46]. In the current model, Total Problems scores for both the CBCL and the TRF were used as endogenous variables (variables with causal links (arrows) leading to them from other variables in the model) [47], and were defined as the outcomes of the model. An epilepsy factor (comprised of number of ASMs and illness duration) and child factor (school placement) were used as the independent variables, and cognitive functions (a latent variable in the model comprised of the four cognitive indices) used as the mediating factor. Parameter estimates were collected using maximum likelihood. The model was tested by evaluating the significance of the estimated path coefficients and by evaluating goodness-of-fit statistics. Chi-square was used as a traditional measure of fit [48]. The comparative fit index (CFI), normed fit index (NFI), incremental fit index (IFI) and root mean square error of approximation (RMSEA) were also reported to complement the data analysis and to allow for a more comprehensive assessment of the model's goodness of fit. A RMSEA of 0.06 or less and a CFI, a NFI, and an IFI of 0.90 or greater represent a good fit between related factors and parents' and teachers' reports on child's emotional and behavioral problems [49].

Finally, records were analyzed for missing data [50] which ranged between 8–13 % for the different study variables. Little's MCAR (missing completely at random) test [51] was non-significant ($\chi^2(8) = 9.474, p = 0.304$), indicating that data were missing completely at random allowing the use of the full sample.

Data analyses were performed using the IBM SPSS 23.0 package and the IBM AMOS 19.0 package (SPSS Inc., Chicago, IL) for the path analyses.

3. Results

3.1. Epilepsy and behavioral and emotional problems

Scores of EBPs of participants with epilepsy according to both parents and teachers are presented in Fig. 2. Paired *t*-test analyses indicated that teachers reported on more problems than parents did, with

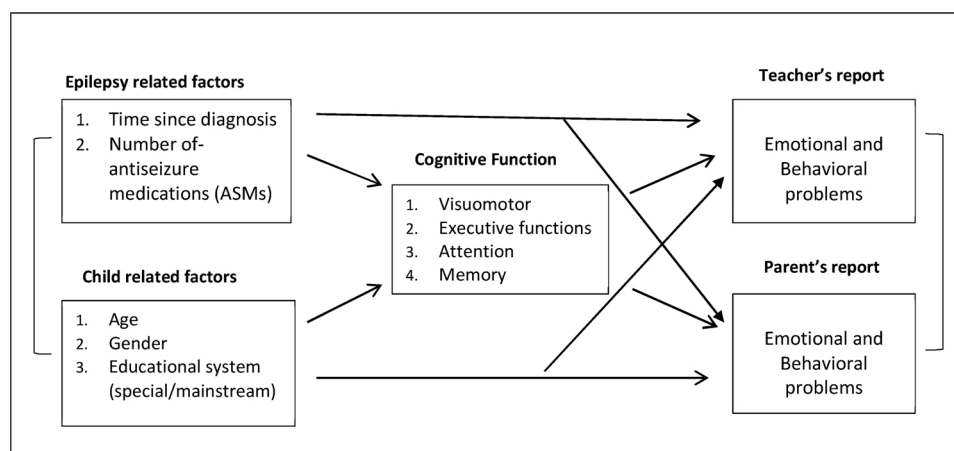


Fig. 1. A theoretical model of the mediation effect of cognition on the associations between child and epilepsy-related factors and between child's emotional and behavioral problems according to both, parents and teachers.

significant differences for the Anxiety and Withdrawn narrow-band subscales [$t(154) = 2.23, p = 0.027$; $t(154) = 2.96, p = 0.004$ respectively], and for all summary scales (ps range 0.001–0.014).

Following Achenbach's distribution of scores into clinical subgroups [41,42], we divided the CAWE in our sample into two groups of below ($T < 60$) and above ($T \geq 60$) clinical band symptoms (referred to as *non-clinical* and *clinical* respectively). As Fig. 3 shows, both teachers' and parents' reports were high above the rate of clinical symptoms in the general population (i.e., 3–5%), with an odds ratio (OR) ranging from 5.8–11.9.

3.2. Associations between child and epilepsy-related factors and a child's EBPs

Relatively weak associations were found between epilepsy-related factors and a child's EBPs, with the number of ASMs positively associated with parents' reports on child's total problems ($r = 0.17, p < 0.05$). Non-significant associations were found between the number of ASM's and teachers' reports ($r = 0.124, p = 0.06$); as well as between the time elapsed since diagnosis and parents' reports ($r = 0.13, p = 0.06$) nor with teacher's reports ($r = 0.05, p = 0.53$). Significant differences in EBP's were found between CAWE placed in mainstream and SE schools, with the latter showing higher levels of EBPs according to both parents ($M_{\text{mainstream}} = 52.8 \pm 10.4$ and $M_{\text{SE}} = 58.5 \pm 11.1, t(153) = -2.97, p = 0.003$) and teachers ($M_{\text{mainstream}} = 56.3 \pm 8.9$ and $M_{\text{SE}} = 61.9 \pm 8.1, t(153) = -2.51, p = 0.01$). No significant associations were found between child's age and gender and the level of EBPs.

3.3. Child and epilepsy-related factors and cognitive functioning

Sample's mean scores for each of the cognitive domains were within the average to low-average range. Specifically, participants' scores on each of the cognitive indices were: $Z_{\text{EF}} = -0.56 \pm 0.85$ (range = -3 to 1.27); $Z_{\text{Attention}} = -0.74 \pm 1.08$ (range = -3 to 1.3); $Z_{\text{Memory}} = -0.81 \pm 0.92$ (range = -3 to 2.2) and $Z_{\text{Visuomotor}} = -0.80 \pm 0.96$ (range = -3 to 1.4). With regard to child and epilepsy-related factors, scores on all cognitive indices were negatively associated with number of ASMs as well as with illness duration (Table 2). Significant differences in all cognitive indices were also found between CAWE placed in SE (Mean scores for: $Z_{\text{EF}} = -1.56 \pm 0.77$; $Z_{\text{Attention}} = -1.56 \pm 1.2$; $Z_{\text{Visuospatial}} = -1.64 \pm 0.9$; $Z_{\text{Memory}} = -1.74 \pm 0.66$) and CAWE placed in mainstream systems (Mean scores for: $Z_{\text{EF}} = -0.36 \pm 0.88$; $Z_{\text{Attention}} = -0.59 \pm 0.98$; $Z_{\text{Visuospatial}} = -0.63 \pm 0.91$; $Z_{\text{Memory}} = -0.63 \pm 0.84$), with the latter scoring higher on each cognitive index. No significant differences were found between girls and boys for any of the cognitive domains.

3.4. Cognitive functioning and emotional and behavioral problems

Negative correlations were found between teachers' reports on the Total Problems scale and child's scores on all cognitive domains. Negative correlations were also found between parents' reports on the Total Problems scale and child's score on the Memory, EF and Visuomotor indices (Table 2).

3.5. Model testing

The full model (Fig. 1) was tested with all variables that were significantly associated with at least one outcome (i.e., Total Problems scale) in the correlation analysis. In the final path analysis (Fig. 4), the standardized regression weights and their significance are indicated along each line. The model indicated that the cognitive factors strongly mediated the association between child (mainstream and SE school placement) and epilepsy (number of ASMs and illness duration) related factors and teachers' reports of child's emotional and behavioral symptoms.

According to the suggested mediation model, a significant positive association was found between epilepsy-related factors and teachers' report on a child's EBPs. No significant association was found between school placement and EBPs according to both informants. Cognitive functions mediated the relationship between child and epilepsy-related factors and between teachers' reports on a child's EBPs, with SE placement, polytherapy and longer illness duration negatively associated with a child's cognitive functions, and the latter negatively associated with higher EBPs.

4. Discussion

The current study examined EBPs among CAWE according to parents' and teachers' reports, and in relation to child's cognitive functioning. To our knowledge, this is the first study to use a mediation model of cognition on behavioral and emotional outcomes among CAWE diagnosed with epilepsy, using a multiple-informant approach.

4.1. Epilepsy and behavioral and emotional problems

In our sample teachers reported higher EBP on all summary scales as well as on the anxiety and depression subscales, as compared to parents. This finding is in accordance with previous findings on differences between parents and teachers reports on EBPs among CAWE [36] and other neurological impairments [35]. Additionally, the percentage of CAWE reported to have above *clinical* level EBPs in our sample was extremely high, with approximately one in three parents and almost one

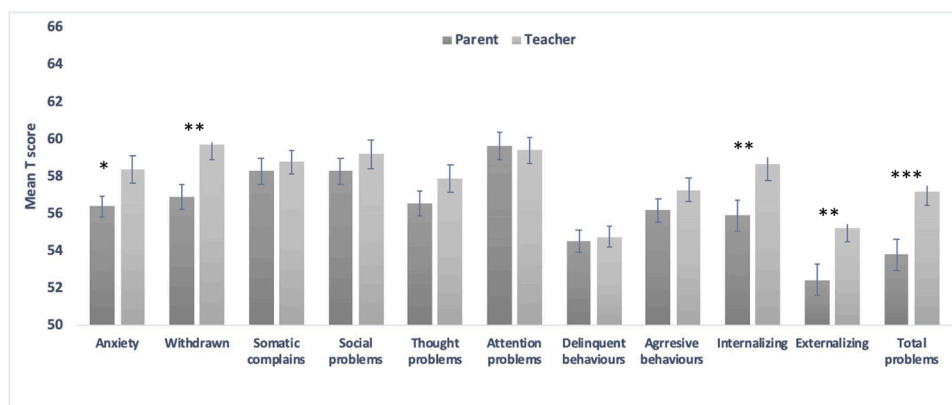


Fig. 2. A comparison between parents and teachers' reports on the ASEBA scales. Scores of $T \geq 65$ on each subscale and $T \geq 60$ on the three summary scales (internalizing, externalizing and total problems) indicate clinical levels of symptomatology.

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

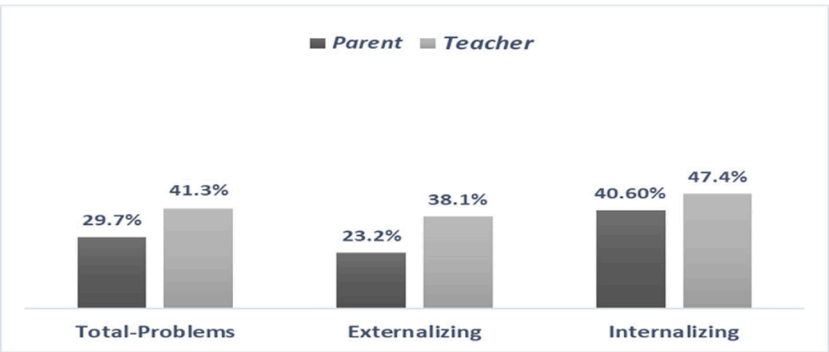


Fig. 3. Percentage of participants reported to have above clinical band levels ($T \geq 60$) of Internalizing, Externalizing and Total symptoms according to both informants (parents and teachers).

Table 2
Correlations between cognitive indices, epilepsy-related factors and child’s total emotional and behavioral problems according to parents’ and teachers’ report.

Cognitive Index	Epilepsy-related factors		Total EBPs	
	Illness duration	Number of ASM	CBCL	TRF
Visuomotor	−0.25**	−0.29**	−0.19*	−0.34**
EF	−0.41**	−0.33**	−0.20*	−0.16*
Attention	−0.16*	−0.25**	−0.12	−0.25**
Memory	−0.33**	−0.29**	−0.22**	−0.25**

Note: Bold indicates correlation is significant at alpha level corrected by sequential Bonferroni method [74]. EBPs = emotional and behavioral problems, EF = executive functions, CBCL = child behavior checklist, TRF = teacher form.
* $p < 0.05$.
** $p < 0.001$.

in two teachers reporting on clinical levels of EBPs. Although these rates are highly above those reported for the general population, they are in line with previous reports on psychiatric symptoms among CAWE [52, 53].

Furthermore, children placed in SE in our sample had higher levels of EBPs according to both, teachers and parents. However, this association was weakened when including epilepsy and cognition factors in the integrated mediation model, indicating that a more holistic approach is warranted when evaluating child’s levels of EPB’s.

With regard to epilepsy-related factors, number of ASMs were

associated with child’s EBPs, according to parents, similar to previous reports indicating that children receiving multiple ASMs (polytherapy) are more likely to demonstrate higher levels of externalizing behavioral symptoms than children receiving monotherapy or no ASMs [7]. This finding may also be attributed to the fact that polytherapy can be viewed as a proxy of illness severity [54]. In contrast to our hypothesis, significant associations between illness duration and a child’s EBPs were not found. Recently, an increase in EBPs was found only among CAWE with an illness duration of above 5 years [13]. As 80 % of our sample had an illness duration below 5-years, the lack of association between illness duration and a child’s EBPs might be explained by the relatively short illness durations in our sample. Future studies should aim to include more CAWE with longer illness durations.

4.2. Child and epilepsy-related factors and cognitive function

The cognitive profile of the CAWE in our sample was within the normal range ($-1 < Z < 1$). However, the range in each cognitive index was negatively skewed, suggesting that the proportion of children with lower than average cognitive functioning was relatively high. This finding is supported by previous reports on subnormal cognitive functioning among CAWE [15].

Similarly to previous findings [55,56], our results demonstrate that the longer the time since diagnosis, the more compromised the child’s cognitive function. This may be understood as a failure to cognitively develop at the expected pace, or as a loss of acquired cognitive abilities

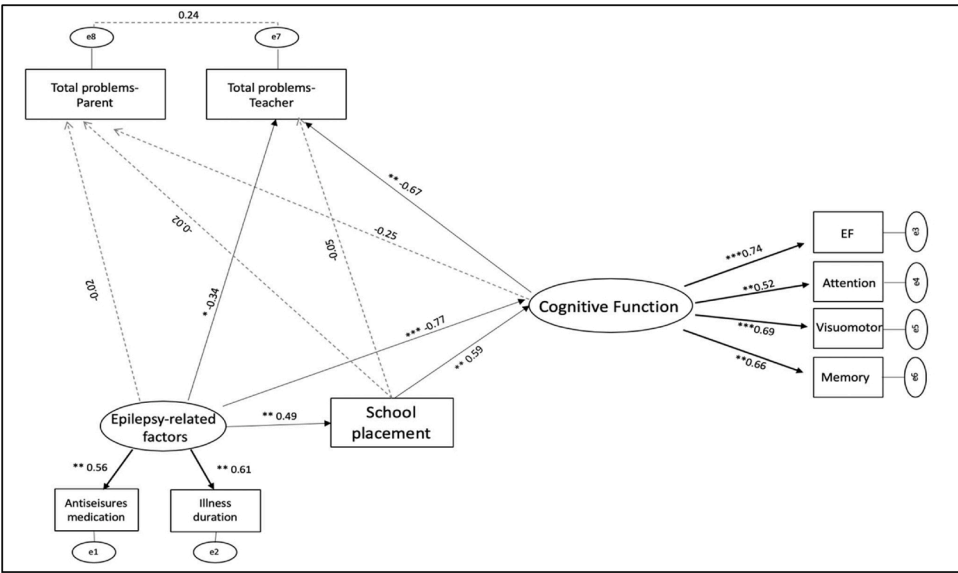


Fig. 4. Final model of the mediating effect of cognition on epilepsy-related emotional and behavioral problems: Standardized regression weights and their significance are indicated along each line, with dashed lines indicating non-significant values. The chi-square for the final model was 28.18, with 20 degrees of freedom ($p = 0.105$), CFI = 0.969, IFI = 0.972, NFI = 0.910, and RMSEA = 0.05 (90 % CI = 0.00–0.092). * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

over time as a result of long seizure duration [57,58]. Similar to previous results [59], our findings show that participants receiving multiple ASMs scored lower on all cognitive measures than participants receiving a single ASM. As previously suggested, this finding has significant clinical implications since number of ASMs may also serve as a proxy for illness severity [54]. Therefore, optimal treatment of epilepsy requires achieving a balance between adequate seizure-control while minimizing the potential cognitive and emotional adverse effects of the employed ASMs [60].

A significant difference in all cognitive domains was found between the type of school placement among CAWE in our sample, with CAWE placed in SE performing more poorly on all cognitive domains. This finding is in accordance with previous studies, indicating that school placement is associated with child's cognitive abilities [61].

4.3. Mediation model of cognitive functioning and child's emotional and behavioral problems

In the current study, child's cognitive function mediated the association between epilepsy-related factors, school placement and EBPs, as perceived by the teachers. Lower cognitive functioning was related to higher rates of EBPs according to teachers' but not parents' reports. This finding is in-line with previous findings indicating that parents of CAWE tend to underestimate cognitive abilities and overestimate behavioral problems [62]. Furthermore, the mediation effect found in this study highlights the important role of cognition in teachers' appraisals of a child's EBPs. This may reflect teachers' natural tendency to rely on academic achievements when evaluating a child's behavior, or their use of age-appropriate comparison groups when making such evaluations [63]. However, a recent systematic review on teachers' attitudes towards epilepsy indicated that deficits in knowledge and negative attitudes were relatively common [64]. Thus, it is important to address the differences between informants' perceptions when planning EBP interventions in the schools or within rehabilitation settings. Furthermore, the fact that educational placement contributed to the mediation effect of cognition on the association between epilepsy and child's EBPs according to teachers' report, resonates with previous findings on the role of school placement on emotional well-being among children with neurological disabilities [25]. However, since we did not have any information regarding the reason why a child was or was not placed in SE, and as most studies use cross-sectional designs limiting the ability to provide more casual conclusions, the actual role of SE placement on a child's EBPs remains unclear. Thus, there is a need for a more comprehensive understanding of the relationship between epilepsy, school environment and child's psychosocial difficulties, when considering the appropriate educational setting for CAWE.

The fact that parents reported high levels of EBPs, but their reports were not affected by either epilepsy-related factors or cognitive abilities, might suggest that EBPs are a major concern in childhood epilepsy, above and beyond other cognitive or epilepsy-related factors. This finding resonates with Livingston's important reflection in the early 70's acknowledging that "the most serious hazard of an epileptic disorder is frequently not the seizures, but the associated emotional disturbances which are prone to develop in a youngster as a result of mismanagement by his family, by his classmates and friends and by society" [65 in 38]. Since both, parents and teachers in our sample reported relatively high levels of symptomatology, we may infer that these reports were representative of a child's psychosocial status. Hence, collecting data from different informants, allows a wider perspective on a child's emotional state [31].

4.4. Limitations

The current study has several limitations. First, although the study adopted a multiple-informant approach, we did not collect self-reports from the children, which is considered as best practice in child

psychopathology [30,52]. Although some health-related questionnaires have been adapted for children younger than 10-years [66], most of the well-established child self-report EBP questionnaires, which also have corresponding parent's and a teacher's forms, are not obtained from children younger than 11 years [67–69]. Since approximately 75 % of the CAWE in our sample were below 11-years, we did not include self-reports in our analysis.

Second, the cognitive functioning of the CAWE in the present sample were within the average to low-average range, representing a relatively well functioning sample of CAWE. Using larger cohorts with a wider range of cognitive functioning may affect the way cognition mediates the association between epilepsy characteristics and EBPs. In addition, the current sample was composed of CAWE referred to a neuropsychological evaluation, with reports on EBPs from both teachers and parents. Subsequently, children who did not have such information were not included in our analysis. This may have increased the risk of bias in our sample as teachers' willingness to provide such reports may reflect a more positive teacher-student relationship, known to predict better school competencies [70].

Third, we did not collect information on seizure frequency or syndromes which has been related with negative effects on cognition and EBPs [71]. The lack of such information may also affect the ability to generalize the reports of the current study to other samples of CAWE.

Forth, data on the sociodemographic (SES) characteristics of parents or teachers, as well as on their emotional state was not collected in our study. As parent-related variables (i.e., SES, attitudes, mood, stress) may be associated with a child's behavioral symptoms and may affect parents' reports [38], follow-up studies should further examine variables related to raters' characteristics. Such information might shed light on how they perceive their child's status.

Finally, participants were recruited from a hospital-based sample, which limits the generalizability of the results to all CAWE. In addition, in the absence of a matched control group, cognitive performance and behavioral reports were compared with population-based norms. Follow-up research is needed to compare our findings with those for healthy controls or children with other neurological conditions.

5. Conclusions

CAWE in our study were reported to have relatively high levels of EBPs, and their cognitive performance fell within the average to low average range. However, our main findings emphasize that the complex interactions between child and epilepsy-related factors and their cognitive and emotional outcomes, are perceived differently by different informants. This perspective is compatible with the ICF-CY [72] framework, which views a child's status not only in terms of a 'medical' or 'biological' dysfunction, but rather as composed of a child's physical and psychological environment. The information collected from multiple informants in different settings reflects the different circumstances in which a child's symptoms manifest, and thus should be recognized as the gold standard representing the interaction between the child and his or her environment [32]. As parents and teachers meet children in different contexts, they develop different expectations regarding the child's behaviors. Therefore, it is not surprising that their views regarding a child's symptoms are not identical. Although these inconsistencies are not perceived as an indication of a 'proxy bias', if left unaddressed they may affect the integration of any evaluation and hamper interventions developed to meet the child's needs. Thus, the current results highlight the importance of providing clinicians information about possible discrepancies in the way different informants perceive the role of cognitive functioning in epilepsy, and its effect on child's psychological state, as well as clear guidelines for managing conflicting perspectives. Such knowledge will help enhance collaboration between a child's parents and the educational staff and support their engagement in providing effective educational and rehabilitation interventions.

Declaration of Competing Interest

All authors have no commercial, financial or other associations to disclose that pose a conflict of interests connected with the publication of the article.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.seizure.2020.09.002>.

References

- [1] Fisher RS, Boas WV, Blume W, Elger C, Genton P, Lee P, Engel Jr J. Epileptic seizures and epilepsy: definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE). *Epilepsia* 2005;46: 470–2.
- [2] Caplan R, Siddarth P, Gurbani S, Hanson R, Sankar R, Shields WD. Depression and anxiety disorders in pediatric epilepsy. *Epilepsia* 2005;46:720–30.
- [3] Davies S, Heyman I, Goodman R. A population survey of mental health problems in children with epilepsy. *Dev Med Child Neurol* 2003;45:292–5.
- [4] Ettinger AB, Weisbrot DM, Nolan EE, Gadow KD, Vitale SA, Andriola MR, Lenn NJ, Novak GP, Hermann BP. Symptoms of depression and anxiety in pediatric epilepsy patients. *Epilepsia* 1998;39:595–9.
- [5] Dunn DW, Austin JK, Perkins SM. Prevalence of psychopathology in childhood epilepsy: categorical and dimensional measures. *Dev Med Child Neurol* 2009;51: 364–72.
- [6] Hermann BP, Jones JE, Jackson DC, Seidenberg M. Starting at the beginning: the neuropsychological status of children with new-onset epilepsies. *Epileptic Disord* 2012;14:12–21.
- [7] Freilinger M, Reisel B, Reiter E, Zelenko M, Hauser E, Seidl R. Behavioral and emotional problems in children with epilepsy. *J Child Neurol* 2006;21:939–45.
- [8] Mitchell WG, Scheier LM, Baker SA. Psychosocial, behavioral, and medical outcomes in children with epilepsy: a. *Pediatrics* 1994;94:471.
- [9] Dunn DW, Austin JK. Behavioral issues in pediatric epilepsy. *Neurology* 1999;53: S96–100.
- [10] Austin JK, Dunn DW, Huster GA. Childhood epilepsy and asthma: changes in behavior problems related to gender and change in condition severity. *Epilepsia* 2000;41:615–23.
- [11] Fleming M, Fittion CA, Steiner MF, McLay JS, Clark D, King A, Mackay DF, Pell JP. Educational and health outcomes of CAWEreceiving antiepileptic medication: scotland-wide record linkage study of 766 244 schoolchildren. *BMC Public Health* 2019;19:595.
- [12] Plioplys S, Dunn DW, Caplan R. 10-year research update review: psychiatric problems in children with epilepsy. *J Am Acad Child Adolesc Psychiatry* 2007;46: 1389–402.
- [13] Valova V, Kochan A, Werry B, John R, Prager C, Schneider J, Kaindl AM. Early onset, long illness duration, epilepsy type, and polypharmacy have an adverse effect on psychosocial outcome in children with epilepsy. *Neuropediatrics* 2020;51: 164–9.
- [14] Caplan R, Siddarth P, Stahl L, Lanphier E, Vona P, Gurbani S, Koh S, Sankar R, Shields WD. Childhood absence epilepsy: behavioral, cognitive, and linguistic comorbidities. *Epilepsia* 2008;49:1838–46.
- [15] Berg AT, Langfitt JT, Testa FM, Levy SR, DiMario F, Westerveld M, Kulas J. Global cognitive function in children with epilepsy: a community-based study. *Epilepsia* 2008;49(April (4)):608–14.
- [16] Reilly C, Atkinson P, Das KB, Chin RF, Aylett SE, Burch V, Gillberg C, Scott RC, Neville BG. Cognition in school-aged children with “active” epilepsy: a population-based study. *J Clin Exp Neuropsychol* 2015;37:429–38.
- [17] Nolan MA, Redoblado MA, Lah S, Sabaz M, Lawson JA, Cunningham AM, Bleasel AF, Bye AM. Memory function in childhood epilepsy syndromes. *J Paediatr Child Health* 2004;40:20–7.
- [18] Love CE, Webbe F, Kim G, Lee KH, Westerveld M, Salinas CM. The role of executive functioning in quality of life in pediatric intractable epilepsy. *Epilepsy Behav* 2016; 64:37–43.
- [19] Reilly CJ. Attention deficit hyperactivity disorder (ADHD) in childhood epilepsy. *Res Dev Disabil* 2011;32(3):883–93.
- [20] Kwan P, Brodie MJ. Neuropsychological effects of epilepsy and antiepileptic drugs. *Lancet* 2001;357(9251):216–22.
- [21] Park J, Yum MS, Choi HW, Kim EH, Kim EHW, Ko TS. Determinants of intelligence in childhood-onset epilepsy: a single-center study. *Epilepsy Behav* 2013;29: 166–71.
- [22] Witt JA, Elger CE, Helmstaedter C. Adverse cognitive effects of antiepileptic pharmacotherapy: each additional drug matters. *Eur Neuropsychopharmacol* 2015; 25:1954–9.
- [23] A Aman MG, Pejeau C, Osborne P, Rohahn J, Handen B. Four-year follow-up of children with low intelligence and ADHD. *Res Dev Disabil* 1996;17:417–32.
- [24] Parkes J, White-Koning M, Dickinson HO, Thyen U, Arnaud C, Beckung E, Fauconner J, Marcelli M, McManus V, Michelsen SI, Parkinson K. Psychological problems in children with cerebral palsy: a cross-sectional European study. *J Child Psychol Psychiatry* 2008;49:405–13.
- [25] Wiener J, Tardif CY. Social and emotional functioning of children with learning disabilities: does special education placement make a difference? *Learn Disabil Res Pract* 2004;19(February):20–32.
- [26] Stainback SB, Stainback WC. Inclusion: a guide for educators. Paul H Brookes Publishing; 1996.
- [27] Achenbach TM, McConaughy SH, Howell CT. Child/adolescent behavioral and emotional problems: implications of cross-informant correlations for situational specificity. *Psychol Bull* 1987;101:213–32.
- [28] (a) Renk K. Cross-informant ratings of the behavior of children and adolescents: the “gold standard”. *J Child Fam Stud* 2005;14:457–68.
(b) Fordham B, Sugavanam T, Hopewell S, Hemming K, Howick J, Kirtley S, et al. Effectiveness of cognitive-behavioural therapy: a protocol for an overview of systematic reviews and meta-analyses. *BMJ Open* 2018;8(12).
- [29] National Institutes of Health. NIH policy and guidelines on the inclusion of children as participants in research involving human subjects. *NIH Guide*; 1998. p. 1–7.
- [30] De Los Reyes A, Augenstein TM, Wang M, Thomas SA, Drabick DA, Burgers DE, Rabinowitz J. The validity of the multi-informant approach to assessing child and adolescent mental health. *Psychol Bull* 2015;141:858–900.
- [31] Smith SR. Making sense of multiple informants in child and adolescent psychopathology: a guide for clinicians. *J Psychoeduc Assess* 2007;25:139–49.
- [32] Durber CM, Yeates KO, Taylor HG, Walz NC, Stancin T, Wade SL. The family environment predicts long-term academic achievement and classroom behavior following traumatic brain injury in early childhood. *Neuropsychology* 2017;315: 499–507.
- [33] N Nelson JM, Harwood HR. A meta-analysis of parent and teacher reports of depression among students with learning disabilities: evidence for the importance of multi-informant assessment. *Psychol Sch* 2011;484:371–84.
- [34] Silberg T, Tal-Jacobi D, Levav M, Breznar A, Rassovsky Y. Parents and teachers reporting on a child’s emotional and behavioural problems following severe traumatic brain injury (TBI): the moderating effect of time. *Brain Inj* 2015;29: 481–9.
- [35] Silberg T, Ahonniksa-Assa J, Levav M, Eliyahu R, Peleg-Pilowsky T, Breznar A, Vakile E. The effect of age-at-testing on verbal memory among children following severe traumatic brain injury. *Child Neuropsychol* 2016;22:600–17.
- [36] Oostrom KJ, Schouten A, Kruitwagen CL, Peters AC, Jennekens-Schinkel A. Dutch Study Group of Epilepsy in Childhood (DuSECh). Behavioral problems in children with newly diagnosed idiopathic or cryptogenic epilepsy attending normal schools are in majority not persistent. *Epilepsia* 2003;44:97–106.
- [37] Huberty TJ, Austin JK, Harezlak J, Dunn DW, Ambrosius WT. Informant agreement in behavior ratings for children with epilepsy. *Epilepsy Behav* 2000;1:427–35.
- [38] Berg AT, Altalib HH, Devinsky O. Psychiatric and behavioral comorbidities in epilepsy: a critical reappraisal. *Epilepsia* 2017;58:1123–30.
- [39] Wang W, Wu J, Dai X, Ma G, Yang B, Wang T, Yuan C, Ding D, Hong Z, Kwan P, Bell GS. Global campaign against epilepsy: assessment of a demonstration project in rural China. *Bull World Health Organ* 2008;86:964–9.
- [40] Fisher RS, Acevedo C, Arzimanoglou A, Bogacz A, Cross HE. A practical clinical definition of epilepsy. *Epilepsia* 2014;55:475–82.
- [41] Achenbach TM. Manual for the child behavior Checklist/4–18 and 1991 profile. University of Vermont, Department of Psychiatry; 1991.
- [42] Achenbach TM, Edelbrock CS. Manual for the Teacher’s Report Form and teacher version of child behavior profile. University of Vermont, Department of Psychiatry; 1986.
- [43] Zilber N, Auerbach J, Lerner Y. Israeli norms for the Achenbach Child Behavior Checklist: comparison of clinically-referred and non-referred children. *Isr J Psychiatry Relat Sci* 1994;31:5–12.
- [44] Baron IS. Neuropsychological evaluation of the child: domains, methods, & case studies. Oxford University Press; 2018.
- [45] Babikian T, Asarnow R. Neurocognitive outcomes and recovery after pediatric TBI: meta-analytic review of the literature. *Neuropsychology* 2009;23:283–96.
- [46] Klem L. In: Grimm LG, Yarnold PR, editors. Path analysis, in Reading and understanding multivariate statistics. Washington DC: APA; 1995. p. 65–97.
- [47] Kline RB. Principles and practice of structural equation modeling. Guilford Publications; 2015.
- [48] Cheung GW, Rensvold RB. Evaluating goodness-of-fit indexes for testing measurement invariance. *Struct Equ Model* 2002;9:233–55.
- [49] Sivo SA, Fan X, Witta EL, Willse JT. The search for “optimal” cutoff properties: fit index criteria in structural equation modeling. *J Exp Educ* 2006;74:267–88.
- [50] Enders CK. Applied missing data analysis. Guilford Press; 2010.
- [51] Little RJ. A test of missing completely at random for multivariate data with missing values. *Am Stat Assoc* 1988;83:1198–202.
- [52] Rodenburg R, Stams GJ, Meijer AM, Aldenkamp AP, Deković M. Psychopathology in children with epilepsy: a meta-analysis. *J Pediatr Psychol* 2005;30:453–68.
- [53] Nickels K, Zaccariello M, Haniwka L, Wirrell E. Cognitive and neurodevelopmental comorbidities in paediatric epilepsy. *Nat Rev Neurol* 2016;12:465–76.
- [54] Rogawski MA, Johnson MR. Intrinsic severity as a determinant of antiepileptic drug refractoriness. *Epilepsy Curr* 2008;8:127–30.
- [55] Hermann BP, Seidenberg M, Dow C, Jones J, Rutecki P, Bhattacharya A, Bell B. Cognitive prognosis in chronic temporal lobe epilepsy. *Ann Neurol* 2006;60:80–7.
- [56] Sherman EM, Brooks BL, Fay-McClymont TB, MacAllister WS. Detecting epilepsy-related cognitive problems in clinically referred children with epilepsy: Is the WISC-IV a useful tool? *Epilepsia* 2012;53:1060–6.
- [57] Lordo DN, Van Patten R, Sudikoff EL, Harker L. Seizure-related variables are predictive of attention and memory in children with epilepsy. *Epilepsy Behav* 2017;73:36–41.

- [58] van Iterson L, Zijlstra BJ, Augustijn PB, van der Leij A, de Jong PF. Duration of epilepsy and cognitive development in children: a longitudinal study. *Neuropsychology* 2014;28:212–21.
- [59] Nolan MA, Redoblado MA, Lah S, Sabaz M, Lawson JA, Cunningham AM, Bleasel AF, Bye AM. Intelligence in childhood epilepsy syndromes. *Epilepsy Res* 2003;53:139–50.
- [60] Hermann B, Meador KJ, Gaillard WD, Cramer JA. Cognition across the lifespan: antiepileptic drugs, epilepsy, or both? *Epilepsy Behav* 2010;17:1–5.
- [61] Bulteau C, Jambaque I, Viguer D, Kieffer V, Dellatolas G, Dulac O. Epileptic syndromes, cognitive assessment and school placement: a study of 251 children. *Dev Med Child Neurol* 2000;42:319–27.
- [62] Helmstaedter C, Pandolfo RV, Hoppe C, Witt JA. Cognitive-behavioral correlates of proxy reports on cognitive capabilities in pediatric patients with epilepsy. *Seizure* 2017;51:193–9.
- [63] Nelson JM, Harwood HR. A meta-analysis of parent and teacher reports of depression among students with learning disabilities: Evidence for the importance of multi-informant assessment. *Psychol Sch* 2011;48:371–84.
- [64] Jones C, Atkinson P, Cross JH, Reilly C. Knowledge of and attitudes towards epilepsy among teachers: a systematic review. *Epilepsy Behav* 2018;87:59–68.
- [65] Livingston S. Comprehensive management of epilepsy in infancy, childhood, and adolescence. Springfield, IL: Charles C. Thomas; 1972.
- [66] Riley AW. Evidence that school-age children can self-report on their health. *Ambul Pediatr* 2004;4:371–6.
- [67] Achenbach TM, Rescorla LA, Maruish ME. The Achenbach system of empirically based assessment (ASEBA) for ages 1.5 to 18 years. The Use of Psychological Testing for Treatment Planning and Outcomes Assessment, 2; 2004. p. 179–213.
- [68] Goodman R. Psychometric properties of the strengths and difficulties questionnaire. *J Am Acad Child Adolesc Psychiatry* 2001;40:1337–45.
- [69] Muris P, Meesters C, Eijkelenboom A, Vincken M. The self-report version of the Strengths and Difficulties Questionnaire: its psychometric properties in 8-to 13-year-old non-clinical children. *Br J Health Psychol* 2004;43:437–48.
- [70] Burchinal MR, et al. Development of academic skills from preschool through second grade: Family and classroom predictors of developmental trajectories. *J. Sch. Psycho* 2002;40:415–36.
- [71] Austin JK, Caplan R. Behavioral and psychiatric comorbidities in pediatric epilepsy: toward an integrative model. *Epilepsia* 2007;48:1639–51.
- [72] Organisation mondiale de la santé. World health organization, world health organization staff. International classification of functioning, disability and health: ICF. World Health Organization; 2001.
- [73] Berg A, Berkovic S, Brodie M, Buchhalter J, Cross J, van Emde Boas W, et al. Revised terminology and concepts for organization of seizures and epilepsies: report of the ILAE Commission on Classification and Terminology, 2005-2009. *Epilepsia* 2010;51:676–85.
- [74] Holm S. A simple sequentially rejective multiple test procedure. *Scand Stat Theory Appl* 1979;65–70.