

Preventing depression in adolescents with epilepsy

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Abstract

Purpose. The goal of the work described in this article was to test the possibility of preventing depression among adolescents with epilepsy.

Methods. Adolescents with newly diagnosed epilepsy (104 patients) were screened for depression. The risk for depression was increased in 30 (28.8%) patients (mean age 17.4, 60% females) who were randomized into two equal treatment groups: (1) cognitive-behavioral intervention (CBI) group and (2) treatment with counseling as usual (TAU) group. The Beck Depression Inventory (BDI), Center for Epidemiological Study on Depression (CES-D) scale, Hamilton Depression Scale (HAMD), and Quality of Life in Epilepsy Inventory (QOLIE-31) were administered at baseline and during the 9-month follow-up.

Results. Initial BDI and HAMD scores for the two groups were comparable. Depression was diagnosed during follow-up in three patients in the TAU group. Subthreshold depressive disorder significantly improved at follow-up in the CBI group compared with the TAU group ($P < 0.05$). QOLIE-31 Total scores significantly correlated with both mood improvement and seizure-free state.

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1. Introduction

Depression is the most common mental disorder of people with epilepsy [1–3]. Depression in people with epilepsy often remains undiagnosed and undertreated [3]. Whether preceding the onset of epilepsy or becoming apparent during the course of epilepsy, depression is a chronic illness that negatively affects the quality of life of people with epilepsy [4,5]. Most depressive disorders in young adults may be preceded by depression in adolescence [6,7]. As depression is a chronic illness, its treatment must be longlasting, and increasing levels of depressive symptoms are associated with increasing levels of psychosocial dysfunction [8]. Furthermore, the abatement of subsyndromal symptoms is fundamental to the achievement of long-term remission [9].

Recent studies designed to prevent depression in children and adolescents without epilepsy have reported

encouraging results [10–12]. The first episode of depression often occurs in adolescence and negatively affects the course of epilepsy. Inversely, long duration of uncontrolled seizures and chronicity of illness are significantly related to the development of a negative attributional style in epilepsy [13]. For these reasons, a study of the effect of psychological treatment on preventing depressive episodes in adolescents with newly diagnosed epilepsy seems justified. The working hypotheses were that the use of selective, indicated, preventive interventions (cognitive-behavioral interventions, or CBI) would be more effective in reducing depressive symptoms of subthreshold depressive disorder and preventing the outbreak of depressive episodes in adolescents with epilepsy than supportive psychotherapy (treatment as usual, or TAU), and that such an effect would be evident in the improvement of other outcome measures such as seizure control and quality-of-life. Therefore, we included assessment of seizure control and quality-of-life measurement together with measurement of depressive symptoms as outcome measures in this small,

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randomized trial of selective psychological treatment in the form of CBI versus TAU in adolescents with newly diagnosed epilepsy.

2. Methods

2.1. Subjects

All patients were adolescents (aged 13–19 at the study onset) recruited from general practices in Belgrade and its surrounding areas. These adolescents were referred, by their general practitioners or neuropsychiatrists in primary health care, to our Outpatient Department of Epilepsy located at the Institute of Mental Health; none of these adolescents had attended a psychiatric clinic. *Inclusion criteria* were newly diagnosed epilepsy (either focal or generalized), subthreshold depression, and normal intelligence. Newly diagnosed epilepsy was defined as the occurrence of at least two unprovoked epileptic seizures within a period not longer than 12 months before inclusion in the study. Depending on age, all patients attended either elementary or high school classes. *Exclusion criteria* at baseline were epilepsy caused by progressive cerebral lesion, mental retardation, and a diagnosis of depression, psychotic symptoms, schizophrenia, bipolar disorder, social phobia, agoraphobia, or panic disorder according to the criteria set forth in the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (DSM-IV) [14]. *Withdrawal criteria* were noncompliance either with antiepileptic drug therapy or with CBI or TAU procedures and a decision by the patient or his or her family to withdraw from the study. All subjects received optimal antiepileptic drug therapy and kept seizure diaries throughout the study. The ethics committee of the Institute of Mental Health, Belgrade, authorized the study. Informed consent was obtained from all subjects included in the study. The subjects were motivated to participate in the randomized treatment study as they had a great need to obtain the support in this early phase of their epilepsy. The mean (SD) age of the 30 subjects with subthreshold depression was 17.4 (1.6); there were 18 (60%) females and 12 (40%) males. Intelligence quotients (IQs) ranged from 85 to 132 (mean 103 ± 14.6).

2.2. Procedures

We used several diagnostic assessment instruments. The diagnostic clinical interview used to screen for depression in subjects aged 13–18 was the semistandardized diagnostic interview for mood disorders and other psychiatric disorders in children and adolescents (Schedule for Affective Disorders and Schizophrenia for School-Age Children, Epidemiologic Version Revised (Kiddie-SADS-E-R) [15]), whereas for patients older than 18, we used the semistandardized interview for adults [16]. Two self-assessment scales—the Beck Depression Inventory (BDI) [17] and the Center for Epidemiological Study on Depression (CES-D) scale [18]—were used to screen for depression and quantitatively assess depressive symptoms. These scales are popular self-administered scales used for adults and adolescents, and are able to increase sensitivity in discovering depressive symptoms. Furthermore, a recent study found that both scales could be used to identify major depression in patients with epilepsy [19]. The main objectives in using these scales, as well as the interviewer-administered Hamilton Depression Scale (HAMD) [20], were to screen for symptoms, assess the severity of depressive symptoms, and monitor clinical improvement. In essence, BDI and CES-D have few false-negative results, but many (25–40%) false-positive results. To decrease the number of false-positive results, we used the three scales (BDI, CES-D, and HAMD) only for quantitative assessment, and used the clinical interviews (performed by two authors, Ž.M. and P.S.) as a diagnostic instrument to determine whether the symptoms were of sufficient intensity, number, and duration to meet the criteria for a mood disorder according to DSM-IV [14] or for subthreshold depression.

On BDI, scores of 0–9 points indicate no depression; 10–15 points, symptoms of mild depression; 16–19 points, symptoms of mild to moderate depression; and 20–63 points, symptoms of moderate to severe depression. On CES-D, scores of 0–14 points indicate no depression; 15–21 points, symptoms of mild to moderate depression; and 22–60 points, symptoms of severe depression. On HAMD, scores of 0–7 indicate no depression; 8–15 points, minor depression; ≥ 16 , severe depression.

Risk factors for depression were elicited in a questionnaire completed by parents of each patient and the patient, at baseline and at the 6- or 9-month follow-up. The questionnaire included screening for the following risk factors:

- Individual: genetic vulnerability, presence of other disorders, presence of anxiety disorders, previous depressive episodes, chronic illness, cognitive-attribitional style, cognitive errors, negative self-perception, personal competencies, social skills, problem solving, peer acceptance.
- Familial: depressed parents—not only related to genetic transmission, parental interaction patterns, parental practices, marital conflicts, exposure to deviant peer groups.
- Environmental: negative life events, chronic daily stressors.

These risk factors were identified in previous studies reviewed in detail by Mrazek and Haggerty [21]. Epileptic seizures were also included among stressors, as defined in our previous study [22].

Because initial subthreshold depressive syndrome in adolescents may often progress to full-blown clinical depression [8], all patients with scores of at least 6–8 on BDI or 9–14 on CES-D were also assessed with HAMD and clinical interview as the criterion for subthreshold depression. After 1 month at baseline, patients with higher scores below the level indicating depression (HAMD 6–8) were randomized into two groups: the group receiving short cognitive-behavioral interventions (CBI) and the control group receiving treatment as usual (TAU). Randomization was accomplished by using a computer-generated list of numbers assigned to the clinical registry numbers of the patients. This was done by one of the authors (Ž.M.), who designed the study and managed epilepsy, but did not administer TAU or CBI.

2.3. Treatment procedures

The aims of the study were explained to each subject before randomization. Briefly, patients and parents were told that various forms of psychological treatment would be used to improve the patients' ability to cope with epilepsy. CBI was administered in eight and seven patients, and TAU in seven and eight patients, by P.S. and R.D., respectively. These authors knew that they had to use psychological means to improve the patients' ability to cope with epilepsy, but were unaware of the study hypotheses.

CBI were applied as part of an individual treatment plan aimed at analyzing and modifying distorted automatic thoughts related to negative depressive thinking [23]. Specifically, patients in the CBI group learned to recognize and correct all main types of cognitive errors: catastrophizing, overgeneralization, personalization, and selective abstraction [24]. CBI were administered in eight sessions during the first 2 months of treatment and then in one session per month (rehearsal) during the next 4 months. Sessions included: activity plans, relaxation, identification and correction of thought distortions—cognitive restructuring, role playing, development of social skills, and problem solving. TAU, administered in the same number of sessions, consisted of therapeutic counseling without CBI. All patients randomized to CBI were instructed to note, in a treatment diary, the occurrence of negative thoughts and countermeasures taken (positive thoughts). Negative and positive thoughts were rated on a 4-point scale, and the results at baseline and the 6- and 9-month follow-ups were compared.

Quantitative assessment during baseline and after 6 and 9 months of follow-up comprised the BDI, CES-D, and HAMD scale scores; the ratings of positive and negative thoughts on a 4-point scale; and the Quality of Life in Epilepsy Inventory Total score (QOLIE-31 Total) [25]. Outcome

measures were: seizure control, diagnosable depression during or at the end of follow-up, depression scale scores, and QOLIE-31 Total score. The study setting was a university department for outpatient care of people with epilepsy (Department of Epilepsy and Clinical Neurophysiology, Institute of Mental Health, Belgrade). Seizures and epilepsy were classified according to the Classification of the International League Against Epilepsy [26–28]. Results are presented as repeated measures at three time points: baseline, 6-month follow-up, and 9-month follow-up.

2.4. *Statistical analysis*

Parametric statistical tests in the form of analysis of variance (ANOVA) for repeated measures with post hoc *t* tests were applied where the data exhibited a normal distribution. Data not normally distributed were transformed into logarithmic values, and if these were distributed normally, ANOVA was used. Correlations between BDI, CES-D, and HAMD scores and seizure control, or quality of life, in the CBI and TAU groups were calculated by computing Pearson correlation coefficients. Categorical data were analyzed using the χ^2 test or Wald–Wolfowitz run test. Data were processed using the SPSS for Windows 8 program. The significance level was set at $P < 0.05$.

3. Results

3.1. *Screening*

Of 104 adolescents screened, diagnosable depression was evident in 9 (8.6%); 63 (60.6%) did not have an increased risk for depression. These 72 patients were excluded from the study. The risk of depression was increased in 32 (30.8%) patients who formed the study sample randomized into the CBI and TAU groups. Two subjects, one in each group, withdrew 1 or 2 months after study onset, so the results represent a study sample of 30 patients.

3.2. *Characteristics of study sample with subthreshold depression*

Demographics and epilepsy characteristics of the two groups are summarized in Table 1. The groups were not significantly different with respect to mean IQ (Table 1) and baseline BDI and CES-D scores (Table 2). Complete seizure control was achieved by 10 patients in the CBI group and eight patients in the TAU group, but this difference was not statistically significant (χ^2 test, $P = 0.44$). At baseline, the two groups did not differ with respect to numbers of all three risk factors for depression (Wald–Wolfowitz run test, $P > 0.05$).

3.3. *Outcome of treatment*

Seven to nine months after baseline, three patients in the TAU group, but none in the CBI group, had their first depressive episode. Because of the small number of patients, the difference is not statistically significant. Precipitating events associated with the occurrence of the first depressive episode were a recent romantic breakup in two

Table 1
Demographics and epilepsy characteristics of the CBI and TAU groups

	CBI group	TAU group
Number of patients	15	15
Age		
Range	13–19	13–19
Mean \pm SD	17.2 \pm 2.5	17.6 \pm 2.2
Male/female ratio	6/9	6/9
IQ		
Range	87–130	85–132
Mean \pm SD	104 \pm 14.6	102 \pm 15.8
Seizure type		
Generalized	6	5
Partial	9	10
Etiology of epilepsy		
Cryptogenic/symptomatic	9	9
Idiopathic	6	6
Duration of epilepsy, years, mean (SD)	0.8 (0.3)	0.7 (0.4)
Antiepileptic drug treatment		
Monotherapy	7	9
Polytherapy	8	6
Seizure control		
Seizure-free	10	8
Uncontrolled	5	7

patients and a major life stress (school failure) in one patient.

Assessment at follow-up (6 and 9 months after baseline) revealed that subthreshold depressive disorder was significantly improved, as demonstrated by lower BDI and CES-D scores, in the CBI group compared with the TAU group (ANOVA, $P < 0.05$) (Table 2). According to the QOLIE 31, the higher the Total score, the better the quality of life. At baseline, QOLIE-31. Total scores of the two groups were comparable, whereas after treatment, at both the 6- and 9-month follow-ups, the CBI group had significantly higher scores compared with the TAU group (Table 2) QOLIE-31. Total scores (Fig. 1) were significantly higher in seizure-free patients than in patients with uncontrolled seizures (*t* test, $P < 0.05$) (see Table 3). The correlation of QOLIE-31. Total scores with BDI scores was highly significantly negative in both the CBI group (Pearson correlation coefficient, $r = -0.6930$, $P < 0.01$) (Fig. 2) and the TAU group ($r = -0.8760$, $P < 0.001$) (Fig. 3). When compared with baseline, the numbers of individual risk factors for depression at the 6- and 9-month follow-ups were significantly smaller in the CBI group than in the TAU group (Wald–Wolfowitz run test, $P < 0.05$). The numbers of familial and environmental risk factors for depression at the 6- and 9-month follow-ups were not significantly different than at baseline. Quantitative assessment of positive and negative thoughts in the CBI group indicated a significant decrease at the 6- and 9-month follow-ups when compared with baseline (Wald–Wolfowitz run test, $P < 0.01$), in parallel with the ability to correct the main types of cognitive errors (catastrophizing, overgeneralization, personalization, selective abstraction). Treatment outcome was not significantly affected by the therapist (R.Dj. or P.S.) to

Table 2
Depression scale scores of BCI and TAU groups (controls)^a

Study instrument	Time of assessment			
	Group	Baseline	6-month follow-up	9-month follow-up
BDI	BCI	8.2 (0.94)	5.4 (2.97) ^b	5.60 (3.03) ^b
	TAU	8.1 (0.96)	7.8 (2.66)	7.7 (1.76)
CES-D	BCI	14.1 (4.52)	9.8 (4.20) ^b	10.5 (5.32) ^b
	TAU	13.9 (4.51)	13.6 (4.64)	13.8 (4.79)
HAMD	BCI	5.9 (0.80)	3.3 (1.29) ^b	3.5 (1.73) ^b
	TAU	5.7 (0.70)	5.8 (1.98)	6.73 (2.76)
QOLIE-31 Total	BCI	36.95 (11.05)	52.78 (6.40) ^c	56.40 (5.51) ^c
	TAU	38.48 (10.18)	41.35 (8.26)	42.23 (9.23)
Cognitive risk factors	BCI	9.4 (1.2)	4.6 (0.8) ^b	4.9 (1.1) ^b
	TAU	9.2 (1.4)	7.8 (1.3)	7.5 (1.8)

^a Values are means (SD).

^{b,c} ANOVA, $P < 0.05$; post hoc t tests: ^b $P < 0.05$, ^c $P < 0.01$.

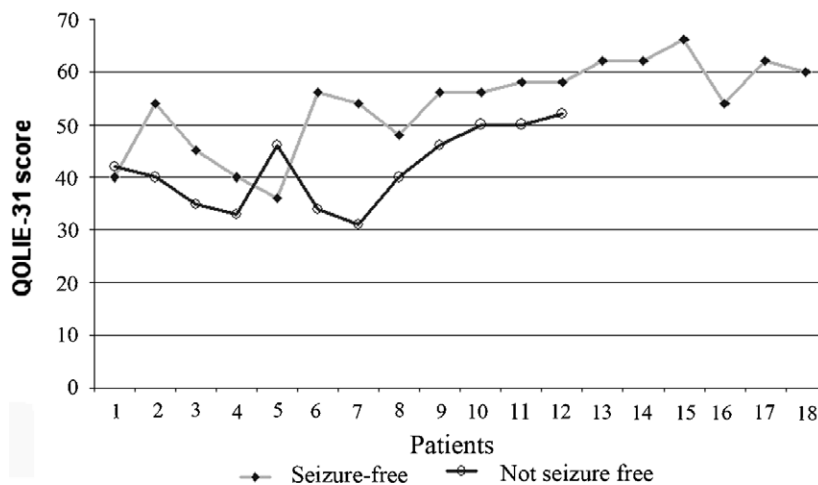


Fig. 1. Relationship of QOLIE-31 Total scores to seizure control for all 30 patients studied, at the 9-month follow-up. Scores of the 18 seizure-free patients are significantly higher than those of the 12 patients with uncontrolled seizures (t test, $P < 0.05$).

Table 3
Correlation of QOLIE-31 Total scores of TAU and CBI groups with seizure control and BDI and CES-D scores at the 9-month follow-up^a

	BDI	CES-D	QOLIE-31 Total
CBI group	5.60 (3.03) ^b	10.5 (5.32) ^b	56.40 (5.51) ^c
TAU group	7.7 (1.76)	13.8 (4.79)	42.23 (9.23)
Seizure-free patients	4.2 (3.62) ^b	11.4 (5.25)	53.72 (8.57) ^c
Patients with uncontrolled seizures	8.5 (3.44)	13.2 (4.86)	41.58 (7.27)

^a Values are means (SD).

^{b,c} ANOVA, ^b $P < 0.05$, ^c $P < 0.01$.

whom a patient was assigned for treatment (Wald–Wolfowitz run test, $P > 0.05$).

4. Discussion

According to a contemporary approach [12], prevention of mental disorders may be universal (targeted toward

whole populations regardless of their risk status), selective (applied to individuals who are considered to be at risk for particular disorders), or indicated (applied to individuals or groups who display mild symptoms of the disorder). Therefore, the type of prevention used in this study was an indicated prevention, as we enrolled in the study adolescents who already manifested mild depressive symptoms. Another type of intervention, the family-based approach [29] or group approach [30], has been demonstrated to be effective for adolescent offspring of depressed parents. Unlike the situation for our patients, this type of intervention is indicated even in adolescents without any depressive symptoms.

Our results are concordant with previous studies using CBI for the treatment of adolescents with depressive symptoms but without epilepsy [11]. However, the results are not directly comparable because of methodological differences between the studies. Contrary to previous studies, TAU was not effective in our patients, which indicates that the

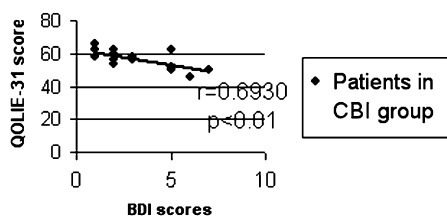


Fig. 2. The correlation of QOLIE-31 Total scores (on y axis) with BDI scores (on x axis) for the CBI group at the 9-month follow-up is highly statistically significant ($P < 0.01$).

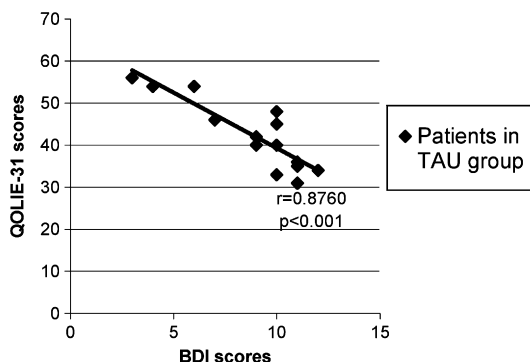


Fig. 3. The correlation of QOLIE-31 Total scores (on y axis) with BDI scores (on x axis) for the TAU group at the 9-month follow-up is highly statistically significant ($P < 0.001$).

nonspecific effects of treatment are not associated with positive therapeutic change. On the other hand, the efficacy of cognitive-behavioral therapy in our patients may be related to its ability to decrease negative thoughts and increase positive thoughts leading to the correction of cognitive errors (see Section 2). Probably, the individual treatment approach used in this study favored the analysis and possible correction of the peculiar features of all four main types of thought distortions in each patient with epilepsy. Because our individual session approach is time consuming, the experience acquired in this study should be used to design a combination of individual and group sessions or a group format only. The latter approach provides a favorable context for training of social skills and coping [10], and manual-assisted cognitive-behavioral therapy would enable the study of preventive interventions by many therapists in randomized large sample(s) [31].

Our results confirm the findings of other studies that achievement of the seizure-free state significantly improves quality of life [4,5,32]. However, we analyzed only the Total scores of the QOLIE-31 scale, as the present study was not designed to determine the relative importance of factors determining the quality of life of patients with epilepsy. Nonetheless, our results suggest that the improved quality of life of our patients in the CBI group, as compared with the TAU group, may be due to the greater reduction of depressive symptoms in

the former group. In fact, the greater persistence of depressive symptoms at follow-up in the TAU group demonstrated an even higher negative correlation with lower QOLIE-31 scores, whereas seizure control did not differ significantly between the CBI and TAU groups. Other studies have found that depression and/or adverse drug effects are more highly correlated with quality of life than seizure frequency or severity [5,33,4,34]. However, these studies included patients with refractory epilepsy and are not strictly comparable to our study with newly diagnosed patients with subthreshold depression who lacked any severe adverse drug effects.

The mechanism of change induced by CBI cannot be deduced from the present study, as we did not measure cognitive functioning in the TAU group. In fact, only one study has examined cognitive functioning in addition to treatment outcome of patients treated with CBI compared with two other types of psychotherapy (nondirective supportive therapy and systemic behavior family therapy) [35]. These authors found that cognitive-behavioral therapy had a greater acute effect on cognitive distortions than other types of psychotherapy. Although further research is needed to identify the underlying mechanisms, it may be hypothesized that CBI may prevent depression in two mutual ways: (1) by stimulating protective factors and, compensatorily, (2) by reducing the effect(s) of risk factors for depression.

Several limitations of the present study must be borne in mind. As a small randomized trial of CBI versus TAU in adolescents with newly diagnosed epilepsy, it does not have the statistical power to determine the significance of all variables influencing outcome measures during follow-up. Further research is needed to replicate findings with larger samples and by independent researchers. Equally, the evaluation of both risk factors and protective factors is also indicated [36]. In this regard, the role of relationship loss as an important trigger of depressive episodes was confirmed as a prospective risk factor for major depressive disorder in adolescents [37].

5. Conclusions

Despite the aforementioned limitations, the results of the present study suggest some effectiveness of selective, indicated, preventive interventions in reducing depressive symptoms of subthreshold depressive disorder in adolescents with epilepsy. The hypothesis that such treatment would have a statistically significant effect in preventing depressive episodes in adolescents with epilepsy was not proven because of the small number of patients. As depressive symptoms were also alleviated significantly by achievement of a seizure-free state, further studies should include larger samples to investigate, on the one hand, the interactions of CBI and seizure control and, on the other hand, the complex relationships between risk factors for depression and protective factors in adolescents with epilepsy.

References

- [1] Kogeorgos J, Fonagy P, Scott D. Psychiatric symptom patterns of chronic epileptics attending a neurological clinic: a controlled investigation. *Br J Psychiatry* 1982;140:236–43.
- [2] Kanner AM. Depression in epilepsy: a frequently neglected multifaceted disorder. *Epilepsy Behav* 2003;4(Suppl. 4):11–9.
- [3] Jones J, Hermann BP, Barry J, Gilliam F, Kanner A, Meador K. Clinical assessment of Axis I psychiatric morbidity in chronic epilepsy: a multicenter investigation. *J Neuropsychiatry Clin Neurosci* 2005;17:172–9.
- [4] Johnson EK, Jones JE, Seidenberg M, Hermann BP. The relative impact of anxiety, depression, and clinical seizure features on health-related quality of life in epilepsy. *Epilepsia* 2004;45:544–50.
- [5] Loring DW, Meador KJ, Lee GP. Determinants of quality of life in epilepsy. *Epilepsy Behav* 2004;5:976–80.
- [6] Pine DS, Cohen P, Gurley D, Brook J, Ma Y. The risk for early-adulthood anxiety and depressive disorders in adolescents with anxiety and depressive disorders. *Arch Gen Psychiatry* 1998;55:56–64.
- [7] Lewinsohn PM, Rohde P, Klein DN, Seeley JR. Natural course of adolescent major depressive disorder: I. Continuity into young adulthood. *J Am Acad Child Adolesc Psychiatry* 1999;38:56–63.
- [8] Lewinsohn PM, Solomon A, Seeley JR, Zeiss A. Clinical implications of “subthreshold” depressive symptoms. *J Abnorm Psychol* 2000;109:345–51.
- [9] Judd LL, Akiskal HS, Maser JD, et al. Major depressive disorder: prospective study of residual subthreshold depressive symptoms as predictor of rapid relapse. *J Affect Disord* 1998;50:97–108.
- [10] Clarke GN, Hornbrook M, Lynch F, et al. A randomized trial of a group cognitive intervention for preventing depression in adolescent offspring of depressed parents. *Arch Gen Psychiatry* 2001;58:1127–34.
- [11] Jaycox LH, Reivich KJ, Gillham J, Seligman MEP. Prevention of depressive symptoms in school children. *Behav Res Ther* 1994;32:801–16.
- [12] Barrett PM, Turner CM. Prevention of childhood anxiety and depression. In: Barrett PM, Ollendick TH, editors. *Handbook of interventions that work with children and adolescents*. Chichester: Wiley; 2004. p. 429–74.
- [13] Kanner AM. Depression in epilepsy is much more than a reactive process. *Epilepsy Curr* 2003;3:202–3.
- [14] Diagnostic and statistical manual of mental disorders, DSM-IV. Washington, DC: American Psychiatric Assoc.; 1994.
- [15] Puig-Antich J, Orvaschel H, Tabrizi MA, Chambers W. The schedule for affective disorders and schizophrenia for school-age children: Epidemiologic version (Kiddie-SADS-E). 3rd ed. New York: New York Psychiatric Institute and Yale Univ. School of Medicine; 1980.
- [16] Endicott J, Spitzer RL. A diagnostic interview: the schedule for affective disorders and schizophrenia. *Arch Gen Psychiatry* 1978;35:837–44.
- [17] Beck AT, Ward CH, Mendelson M. An inventory for measuring depression. *Arch Gen Psychiatry* 1961;4:861–71.
- [18] Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. *Appl Psychol Meas* 1977;1:385–401.
- [19] Jones JE, Hermann BP, Woodard JL, et al. Screening for major depression in epilepsy with common self-report depression inventories. *Epilepsia* 2005;46:731–5.
- [20] Hamilton M. Development of a rating scale for primary depressive illness. *Br J Doc Clin Psychol* 1967;6:278–96.
- [21] Mrazek PJ, Haggerty RJ. Reducing risks for mental disorders: frontiers for preventive intervention research. Washington, DC: Natl. Academy Press; 1994.
- [22] Martinović Ž. Adjunctive behavioural treatment in adolescents and young adults with juvenile myoclonic epilepsy. *Seizure* 2001;10:42–7.
- [23] Beck AT, Rush AJ, Shaw BF, Emery G. *Cognitive therapy of depression*. New York: Guilford Press; 1979.
- [24] Beck AT. *Depression: causes and treatment*. Philadelphia: Univ. of Pennsylvania Press; 1967.
- [25] Cramer JA, Perrine K, Devinsky O, Bryant-Comstock L, Meador K, Hermann B. Development and cross-cultural translations of 31-item Quality of Life in Epilepsy Inventory (QUOLIE-31). *Epilepsia* 1998;39:81–8.
- [26] Commission on Classification and Terminology of International League Against Epilepsy. Proposal for revised clinical and electroencephalographic classification of epileptic seizures. *Epilepsia* 1981;22:489–501.
- [27] Commission on Classification and Terminology of International League Against Epilepsy. Proposal for revised classification of epilepsies and epileptic syndromes. *Epilepsia* 1989;30:389–399.
- [28] Engel J. A proposed diagnostic scheme for people with epileptic seizures and with epilepsy: report of ILAE Task Force on Classification and Terminology. *Epilepsia* 2001;42:796–803.
- [29] Beardslee WR, Gladstone TR, Wright EJ, Cooper AB. A family-based approach to the prevention of depressive symptoms in children at risk: evidence of parental and child change. *Pediatrics* 2003;112:e119–31.
- [30] Gregory CN, Hornbrook M, Lynch F, et al. A randomized trial of a group cognitive intervention for preventing depression in adolescent offspring of depressed parents. *Arch Gen Psychiatry* 2001;58:1127–34.
- [31] Tyrer P, Thompson S, Schmidt U, et al. Randomized controlled trial of brief cognitive behaviour therapy versus treatment as usual in recurrent deliberate self-harm: the POPMACT study. *Psychol Med* 2003;33:969–76.
- [32] Boylan LS, Flint LA, Labovitz DL, et al. Depression but not seizure frequency predicts quality of life in treatment-resistant epilepsy. *Neurology* 2004;62:258–61.
- [33] Birbeck GL, Hays RD, Cui X, Vickrey BG. Seizure reduction and quality of life improvements in people with epilepsy. *Epilepsia* 2002;43:535–8.
- [34] Gilliam FG, Fessler AJ, Baker G, et al. Systematic screening allows reduction of adverse antiepileptic drug effects: a randomized trial. *Neurology* 2004;62:23–7.
- [35] Kolko DJ, Brent DA, Bauger M, Bridge J, Birmaher B. Cognitive and family therapies for adolescent depression: treatment specificity, mediation, and moderation. *J Consult Clin Psychol* 2000;68:603–14.
- [36] Resnick MD, Bearman PS, Blum RW, et al. Protecting adolescents from harm: findings from the National Longitudinal Study of Adolescent Health. *JAMA* 1997;278:823–32.
- [37] Monroe SM, Rohde P, Seeley JR, Lewinsohn PM. Life events and depression in adolescence: relationship loss as a prospective risk factor for first onset of major depressive disorder. *J Abnorm Psychol* 1999;108:606–14.