

Monitoring and Managing Depressive Symptoms in Adolescents with Epilepsy

Giangennaro COPPOLA¹,
Grazia PASTORINO²,
Francesca Felicia OPERTO³

¹ Child and Adolescent
Neuropsychiatry, Salerno, Italy,
gcoppola@unisa.it

² Child and Adolescent
Neuropsychiatry, Salerno, Italy

³ Child and Adolescent
Neuropsychiatry, Salerno, Italy

Abstract: *Depressive disorders are the most frequent psychiatric disturbances associated with epilepsy in adolescents and include a broad and heterogeneous spectrum of conditions that share hallmark features and symptoms such as sadness, irritability, decreased motivation or interests, fatigue, withdrawal, hopelessness, anhedonia, changes in appetite and weight, and sleep disturbances that are persistent and pervasive most days for at least 2 weeks. Using generic self-report depression surveys and current diagnostic codes, clinical and surveillance studies have revealed prevalence rates of 20–25% for depression in youth with epilepsy, with adolescents showing particular vulnerability. Furthermore, 20% of youth with epilepsy endorse suicidal ideation, and youth endorsing suicidal ideation do not necessarily have clinical symptoms of depression. Considering that depression in youth with epilepsy is a common comorbidity, characterized by poorer psychosocial and healthy-related outcomes and increased risk of suicide, a brief, free measure of specific depressive symptoms in youth with epilepsy would be beneficial. Recently, the NDDI-E-Y inventory has been developed from the adult NDDI-E, and validated in many countries. NDDI-E-Y showed reliable and construct validity, being a brief screening tool (12 items) that can be easily included in routine epilepsy care. For the management of depressive symptoms in adolescents, interventions can be distinguished in non-pharmacological and pharmacological. The first includes psychoeducation which should clarify to adolescents and parents the main features of epileptic disorder, side effects of antiepileptic drugs, treatment modalities, how to cope with learning and social difficulties, in order to improve quality of life. Concurrently, a cognitive-behavioral therapy (CBT) including individual therapy, supportive and family therapy and school services, should be carried on. Psychopharmacology for depressive symptoms should be deserved to moderate to severe depressive symptomatology, only after deep assessment of prior and current antiepileptic and/or psychopharmacologic treatment. SSRIs including fluoxetine, sertraline, fluvoxamine and escitalopram should be first considered. Data coming from experimental studies in animals and humans seem to confirm no decrease of seizure threshold by SSRI adjunctive therapy.*

Keywords: *screening tools; NDDI-E-Y; depression; anxiety; adolescents; monitoring; managing; psychopharmacology.*

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Introduction

Seizure disorders are the most common childhood neurologic condition, with 4-10% of children experiencing at least one seizure. Children with epilepsy have higher rates of emotional and behavioral problems than their healthy peers. In particular, mood disorders are increasingly present in pre-adolescent ages compared to younger children. Adolescence, indeed, is a particularly vulnerable period marked by profound developmental changes in the biological, social and psychological domains. Coping with these changes may be especially challenging for adolescents with epilepsy. Conflicts between life expectations and the limitations of a chronic disease could also reduce quality of life and result in increased emotional problems. Recent studies report anxiety and depression in adolescents in 15-36% and 8-35%, respectively; noteworthy, clinical-based studies report higher rates of mood disorders (20-36%) compared to population-based studies (5-13%).

Furthermore, 20% of suicidal ideation youth with epilepsy endorse suicidal ideation, and youth endorsing suicidal ideation do not necessarily have clinical symptoms of depression (Jones et al., 2013). In a case-control study, 53 children aged 8 to 18 years with recent onset epilepsy of idiopathic etiology, Jones et al. (2007) showed higher rates of depressive and anxiety disorders, and less prevalent rates of attention-deficit-hyperactivity disorder, oppositional defiant and tic disorders, with no significant difference between focal and generalized epilepsy. Depression symptoms comprised tearfulness, sadness, becoming easily upset, separation anxiety, and social phobia.

Risk for depression was found significantly higher by Kwong et al. (2016) in adolescents with epilepsy and lower IQ, with persisting seizures vs well controlled, depending on seizure focus localization and type of antiepileptic drug. In addition, significant contributors to internalizing problems were psychologic response to disease, hopelessness, seizure adverse effects on family, poor emotional and communication support and maternal depression.

With respect to seizure focus localization, a recent study by Schraegle and Titus (2017) reported that children and adolescents with temporal lobe epilepsy developed more frequently depression with respect to those with frontal lobe epilepsy.

Depressive episodes may also be triggered after starting with an antiseizure medication with negative psychotropic properties, after withdrawal of an antiseizure medication with mood stabilizing effect or after

adding an enzyme-inducing AED leading to a serum level decrease of ongoing antidepressant therapy (Barry et al., 2008).

Every AED, including those positive psychotropic properties, can trigger psychiatric symptoms in epileptic patients, some with a greater severity than others. In some cases, Phenobarbital can result in depression that may occasionally be related to the presence of suicidal ideation and behavior. Seemingly, primidone, tiagabine, vigabatrin, felbamate, topiramate, levetiracetam and zonisamide have been reported to trigger symptoms of depression, particularly in subjects with a prior history of depressive symptoms of mood disorder. Adverse cognitive events as those linked to topiramate therapy should be considered in order to avoid depression also in adolescents and young adults. Interestingly, children and adults with incident unprovoked seizures are 1.7-fold more likely to have a history of major depression before seizure onset, and major depression is a risk factor for unprovoked seizures (Hersdorffer et al., 2006).

With respect to suicidal ideation, nearly 20% of youth with epilepsy endorse it, but they do not necessarily have clinical symptoms of depression. Luckily, suicidal attempts are very rare among adolescents with epilepsy compared with suicidal ideation (20-25%) (Fulga, Perju-Dumbravă & Crassas, 2008; Perju-Dumbravă et al., 2019; Zamari, Mehdizadeh, & Sadeghi, 2012).

Among the several methods so far available to detect and screen depressive symptoms in young patients with epilepsy, today CDI-2 questionnaire has to be considered the gold standard. Nonetheless CBCL questionnaire for teenagers and the recently validated NEDDI-E-Y questionnaire (Wagner et al., 2016). (Fig.1) are particularly useful and sensitive screening tools, also for suicidal ideation screening. Of course, a thorough psychiatric evaluation should always follow, to confirm depression, and all the etiologic components (familial, socio-educational, treatment - dependant and so on)

(Perju-Dumbravă et al., 2013).

Fig. 1. The 12-item revised NDDI-E-Y for children and adolescents with epilepsy, aged 12-17 years

Factor Pattern		Factor I
NDDIEY 1	Everything is a struggle	0.67407
NDDIEY 2	I have trouble finding anything that makes me happy	0.71354
NDDIEY 3	I feel like crying	0.74924
NDDIEY 4	I feel frustrated	0.71954
NDDIEY 5	I feel unhappy	0.75388
NDDIEY 6	I think about dying or killing myself	0.54603
NDDIEY 7	Nothing I do is ever right	0.65103
NDDIEY 8	I feel sorry about things	0.62544
NDDIEY 9	I feel sad	0.80397
NDDIEY 10	I feel guilty	0.65280
NDDIEY 11	I feel cranky or irritated	0.61863
NDDIEY 12	I feel alone	0.76142

Management of depressive symptoms in adolescents with epilepsy

The first step to be considered when treating adolescents with epilepsy and depressive symptoms is the potential detrimental role of antiseizure medications together with the effect of seizure persistence.

Some antiseizure medications, as monotherapy or in combination as phenobarbital, carbamazepine and lacosamide, may easily cause cognitive impairment and lethargy, thus leading to mood worsening. Sometimes it is quite enough to shift to other drugs like valproic acid, lamotrigine or levetiracetam to get clinical improvement. It is as well mandatory to consider if depressive symptoms are developing early after seizure onset or during follow-up. Seizure onset in a teen-ager frequently means loss of freedom due to parental worries and anxiety. Life suddenly changes and the adolescent is heavily limited as to daily activities (go out alone for a walk, motorbike forbidden, etc.). Consequently, psychoeducation through an improved knowledge of epilepsy disorder both to the patient and his/her parents has great importance. A cognitive-behavioral approach is as well indicated.

A psychopharmacological treatment including SSRI like sertraline, fluoxetine, fluvoxamine and escitalopram should be considered mainly in moderate to severe cases. As reported in animal studies, seizure threshold is not lowered by these drugs. Nonetheless, drug-drug interactions has to be considered as enzyme-inducing antiepileptic drugs like phenytoin, carbamazepine and phenobarbital can decrease SSRI blood- levels. On the other hand, fluoxetine/fluvoxamine increase phenytoin, carbamazepine and valproic acid serum levels, by directly inhibiting P450 liver enzyme.

In conclusion, monitoring mood disorders is strongly indicated in adolescents and young patients with epilepsy. Validated scales and questionnaires as the NEDDI-E-Y and CBCL are particularly useful tools in this regard.

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