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DEPRESSIVE DISORDERS IN CHILDHOOD AND ADOLESCENCE: PECULIARITIES AND PROBLEMS OF TAKING CARE. A LITERATURE REVIEW

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ABSTRACT

Depressive disorders in developmental age represent a significant healthcare challenge, both for the growing prevalence and for the clinical and psychosocial peculiarities. This issue is connected to the problem of emotional dysregulation in childhood and adolescence and to the problem of suicidal risk. The authors describe the characteristics of depression in childhood and adolescence reporting the state of the art with respect to the current needs of care and therapy with reference also to pharmacological therapy.

KEYWORDS: depression, taking care, emotion dysregulation, child and adolescent

1. INTRODUCTION

Depressive disorders represent a clinical picture that also affects developmental age, with different clinical peculiarities and significant care issues.

Over the last 10 years, anxiety and depression have increased significantly among children and young people. Internalizing disorders were already on the rise before the COVID-19 emergency [1]; in the USA in 2016, approximately 5% of twelve-year-old and 17% of seventeen-year-olds reported having experienced a major depressive episode in the previous 12 months [2].

The pandemic and then the international war scenarios, which generate concern and uncertainty about the future, have further accentuated this trend. Requests for help from services have increased and disorders have increased in prevalence and incidence, especially among minors and young people [3]-[4]-[5].

“Just think that most depressive conditions begin in adolescence (1 in 4 females and 1 in 10 males), but are often preceded by other disorders such as sleep disorders, 59% of cases of eating disorders occur between 13 and 25 years of age, 6% are under 12 years of age, and that suicide is the leading

cause of death in Italy among adolescents (2019 data). The early onset of these pathologies is also associated with more serious and complex conditions” [6].

49.4% of young Italians between 18 and 25 years of age said they suffered from anxiety and depression due to the COVID-19 health emergency. For the same reason, 62.1% changed their vision of the future [7].

Similar data emerged from the Report “Generazione Post Pandemic: bisogni e aspetti dei giovani italiani nel post Covid 19”, developed in collaboration with Censis, the National Youth Council and the National Youth Agency in June 2022 [8].

We are therefore talking about huge numbers in Europe and in the world [9]. For this reason, it is very timely to organize services for the detection and management of this significant public health problem [10].

Today, the clinical interest in this condition is therefore constituted first of all by the emergency of data from the last 3-4 years, certainly not addressable by services with ordinary resources; then by the extent of the functional impairment with scholastic and social repercussions, by the peculiarity of the symptoms depending on the age group, [11] and by the short- and long-term outcomes for the entire development of the individual. Another important element is the risk of suicide in adolescence, strongly correlated to these issues, and always of great media and social impact.

The genesis of the disorder must be traced back to the bio-psycho-social paradigm, with a genetic predisposition and vulnerability (familiarity), associated with relational factors (early relationships, attachment characteristics), educational, environmental, possible stressful factors and life events of various types. Studies on parenting [12]-[13], correlate “parenting” with the onset of depression, that is, difficulties in managing intra-family conflicts determine an increase in the risk of depression in children.

Very recent data [14] also correlate child abuse and maltreatment with the onset of childhood-adolescent depression.

Currently [15] we are therefore looking for old and new etiological factors (e.g. digitalization, new forms of communication, social media) of this increase in internalizing disorders in general.

However, from an organic point of view, neuroimaging data [16] show early the same atypias that are later detected in adults in frontal, limbic and temporal areas, which justifies the need for an early diagnosis and above all for adequate interventions.

For the categorical diagnostic framework, the references of the DSM 5-TR [17] and the ICD 10 [18] are valid, which highlight 2 main forms: Major Depressive Disorder and Persistent Depressive

Disorder (formerly called Dysthymia, chronic form) with the difference that to make a diagnosis of persistent depressive disorder in developmental age, 12 months and not 2 years of symptoms are enough.

In this examination, for diagnostic purposes, 2 crucial aspects must be considered first of all: the first corresponds to the distinction between subthreshold symptoms and "paraphysiological mood" alterations on the one hand and a structured clinical picture on the other, the second aspect concerns the peculiarity of the depressive clinic in children and adolescents.

In general, typical of the clinical presentation of depression in developmental age is the cyclicity during the same day, the alternation with altered or elevated mood and the comorbidity with different disorders. In fact, one is often induced to make a diagnosis of unspecified mood disorder, a term reintroduced by the DSM5-TR, both for the vagueness and variety of symptoms, and for the detection of clear elements of developmental risk in a psychotic or bipolar sense.

That said, the basic manifestations of depressive disorders in children and adolescents can be considered substantially similar to those of adults but are related to ideational contents and worries typical of children, such as study, sports and play activities. Children may not be able to express their emotional conditions or internal experiences. Depression or mood disorder must be taken into consideration when a young person or a child, who previously behaved adequately, begins to show a decline in school performance, isolates himself or becomes too reactive or commits socially problematic actions [19]. A decline in school performance is always a relevant symptom in the history of a minor, both with respect to depressive symptoms and with respect to the prodromes of schizophrenia, which, as is known, can also be preceded by a long prodromal period that can be mistaken for a simple cognitive decline. In some children with a major depressive disorder, the predominant mood is irritability rather than sadness (an important difference between the infantile form and the adult forms). Irritability associated with childhood depression can also manifest as hyperactivity and aggressive, antisocial behavior [20].

In children with intellectual disabilities, depression or other mood disorders can manifest as somatic symptoms and behavioral disorders.

Similarly, as age increases, the discomfort shifts from the somatic and behavioral side to the internalized side, because the capacity for self-observation and introspection grows. On the other hand, in immigrant minors, for socio-cultural or linguistic reasons, it is more frequent that depressive symptoms remain in the somatic or behavioral area, with anxious-depressive disorders and manifestations, in comorbidity with PTDS, typical of these conditions.

In preschool age, the symptoms are mainly non-verbal: the child is apathetic, sad, slow, scarcely interested in the environment and play, the facial expressions are little varied, so much so that they

can simulate some aspects of autism, from which these pictures differ for a greater and more physiological capacity to respond to environmental stimuli. Somatizations and regressive phenomena are possible.

With school age, the ability to verbalize psychic suffering increases, with experiences of low self-esteem, abandonment, loss, or boredom and apathy with respect to age-appropriate activities. Instability and impulsivity are also possible, with the risk of confusion with a picture of ADHD, with which it can also be in comorbidity, even if in depression the experiences of loss and sadness prevail.

In adolescence, on the one hand, the picture reflects a greater awareness of one's experiences, but on the other hand, it can highlight a more severe psychosocial impairment, both due to serious learning difficulties, thoughts of death with suicidal risk, dysfunctional behaviors and possible access to psychotropic substances.

It is also necessary to remember the atypia of symptomatic manifestations in preadolescence and adolescence. Sometimes apathetic and withdrawn forms prevail, or with a tendency to demonstrative behavior, or elements in common with borderline PD, or the alternation or rather the imbrication with hypomanic symptoms that pose the problem of diagnosing bipolar disorder and the need for targeted therapeutic strategies.

In the case of more complex pictures, psychotic symptoms may appear, usually consistent with mood, which make it necessary to make a differential diagnosis with respect to a schizophrenic-type psychotic onset, while more likely these symptoms can orient towards a picture of current or future bipolarism.

In this regard, the importance of emotional dysregulation as a cross-cutting substrate for many developmental pathologies, but in particular mood disorders, should be considered.

2. The Emotional Dysregulation

Emotional dysregulation has been defined as “the frequent and intense experience of emotions combined with the inability to cope with their occurrence” [21].

ED can be related to constitutional and genetic factors, traumatic environmental events and characteristics of early relational experiences.

Emotional dysregulation is therefore a condition that underlies all the symptomatic pictures of developmental psychopathology and basically consists in a maladaptive processing of internal or external stimuli when the regulation systems function impaired. Most of the time this impairment is significant and disabling in all life ambitions. The reactions appear incongruous and excessive, compared to the elementary rules of social life: at school and in different social, sporting or recreational

contexts in general, with adults or with peers in sport, reactions of high excitability, unstable mood, irritability, up to behavioral excesses and aggression occur.

In childhood, emotional dysregulation is structured as a path of great difficulty that intensely involves family members, school and other life contexts. In adolescence, specific transformations of the period are intertwined with emotional dysregulation, determining marked dysfunctionality of thymus, behavior and active functioning as a whole.

The mechanism of self-regulation and its failure in bipolarism in developmental age would be relevant [22].

A recent study by Hollender [23] correlates emotional dysregulation in preschool age with the onset of affective disorders and depression in adolescence.

DE is considered crucial for the development and maintenance of depressive and especially affective symptoms in developmental age. This is due to the attenuation of positive emotions and gratification and accentuation of negative emotions such as sadness, boredom and apathy, as well as poor regulation of the emotions themselves with irritability and reactivity to the environment with a relative sense of unworthiness and low self-esteem. The tendency to ruminate and the underlying negative pathogenic beliefs as well as the poor awareness of emotions are able to maintain a low or irritable mood throughout the day.

3. Taking care and diagnosis

Meanwhile, the environment and even clinicians show difficulty in distinguishing clear symptoms of depression and “traits” reactive to stressful events or to the pre- and adolescent phase. In recent years, efforts have been directed precisely towards the distinction between an adolescent “crisis” and diagnostically structured depressive (or sometimes psychotic) symptoms.

While it is true that at least 2 weeks of symptoms are needed, this is not a significant enough criterion to distinguish between those who have difficulty going through this phase and those who remain blocked in some way [24]. Therefore, only the latter should be considered as “sick” [25].

What makes depressive symptoms so frequent at this age is the fact that adolescence involves a process of loss and pain. In order to become adults, adolescents must process a mourning experience, that is, they must face the loss of the ideal of parents possessed during childhood, mourn the loss of their childhood and the happy lifestyle associated with it, and, finally, they must face the loss of their bisexuality, dealing with the dynamics related to separation-individuation and the elaboration of the concept of a sexual body with a defined gender identity.

Dealing with developmental tasks therefore involves mourning, but the elaboration of this mourning heralds an expansion of existential boundaries, with an increase in cognitive potential, emotional investment in the body, in the activities of the peer group and the first relationships as a couple.

If many adolescents present symptoms of depression, then, when should we worry about the existence of a true depressive picture? There are several indicators: first of all, the presence of an accentuated sense of guilt and anxiety in a very inhibited adolescent constitutes an alarm signal. Generally, an adolescent of this type has probably had stressful events during childhood and then we speak of a progression from childhood to adolescence towards a depressive disorder. Depression can at the same time be camouflaged behind a mosaic of somatizations, dysmorphophobia or behavioral and/or eating disorders. In a depressive picture, the existence of derealization, suicidal ideas or acts and a disinvestment in commitments and relationships represent aggravating factors. Furthermore, it is worth remembering that the most serious depressive states are not necessarily the most evident and that parents tend to be more alarmed by challenging attitudes than by those of excessive submissiveness and emotional flattening, which are equally if not more dangerous. Obviously, the distinction, apart from the references of the diagnostic systems, is to be found in the quality and intensity of the symptoms, in the degree of dysfunction they entail, in the degree of alienation from significant relationships both with peers and with reference adults; conflict at home, irritability, opposition, should not lead us to a diagnosis if several or all areas of functioning are preserved, such as an emotional relationship or with the sports group, the evaluation of the role of reference adults, planning and hope for the future. I repeat, in addition to the diagnostic manuals, and the verbalization of suffering, in adolescents it is often the sensation of loss of hope and lack of a "way out" that must activate the attention of the clinician, also with respect to a possible anti-conservative act.

It should not be forgotten that access to psychoactive substances can modify the symptoms of thymism, both as a contributory cause of a mood disorder, and as self-treatment of suffering, which subsequently activates a structured addiction. In adolescents, the relationship with substances of abuse should always be investigated, especially cannabis, which is the most socially accepted and which is particularly involved in the risk of early psychosis and emotional imbalances [26].

To aid diagnosis, there are several self-administration tools that can be used with children aged 6-7 years and older, although it is advisable to take their duration into consideration to avoid excessively tiring the subjects. In first place are the CDI [27] and the K-SADS [28]-[29].

The Children's Depression Inventory-CDI, is based on the Beck Depression Inventory-BDI [30], therefore, it is based on Beck's cognitive theory of depression. Following this same theoretical line, the Children's Depression Scale-CDS [31] was designed, from the beginning it was conceived exclusively to assess childhood depression. According to Chorpita et al. [32] the CDI measures a broader construct of negative affectivity rather than depression as a separate construct, and that can be useful for screening the dimensions of personality traits or characteristics, while other instruments,

such as the Revised Child Anxiety and Depression Scale -RCADS, tend to measure a specific clinical syndrome. We also use the SAFA battery, a self-administered diagnostic tool, consisting of a coordinated set of scales that explores a wide range of symptoms and psychic states in the area of internalizing disorders in developmental age. The items that make up the SAFA are adapted to the age of the subject, a feature that allows a high reliability of the instrument. The scales can be administered together (for a comprehensive screening of the person) or individually (to answer specific clinical questions) [33].

To arrive at a diagnosis, as always in developmental age, it is necessary to collect information from all the people who are part of the child's life context, as well as from the child himself. The diagnosis is always clinical, but the aforementioned tools can give us an idea of the severity of the condition and the possible effects of ongoing treatment.

It is essential to look for stressful events and the correlation with negative experiences such as abuse, mistreatment or bullying. It is important not to forget to exclude medical conditions or the effect of pharmacological therapies and/or substances of abuse. A careful evaluation of the anamnesis and appropriate laboratory tests are therefore often necessary to exclude other pathologies (e.g. mononucleosis or thyroid disease) that can cause similar symptoms such as apathy, slowness and hypersomnia

As regards the management and care of childhood-youth depression, the NICE guidelines of June 2019 [34] should be mentioned: they propose a “gradual” treatment model for depression, drawing attention to the different needs of minors affected by depression - depending on their clinical and psychosocial characteristics - and to the necessary care responses. The stages are:

- Identification of depression and risk profile in primary care;
- Identification of depression in children and young people who turn to specialist services;
- Management of depression recognised in primary care - mild depression;
- Management of depression recognised at a specialist level - moderate to severe depression;
- Management of depression recognised in a hospital setting, such as drug-resistant, recurrent and psychotic depression, including conditions requiring hospitalisation.

Obviously, the management of depression also raises the question of the transition to adult services, in the case of persistence of the clinical picture before the age of 18, with particular attention to the continuity of care and to an adequate juxtaposition of the interventions of the 2 teams, one for minors and one for adults.

4. Suicidal risk

Depression is of importance in developmental age and especially in adolescence because it correlates with the risk of suicide, and we know that suicide is one of the main causes of death in adolescence, together with accidents.

This is in accordance with the World Health Organization (WHO) [35], which indicates suicide as the second cause of death in young people between 15 and 29 years.

Depression, emotional dysregulation and suicidal ideation are correlated, even if it is not yet known to what extent, to non-suicidal self-harm, which are proving to be very widespread in recent years and which the DSM 5_TR has included in its Nosographic schemes. From this point of view, emotional dysregulation often underlies these symptoms correlating in comorbid conditions mood disorder, gender incongruence, DNA-type problems and self-harm.

However, suicidality, which includes a wide spectrum of situations ranging from sporadic ideation to frankly self-harmful behavior, must be well investigated. Where there is a plan and not a vague idea, where there are risk factors, some form of protection must be activated, from 24-hour monitoring in a protected family environment to hospitalization in a suitable environment. Risk factors are a previous attempt, a family history of suicide, comorbidity with bipolar disorder, substance use, an impulsive temperament in the child or in the family.

Recent research [36] correlates child abuse with the risk of youth suicidality, as other authors correlate it, precisely, as previously highlighted, with the risk of depression.

In a very large recent study [37] it seems that relationality in life contexts can be a very important protective factor, if the child does not have particular associated risk factors, such as a recent suicide attempt or other life events.

Therefore, in the diagnostic evaluation questions [38] regarding the risk of suicidality (which goes, we repeat, from the idea, to the planning, to the attempts) must never be omitted. Even sudden changes from discomfort to calm should not be ignored as a warning signal, and the child's environment must be well informed of this.

5. Comorbidity

Often, MDD and DPD coexist in the same patient, which represents a negative prognostic factor. Often, the depressed patient is at risk of developing bipolar disorder, especially if there is a family history and psychotic symptoms coexist [39].

Bipolar disorder in developmental age is equally problematic as a diagnosis, often due to its atypicality, sometimes due to the finding of chronic hyperexcitability without defined episodicity, and often also due to the mixture with symptoms such as ADHD and Oppositional Defiant Disorder.

Furthermore, recent studies [40] maintain that inattention and deficits in executive functions (EF) typical of ADHD-type disorders can be predictors of depression in adolescence.

Often, in cases of significant dysregulation of mood and behavior, it is still worth looking for symptoms that satisfy the diagnosis of bipolar disorder or Borderline PD.

We also recall that the DSM 5 [41] has identified a separate form, disruptive mood dysregulation, as a result of the clinical and research need to identify particular forms of mood disorder in developmental age. An anxiety disorder in its various manifestations can typically be comorbid with depression but can very often precede the emergence of a depressive disorder in developmental age.

It is not uncommon for mood disorders, eating disorders and anxiety disorders to occur in comorbidity with diverse symptomatic manifestations.

Recent research [42] highlights how anxiety and depression in comorbidity with other disorders are less present in adolescence than in childhood, as if internalizing symptoms can take on a different value and meaning as age passes.

Comorbidity, especially with externalizing disorders, seems to be an unfavorable prognostic factor [43].

Although most children and adolescents recover from the first depressive episode, a percentage of children, 30-70%, especially those with risk factors, experience one or more relapses. We specify that remission means a period of at least 2 weeks without symptoms. Recovery means a period of at least 2 months without symptoms

Risk factors can be considered a significant family history, comorbid psychiatric disorders, chronicity of depressive symptoms, anxiety, negative cognitive style and exposure to negative life events (for example, family conflicts, mistreatment and abuse), low IQ.

6. Therapeutic Interventions

Treatment of depressive disorder must include:

- 1- Interventions directed simultaneously at the family and school and reference contexts;
- 2- For adolescents, usually psychotherapy and pharmacological therapy with antidepressants;
- 3- For children and preadolescents, psychotherapy alone is often preferred, followed, if necessary, by antidepressant pharmacological therapy.

Therefore, it is believed that appropriate measures aimed at the family and school should be combined with direct treatment for the child or adolescent. The intervention for parents is of a psychoeducational nature, according to the most accredited models, which include information, problem solving and interventions on communication styles [44]. A short hospital stay may be necessary in acute crises, especially if a suicidal risk is identified. Likewise, in severe forms, a socio-rehabilitative intervention in a community for minors should not be excluded.

For adolescents (as for adults), the combination of psychotherapy and antidepressant drug therapy is usually much more effective [45]. Clinicians tend to focus on psychotherapy in younger children; however, drugs can also be used in very young subjects (fluoxetine can be used in children aged ≥ 8 years), especially when depression is severe or does not respond to psychotherapy [46].

Basically, one can focus on the functional impairment. In mild depression, in which functioning is not much compromised, psychotherapy alone can be used; in moderate depression, there are many symptoms and a significant weakening of general functioning; in the severe form there is general impairment of adaptive functioning. In these last 2 forms, it is also necessary to refer to pharmacological therapy. Generally, among other things, after 3 months of a psychotherapeutic intervention it is necessary to evaluate whether there are results and what the boy's experience is with respect to the path itself.

Regarding medications, an SSR-I is usually the first-choice antidepressant [47]. Children should be closely monitored for behavioral side effects (e.g., disinhibition, behavioral activation), which are common but usually mild to moderate, decrease with dose reduction, and are rarely serious. Behavioral adverse effects can occur with any antidepressant and at any time during treatment, so children and adolescents taking these medications should be closely monitored.

A recent 2020 meta-analysis [48] found that fluoxetine was the drug that offers the best results in moderate and severe forms of depression, although assessments should be made on a case-by-case basis. Another 2022 meta-analysis also highlighted the significant role of fluoxetine, combined with cognitive-behavioral therapy [49].

In very severe depression, psychotic and/or manic symptoms may require treatment with an antipsychotic drug [50]-[51] or a mood stabilizer.

In forms with bipolar features, a mood stabilizer can be started at the first episode, together with psychotherapeutic and psychoeducational interventions [52]. Lithium and lamotrigine are considered the most suitable molecules [53] together with psychotherapeutic and psychosocial interventions.

Children and adolescents must remain in treatment for at least 1 year after remission, but subjects who have experienced a number of major depressive episodes ≥ 2 must be treated permanently.

There has been much discussion in the last 20 years about the risk of suicide associated with treatment with antidepressants [54]. In fact, 2 meta-analyses, one in 2004 in the USA and one in 2006 in the UK have raised considerable doubts. In 2004, the American FDA (Food and Drug Administration) [55] performed a meta-analysis of 23 studies previously conducted on 9 different antidepressants. Although no patient had completed suicide in these studies, a small but statistically significant increase in

suicidal ideation was observed in children and adolescents treated with an antidepressant (about 4% versus about 2%), leading to a black box warning (black box warning by the FDA) on all classes of antidepressants, and in the second case, a small increase in self-harm and suicide-related events, but no significant increase in ideation [56]. In fact, observational studies have excluded an increase in actual suicidal acts linked to the therapy, acts that would have actually increased subsequently by about 14% due to a lower tendency to prescribe precisely because of this alert.

Some recent rather accredited publications had tended to interpret the benefit/risk ratio for the use of antidepressants in adolescent depression as unfavorable [57].

On the contrary, for example, a 2017 editorial by Dubicka [58] examines clinical studies and pharmaco-epidemiological data that support the maintenance of the use of antidepressants in the management of depressed adolescents and the need for adequate information in this regard.

In general, although antidepressants have a variable efficacy in developmental age from one subject to another, and despite the "chronic" "cultural" perplexities on the use of psychotropic drugs in children and adolescents, on the part of family members but also on the part of mental health workers, it can be assumed that the benefits seem to prevail over the risks.

The best approach seems to be ultimately the association of pharmacological treatment with psychotherapy and adequate and accurate monitoring of the patient throughout the treatment process.

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