Jornal de Pediatria

REFERÊNCIA

LIMA, Dênio. Bipolar disorder and depression in childhood and adolescence. **Jornal de Pediatria**, v. 80, supl. 2, p. 11-20, 2004. DOI: https://doi.org/10.1590/S0021-75572004000300003. Disponível em: https://www.scielo.br/j/jped/a/BhRWN6Ds8F5h53VQ54GBScF/?lang=pt#. Acesso em: 10 ago. 2021.

0021-7557/04/80-02-Suppl/S11
Jornal de Pediatria

Bipolar disorder and depression in childhood and adolescence

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Abstract

Objectives: To provide a historical review of childhood depression and bipolar disorder, covering concepts, diagnostic categories, epidemiology, genetic and neurobiological aspects as well as predisposing factors and treatment modalities.

Sources of data: Extensive review of the literature on child depression and bipolar disorder.

Summary of the findings: Child depression and bipolar disorder are associated with genetic factors, mood, adverse life events, divorce, academic problems, physical and sexual abuse, and neurobiological factors. Treatment usually includes medication and psychotherapy.

Conclusions: These are important childhood disorders whose diagnosis is often difficult. The identification and treatment of depression and bipolar disorder reduces the suffering of affected children and adolescents. The pediatrician can intervene by orienting the family in mild cases, but must be alert to cases requiring more aggressive treatment.

J Pediatr (Rio J). 2004;80(2 Suppl):S11-S20: Child depression, mood disorder, mania, bipolar disorder.

Introduction

The definition of childhood depression is still controversial. Until recently, childhood depression was believed not to exist or was inconspicuous.

In the last 20 years, the depressive disorders that affect adults have been considered to afflict children as well.[1-3] However, this comparison between depression in children and in adults is not quite correct and many authors are still skeptical about the actual frequency of depressive syndromes in prepubertal individuals.[4-6] The definition of depressive disorder in adults is a controversial issue. Although great improvement has been recently made in the diagnosis and classification of affective disorders in adults, many problems remain unsolved.[7] As a matter of fact, the problems that are observed in the study of childhood depression are similar to those found in studies with adults.

Feeling sad is a normal experience in everyone's life. However, depression is not synonymous with sadness or unhappiness, although unhappiness is a common symptom of depressive mood, associated with depression. Depression can occur as a symptom when affection is synonymous with sadness, or as a syndrome or disorder when a group of symptoms occur together and when sadness is part of an array of problems, which may include loss of interest in activities, feeling of worthlessness, sleep disorders, changes in appetite, etc.

Negative mood in depression may be represented by aspects such as *a feeling of emotional emptiness or a lowered emotional feeling.* Several patients describe their mood as a "black cloud" over their heads. There is a daily oscillation, and one day can be worse than the other. Anhedonia (inability to gain pleasure from normally pleasurable experiences) is also a symptom of depression.

Quite recently, the importance of the so-called "cognitive aspects" of depression has been underscored, and some

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authors believe that this definition is essential. Some depressive patients have an intense feeling of personal inadequacy and tend to have low self-esteem (disparaging opinion of themselves), believing that others see them disparagingly.

Depressive affect and depressive cognition are experienced by many people in the course of their lives, being part of their normal life without any pathological connotation. The term syndrome does not mean only one isolated symptom, but a combination of several symptoms that form a complex and determine the depressive syndrome.

According to the Diagnostic and Statistical Manual of Mental Disorders (DSM IV),[8] major depression should include the following symptoms, regardless of age:

- Five or more of the following symptoms and at least one of the symptoms: depressed mood or loss of all interest and pleasure; depressed mood almost every day; pronounced loss of pleasure; weight loss or gain (over 5% in one month); insomnia or hypersomnia; psychomotor agitation or retardation; fatigue or loss of energy; feeling of uselessness or excessive guilt; poor concentration; recurrent thoughts of death, suicidal ideation without specific plan or attempt.
- Symptoms do not meet the criteria for mixed episode.
- Symptoms cause clinically significant distress or impairment of social functioning.
- Symptoms are not due to the effect of substances or general medical condition.
- Symptoms are not due to normal bereavement.

According to ICD-10 Classification of Mental and Behavioral Disorders,[9] mood disorders (affective disorders belong to F.30–39 groups, which are classifications for adults; there is, however, an exception for mood disorders that appear in childhood or adolescence) should be registered using the categories in this section, provided that they match the descriptions provided (mixed disorders of conduct F.92.0).

Depressive episode

In typical mild, moderate or severe depressive episodes, patients suffer from lowering of mood, loss of energy and reduced activity. Ability to feel pleasure, show interest and concentrate is reduced, and marked fatigue after effort (even if minimum) is common. There is sleep disturbance and loss of appetite. Lowering of self-esteem, feeling of guilt and worthlessness are often frequent, in addition to lowered mood, waking up earlier than usual, marked psychomotor retardation, agitation, loss of appetite, weight loss, and loss of libido.

In children and adolescents, ICD-10 includes depressive conduct disorder, which is the combination of childhood conduct disorder (F 91. -) with persistent and marked mood depression (F 32. -) characterized by symptoms such as excessive distress, loss of interest and pleasure in usual activities, self-reproach and hopelessness; sleep disturbances or loss of appetite may be present.

- General criteria for conduct disorders (F 91) should be met.
- General criteria for mood (affective) disorder (F 30-39) should be met.

There is some reluctance to accept cases of depression identified in the community and those treated by psychiatrists. This reluctance is due to the definition of anguish and disease. The key to this issue lies in the distinction between depression and a normal reaction to the stress caused by every-day events (demoralization). Unfortunately, the pieces of evidence are inconclusive or often contradictory. The relationship between the onset of the depressive episode and the adverse effect that precedes it is well established in adults.

Definition and classification

Definitions are comparable to those of adults. However, there are some problems with the use of the definition of adult depression in children.

Children may have different symptoms depending on their age. When they are too young, they cannot express themselves properly. They may snivel or become irritable and have somatic complaints. Some authors think that refusal to go to school is a symptom that should be highly valued. Older children and adolescents have symptoms that resemble those of adults.

Anaclitic depression

The first study to correlate childhood depression with adult major depression was that conducted by Spitz.,[10] who described the "anaclitic depression" syndrome. According to Spitz, children who were separated from their mothers and placed in day care center presented crying, withdrawal, psychomotor retardation, slow reaction, delayed movements, and some of them had stupor and loss of appetite. Spitz posited that the loss of a cherished object was the most important factor in the etiology of the disease. Other authors observed a change in behavior similar to that described by Spitz, in institutionalized children[11] who were passive and apathetic. Spitz is criticized, especially because he suggested that anaclitic depression led to severe developmental delay. His methodology was also criticized. In spite of this, the definition of anaclitic depression is still used nowadays.

Harmon, Wagonfield and Emde report the case of an institutionalized three-month-old infant who showed symptoms of anaclitic depression at eight months: sniveling, withdrawal, apathy, weight loss and sleep disturbance.[12]

Masked depression

According to the predominantly psychoanalytic literature of the 60s, depressive conditions could not occur in children, since children's personality structure was too immature. Rochlin considered that depression could not occur in middle childhood, because children did not have a sufficiently structured superego to drive their aggressiveness towards their own ego and, in middle childhood (6 to 10 years), it was masked depression that was actually present.[13] Glaser included the following symptoms in the definition of masked depression: phobias, "delinquency", somatic symptoms and others such as: social withdrawal, aggressiveness, fear of death and enuresis.[14] Frommer suggests three types of depression: a) – uncomplicated or pure depression– with the following symptoms: irritability, sniveling, sleep disturbance, and suicidal ideation or attempt. Symptoms of depression were spontaneous and common; b) – enuretic depression– children frequently showed severe learning disabilities and problems at school, antisocial behavior, family conflict and rejection of parents. Children suffered from maturational delay, which resulted in enuresis; c)– phobic depression – characterized by intense anxiety, somatic symptoms and some depressive symptoms.[15] Cytryn & McNew thought that masked depression could be diagnosed by children's facial expression and fantasy content. However, they also described the "typical" depressive syndrome, which consisted of: hopelessness, psychomotor retardation, sleep disturbance, loss of appetite, social withdrawal, and other symptoms observed in adult depression. They classified depression into: a) Acute depression – without previous psychiatric disorders and without pronounced familial psychopathology; b) Chronic depression – typical depression, usually with poor adjustment before the onset of the disorder and tendency to result from a maladjusted environment.[16]

Childhood depression is often expressed by nondepressive symptoms with few and obvious signs of the state of mood. The problem is that no one has been able to establish a set of criteria to identify the different symptoms caused by depression, and identical symptoms, which occur in different underlying disorders. Nevertheless, irritability may be an important sign for the diagnosis of depression.

Thus, symptoms of masked depression include all those psychiatric symptoms observed in children. Since the symptoms in the ICD and DSM classifications are specific and descriptive and quite etiological, descriptive symptoms may be important to indicate depression in an individual.

Kovacs & Beck state that masked depression should not be considered. They showed that many of these behavioral symptoms, observed in masked depression, are prominent in adults. Careful clinical examination may reveal underlying depression.[17]

Diagnostic criteria

Several suggestions for the diagnosis of depression in children have been made, all of them based on symptoms that are similar to those observed in adults. The first one was proposed by Feighner in 1971, and included the following: presence of dysphoric mood and low self-esteem; two or more of the following eight symptoms: aggressive behavior (or agitation), sleep disorder, change in school performance, poor social interaction, changes in attitude towards school, somatic symptoms; loss of energy and appetite, and weight loss; these symptoms represent a change in children's general behavior; these symptoms should occur for at least one month.[18]

Pearce in 1978, in a study with depressive children, shows the most common symptoms based on statistical data; determines the diagnostic criteria for childhood depression, among which he includes that depressive disorder is defined by "depressive mood" and two of the following symptoms: morbid or suicidal thoughts, sleep disorders, eating disorders, obsessions, irritability, hypochondriasis, eating symptoms, refusal to go to school, impaired perception such as delusions or excessive guilt and low self-esteem.[19]

These criteria are an improvement to the current definition of depressive disorders in children. These two types of criteria are not specific, because depressive disorder could be diagnosed in the absence of most symptoms. As we can observe, there is no consistency in the diagnostic criteria for childhood depression. In spite of this, there is considerable evidence to support the validity of adult depressive symptoms found in children and adolescents.

Symptoms vary with age. The younger the child, the more somatic the symptoms, and irritability is also present; as the child grows up, he/she may present symptoms of the adult type, such as withdrawal, guilt, easy crying, suicidal thoughts, anhedonia. Mood swings should also be considered.

Studies show that there is an increase in the prevalence of depressive disorders in relatives of children who suffer from depression; therefore, it seems that the increase in

risk is specific to depressive disorders in these families where prevalence is higher.

Diagnostic categories

Dysthymia

The etymological meaning of dysthymia is "ill-tempered", referring to a temper that tends towards melancholy. Its intensity is weaker than that of major depression; its onset often occurs in childhood or adolescence; and it is long-lasting and may continue into adulthood. The diagnosis of dysthymia requires that depressive or irritable symptoms be present. Irritable mood is more common in children than in adults, and should be present almost every day including at least two of the following associated symptoms: increased or poor appetite; insomnia or hypersomnia; fatigue; low self-esteem; poor concentration or indecisiveness; and hopelessness. Symptoms may also cause intense distress or impairment to social functioning, poor performance at school and in other areas. Symptoms may be chronic, lasting for one year (up to two years in adults), in children and adolescents.[20,21]

Separation anxiety

Many of depressive symptoms such as sadness, preoccupation, sleep disturbance, somatic symptoms, apathy, and social withdrawal may occur as part of the fear of separation from persons to whom the child is attached. In these cases, the symptoms may be clearly associated with separation, such as the worry about staying away from a parent. Likewise, a somatic symptom may appear so that the child can stay at home or to draw attention to himself/herself.[20,21]

Adjustment disorder with depressive mood

Depressive symptoms may occur as a reaction to a psychological stressor, such as divorce of parents, separation from friends for having to move away or a severe disease affecting a parent. In these cases, the symptoms appear right after the stressor has occurred (within three months). The reaction is seen as maladaptation to every-day functioning. The reaction is exacerbated, more pronounced than that usually expected for a given action. Symptoms tend to disappear after adjustment to the new situation or circumstance.[20,21]

Uncomplicated bereavement

Bereavement is similar to an adjustment disorder in terms of association with a particular event. However, it is not a disorder, because it is considered to be a normal reaction to the loss of a loved one. Bereavement is often associated with several depressive symptoms, or with a complete depressive syndrome with temporarily impaired social and school functioning. Nevertheless, the reaction does not have a clinical meaning, unless it persists for a reasonable period of time, way beyond that of adjustment, or long episodes recur after the loss.[20,21]

Mania

Mania is a severe symptom that often produces a remarkable decrease in school performance. It may be considered mild, moderate or severe. The following categories exist:

- Bipolar disorder, mixed episode: combination of mania and depression, with a depressive episode lasting at least one day, quickly interspersed with mania;
- Bipolar disorder, depressive type: current depressive episode with one or more previous manic episodes;
- Cyclothymia: several episodes of hypomania for one year, with depressive mood or loss of interest or pleasure, which do not meet all the criteria for major depression;
- Unspecified bipolar disorder, with manic or depressive characteristics that do not meet the criteria for other specific bipolar disorders.[22]

Symptoms include increased irritability, unstable mood, with isolated crying episodes. Individuals with this type of disorder may cause harm to others or to themselves. They are restless, speak faster than usual, with pronounced lack of concentration, and may need only few hours of sleep. Thoughts permeated with fantasy and greatness may be present. These children may suffer accidents for believing they have magical powers. Due to the similarity between the symptoms of hypomania and attention deficit hyperactivity disorder, which may often accompany parental complaints regarding excessive talking and anxiety, they may also show cognitive blunting and impairment of concentration, as well as depressive psychomotor agitation, hyperactivity and excessive talking, impulsivity, and anhedonia in children with ADHD, who have difficulty in gaining continuous pleasure in activities that would normally keep the interest of healthy children. It should be underscored that children with ADHD have irritable mood, which may be understood as masked depression. However, ADHD is a long-lasting problem and the follow-up of these children does not show progression into bipolar disorder, or at least not into the classic bipolar or uncomplicated bipolar type, which often leads to confusion and may hinder the diagnosis.[20-23]

Epidemiology

Prevalence

Age difference

Population-based epidemiological studies are usually rare and difficult to be carried out. They consist of

sampling, since it is impossible to collect data from the whole population.

Rutter et al. assessed the whole population on the Isle of Wight, in a classic study of childhood and adolescence psychiatry. They conducted the study in two different moments, focusing on childhood psychiatric disorders. Data were collected through questionnaires answered by parents and teachers at school, records from clinics and hospitals, and pediatric medical charts. The diagnosis was established based on behavior.[24]

Age of onset seems to vary during childhood. Children aged between 1–6 years, referred to treatment, showed low rates (1%) of major depression than those aged between 9 and 12 years (13%). Depressive disorder was rare in children, both in those aged 10-11 years (0.14%) and in those aged 14-15 years (1.5%), but depressive mood occurred in 13% of children aged less than 10-11 years and in 40% of adolescents aged 14-15 years, among which 7-8% showed suicidal thoughts. However, depressive symptoms were common in both ages (sadness/unhappiness in 12-45%). Adolescents showed affective symptoms with more frequency, and these symptoms were also evident in their parents' reports.[24]

Lima, in a retrospective study of 2,689 male and female children aged between 12 and 15 years (conducted at the Department of Child and Adolescent Psychiatry of Maudsley Hospital, London,) found that 38.8% of children aged between 12 and 13 years and 61.2% of those aged 14-15 years had depressive disorder after using Pearce criteria for depressive disorder in 18% of all children. No significant difference was observed between male and female subjects, but 65.8% of children at the pubertal stage and 34.5% of those at the prepubertal stage had depression.[25]

Emotional symptoms significantly associated with depressive disorder included sadness (100%), suicidal ideation, threats or attempts (38.4%), refusal to go to school or phobias (38.2%), irritability, bad humor (30.5%), isolated phobias (18%) and rumination, obsessions and rituals (12%). Somatic symptoms included: eating disorders (19.4%) and sleep disorders (29.9%). Abnormal relationship with the family was significantly associated with the mother (50.4%) and with the father (43.8%); the association of relationship of depressive children with other family members or adults was not significant.[25]

Gender differences

No gender-specific differences were observed in the 6-12 age group as to the prevalence of depression, but there was an increase in depression among female subjects at the beginning of adolescence, in women and in adulthood.

Socioeconomic status

According to Costello and Bird et al.,[26,27] socioeconomic status was not significantly associated with depressive disorder in young individuals. Cohen used to say that socioeconomic class is not a predictive factor for depression in children, whereas Kaplan thought that low socioeconomic status resulted in less depression than a high socioeconomic status, and Kandel and Davis pointed out that low family income was associated with depressive symptoms.[28-30]

Race

Studies have yielded controversial results. Some authors say that race has no effect on the prevalence of depressive disorder, while others claim that depressive symptoms affect more blacks than whites.[26,30,31]

Predisposing factors

Predisposing factors may be multifactorial: genetic, social and psychological. Childhood depression may be triggered by long-lasting adverse events, family problems and personality factors.

Depressive disorder in parents

Studies often suggest that genetic factors are involved; family studies suggest that a high rate of psychiatric disorders is found in relatives of depressive children; children whose parents are depressive are at risk for a wide variety of psychiatric disorders, including depressive conditions.

Genetic factors

Gershon et al. and Andreasen et al. carried out a very consistent study with adults and suggest that affective disorders tend to be family-related. Molecular biology has been used to determine whether the severe forms of bipolar affective disorders are related or not to genetic markers, as occurs with the relation of affective disorders to chromosome 11. However, the early occurrence of depression is associated with an increase in the familial loading. Weissman et al. assert that when depression occurs before the age of 20 years, it is strongly associated with familial loading. If it appears after the age of 40 years, no familial relation is present. In a study conducted by Weissman et al., children of parents who had depressive disorder before their twenties showed a risk 14 times higher for major depression before the age of 15 years, compared to controls.[33]

Studies suggest that depression in children is associated with depression of their parents through several mechanisms, such as: direct genetic effect on the system that regulates mood, which seems to be the cause of

bipolar disorder in adults; other genetic effects, mediated by factors such as child's temperament, which indirectly increases the risk of depression; or perhaps the symptoms of the parents, directly affecting the child's environment and upbringing; or factors related to parents' personality or social circumstances.[32]

Depression and anxiety

The association between depressive disorder and separation anxiety was significant in 58% of children and in 37% of adolescents; 45% of children and 27% of adolescents with phobia and avoidance had depressive disorder.[33]

Temperament

Temperament is associated with high risk of psychiatric disorder in middle childhood. Dunn & Kendrick found out that some temperamental characteristics can be strongly associated with anxiety disorder after the birth of a sibling. Adversity is more easily dealt with in adaptable children. Certain temperamental characteristics in children may favor the occurrence of accidents. Children with an aggressive temperament can be criticized or be attacked. Temperament can predispose children to or protect them from depressive disorder in varied ways. It has been suggested that temperamental characteristics are closely related to depression in young children. Too little has been written about temperament and depression; however, we need more information and studies to determine whether temperament acts directly or indirectly on depressive disorders.[34]

Adverse life events

Death depends on age; children aged between three and six years have depression as a reaction. Approximately one third of prepubertal children will have clinical signs of major depression. Bereavement is a feeling that is observed in all ages, but depression occurs in most age groups.[35]

Divorce

It is age-dependent: preschool children show regression, become active, anxious, trying to draw attention. In middle childhood, children get depressive, are afraid that their mother or father could be replaced. For adolescents, separation has a striking effect, they may have severe depression, anger is also present, and they tend to blame the parent that leaves the family.[36]

Academic problems

Association between academic problems and depression in young individuals has been reported in several studies. However, academic performance of patients does not differ from those individuals with psychiatric problems. Some reports show that depressive children tend to be more absent from school than those with nondepressive psychiatric problems. One third of students with "pure" depression" (without any other learning or behavioral disorder) needs special educational guidance.[37,38]

Physical and sexual abuse

There are two reasons for us to think that child abuse may be a cause for depression; – physically abused children show more physical aggressiveness and are at risk of having a wide variety of cognitive disorders.[39-41] Nevertheless, there are several reasons to think that physically abused children are at risk of having depressive symptoms. They may present characteristics such as anhedonia, low self-esteem, withdrawal, and poor social interaction. Parents who abuse their children physically tend to teach their children hopelessness.[40-44] Studies show that sexually abused children have anxiety, guilt, shame, aggressiveness, and negative symptoms, or other psychiatric disorders. Investigations suggest that sexual abuse victims do not have a psychiatric diagnosis and no relation to depression is apparently present, but an adjustment reaction with depressive mood may occur. Other studies show that 36% of children aged between 2 and 11 years have symptoms of depressive mood. Sexually abused adolescents (12-18 years), when compared to non-sexually abused ones, show no difference as to depressive symptoms. However, approximately 50% of sexually abused adolescents had suicidal ideas and 50% of them attempted suicide, but the results do not differ from non-sexually abused adolescents.[45-49]

Neurobiology of depression

The monoamine theory of depression established that depression was due to deficiencies of neurotransmitters, especially to the depletion of norepinephrine and serotonin. Certain drugs (e.g.: reserpine, used to treat hypertension) that depleted these neurotransmitters were able to induce depression. The pharmacological action of antidepressants used at the time (tricyclics and MAOI) increased the concentration of these neurotransmitters. A "normal" amount of monoamines was believed to decrease as a result of an unknown pathological process, stress or drugs.[50] It was also observed that reserpine depletes norepinephrine and dopamine in animal brains. On the other hand, iproniazid sometimes improved mood. Substances such as iproniazid are known to inhibit monoaminoxidase, whose main function is the metabolization of amines such as norepinephrine. Various controlled studies showed that tricyclics (e.g.: amitriptyline) have an effect on the amine pathway and are efficient as

antidepressants.[51] In general, affective disorders are characterized by a deficit (depression) or excess (mania) of one or more neurotransmitters or by an unbalance of these neurotransmitters.[20]

Two hypotheses were formulated regarding the pathophysiology of affective disorders: the first one focuses on catecholamines and the other one focuses on indolamine 5-hydroxytryptamine. The hypothesis of catecholamine proposed that some depressions are associated with catecholamine deficiency in important functional regions of the brain, and that mania is due to an excess of catecholamines.[52] Recent studies found that children with major depression have an increased secretion of the growth hormone (GH) during sleep. Several mechanisms can explain the increased secretion of GH during sleep in major depression, but the major two mechanisms are: a) functional deficit of the serotonin hypothalamic system (e.g.: nocturnal GH inhibitor) and b) increase in cholinergic activity (e.g.: system that increases the nocturnal secretion of GH). Puig-Antich concluded that serotonin deficit could explain these findings better than cholinergic hyperactivity; however, a simple serotonin deficit could not occur as a result of the findings obtained. On the other hand, few biological studies on serotonin concentration could be interpreted as consistent with the increase or decrease in the activity of this system.[52-56]

Receptor hypothesis of depression

According to this hypothesis, abnormal functioning of monoamine receptors produces depression. This disorder may be caused by monoamine depletion. Monoamine depletion causes compensatory up-regulation of postsynaptic neuronal receptors. However, no direct evidence of this hypothesis has been found, but postmortem studies consistently show an increased number of serotonin-2 receptors in the frontal cortex of patients that committed suicide. Indirect studies of the functioning of receptors in patients with major depressive disorder suggest abnormal findings in several receptors when neuroendocrine markers or peripheral tissues (e.g.: platelets or lymphocytes) are used. Modern molecular techniques investigate the abnormal gene expression of enzymes and receptors, of neurotransmitters in depressive families, but they have not successfully identified molecular deficiencies.[57]

Stress and glucocorticoids

Stress activates the release of hypothalamic neuropeptides. This effect leads to ACTH release into the bloodstream, which will induce adrenal release of glucocorticoids. Glucocorticoids act in a wide variety of tissues, and also in the brain by binding to hippocampal receptors, affecting cognition. They also have a negative feedback effect on its own release by inhibiting ACTH release. This feedback is impaired in depressive patients, being known as resistant negative feedback.

Adrenal steroids released during stress contribute to hippocampal atrophy. The subtypes of depression more commonly associated with hippocampal atrophy are involved in increased secretion of glucocorticoids. These hormones have several adverse effects that are more active or restricted to the hippocampus, such as regression of dendritic processes; inhibition of neurogenesis; reduced ability of neurons to survive injury. Selective hippocampal atrophy occurs in Cushing's syndrome, in which there is increased secretion of glucocorticoids, and in posttraumatic stress disorder, in which the concentration of glucocorticoids is also elevated.[58]

Morphological brain abnormalities

There has been strong interest in morphological changes that occur in prolonged major depression. Reduced hippocampal volume in depression has been considered because of the vital role that this structure has in learning and memory, fear conditioning, and neuroendocrine regulation. An atrophy of approximately 20% of hippocampal volume is shown after control of total brain volume or temporal lobe and amygdala volume. However, atrophy increases in prolonged depressions and persists for decades after its resolution. One of the possible mechanisms is that depression induces regression of the dendritic processes; another possibility is the loss of hippocampal neurons in prolonged depression.[59]

Treatment

Management of depressive children should be implemented as early as possible.

Assessment of depressive symptoms and possible associations: diagnosis; inappropriate education; impairment of psychosocial functioning; psychiatric disorders; maltreatment.

Mild depression – regular meetings including comprehensive discussions with children and their parents, and support in order to relieve stress and improve mood.

Severe depression – specific treatment and hospital admission in some cases. For prevention of suicide risks, the situation should be analyzed before deciding on a divorce or on leaving home.[21,22]

Psychological treatment

Cognitive-behavioral therapy involving children and their families; training of social needs– similar to cognitive-behavioral therapy, focusing on open activities and development of specific skills; interpersonal

psychotherapy– focused on relationship; family therapy.[21,22]

Drugs

For adjustment disorders with depressive mood, dysthymia and major depression, antidepressants such as tricyclics (imipramine, clomipramine, maprotiline, amitryptine or nortriptyline)[21] may be used. These drugs are the oldest and most widely used in children. When compared to placebo, these drugs showed no statistically significant differences, but they are still used, although they often produce marked adverse reactions, due to their muscarinic effects. Before implementing treatment, the following exams should be performed: ECG, urea, creatinine, oxaloacetic and pyruvic transaminases. Patients should be monitored every six months.[60]

Selective serotonin reuptake inhibitors (SSRI), approved by the FDA to be used in children are: sertraline chlorhydrate - safe and efficient and frequently used in obsessive-compulsive disorders in children and adolescents; fluoxetine - widely used and should be initially given in a low dose, due to its slow clearance and also because it may interact with other drugs. This drug has a good result and few side effects. Paroxetine - very efficient in treating depression, even though there are few systematic studies on its pharmacokinetics and efficiency in children; citalopram - should be avoided due to insufficient evidence of its efficacy in this age group; venlafaxine - inhibits norepinephrine reuptake, and to a lesser extent, serotonin and dopamine reuptake. It has been widely used in adults, but due to little evidence of its benefits to children, it is not indicated for patients younger than 16 years.[21,22,60-65]

Lithium carbonate, carbamazepine and valproic acid are used for mood stabilization and improvement of irritability in cases of bipolar disorder. These drugs are widely accepted by physicians; however, clinical and laboratory assessments should be considered before the use of these drugs.[21,22,60]

Biological treatment: - treatment with electroconvulsive therapy (ECT) has been rarely used in this age group. There are few studies on this technique, mainly case reports. In general, it is a very efficient and safe technique, used only when all other treatments have failed. No striking difference has been observed as to indication, response, and side effects compared to adults.[3,22,63,65]

Conclusion

The quick improvement in the investigation of childhood depression is partly due to the transfer of concepts from adult depression. In the last 30 years, researchers have investigated childhood depression by means of medical interviews, questionnaires or semistructured interviews, and lab exams. However, childhood depression has its own characteristics, and adult-type symptoms occur in adolescence. Several factors may cause childhood depression, such as the role of the family in children's daily routine (parents have a key role), and genetic factors (depressive children are more commonly found in families where one of the parents is depressive, compared to those who do not have this diagnosis). Children of depressive parents will have more problems, since there will be less affection and happiness, in addition to ambivalent behavior on the part of their parents, which results in complicated communication, associated with dysphoric affect. Physical and sexual abuse, academic problems, separation or divorce of parents are important risk factors. When establishing the differential diagnosis with dysthymia, separation anxiety disorder, adjustment disorder with depressive mood, cyclothymia, uncomplicated bereavement, it is important to distinguish attention deficit hyperactivity disorder from hyperactivity and mania. Intervention may include parental counseling, individual and/or family psychotherapy, and drug therapy. Those that produce fewer side effects should be preferred (e.g.: selective serotonin reuptake inhibitors). Tricyclics should be used only if no other option is available, since they produce remarkable adverse effects.

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