

# Neurological and behavioural symptoms of attention deficit hyperactivity disorder: from diagnosis to the treatment

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The Attention-Deficit/Hyperactivity Disorder (ADHD) is a behavioral disorder characterized by inattention, impulsivity, and hyperactivity that makes it difficult and in some cases prevents normal development and social integration of children [1]. It is a heterogeneous and complex disorder, multifactorial in that 70 - 80% of cases coexists with another or other disorders (termed comorbidities). The coexistence of multiple complaints aggravates the symptoms complicating both diagnosis and therapy. Those are the most frequently associated with oppositional defiant disorder and conduct disorder, specific learning disorders (dyslexia, dysgraphia, etc.), Anxiety disorders, and, less frequently, depression, obsessive-compulsive disorder, tic disorder, bipolar [2].

The presence in the classroom of children with problems related to ADHD is not uncommon. In the United States it is believed that 2-6% of children suffer from the disorder and attention deficit hyperactivity disorder (ADHD) and it is thought that in every classroom there are at least 1 or 2.

The fundamental characteristic of the disorder is a persistent mode of inattention often accompanied by hyperactivity and impulsivity. Children with ADHD show very high levels of activity with respect to their age, are unable to keep the attention, interest and perseverance in what they are doing, they are games, activities, objectives long-term or tasks that are assigned to them; impulsiveness and self-control delay greatly to be compared with the present stage of development where they belong.

It is possible that manifest excessive anger and rage at both verbal and physical instructions and orders given by adults, parents or teachers, are ignored, challenged or disrespected. For this reason it is particularly difficult to take care of children who experience this disorder, and their behavior, with the reactions that accompany them, create a family context in which relationships are characterized by a strong directivity and control, anger and antagonism, even because the behaviors related to the disorder, characterized by a certain degree of variability, often are mistaken for volitions and as a result the children are perceived as hostile and rude.

Difficulties also arise among peers, siblings or classmates, both in the sharing of space, toys and activities, and is at times playful, free play, if they involve cooperation, observance of rules or social labels. For adults, the problem does not change much, they continue to experience a number of difficulties both in interpersonal and both in study and work [3].

The level of emotional development of children with ADHD is 30% slower than that of their peers, so a 10 year old child with ADHD act with the maturity level of a child of about 7. There is no cure for ADHD

and an adult untreated live a very difficult life that has not always had serious problems with the law or that is not landed in the world of drug addiction or alcoholism. Adults depressed, anxious, emotionally unstable and in their work, in social life, family, constantly changing job, wife, car and who have frequent fines and traffic accidents, easily addicted to alcohol or drugs, almost always heavy smokers, could be ADHD [4].

## ADHD etiology

It is important to note that currently the ADHD causes are unknown. There is no doubt that the disorder has multiple etiology. Initially it was thought that brain damage, due, for example, a brain infection, a trauma or other damage and complications that occurred during pregnancy or at birth, was the main cause of ADHD symptoms, and many studies have found a correlation with complications occurring during pregnancy or at birth (unusually short or long labor pains during childbirth, fetal risk, difficult parts where you need the help of forceps, toxemia or eclampsia) [5-8]. Other studies have found a relationship between smoking during and before pregnancy, and the level of hyperactivity and inattention, and that exposure to smoking, both direct and environmental during pregnancy is higher in children with ADHD and that this can be associated with damage to the brain from anoxia. Similar relationships were found with alcohol consumption by the mother during pregnancy, and even if there are no relations of cause and effect with respect to hyperactivity or inattention in the offspring, we think of a teratogenic effect of alcohol on the development of the brain. The amount of alcohol taken seems to be directly proportional to the degree of distractibility of children to four anni [5-8].

In summary were identified three possible etiological areas:

- 1) psychosocial
- 2) neurological
- 3) genetic

## Psychosocial factors

It is important to note that environmental factors can strongly affect the severity of the disorder and the occurrence of certain

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**Key words:** attention-deficit/hyperactivity disorder, children, cognitive disorders

**Received:** February 09, 2018; **Accepted:** March 01, 2018; **Published:** March 05, 2018

disorders associated considered, the latter, the strongest predictors of subsequent developmental risks and negative outcomes. For this reason, the environment in which the child is raised and educated has an important role [9].

## Neurological factors

Significant similarities were found between ADHD symptoms and those produced by injury or injuries to the frontal lobes, especially the prefrontal cortex, a figure which, together with the early onset of symptoms, their nature relatively persistent over time, the association with other developmental disorders (learning disabilities, speech disorders, motor abnormalities and IQ) believed to be associated with a neurological impediment to their significant relationship to peri- and postnatal difficulties and, finally, the significant improvement with pharmacological interventions have reinforced the idea that the cause was from attributed to neurodevelopmental factors. Still, the results of neuropsychological tests associated with the functions of the prefrontal lobes (inhibition, planning, persistence, motor control and even verbal fluency, etc..) Together with significantly greater risk of the disorder in other family members proving the presence of factors biologic [8-10]. A number of studies suggest the hypothesis that there are some difficulties with brain neurotransmitters, and reactions to different substances that subjects have ADHD, support this idea. Studies on the liquid cefalospinale show that ADHD in children, a decrease of dopamine may underlie the disorder. Experimental results conducted on metabolites of neurotransmitters in the brain, present in the blood and urine are not consistent and show a selective problem of availability of dopamine and norepinephrine, but at present, these tests can not be considered decisive [8]. Finally, some studies show a decrease in blood flow in the prefrontal regions, in the circuits that connect these regions to the limbic system, across the street caudata, specifically in the region of striato10. From the point of view of morphological differences were observed in the right hemisphere temporal plana, smaller in children with ADHD [8]. Starting from the research of Lou et al. [11] on the reduced blood flow in the caudate regions and streaked and in frontal regions, studies have been concerned to assess the morphology of these regions in children with ADHD and have demonstrated the presence of a left caudate nucleus significantly smaller. In summary, it probably has a significant role in ADHD a mechanism that involves the circuitry between the prefrontal and limbic system, and especially the striatum, the brain areas that are the basis of inhibitory reactions, distraction, and that stimulate ' learning and sensitivity to rewards and who are some of the richest areas of dopamine in the brain [8].

## Genetic factors

There are no evidences that ADHD is the result of an abnormal chromosome structure, but most of the research indicates that this disorder is of hereditary nature [12]. The research is focused on the gene of dopamine type 2, starting from the results about its association with increased alcoholism, Tourette's syndrome and the same ADHD. In the light of the latest research on the possibilities opened up by the map of the human genome will be able to probably know more precisely the mechanisms that lead to ADHD. ADHD is a biological disorder rather than a learning disorder due to a variety of neurological causes. Hereditary factors seem to play a large role in the occurrence of these symptoms in the child. What is transmitted may be genetically or the tendency to produce low amounts of dopamine or a lower activity of the prefrontal areas, striata and the limbic brain and their vast interconnections. Their condition may be exacerbated by complications during pregnancy, exposure to toxins, or neurological

diseases and social factors such as family and environmental adversity, lack of child care in breeding or poor environmental education. There may also be cases of children with ADHD in which there is not a genetic predisposition to the disorder, but exhibiting a significant neurological damage, although this seems to be true for a small minority of cases of ADHD [12]. On the contrary, there is little evidence to support the fact that ADHD may depend on social and environmental factors such as poverty, family chaos, diet or lack of parental care of bambino [8]. Regarding the affective and relational components of the disorder ADHD in childhood, it seems that, with his tireless and relentless move that no one seems able to stem the hyperkinetic child looks around in circles, like a spinning top always on the same point: turning on itself fills an empty space, and fills him with anguish. He appears as the guardian of a world fantasized as catastrophic, dominated by the destruction in the form of blast and fragmentation. The movement does not result in anything and never never gradual or finalized. Never stops: he wants to do only what he wants, always, first and foremost. In dealing with these children we can better recognize and understand archaic mechanisms of functioning of the mind, designed to protect anguish, such as identification, projective identification, denial. In other words, in these cases, more than ever, recognize countertransference reactions can help to formulate hypotheses about the psychological situation inherent in the relationship with these children and then to identify the most appropriate ways to help them change their attitude.

## Diagnosis

ADHD is "a situation / persistent state of inattention and / or hyperactivity and impulsivity more frequent and severe than is typically observed in children of the same level of development." Inattention, hyperactivity, and impulsivity are commonly known as the key symptoms of this syndrome. They must be present for at least 6 months and have made their appearance before the age of 7 years [13-25].

The International Statistical Classification of Diseases and Related Health Problems (ICD-10) World Health Organization uses the term "hyperkinetic disorder" for a more narrowly defined diagnosis (ICD-10 WHO 1994). It differs from the classification of the DSM-IV as all three problems of attention, hyperactivity and impulsivity must be present and must be simultaneously satisfied the more stringent criterion of their presence in a variety of setting, while the presence of another disorder constitutes an exclusion criterion. Based on the diagnostic criteria systematized in the Diagnostic and Statistical Manual of Mental Disorders (DSM-III, DSM-IIIR, DSM-IV) and in the Diagnostic and Statistical Manual for Primary Care, child and adolescent version (DSM-PC) diagnosis of ADHD is based on the presence of: 6 or more of 9 symptoms of inattention or 6 of 9 or more symptoms of hyperactivity \ impulsivity.

## Therapies

ADHD patients may be subjected to the following treatment:

Psycho-behavioral

Pharmacological (methylphenidate, atomoxetine)

Combine (Psycho-behavioral + pharmacological).

## Pharmacological therapies

In recent years in the United States the use of psychostimulants, including methylphenidate and amphetamines, for the pharmacological treatment of ADHD, raised a strong debate focused mainly on the easy availability and frequent prescription of these substances, as well as on

their potential abuse. In the U.S., the diagnosis of ADHD is made by the physician and the first approach is pharmacological, it follows that at a high rate of diagnosis, often incorrect, are associated treatments inappropriate [13-25].

In the European context, however, the approach is multidisciplinary ADHD and drug therapy is reserved for severe cases and in the context of a multimodal program (psychotherapy and pharmacotherapy). Methylphenidate is used in the treatment of patients suffering from attention deficit disorder with or without hyperactivity disorder and narcolepsy (uncontrollable desire for sleep or sudden attacks of deep sleep). This medication is a central stimulant, amphetamine variant, and as such belongs to the drugs of abuse regulated by Presidential Decree 309/90, recently amended by Law 21/02/2006 n. 49. Psychostimulants are considered the most effective therapy for ADHD and methylphenidate is the drug of which, until now, has been the largest collection used [26]. Stimulants act on the monoamine transporters: methylphenidate modulates especially the amount of dopamine and norepinephrine, present in the inter-synaptic. Boost a deficient dopaminergic transmission and attenuates a state of dopaminergic hyperactivity. It can improve the inhibition of responses, the working memory and the processes of discrimination of the stimuli [13-25]. The results of some controlled clinical trials have shown that methylphenidate is effective in about 70% of children with ADHD. The therapeutic effect is rapid. A week of treatment is usually sufficient to achieve measurable benefits even in the school environment: increased attention, the ability to accomplish the assigned tasks, in addition to reducing impulsivity, distraction and interactions interpersonal conflict. In studies conducted to date it has been noticed that the same dose of methylphenidate can however produce in children with ADHD changes in positive, negative or zero, according to the evaluation method used [27]. This paradox highlights the heterogeneity of the valuation methods used to date in clinical trials, ranging from a subjective perception of improvement on the part of parents, outpatient clinical assessments, analysis of the child's academic performance.

The most common side effects of psychostimulants and methylphenidate are decreased appetite, insomnia, and gastrointestinal irritation: insomnia can be prevented by avoiding the evening dosing, lack of appetite and gastrointestinal disorders by administering the drug after meals. When the drug is administered incorrectly, headache and abdominal pain are rare, temporary and rarely require modification or discontinuation of therapy. Rare, although documented, are neutropenia and eosinophilia. In susceptible individuals, may occur or worsen involuntary movements, tics and obsessive ideas. In some children, can induce rapid changes in mood with increase or decrease in speech, anxiety, excessive elation, irritability, sadness (dysphoria) [13-25]. In children, high doses of the drug can lead, paradoxically sedation and decreased learning ability. In children, the abuse and addiction are virtually non-existent.

The subjects treated with psychostimulants are at greater risk of cardiovascular events. The risk is a direct function of age: younger children, adolescents, and greater adults [28]. Numerous drugs, capable of blocking in a more or less selective reuptake of norepinephrine, are effective in the treatment of ADHD. The noradrenergic system modulates the function of several brain areas involved in the mechanisms of vigilance, alertness and attention. The drugs can modulate the noradrenergic function are: tricyclic antidepressants,  $\alpha_2$  adrenergic agonists, selective noradrenaline reuptake blockers. Some of these drugs, however, have less tolerability (desipramine: anticholinergic effects and risk of cardiotoxicity), tolerance to the therapeutic effects after a few months (clonidine).

The atomoxetine, a norepinephrine reuptake inhibitor, has shown efficacy and tolerability similar to psychostimulants, without potential abuse [29]. Atomoxetine was first introduced to the U.S.A market in November 2002 and then subsequently in the UK in May 2004, the last year has also been introduced in Italy.

To date the drugs registered in Italy for drug therapy of ADHD are methylphenidate administered according to body weight, on average, 0.3 to 0.6 mg / kg / dose in 2:00 to 3:00 daily doses, and atomoxetine administered in according to body weight, on average, 1.2 mg / kg / dose in a single daily dose (rarely in two half doses) [29].

## Other pharmacological treatments

Tricyclic antidepressants, SSRIs, antipsychotics, neuroleptics, benzodiazepines and other CNS-acting drugs are sometimes used in the pharmacological treatment of ADHD patients. Typically these are cases of comorbidity in which you need to associate psychostimulants, drugs of choice for the ADHD, other substances for specific illnesses associated with ADHD [30].

## Combined treatments

The study conducted by the NIH MTS has shown that the best results in the treatment of ADHD are obtained with combination therapy (psycho-behavioral and pharmacological). Where the psycho-behavioral therapy alone is not sufficient for the treatment of the syndrome, should be implemented through the combination therapy, pharmacological and non-pharmacological [30].

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