The Story of Filippo, Who Rocked Back and Forth (i.e., ADHD)

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In 1882, Gaetano Negri translated into Italian a little book—well known among German-speaking children—originally titled "Der Struwwelpeter" and written by Heinrich Hoffmann, a psychiatrist and writer.

Among the nursery rhymes that make up this book—all strongly aimed at showing the most morally upstanding behaviour and the harm that can come from wrongful actions—the one most interesting for the purposes of this work is the eighth, that is the Story of Filippo, Who Rocked Back and Forth. A boy who "gave no thought to stern reprimand as he ought" and is undeterred, "stomping and pounding, shouting, battering his fists on the table, rocking back and forth in his chair and dangling while pulling on the tablecloth".

Obviously, the child then falls and drags the fully laden table with the family dinner down with him: "Oh, what a fright! Oh, look what a horrible mess!". But the parents can only resign themselves to this unfortunate event: "Too heavy were their hearts with thoughts of their misbegotten son, who forced an unwilling fast down on them all".

Certainly, the form and style of the nursery rhyme don't sound very up-to-date anymore, just as the moralistic claim of these compositions also appears a bit naive.

Yet these words still depict the experiences told by current families living with a child affected by Attention Deficit/Hyperactivity Disorder (ADHD).

These children greatly exceed the limits of a healthy amount of liveliness for their age, continually in motion as if driven by an engine (hyperactivity), easily distractible and therefore forgetful of what they are told or what they are doing (inattention), with a tendency to act before thinking things through and with no regard for social rules and norms (impulsiveness) (1).

This is a neurodevelopmental disorder, i.e. an alteration of the normal development of the functioning of the Central Nervous System, with onset in the first few years of life and definable as a stable trait, a "way of being in the world", which in turn becomes a disorder (i.e. pathology) to the extent that it ends up compromising the child's ability to maintain adequate relationships with their peers and adults, to learn and to create useful experiences for their growth.

Furthermore, this diagnosis does not apply to situations in which the child presents this type of dysfunction only in a specific context nor when dealing with temporary occurrences, which disappear relatively quickly (less than six months) (2).

The first scientific work on ADHD appeared in scientific literature in 1902 signed by George Frederic Still (known as "the father of British paediatrics").

This author interpreted behavioural symptoms as a consequence of a defect of moral control, not resulting from organic pathology or what we currently call Intellectual Disability (the currently preferred term to indicate the clinical entity known in the past as Mental Retardation) (3). This reading, substantially in line with Hoffmann's text, now appears to be obsolete and in some ways dangerous.

Indeed, many children with ADHD are quickly labelled as rude and misbehaved, or just simply defined as "bad". However, this does a great injustice to both them and their parents.

For several decades, direct and indirect evidence of the neurobiological nature of this disorder has been observed.

The frequent association with "non-optimal" situations during pregnancy and childbirth had in the past led to hypothesising the existence of "minimal brain damage", which did not express itself with the motor (but also visual and cognitive) symptoms typical of Infantile Cerebral Palsy, but rather interfered with the ability to focus and maintain attention, as well as regulate (in an inhibitory sense) behaviour.

Over time, this hypothesis has found little confirmation and there is presently no single theory for the neurobiological peculiarities that are the basis of an ADHD diagnosis (4): several studies have documented a reduction in the functionality of the connective pathways between the frontal lobe and the basal ganglia, starting from the striatum, though finding a high variability in the neurotransmitters that could be involved (5).

The involvement of the frontal lobe, and in particular of the so-called "prefrontal cortex", is particularly fascinating because this portion of the brain is known to be fundamental for performing what are usually called the Executive Functions. These are the ability to plan, organise and perform activities of varying degrees of complexity, monitoring the outcome of these actions and taking steps to correct them where necessary to achieve set objectives. A close relative of the Executive Functions, from a neuropsychological point of view, is the attention span, a complex function that is responsible for selecting and putting a certain objective at the centre of the subject's cognitive function, resisting non-essential stimuli (so-called "distractors") until the subject decides to move their "target".

In subjects with ADHD, difficulties are found that can be easily interpreted as a malfunctioning of these skills: poor selectiveness in stimuli and/or excess of distributed attention to indistinctly accommodate information from the surrounding environment, insufficient ability to functionally regulate both motor and cognitive activity, both of which are accelerated to a frenzied state, and a tendency to act in a manner that cannot be controlled by sufficient self-reflection time (6). As a younger patient, who thanks in part to their own intellect had been able to take advantage of a good self-management course, once explained to me: "The problem is that there are too many interesting things in the world".

Described in this manner, the ADHD framework unfortunately lends itself to the risk of trivialisation, which is neatly summed up in the sadly all too common phrase that a child "only has ADHD". This expression is, however, flawed. Firstly, ADHD by definition is diagnosed in the presence of significant impairment of a child's functionality, in terms of learning and social and life experiences necessary for mental and physical growth.

In addition, children with ADHD tend to present neuropsychological disorders a little more frequently (both neurocognitive, such as Intellectual Disability or Specific Learning Disorders, as well as psychopathological disorders, starting with anxiety and depression). When these disorders occur—to make matters worse—they tend to occur earlier and in a more severe form. Again, over time, subjects with ADHD have a risk of developing negatively, presenting more serious behavioural disorders, personality changes accompanied by severe impulsive behaviour, including the use of substances and all the way up to outright anti-social disorders. Studies conducted in various countries have shown a very high prevalence of ADHD among imprisoned adult subjects. Finally, failure to recognise these disorders can often lead to a delay in the implementation of appropriate therapeutic intervention, increasing the risks already mentioned.

Regarding the recognition of these disorders, it should be noted that it is not easy to formulate a precise diagnosis, especially in younger children. With the notable exception of particularly serious forms or those associated with other neurodevelopmental disorders (such as Intellectual Disabilities or Autistic Spectrum Disorders, but also Primary Language Impairment and Developmental Coordination Disorder), it is rare to reach a diagnostic definition before six years of age (coinciding with access to primary school, a context that, due to the high demand in terms of rules to be followed for prolonged periods of time, tends to make the typical symptoms more clear). Because of this, it is a common experience for all paediatricians to see certain children described in various terms (unruly, inattentive, etc.), who, due to their behaviour, end up making things difficult for their families (and often the doctors who have to take care of them, as well!).

The genetic aspect, which is (also) undoubtedly relevant for ADHD, only adds to the difficulty in recognising and discerning between the different neurodevelopmental disorders. In addition to the frequent clinical observation which attests that parents often possess behavioural traits and methods that can be seen as mitigated versions of the typical problems their children suffer from, there are now also numerous studies that have evaluated the aspect of genetic disorder transmission, estimating that genetic factors can explain up to 80% of the variability between subjects with and without ADHD (*7*).

Taking these diagnostic precision limits into account, it is possible for a Family Paediatrician to immediately intervene to help a child and their family. Naturally, empathetic listening to what the parents say, of the difficulties they experience, of their sadness and anger in not being able to "control" their child is in itself invaluable and therapeutic. Some useful and practical advice can then be provided, specifying that there are no magic recipes, but rather methods that are particularly useful for allowing the child to find better ways to balance and function.

These tips include: clearly stressing the importance that an agitated and restless attitude is not productive, and tends to merely worsen a child's behavioural disorders, whereas the positive aspects of what the child does should be outlined and emphasised, only at a later date (and even then only if necessary) bringing attention to what was inadequate. It is also necessary to clearly and explicitly define what the child must and must not do, as well as the consequences that will follow their behavioural choices (in terms of rewards or, if necessary, punishments). Particularly important is that commands and instructions always be clear, explicit and worded positively: for these children, the sentence "don't run in the hallways" is an invitation to jump, cartwheel or do similar actions, while "walk slowly in the hallways" leaves no room for unwanted (and perhaps potentially dangerous) interpretation.

This type of advice, expanded and adapted, is the basis of so-called parent training, i.e., helping to support parents in the management of their child and their ADHD. Likewise, there are teaching and educational methods for teachers examined in the aptly named teacher training. While taking action within a child's environment can be extraordinarily useful, and sometimes absolutely necessary, a paediatrician

may often request or consider it important to intervene directly with the child. Several psychological approaches have been developed that can be used to help a child improve their ability to self-regulate and to prevent (or address) symptoms and disorders present in comorbidities related to ADHD.

Within a framework that must be articulated and multi-modal, the hypothesis of drug therapy is then suggested in some cases. In this regard, all scientific literature agrees in recognising the role of methylphenidate. This molecule, which is classified as a psychostimulant and in biochemical terms has a structural affinity with amphetamines, has an extremely significant and specific effect on the typical symptoms of ADHD. While the way it works is not yet fully understood, the most likely hypothesis involves the inhibition of dopamine reuptake and, to a lesser extent, of noradrenaline at the striatum. The use of this drug is particularly carefully regulated in Italy. More specifically, after confirming the diagnosis, administering a first dose under medical and nursing oversight (the "test dose") is required, as well as a control protocol in conjunction with a dedicated National Registry. Methylphenidate has a relatively short half-life, so even the modified-release products currently available have an effect that generally lasts no longer than 8–9 hours. Therefore, treatment planning that takes into account the needs of the child and their family becomes particularly important (8).

Similarly, the use of atomoxetine, a drug that selectively inhibits noradrenaline reuptake, is approved in Italy with the same indications. This molecule has, according to many authors, a lower efficacy rate compared to methylphenidate and appears to present greater risks of cardiovascular toxicity. Other molecules (e.g., amphetamines) are used abroad but are not approved for use in Italy (9).

The introduction of drug therapy requires synergy between a Family Paediatrician and the Reference Centre. Indeed, while the latter is responsible for the process of evaluating and introducing the drug, the paediatrician always and in all circumstances maintains a central role in monitoring the child's health conditions as a whole. In particular, it is important to monitor the trend in staturo-ponderal growth (although the most recent data seems to be scaling back the risks of slowdown in this context), the regularity of the sleep-wake rhythm, adequate nutritional intake (considering that during effective hours a decrease in appetite is frequently observed), and cardiovascular parameter trend, with particular reference to cardiac electrical conduction parameters and blood pressure.

Although methylphenidate has particularly significant efficacy and safety data, higher than that available in drug therapies for other neuropsychological disorders during developmental age (and often present in adulthood ones, as well), current regulations significantly limit access to this type of treatment.

This is because, on the one hand, the use of drug therapies is not expected before the age of 6, essentially because the data available for the younger age range is considered insufficient to ensure an adequate risk-benefit ratio. On the other hand, the need to pass through the network of Centres authorised to prescribe said medication causes "bottlenecking". In addition to this, there are family concerns, sometimes exacerbated by the fact that this therapy has been the subject of non-scientific but strongly negative and critical publicity spread over the Internet for a long time. It is therefore not surprising that, in Italy, it is estimated that only 3% of children who could be eligible for drug therapy are actually prescribed it (compared to an average of around 25% in other Western countries).

The Family Paediatrician may therefore be in a position to consider additional treatment necessary, even after having already taken, in collaboration with the dedicated services, the clinical measures required to support the child, their family and their school. Over time, numerous non-pharmacological strategies have been proposed, mainly related to dietary guidelines or the use of food supplements. It is important that the paediatrician offer authoritative, competent guidance given that the risk of resorting to an uncontrolled information source such as the Internet as an alternative, in its various forms and permutations, is otherwise quite high. These types of measures may mean providing initial help while waiting to access potential drug therapy, and possibly avoiding the latter if the benefit obtained is already sufficient.

Dietary guidelines essentially involve a reduction in simple sugars and substances with psychostimulant potential. The usefulness of limiting artificial preservatives and food colouring has also been suggested, though it is currently quite difficult to carry out.

At the nutraceutical level, some interesting evidence has been reported relating to the use of Polyunsaturated Fatty Acids (PUFAs). These substances are essentially classified in relation to the position of the first C=C double bond to the end carbon atom. In particular, Omega-3 polyunsaturated fatty acids play an emerging role in multiple diseases, including various neuropsychiatric diseases. In nature, they are mainly produced by marine algae and are concentrated in various fish species. Specifically, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are generally found in fish, fish oil and shellfish, while alpha-linolenic acid (ALA) is found in walnuts, almonds and vegetable oil (flaxseed oil and colza oil). It has been shown that the current Western diet is lacking in Omega-3 PUFAs, both for the most widespread food choices and because even the foods that could contain these substances are increasingly less rich in them (likely due to livestock farming methods) (10).

Although their effects are only partially known, there are now numerous studies that have demonstrated a possible use when implemented in treatments for various neuropsychiatric disorders in children. The Omega-3 PUFAs influence the physical and chemical structure of cell membranes and modulate gene expression, acting on ion channels and the biosynthesis of eicosanoids. EPA and DHA are among the main Omega-3 PUFAs that, in addition to modulating the production of active prostanoids and leukotrienes, compete with arachidonic acid (AA) in being converted by cytochrome P450 enzymes and forming physiologically active metabolites. Although the evidence is not yet definitive, it is clear that it is important for doctors to know these substances and their possible uses, due also to the manageability of Omega-3 PUFAs in clinical practice.

There are now numerous studies related to the use of Omega-3 PUFAs in ADHD. Despite having a lower efficacy than methylphenidate (11), they represent a possible alternative, both due to the substantial absence of side effects (essentially limited to a not always pleasant taste when the preparation is not ingested as a capsule), as well as for the possibility of observing benefits even in non-neuropsychiatric aspects (as the potential benefits on cardiovascular health, hepatic metabolism and their supplementation are all already well-known). More recent data also highlights a possible positive effect on praxis skills (planning and sequencing of end actions) and learning skills, which appears to be further optimised by preparations containing all the main Omega-3 PUFAs in optimal proportions. The hypothesis here is that this balance prevents the activation of the conversion pathways that could lead to the creation of Omega-6 PUFAs (known for their pro-inflammatory properties) to an excessive degree.

Obviously, intake should continue for a sufficient period of time, generally no less than three months (although personal experience can attest a prolonged use, even for up to 18 months, has no detectable side effects, either clinically or from basic blood chemistry tests).

With regard to this approach, it should also be emphasised that the choice of the product used is particularly important. Although it is possible, through different channels, to find preparations that boast high concentrations of Omega-3 PUFAs,

it is particularly important to consider that these substances are sensitive to oxygen exposure in the air and therefore must be processed in accordance with strict procedures. As such, there is no real "exchangeability" between the different products and it would, in fact, be advisable to know which of them are certified for the use of rigorous production methods capable of preserving the potential of these substances.

Key Points

- Attention Deficit/Hyperactivity Disorder is frequently encountered in a Family Paediatrician's practice, both in its typical form and its variants, which are nevertheless contextualised as neurodevelopmental disorders.
- Diagnostic recognition is important, but adequate intervention is even more significant for the well-being of families and the prevention of future hardships for their child.
- The Family Paediatrician must take on a directing role in selecting appropriate measures and may act in person, in addition to mobilising specialist services (if they deem it appropriate).
- In addition to family support, nutraceutical strategies may also be implemented, among which polyunsaturated fatty acids seem to be particularly promising, as they can be effective and are well tolerated.

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