Medication-based supportive brain maturation therapy in childhood and adolescence

By Fritz Held

Following the development of medications that can activate the cerebral metabolism and cerebral blood flow in a physiological way (Piracetam, Centrophenoxine), these are being used in the supportive intensive care treatment of severe brain damage (trauma, apoplexy, tumor operations, alcoholic delirium and predelirium), as these brain function-enhancing medications also stimulate the cerebral regeneration, repair and compensation processes. These medicinal substances are also beneficial to geriatric patients as the stimulation of the cerebral metabolism and, subsequently, cerebral blood flow can improve the impaired brain functions of this age group.

Indication: children whose development is (partially) delayed

While these two areas of indication are now part of common medical knowledge and experience there is, however, another important and large area of indication for these medications, which is still far too little known, viz. the treatment of children and adolescents with delays of various types and geneses. Apart from the fact that, when treating children or adolescents, we are generally grateful for medicines which work physiologically, are nontoxic, free of side effects, and without any risk of addictions, the above-mentioned medications have made it possible for the first time, in addition to non-medicinal treatment measures, to directly draw on the functions of “maturation” and “subsequent maturation”.

The biological function “maturation” is specific to childhood and adolescence. In a sense, it is thus a child-specific brain function that no longer exists in adults, and which ensures that all physical and mental functions (e.g., the maturity of motor functions, sensory functions, speech, reading and writing functions, social behaviour etc.) mature on time and in a coordinated manner and thus become functional, whereby the different ontogenetic maturation dates of these functions often correspond to their different phylogenetic development dates in human phylogeny.

Maturation delays

In all these functional areas, delays in maturation, delays, can occur for the most diverse reasons and in the most diverse forms. As far as the various causes of such delays or partial delays are concerned, there are congenital, i.e., genetically fixed delays of certain functions, which also appear in the medical history of the family. Acquired delays and partial delays may occur, too, whereby not only physical factors can have a delaying effect without damaging the brain (e.g., premature birth, perinatal hypoxia, nutritional disorders, etc.), but in which, due to the close interconnection of physical and mental functions, psychological factors may also slow down maturation (e.g., being separated from the mother during the imprinting period of the first three years of life, or frequent changes of the people the child relates to most closely).

With regard to **the different forms**: there are delays of the entire physical or mental maturity, there are isolated partial delays, e.g., only of linguistic, motor, or social maturity, and there are dissociations of maturations, e.g., between accelerated physical maturity and delayed mental maturity (such as in puberty crisis).

Activation of maturation in practice

If we now consider this biological function “maturation” and “maturation to proper functioning" as a specific brain function of childhood and adolescence, and if there are medications that can physiologically activate the cerebral metabolism, and thus inevitably also the brain functions, then it is obvious that in this way the brain function “maturation” can be activated if it is delayed for any of

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the causes mentioned and remains behind. Since these are physiologically active medicines, this happens without the risk of on overactivation of maturation, which in the end may turn a late development into an equally undesirable prematurity.

Since neither the range of indications for such a medicinal-based supportive maturation therapy for children and adolescents are sufficiently known, nor the symptoms that can arise, e.g., from a partial suspension of social maturity, in the form of a wide variety of behavioral and performance disorders, this report aims to delineate the experience gained over many years in the author's surgery of child and adolescent psychiatry with the diagnosis and therapy of delays and partial delays in by now hundreds of children and adolescents of all ages who have been treated with Piracetam[1].

The biochemistry of Piracetam

To start with, I would like to briefly describe the biochemistry of Piracetam, by means of which the therapeutically effective activation of the cerebral metabolism in a physiological way is achieved.

Biochemical studies in animals indicate an improvement of the energy potential of the cerebral cell through an accelerated ATP turnover. Piracetam increases the incorporation rate of radioactively labeled phosphate into the cerebral organic phosphate compounds and stimulates the metabolism of phospholipids and nucleic acids (*Giurgea, Gobert*). The increase in neuronal protein formation could be indirectly determined by an increase of polysomes, the protein synthesis apparatus of the nerve cell (*Burnotte*).

This means that Piracetam enhances the cerebral metabolism which is an indispensable prerequisite for the healthy operation of all brain functions.

Supportive therapy and dosage

Various studies (*Fiegel, Wilsher*) have demonstrated good success with supportive Piracetam therapy for learning and adjustment difficulties in children and partial performance deficits in adolescents. Concentration and attentiveness were improved; behavioral and social contact disorders decreased.

It should be noted in advance that in children under 10 years of age, the preparation is usually most effective at a dosage of 2x400mg per day, in children over 10 years of age at a dosage of 2x800mg per day, to be given in the morning and at noon. It proved advantageous that the preparation is also available as an oral solution as there are many who are incapable of swallowing capsules or tablets.

No side effects

Furthermore, it should be noted that till now it has never been necessary to discontinue the treatment prematurely owing to intolerance or toxic effects, and that there has never been a case of medication dependence. Once the therapeutic goal of subsequent maturation had been achieved, the medication could be discontinued without complications.

Due to the evident and plausible physiological mode of action as well as the innocuousness of the medication, **compliance** was high, as the general fear of psychotropic medications, dependence, or addiction was not attributed to this class of preparations so that there was no obstacle to long-term treatment. (Required duration between 3 and 12 months or longer, depending on indication).

[1] NORMABRAIN ®, Cassella-Riedel Pharma, Frankfurt

Finally, it should be noted that in no case an isolated activation of sexual maturation occurred, but that, on the contrary, the therapy proved to be effective only in delayed mental functions while it did not have an activating effect on physical development.

Ranges of indication

Before describing the individual areas of indication, it should be noted that, irrespective of age and symptoms, there are children who respond better to Piracetam from the outset and others who respond better to Centrophenoxine. Why there seem to be Piracetam and Centrophenoxine types in this maturation therapy is not yet clear. Herein, we shall discuss the ranges of indication of such children who responded to Piracetam. In detail, these were the following ranges of indication:

Partial delays

It has become apparent that in children with partial delay development of speech (stammering, agrammatism), motor skills (clumsy fine motor skills), or reading and writing functions (dyslexia, dyslexic syndrome), a subsequent maturation and thus normalization of the respective functions was achieved significantly more quickly when the respective specific remedial functional training (speech therapy, remedial gymnastics, orthography training) was combined with a medication-based maturation therapy.

Educationally impaired children and developmentally challenged children

Another area of indication for a medicinal-based maturation therapy are those children whose late development is not reversible, i.e., capable of subsequent maturation, but in whom optimal mental maturation is restricted by cerebral damage or genetic factors.

Even for them, a medicinal-based maturation therapy together with the appropriate special educational measures (special school for educationally impaired children, special school for developmentally challenged children) can achieve an optimal activation of all developmental potentials up to the limits of what is possible better and faster than would be possible using educational and psychological measures alone. At that, it was found that, in many cases, in developmentally challenged children of the erethistic type, the same behavioural regulation can be achieved with Piracetam as with the much less harmless stimulants (e.g., methylphenidate). Apparently, it is the same operating principle: instead of a biochemical sedation of the restlessness itself a biochemical activation and enhancement of the insufficient developed functions.

Partial developmental lag of social maturity

Children with partial developmental lag of social maturity are a particular case. This, like any other partial developmental lag, can result from various causes already described. It is particular not only because this partial developmental lag of social maturity is very frequent, but also because it is far too seldom recognised and considered as a possible cause for the most diverse behavioural and performance disorders of childhood and adolescence.

This is mainly due to the fact that in the depth-psychological era, there is too strong a tendency to view child behavioural disorders in a one-sided milieu-oriented way and to search for the causes in the milieu in an often almost dogmatic stubbornness. In doing so, it is overlooked that the causes of such behavioural disorders can also lie in the child itself (e.g., in precisely such a delay in and of social maturity), and that the identified misbehaviour of the mother does not necessarily have to be the cause of the behavioural disorders of the child, but may also be their consequence. For there are behavioural disorders which are quite capable of transforming even the most intact family milieu into a troubled one over time.

This one-sided, milieu-oriented in-depth psychological approach not only causes incorrect diagnoses and unsuccessful false treatments (e.g., years-long play therapy), but also leads to the fact that the actual causes in the child remain undetected and can therefore continue to have an effect. (And if, sometimes, years of psychotherapy prove successful, it was, in fact, not the method, but simply the time that was available for a spontaneous subsequent maturation.)

Which behavioural disorders can result from such a partial lag in social maturity, irrespective of how it developed?

In general, these behavioural disorders are characterised by the fact that, due to this delay in maturation, physiological patterns of behaviour of earlier maturational stages do not appear at the normal time, but much later. Or they do appear at the normal time without regressing as normal. Instead, they persist and thus still appear in later developmental stages, into which they no longer belong, and therefore act as behavioural disorders.

Hence, for example, in case of a lag in social maturity, the physiological phase of defiance may persist into school age where it is no longer recognised and accepted as such.

Or the physiological phase of separation anxiety and clinging to the mother persists into school age – these children do not go to school without their mother, or to bed without their mother, or they come to their mother's bed every night.

Or both phases may persist simultaneously, resulting in a paradoxical behaviour towards the mother.

Or there is a delayed development of the ability to socialise with fear of contact, the inability to assert and defend oneself, the inability to assimilate and the typical omega position within a group.

Or there is a delayed development of bladder and bowel control (which is also a part of social maturity) along with persistent enuresis and encopresis.

Or there is a delayed development of the ability to control and restrain one's temper, affects, and reactions, or to abide by the social rules of the family or school.

Confusion with milieu-related neuroses and negative character traits

It is obvious that such delayed developmental-related behavioural disorders are all too easily mistaken for milieu- related neuroses or negative character traits, when in reality they are merely reversible late developments of social maturity that respond particularly well and quickly to a medicinal-based maturation therapy.

One can often watch from week to week how the inhibited children become more and more outgoing and are suddenly able to defend and assert themselves (often via an aggressive transition phase, which is therapeutically desirable in these cases). Or one can watch, in case of a persisting phase of defiance, how the aggressiveness lessens during such a maturation therapy without any sedation and gives way to a controlled behaviour. (Regrettably, instead of a maturation therapy, tranquilisers with all their associated risk factors are often wrongly used here.)

Behavioural disorders in puberty

Normal pubertal behaviours become behavioural disorders when they are excessive in quantity as a result of maturational dissociation. Here, too, normalisation could often be achieved more quickly and effectively with Piracetam (in conjunction with intensive talk therapy and parental counselling) than by often all too rapidly resorting to tranquilisers, which pose a particularly high risk of dependence and addiction, especially in this age group (tranquilisers as a first step towards addiction).

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Concentration difficulties

Since both the ability to concentrate and intelligence are also brain functions and, like all brain functions, are subject to a maturation process, an activation of the ability to concentrate and thus an improvement in school performance can also be achieved by means of a medicinal-based maturation therapy.

Celebral electrical signs of developmental lag

In many delays and partial delays, cerebral electrical signs of developmental lag can simultaneously be found in the electroencephalogram, which are often mistaken for signs of irreversible brain damage and thus lead to further misdiagnosis. However, these cerebral electrical signs of developmental lag prove to be reversible in the course of subsequent maturation and regress visibly.

Yet, this can only be recognised if several follow-up electroencephalograms are performed, thus protecting against the misdiagnosis “brain damage”. After all, the often hastily made diagnosis “brain damage”, which is derived from a single electroencephalogram or even only from the anamnesis or the symptoms, is more than a medical misdiagnosis. It becomes a permanent social label involving all the elements of devaluation which can impair a child’s psychological development just as much as actual brain damage.

Duration of subsequent maturation

Based on my 30 years of experience as a child and adolescent psychiatrist, I would like to answer the question of how long an underdeveloped brain function of whichever kind is capable of subsequent maturation at all as follows: It is capable of subsequent maturation as long as it is not fully developed if no brain-organic or genetic restrictions exist. I.e., a supportive medication-based maturation therapy is indicated regardless of age, as long as the children and adolescents are still in the developmental age and have not yet reached their final maturity, which may well extend beyond the age of 20.

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