Neurobiological Principles of Mental Development in the Child

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Abstract. The mental development of a child is closely linked to the development of the brain. This does not mean that this development can be understood to be purely neurobiological. Rather, the brain is the organ of feeling, thinking, and action planning, where a number of factors concur and interact with each other in complex ways. These include (1) genetic predispositions and characteristics of individual brain development, (2) early attachment experience, (3) psychosocial and imprinting experience during infancy, and (4) education and training in later childhood, adolescence, and adulthood.
These factors act at different times upon the individual development and thus enter brain development, i.e. genetic predisposition and brain development conditions show an early influence on the structuring of the personality, followed by the early bonding experience and early psychosocial experience in childhood. For both factors it is very difficult to determine their individual effect, as they sometimes interact intensely before birth. Taken together they deeply influence most certainly the development of personality. Education and training in adolescence and adulthood have, by contrast, a lesser impact on the shaping of the individual and social personality.

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1 Early brain development

The brain shapes very early its basic structure in the development of an embryo, which is common for all mammals and consists of a paired end brain (telencephalon) and an unpaired interbrain (diencephalon), midbrain (mesencephalon), bridge (pons) and extended mark (medulla oblongata) as well as a cerebellum [1]. The resulting brain parts slide against each other, bend down, or one part overgrows the other as happens in the human brain. The relative sequence of the parts of the brain remains strictly intact. During brain growth the formation of nerve cells is extremely high and amounts throughout pregnancy to about 250,000 neurons per minute with a maximum of 500,000 per minute. Whereas the cell division in the human brain is largely completed in the twentieth week of pregnancy, cell migration continues long after the birth.

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Important for the function of the brain as a system of information processing is not only the formation of nerve cells, which is substantially completed in humans at birth with local exceptions, but also the formation of cell contacts (synapses) in cell bodies, dendrites and axons, called synaptogenesis [2, 3]. Axonal projections are already formed from the nerve cells during their migration, while dendrites usually develop only after the cells have reached their final destination. The formation of dendrites and synapses as points of contact between axons and dendrites, or between dendrites of different neurons starts to a large extent with the fifth month of pregnancy, but increases after birth again massively together with the formation of dendrites. However, this happens differently in different parts of the brain. In the visual cortex, for example, a doubling of the synaptic density takes place between the second and fourth month after birth and the maximum number is approximately reached within one year. Subsequently, the number of synapses drops, and the adult level is reached at about eleven years. In the frontal cortex, the maximum synaptic density is likewise achieved within a year, but the number of synapses is twice as high as in the visual cortex; synapse reduction begins here only with five to seven years and does not come to a certain stop before an age of eighteen years.

The main principle of the development of specific neuronal connections, formed in the brain, is that initially far more synapses are formed than are needed later on. This means that at first an overproduction of synapses, and then a dramatic reduction occurs. It is believed that among the billions and billions of synapses a local competition takes place, which is essentially conducted about nutrients and growth substances (called trophic factors) as well as about to ensure a minimum of neuronal excitation. In fact, does a synapse receive too little of everything, then it dies. As a consequence first diffuse, i.e. nonspecific synaptic links are installed, then they are reduced selectively and adaptively due to the competition between synapses. Thereby, the respective network is made more efficient [4]. In the provision of adequate neuronal excitation both internally generated stimuli and those derived from the environment play a major role.

Another important factor in the structural and functional maturation of the brain is the myelination of nerve fibers. To this end a so-called myelin sheath is formed around an axon. The myelination of an axonal extension allows a much (in some cases hundreds of times) faster propagation of action potentials through the axons than in unmyelinated fibers. Without a massive myelination in the brain excitation processes would run much slower, this would severely impair the cerebral cortex with its trillions of axonal connections and would make many complex cognitive performances impossible. Therefore, the process of myelination of the cerebral cortex is an important component in the development of higher cognitive and psychological benefits [5].

The myelination of axons in the brain begins after completion of cell migration and finishes gradually until they reach adulthood. Thereby, there is a clear gradient. Before birth, the axons of cells are myelinated in the spinal cord and the medulla oblongata and immediately after birth the axons of cells in

the mesencephalon and cerebellum. In the first and second year follow axons in the thalamus and in limbic centers of the end-brain and in the basal ganglia and then those in the primary sensory and motor areas of the cerebral cortex. Subsequently, the secondary sensory and motor areas are myelinated. Still later myelination takes place in the associative areas of the cortex. Here the fibers of the prefrontal and particularly the orbitofrontal cortex are myelinated at last; this may drag on until the age of 20. The growth of dendrites, the death of synapses, and the myelination are accompanied by a parcellation of the brain into structural units, namely into nuclei outside the cortex and later into cortical areas. The final step in the differentiation is the fine wiring in these structures. Thereby, the neurochemical specificity of neurons develops, i.e. the equipment with specific excitatory, inhibitory and modulating neurotransmitters and neuropeptides.

The aforementioned brain centers develop in the vertebrate brain in a very specific sequence [6]. At first, the hypothalamus and the amygdala as well as the tracks connected with the brainstem are developed very early, namely, around the fifth and sixth week of pregnancy, followed by the nucleus accumbens, the septum, and the limbic main communication routes in the sixth and seventh week. Already in the third month of pregnancy one can differentiate the various nuclei of the amygdala. The basal ganglia begin their development in the seventh and eighth week as well as the deep cerebellar nuclei and parts of the vestibulo- and spinocerebellum and parts of the limbic cortex (e.g. the insular cortex). However, although only little is known about the process of fine wiring within these centers, one can assume that it begins very early. At least, the main centers and the limbic connecting tracts are available well before birth. The hippocampus begins to bend in the middle third of the embryonic development in a characteristic "sea horse-like" manner and the connections of the three parts of the hippocampus (ammon's horn, subiculum, gyrus dentatus) among each other and with the adjacent entorhinal cortex form starting with the twentieth week. The first links of the hippocampus formation with the isocortex do not occur prior to the twenty-second week.

The actual training of the isocortex with its convolutions and fissures, which represent signs of increased cell formation, begins to a significant extent in the fourteenth to the seventeenth week in the cingulate cortex and in the occipital cortex as well as in the adjacent parietal lobe. Then the central groove and the upper temporal sulcus follow in the eighteenth to the twenty-first week of pregnancy, followed by further sulci and gyri in the parietal, temporal and occipital lobes. In the twenty-sixth to the twenty-ninth week both sulci and gyri of the frontal lobe are added. The formation of secondary temporal, frontal and orbital sulci and gyri marks the end between the 30th and 37th week, i.e. just before birth. The sequence of cognitive, mental and motor development of a child corresponds very closely to the first occurrence of the sensory, motor, cognitive and executive functions of the cerebral cortex.

The brain of the newborn has all the sulci and gyri of the mature brain. It weighs 300 to 400 grams and already contains the final number of neurons

(except those born postnatally in the hyppocampus), which, however, are still relatively immature. The subsequent massive increase in mass of the brain to an average of 1300 to 1400 grams in adults is primarily due to the length growth of dentrites and the myelination of axons as well as the increase in glial cells and brain blood vessels. The fine wiring of the cerebral cortex is thus taking place essentially after birth [3].

According to the anatomical development of the brain the sensory systems mature at different times. The sense of balance develops first; it is formed up to the end of the 5th month of pregnancy, followed by olfaction and the sense of taste. The visual system is also developing prenatally. From the 5th month the first visual synapses form, a strong growth takes place between the 14th und and 28th week of pregnancy. However, the highlight of this development lies in the first postnatal age, as already described. Like seeing, hearing takes place even before birth, but this happens apparently subcortical, because the auditory cortex develops only in the first two years after birth. The gross motor skills are present along with the sense of balance well before birth, also specific forms of arm and hand movements, such as thumb-sucking. Targeted access occurs from the 4th month, the fine motor skills between the eighth and the eleventh month, the release of a grasped object starting with the 13th month. Upright walking takes place at the end of the first year, that is when the motor cortical fields are mature enough for leg movements. This relatively late maturing is explained by the fact that the myelination and the fine wiring of these cortical fields progresses from head to foot.

From the second half of the first year, the areas of the frontal lobe slowly start working. Clearly the number of synapses is increased, and this comes along for an infant with nuanced perceptions and feelings from the 10th month on. With two and a half years a further maturation of the prefrontal cortex occurs in terms of the dendritic length and growth as well as the synaptic fine connection, especially as far as the prefrontal cortex and the Broca area are concerned. This is viewed to be the basis for the formation of conscious thought and other higher cognitive functions, the syntactic-grammatical language and self-consciousness. Apparently at this very time, i.e. at an age between two and three years, the development begins when the human child leaves behind both cognitively and communicatively his nonhuman contemporaries, see Ref. [7].

The development of language begins with the sensibility for the affective and emotional tone of language and intonation. This already happens before birth in the right hemisphere, which dominates in the first months after birth. Only then the left hemisphere begins to become active with the temporal region, i.e. with the later Wernicke area. The right frontal area, which is opposite to the Broca area, is developed in advance in its neuronal fine structure, e.g. the dendrite length, until the 12th month. Between the twelfth and fifteenth month the dendrite length increases faster at the left hemisphere, but between the twenty-fourth and thirty-sixth month after birth both right and left frontal areas develop at the same rate. Between three and six years, however, the left frontal

area dominates, i.e. the Broca area. This is consistent with the fast development of a syntactic language, which takes place afterwards.

In summary, the limbic system and the subcortical system of behavioral control, i.e. the basal ganglia, are formed early prenatally and well before the hippo campo-cortical system form, i.e. as early as the fifth embryonic week. The cortical system as the site of the conscious ego matures, however, only after birth, and this maturation process is completed not before the end of puberty. Until recently little was known on the development of the brain during adolescence. But meanwhile we know that, during this important stage of life, new connections are made in many parts of the brain, among others stimulated by sex hormones, which are then selectively degraded. The word of the "construction site of the adolescent brain" does apply, in particular to the frontal and the temporal lobe.

2 The structure of the "psychic apparatus"

The shaping of the human psyche is largely determined by subcortical and limbic cortical centers and areas of the brain, which interact with cognitive and motor centers in a characteristic way, see Refs. [6, 8]. Thus, large parts of the brain are involved in the constitution of the personality of a person. Though there is some overlap, one can differentiate four levels of the brain, which run on personality-related processes. At each level there are again several to many centers, which interact among each other and with other centers. In this respect, the level structure shown below should not be viewed selective.

The lowest level is the autonomic-affective level. It is represented by the limbic-autonomic main axis of the brain, which include parts of the septal and hypothalamic region, the central amygdala, the central gray matter and the autonomic-visceral centers of the brain stem (midbrain, pons, medulla oblongata). These areas of the brain secure our biological existence via controlling the metabolic balance, circulation and blood pressure, temperature regulation, the digestive and endocrine system as well as nutrition and fluid intake, waking and sleeping. Deficits in these regulation systems can lead to severe physical impairment. This level also controls our most fundamental affective behaviors and sensations such as offensive and defensive behavior, flight and freezing, aggressiveness, anger and sexual behavior. These drives and emotional states are in their way largely genetically determined - we share them with other mammals and especially primates - and are therefore only slightly influenced by experience and voluntary control. In particular, they run completely unconscious; they are aware only via excitations which travel from there to the cortex.

In their individual shaping these centers set the properties of the temperament, with which the people come into the world, i.e. whether a person is curious, daredevil or careful, communicative or taciturn, brave or timid, etc. This layer is formed in the brain already during the first few weeks of pregnancy. Here one finds also innate mechanisms of the interaction of the later infant with his mother, in particular the an attachment behavior, and his other close environment, see below.

The second level arranged above is that of emotional conditioning and emotional learning. To this end the corticale, mediale und basolaterale amygdala, the mesolimbic system (nucleus accumbens, ventral tegmental area and substantia nigra) are involved. The basolateral amygdala is the site of conditioned linkage of emotionally relevant, mostly negative or surprising, but also positive events with the basic feelings of fear, anxiety, defense and surprise. This includes the recognition of the importance of emotional and communicative signals such as facial expressions, gestures, voice intonation and posture. The medial and cortical amygdala handles smell and taste preferences as well as social smell signals called pheromones which play an important role for the individual likes and dislikes. These preferences are partly genetically determined and partly experience-dependent.

Interaction partner and simultaneously "opponent" of the amygdala is the mesolimbic system. It dominates during the registration and processing of natural reward events ("this has gone well" and "that was fun") and represents the cerebral reward system via the release of pleasure-producing substances of the brain (the so-called endogenous opioids). This means that everything which produces lust, joy, satisfaction etc. in us is bound to the distribution of certain substances in the brain. On the other hand, it is the basic motivation system which "promises" a reward via the distribution of the neuromodulator dopamine and, thus, "motivates" our behavior, as we shall see. The activity of dopaminergic neurons in the nucleus accumbens depends on the prediction of rewards [9].

This middle limbic level arises somewhat later than the lower level, but also before birth, and develops primarily in the early days after birth. It shapes the unconscious parts of the self, due to early childhood experiences, especially early attachment experiences. This produces in a recursive way the basic structures of the relationship to ourselves (self-image) and to others (empathy) as well as the basic categories of what is considered to be good or bad from an "infantile" way. Although these basic structures and categories result partly from unconscious and partly from conscious learning processes, they solidify step by step, and thus become "angel" or "vicious" circle in the sense of Papusek [10], i.e. experiences are selectively made in order to confirm anticipations and preferences. At this central limbic level it is determined what we seek out or have to repeat as it is connected with gratification and pleasure and what we have to avoid, as it is associated with an increase in the needs, pain and aversion. It is thus crucial for the mental level, both in terms of a normal and an abnormal development.

The third level is that of conscious, predominantly socially mediated emotions and motives. It includes the limbic parts of the cerebral cortex. These include the insular, the cingulate and the orbitofrontal cortex, which interact in turn partly parallel and partly hierarchically with each other. The insular cortex is the processing site of affective sensations, including the affective pain perception, i.e. it determines when and how a body injury hurts, and is also the place of the affective-emotional visceral perception of the famous "gut feelings". The anterior cingulate cortex with its lower, ventral part is related to risk perception and risk

assessment and with the affective tone of pain sensations, especially with pain expectation, whereas the dorsal part is concerned with cognitive attention and error monitoring.

The orbitofrontal cortex (OFC), i.e. the lower frontal lobe, which is located above the eye sockets (orbita), and the adjacent ventromedial frontal cortex (VMC, with transitions to the anterior cingular cortex, ACC) are in a certain sense the "highest" limbic cortex. Lesions in OFC and VMC lead to the inability to capture the social communicative context, for example the importance of scene representations or the expressions of faces. The OFC is the seat of networks, which represent the rules for moral and ethical behavior, i.e. those behaviors that are appropriate to preserve us the support and appreciation of our fellow human beings in the narrow sense and the society in the broader sense. It is that part of the brain, which needs the longest maturity and is reasonably "mature" not until the age of 18-20 years. Both OFC and VMC play a major role in the control of the affective limbic level and of the selfish-infantile drive from the centers of limbic middle level, the amygdala and the mesolimbic system, on the basis of socially mediated experience. It is the site of development of the components of the conscious itself and the affective-emotional, also socially mediated ego, and here elements of morality and ethics are formed, which as described by Sigmund Freud as the superego.

These three limbic levels contrast with the cognitive-linguistic level, which forms inside the cerebral cortex in the stricter sense, the six-layeredisocortex. It includes executive, i.e. preparatory treatment areas, in particular the dorsolateral prefrontal cortex (PFC). In the left PFC also resides the Broca speech area that represents the neural basis of the human syntactic-grammatical language. The dorsolateral PFC is part of working memory and, thus, of intelligence and mind. It is related with the spatio-temperal structuring of sensory perceptions, with tactical and contextual acting and speaking as well with the development of goals.

This is the level of the cognitive-linguistic ego and of grammatical-syntactical communication. On the one hand it is examined "which side one's bread is buttered on", and on the other hand it is about problem solving and purpose-rational action planning. Finally, this is the level of rational or pseudo-rational representation and justification of the conscious ego in front of oneself and of others. This level is closely connnected with the sensory (i.e. visual, auditory and tactile) areas as well as with the motoric centers of the cerebral cortex, but it has only few links to those limbic centers, including the OFC and VMC. This means that the upper frontal lobe, as the seat of intelligence and understanding, hardly interacts with the lower frontal lobe as an instance of moral-ethical control, risk assessment and control feeling.

The presented "four-layer model" of psyche and personality explains well the complexity of personality. There are largely genetically or prenatally fixed portions of temperament, above resides probably the most important limbic level of emotional conditioning in early childhood. Both together make up the core of our self-centered personality, which works largely unconsciously or cannot be

recalled (Freud's "infantile amnesia"). The development of this core of our personality is largely finished with 5-6 years. At about four years the development of the third limbic level begins at which we socialize through early childhood attachment experience through our extended family, i.e. father, siblings, grandparents, uncles, aunts as well as playmates and classmates. Here we learn how to behave, such that others like us and help us when necessary. We do this not necessarily out of pure human love, but because of the experience acquired early in life, that the others (apart from our parents) do not help us, if we do not help them, i.e. if we do not develop "reciprocal altruism". This socialization takes a long time and is largely completeled not before twenty years when the personality is more or less "consolidated".

The fourth level of intelligence, mind and language develops roughly in parallel to the upper limbic level, but largely independent of it. This fact is of great importance for the school, because here you will often find that boys and girls are "highly intelligent", but their personalities are not sufficiently developed (which is a problem when skipping classes). The opposite can also happen that someone is relatively "mature" of his or her personality, i.e. reveals a good social conduct, but remains somewhat slow in his/her cognitive abilities.

3 Neuromodulators and personality

In first approximation one can identify six neurobiological-psychological basic systems which are characterized by the specific interaction of neuroactive substances in the above mentioned limbic and cognitive centers of the brain. These basic systems also arise partly at different times in cooperation of genetic and environmental factors.

The first neurobiological-psychological system is the stress management system, which is also called the stress axis. Its function is to direct the organism towards coping with physical and psychological stress and strains. It emerges quite early in the development of the brain, that is already in the first weeks of pregnancy, but is functioning well only at the end of the first postnatal year of life. This system is activated by the limbic centers, which are responsible for detecting potentially threatening or negative events (e.g. the amygdala), and reacts hereupon in two steps. The first and fast stress response is based on the activation of neuromodulators adrenaline (epinephrine) in the adrenal medulla and noradrenaline in the locus coeruleus ("blue core") of the brain stem. The release of adrenaline into the blood stream and then into the body and of noradrenaline in the autonomic centers of the brain lead in a matter of seconds to an increase in muscle tone, responsiveness and attention. Adrenaline and noradrenaline in turn trigger the second and slower stress reaction [11]. This begins with the release of corticotropin releasing factor (CRF) in cells of the hypothalamus, which then migrates to the anterior part of the pituitary gland. There it effects both the production and the release of the adrenocorticotropic hormone (ACTH). ACTH travels through the blood stream to the adrenal cortex, where it stimulates the formation of glucocorticoids, in humans mainly cortisol. Cortisol in turn moves

through the blood stream into the body and the brain, where it triggers a variety of effects. It mobilizes our metabolism by increasing glucose and fatty acid levels in the blood and, thus, puts the body in a position to accomplish demanding achievements.

In the brain cortisol acts on two different receptors, especially in the amygdala, the hippocampus and the orbitofrontal cortex, namely the mineralocorticoid and the glucocorticoid receptors. Low doses of cortisol and mild stress activate primarily the mineralocorticoid, stronger stress the glucocorticoid receptors. Due to the latter the activation of those brain centers is increased which control the reactions for eliminating the threat or stress, for instance, escape, defense, fight or more complex countermeasures. The effect of this stress hormone is slower and more long-lasting than that of adrenaline and noradrenaline [12]. Simultaneously cortisol controls directly via the glucocorticoid receptors or indirectly via the hippocampus and the orbitofrontal cortex the release of CRF and ACTH in the hypothalamus or in the pituitary. Thus, there exists a negative feedback between cortisol on the one hand and CRF and ACTH on the other hand, which should prevent that too much CRF, ACTH and cortisol are produced at a stress reaction [11]. A special role in this negative feedback of the CRF-ACTH-cortisol system plays the hippocampus, which has a particularly large number of corticosteroid receptors and, therefore, reacts particularly sensitive to severe stress. The reduction of the stress-related cxcitement is enhanced by the simultaneous release of endogenous opioids and other "primary brain drugs" and of serotonin, which has a sedative and anxiety-dampening effect in this context.

Mild stress is necessary in order to prepare body and brain for dealing with and addressing problems and dangers, and high stress can temporarily lead to a release of unsuspected forces. Chronic high levels of stress on the other hand leads to physical and mental decline in performance, insomnia, over-excitement, depression, stomach aches and headaches, forgetfulness and a strong decrease of sexual activity. Here it is the failure of the aforementioned negative feedback of the stress axis and, correspondingly, an ongoing overproduction of CRF, ACTH and cortisol, called "hypercortisolism", which damages in particular the hippocampus (although mostly reversible). During the course of the stress response one speaks of an "inverted U" shape. People strongly differ in the way they deal with stress, i.e. it belongs to the personality of a person, how much stress he or she can withstand, i.e. "stress resilience", determining how quickly and effectively potentially negative and threatening events are recognized, how fast the stress axis "boots up" body and brain and how quickly the excitement may be "shut down". Some people can tolerate a lot of stress and under stress reach a "top form", while others are very sensitive to stress and barely tolerate some stress or excitement. Some are excited and calm down quickly, others are slowly excited and have trouble to calm down later on.

The just mentioned U-shaped pattern of stress response can therefore turn out to be highly individual. This is supported by the highly individual production rates of CRF, ACTH, and cortisol, by the distribution pattern, by the number

of glucocorticoid receptors, and by the effect of soothing substances (endogenous opioids, serotonin, etc.), and all this is determined partly genetically and partly environmentally. High levels of stress can cause great damage for an unborn child via the mother, or after birth directly on the infant, because the stress axis is yet unfinished and especially vulnerable [13–15]. But also in the later life severe acute stress (a serious accident, physical abuse, great mental suffering) may cause a psychological trauma and may lead to the formation of post-traumatic stress disorder (PTSD), which is associated with structural and functional deficits, especially in the hippocampus and the frontal cortex [16].

The second neurobiological-psychological system is the self-calming system. It develops partly before birth and partly postnatally. It is mainly determined by the meuromodulator serotonin (5-hydroxytryptamine, abbreviated 5-HT) Serotonin is produced in the nuclei, which sit on the midline (the "seam", greek and latin "raphe") of the lower brain stem and, therefore, are called "raphe nuclei". From here serotonin is spread via different nerve fiber tracts in the brain, especially in limbic centers such as the amygdala, hypothalamus, mesolimbic system, hippocampus, basal ganglia, orbitofrontal, cingulate, and insular cortex. Serotonin acts there, but also directly at its place of origin, the raphe nuclei, on a variety of receptors, which may have very different effects on their support cells. A group of receptors, the so-called 5-HT-1A receptors, are involved in the regulation of food intake, of sleep and of temperature; psychologically they cause a damping and calming-down and are significantly involved in the oppression of harmful activity stimuli (see below). A deficiency in serotonin production and increase, a deterioration of its effect via the so-called serotonin transporter as well as an activation of 5-HT-2A receptors initiates insomnia, depression, anxiety, risk aversion, reactive aggression and impulsivity. Such people typically interpret the world as threatening and feel constantly worried which manifests itself - most often in men - in "reactive" physical violence ("you have to fight after all!"), in women more in self-harm ("I am myself to blame for everything") and in both sexes in depression.

Human personality is characterized by their ability, how to deal with stress, and more significantly by the degree of confidence or anxiety, balance or inner serenity, frustration tolerance and sense of threat; and all this is essentially determined by the functional state of the serotonergic system, which closely interacts with the stress system and with substances such as the endogenous opioids and the "attachment hormone" oxytocin (see below). The management of acute high stress therefore depends also strongly on the effectiveness of the self-calming system, while, conversely, humans with deficiencies in this system, which show a high degree of anxiety and risk aversion, also show strong deficits in coping with stress. Just as the stress processing system, the performance of the self-calming system is partly genetically determined and partly influenced by environmental factors. Severe stress and strong psychological trauma in early childhood, for instance in form of physical or psychological abuse or neglect, and sexual abuse, lead to a sustainable, partly irreversible damage to the self-calming system [13, 17].

The third neurobiological-psychological system is the internal evaluation system. This system essentially comprises the activity of the amygdala and the mesolimbic system, which rate - metaphorically speaking - everything what a person experiences and is doing, according to the consequences for one's own welfare and draw conclusions for the further behavior. The recording of positive events is connected with the release of brain's own opioids through centers of the hypothalamus, which act upon receptors in the mesolimbic system, mainly in the nucleus accumbens, but also in the amygdala and in the orbitofrontal, cingulate, and insular limbic cortex, and which are linked with the feeling of reward and, thus, with joy, pleasure and desire. The recording of negative events is related to the release of substance P ("P" for "pain"), arginine vasopressin, and cholecystokinin and generates feelings of aversion, pain, and threat up to panic. Closely connected to this are also a serotonin deficit as well as an increased production of the stress factors CRF, ACTH, and cortisol. In addition comes the effect of noradrenaline associated with stress, fear, anxiety, the increase of the general awareness and the sense of threat and the consolidation of negative aversive memories. This positive-negative rating develops very early, no later than the first birthday, and determines how strong a person responds to reward and punishment, and whether one is more reward receptive ("extraverted") or punishment receptive ("neuroticistic").

The evaluation system forms the basis of the motivation system, by establishing that things and actions leading to reward should be repeated, whereas things and actions leading to pain or punishment should be avoided. The repetition tendency is based on the conscious or unconscious assumption that the reward will return upon repetition, i.e. it is driven by the expectation of reward. In the brain, this is achieved by the dopamine system, see Ref. [9]. Dopamine is primarily produced in the substantia nigra and the ventral tegmental area of the brain stem and acts upon many limbic brain centers, mainly the nucleus accumbens, the amygdala, the hippocampus and the orbitofrontal prefrontal and anterior cingulate cortex. Different types of dopamine-producing and dopamine-affected neurons register type, intensity and probability of occurrence of rewards and store it in the reward memory, which becomes the basis for reward expectancy and prediction. Still other dopaminergic nerve cells register, whether and to what extent an expected reward has actually occurred, and, thus, act - metaphorically speaking - as "confirmation" or "disappointment" neurons; their activity naturally influences the reward memory.

A pulse-like increase of the dopamine level is associated with the drive to seek or perform a reward-promising object or action. Accordingly an elevated dopamine level is connected with mental activation, reward expectation, sensation seeking and increased creativity, a lack of dopamine leads to a lack of ideas and imagination, lack of motivation and depression. A strong and sustainable increase of the dopamine level leads to a desire for adventure and variety, mental restlessness, impulsiveness, aggressiveness, flight of ideas and delusions.

The same applies for the registration of adverse events, in particular pain and punishment and for the memory of punishment, which defines what should be

avoided. It is connected with the activity of neurons in the amygdala, the nucleus accumbens and the orbitofrontal cortex, which are sensitive to serotonin, substance P and arginine-vasopressine. A low level of serotonin may be congenital-constitutive, but may also be caused, as already mentioned, by strongly negative early childhood experiences such as neglect, physical and sexual violence or inconsistent education. This leads to a preponderance of the punishment memory in the child and, thus, to avoidance behavior up to total inaction or, in women, to a tendency to self-harm, and in men to increased levels of aggression and violence or other anti-social behavior.

These three systems (or four systems if one considers the dopaminergic motivational system as a system of its own) form together predominantly on the lower and middle limbic level the core of our self-centered personality by defining how we handle stress, deal with frustrations, how we respond to rewards and punishments and what motives us. They also form the basis of three other psychological basic systems that develop subsequently and add a socially mediated part to the self-centered core of our personality.

This includes the impulse inhibition system. The behavior of infants and young children is usually impulsive and does not tolerate delayed gratification ("I want everything, and immediately"). Inhibition and tolerance for delayed gratification or postponement of elimination of negative things start developing from the first year until adulthood. Responsible for this on the brain side is the maturation of the lower and inner frontal lobe, i.e. the orbitofrontal, anterior and ventromedial cingulate cortex, as the upper limbic level, see above. They form inhibitory pathways to the subcortical limbic centers of the lower and middle limbic level (hypothalamus, amygdala, mesolimbic system), which in turn are designed for impulsive reactions and immediate gratification of egocentric motives [18]. The impulsive system is driven by the just described motivational dopamine system, inhibition essentially takes place via the serotonin system [19–21]. The bottom and medial frontal lobe contains many serotonin receptors, and an activation of the frontal lobe via these receptors increases over the descending pathways the inhibition of the mentioned subcortical limbic centers via their inhibitory neurons. This applies both to appetitive as aversive reactions, i.e. the urge for immediate reward as well as the tendency to immediate escape, defense or immediate attack. This explains why the lack of serotonin and, thus, a sub-activity of the frontal cortex usually occurs with anxiety disorders and violent antisocial behavior, as well as with experience with addiction, gambling addiction and high-risk behavior [22].

The next system is the attachment and empathy system. In its primary stage as an attachment system it is developing in a few weeks after birth, when the infant begins to smile at his mother or other primary attachment person and interacts with her increasingly complex ways. It is believed that this strenghens the emotional coupling between infant and attachment person and increases the differentiation of the emotional world of infants and small children, and is coined in the emotion of the mother. Accordingly, a depressive mother will strengthen the negative feelings of her child and, apart from disseminating depression pro-

moting genes, reinforces the tendency to depression of a child in non-genetic ways.

An essential role in this binding plays the neuropeptide oxytocin, which is produced in the hypothalamus and promotes the uterus contractions and milk flow. In mammals including humans, it occurs as a "attachment hormone" in mother-child and also in adult couple relationships and sexual behavior, but also generally in trusting social contacts [23, 24]. This effect of oxytocin is reinforced by the release of endogenous opioids and serotonin, which enhance the sense of well being during intense social relationships. Disturbances in social behavior, for example autism, Asperger's syndrome, antisocial personality disorder and psychopathy, are associated with deficits in the oxytocin budget.

These disorders are associated with deficits in the empathy system, which develop from the attachment system. Empathy includes the ability to "read" thoughts and intentions of others, which is also called "theory of mind". One has to add the ability to show "compassion", i.e. empathy in the strict sense. The former may well occur without the latter, for example, psychopaths who can superbly read and take advantage of the thoughts, desires and fears of other people, but act ruthlessly [25, 26].

The human empathy system encompasses both subcortical limbic centers such as the mesolimbic system and the amygdala (especially when recognizing the facial expression) and cortical limbic centers, especially the anterior orbitofrontal, cingulate and insular cortex for the perception of "pain" in others, as well as areas of the parietal and temporal lobes, which are involved in the recognition of faces and gestures. Unfortunately, this system is often referred to as cortical "mirror neuron system" on the basis of "mirror neurons" which were discovered and closely examined in macaque monkeys, see Refs. [27, 28]. The one is completely unrelated to the other, because in macaques the mirror neurons are not involved in empathy or imitation (macaques show neither the one nor the other) and are found in a premotor and not in a limbic or a cognitive region of the cortex as in humans [29].

The last neurobiological-physiological system is the system of sense of reality and the perception of risk. It develops after the age of three, when the cognitive abilities of the brain develop gradually, in particular in terms of attention and memory skills. This system is primarily bound to the neurotransmitter and neuromodulator acetylcholine, which is mainly formed in the so-called basal forebrain. The basal forebrain affects massively the cognitive areas of the cortex via the release of acetylcholine, in particular the frontal lobes as well as the hippocampus wich is central to learning and memory. Acetylcholine increases both attention and concentration by "focusing" neuronal activity in the frontal lobes and in the selective retrieval memory contents; a disturbance of the basal forebrain (e.g. in case of Alzheimer's desease) and thus a reduction of the acetylcholine level cause a lack of concentration and a reduced memory performance up to dementia. The states of the attention and concentration is also supported by the release of noradrenaline in the locus coeruleus, which causes either a

general arousal or a specific task-related response via a tonic or phasic effect, respectively.

The features of this system also include the ability to recognize risks of a particular situation and, thus, potential negative consequences of our actions. Here, mainly the activity of the dorsal portion of the anterior cingulate cortex plays a role, which has a close relationship with the adjacent dorsolateral prefrontal cortex. It is believed that the anterior cingulate cortex "recognizes" the risks and sends corresponding signals to the prefrontal (cognitive) and orbitofrontal (emotional and ethic) cortex, which results in certain global strategies of action (see above). Persons with deficits in the anterior cingulate and prefrontal cortex fail to detect risks, whereas people with deficits in the orbitofrontal cortex are able to do high-risk things, even if they know these risks [30].

This rational-cognitive system of the prefrontal and dorsal cingulate cortex is the one which together with the orbitofrontal system of social control develops slowest and is more or less mature only at the beginning of adult life - i.e. the attainment of adulthood is characterized by the fact that young people slowly come "to reason and understanding" and have learned simultaneously "how to behave".

4 Final remarks

During the past years, neuroscientists, together with psychologists of personality and psychiatrists, have studied intensively the relationship between neuroanatomical, neurophysiological and neuropharmacological properties of the brain and personality traits, including their individual characteristics and diseases [31]. Therefore, it becomes increasingly better to relate the prevailing classifications of personality, for instance after the "Big Five" of Costa and McGrae, with these brain properties and to explain why the basic features used in these classifications (neuroticism, extraversion, openness, conscientiousness, and compatibility) are not truely selective, because the underlying psychological basic systems interact pharmacologically and functionally both positively and negatively. This could be addressed here only in a very superficial way.

The emotional and cognitive development of the child is determined by a sequential maturation of limbic structures at the three limbic levels plus the cognitive-linguistic level and the corresponding maturation of the neuropharmacological systems which drives the interaction between the levels. The most important finding here is that both maturation processes are based on a complex interaction between genetic-epigenetic and environmental processes, in which early attachment experience during early childhood play a major role. To explain all this in more detail has to be left to future publications.

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