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The Programming of Afferent and Efferent Nervous Fibers in Man

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Summary. After differentiations were known to be partial processes of the growth of the total organism it had been investigated whether or not the appearance of the reacting organs has a programming importance for the development of nervous fibers. By means of total serial reconstructions of 2 to 7 mm human embryos the topokinetics of the afferent and efferent nervous fibers have been ascertained and the different topodynamics have been explained. From these investigations it has become evident that the pathways of both the arising brain nerves and the spinal nerves are traced out by mesenchymal guiding structures which are initiated by the topogenesis of the blood vessels. The growth of the nerves in these guiding structures provides the growing nervous fibers as pull structures. By means of their growth pull the nervous fibers contribute biodynamically to the formation of the total embryonic organism.

Even in the early development the anlagen of the reacting organs and the nerves were regularly connected to each other by aligned tissual structures. Therefore, neither should be understood as being disconnected in any phase of development. Total reconstructions and suitable accompanying serial sections regularly show that the peripheral differentiation processes determine biodynamically the alignment of the nervous fibers. In other words: the programming of the nerves begins in the periphery.

Comparisons of the developmental movements of the dendrites with the movements of the neurites make clear that the dendrites grow by afferent growth at the peripheral side of their tips. On the other hand, the axons grow at their tips by metabolic movements in the opposite direction (i.e. efferent). In this manner the later physiological afferent and efferent conductions are topodynamically programmed by differently directed growth processes. Even the growth of each neuron occurs as an afferent and efferent kinetic process that is topodynamically programmed.

Key words: Nervous fibers (homo) – Afferent and efferent growth – Programming – Topodynamics – Developmental movements.

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Zusammenfassung. Nachdem bekannt ist, daß Differenzierungen Teilprozesse vom Wachstum des ganzen Organismus sind, wurde untersucht, ob die Entstehung der Erfolgsorgane für die Entwicklung der Nervenfasern eine programmierende Bedeutung hat. Hierzu wurde mit Hilfe von Totalrekonstruktionen 2—7 mm großer menschlicher Embryonen die Topokinetik der afferenten und efferenten Nervenfasern ermittelt und auf dieser Grundlage ihre unterschiedliche Topodynamik erläutert. Dabei zeigte sich, daß der Weg aller entstehenden Gehirn- und Spinalnerven durch mesenchymale Leitstrukturen vorgezeichnet wird, die regelmäßig von den ersten Blutgefäßen initiiert werden. Die Beziehungen der Nerven zu ihren Leitstrukturen bedingt, daß die Nervenfasern als Zugstrukturen wachsen. Sie sind dadurch an der Gestaltung des ganzen embryonalen Organismus entwicklungsdynamisch beteiligt.

Da die Anlagen der Erfolgsorgane schon frühembryonal ausnahmslos durch gerichtete Gewebsstrukturen mit den Anlagen der Nerven in Verbindung stehen, kann man beide in keiner Entwicklungsphase als zusammenhanglos verstehen. Regelmäßig bestätigen Totalrekonstruktionen mit geeigneten zugehörigen Präparaten, daß die peripheren Differenzierungsvorgänge die Ausrichtung der Nervenfasern entwicklungsdynamisch steuern.

Vergleiche der Entwicklungsbewegungen der Dendriten mit denen der Neuriten ergeben, daß die Dendriten durch afferentes Wachstum an ihren Spitzen wachsen und daß umgekehrt die Axone durch Spitzenwachstum mit Stoffwechselbewegungen in umgekehrter Richtung efferent (von innen) wachsen.

Auf diese Weise werden die späteren physiologischen Afferenzen und Efferenzen durch unterschiedlich gerichtete Wachstumsvorgänge topodynamisch programmiert. Schon das Wachstum einzelner Neurone ist ein afferentes und efferentes topodynamisch programmiertes Geschehen.

Schlüsselwörter: Nervenfasern (Homo) – Afferentes und efferentes Wachstum – Programmierung – Topodynamik – Entwicklungsbewegungen.

Introduction

Starting from the common concept that the nervous system is programmed, it seems evident that we should investigate the development of the nervous system because its development necessarily implicates its programming. Because the tips of the afferent and efferent nervous fibers act in an opposite direction it should be assumed that they are even growing differently.

There are no suitable ontogenetic studies on the programming of the nervous system. For such studies the knowledge of relationships is necessary in order to understand the differentiations as being growth processes of the total organism. For finding such relationships, concrete observations of the structural development of the organism as a totality are required. For that purpose a complete set of total serial reconstructions of early human embryos is prerequisite. Because there were not total reconstructions at disposal, it was impossible to give well-founded statements about the programming of the nervous fibers.

Indeed, it is not only imaginable but also obvious that the site of the arising nervous system has a programming importance. It is known that even the most complicated connexions become established as the nervous cells grow. Therefore it is reasonable to comprehend their growth as an important factor. In fact, here relationships are demonstrable which call our attention to rules of differentiations. These rules are based on the developmental dynamics of the growing embryo. In the following paper this will be shown for the nervous fibers.

Material and Methods

Human embryos (approx. 18 to 32 days old) from 2 to 7 mm in size were investigated. At these stages of growth, the brain nerves first arise followed in a similar way by the spinal nerves succeeding each other exactly craniodaudally. In the following discussion, this will be explained using serial reconstructions of total human embryos[1].

It is possible to recognize common features of brain and spinal nerves by the serial reconstructions. These reconstructions point to principles (unknown until now) of the development of nerves. Comparing the succeeding positional relationships of the sites where nerves arise, it is possible to describe the developmental movements of the arising nerves and to show these as being components of the differentiation of the whole embryos. The developmental movements give us a hint of how the functional behaviour is a base of all the later actions of the nervous system. The investigation of the biokinetics is a way to gain knowledge of the early behavior of man (Blechschmidt, 1977); this knowledge cannot be gotten from experimental methods as they have been employed by Droz (1963) and Schubert (1974; 1975). Since it is known from the thalidomid catastrophe in the sixties that results of animal experiments must not be transferred to man without more ado, comprehensive developmental kinetic studies have been made to learn something about early human behavior.

Results

If it were to be accepted that both the tips of the nervous fibers and the receptors arise independent from each other, then it would be difficult to understand how the 'correct' fiber tips find the 'correct' receptors. But, if one does not neglect the fact that the fiber tips, as well as the receptors, are partial structures of the whole embryo and consequently cannot be independent structures in any phase of development, then one must see the problem of innervation otherwise: the innervation appears to be the result of even primary existent connexions. These connexions are implicated with the positional relationships of the arising nervous cell aggregations.

In the following discussion we shall prove that the nervous pathways are dictated to the fibers from the periphery that means a stepwise programming by the peripheral cell structures. In every phase of development there are positional relationships for the nerves that are sufficient to determine their differentiations. This is so evident that there is no reason to assume programming other than a peripheral one in which other than physical forces are immediately position-determining for the kinetics of the innervation processes. Those physical forces are already discernible during the early growth. They result in movements against

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[1] Blechschmidt collection of human embryos. Institute of Anatomy, University of Göttingen. Catalogued in the Carnegie Institution, Davis (USA) (Blechschmidt, 1973)

resistance, i.e., in actions with work in a physical sense. These actions are growth functions. The later abilities of the nervous system are prepared by those growth functions (development of functions of the nervous sytem).

There are no actions of the nervous system which are so original and so characteristic as its first growth functions. But even these were not usually investigated because they are not in accordance with the common schematic concept of nervous functions.

The Development of the Cells in the Neural Tube

The early neural tube shows the following topokinetics. Already in a human embryo with 13 paired somites characteristic nervous differentiations can be observed. In this stage, the neural tube forms three layers which merge into each other. Thus there cannot be a doubt about ordered metabolic movements (Fig. 1).

The still undifferentiated cells are located generally inside forming the layer of the ventricular mitoses. When suitable stained this zone appears black in transmitted light because of its abundance of nuclei. Outside, a zone with densely-packed cell processes, which have been aligned perpendicular to the pia and are so thin that there usually is no space for nuclei, is found. Consequently this outer layer appears white in transmitted light. Between these layers a grey zone becomes established. It exhibits processes of cell bodies as well as thick cell bodies with large dark nuclei.

The described microscopic picture is a momentary aspect of the first biodynamics of the neural tube. One could get an idea of the forces existing here by considering not only the movements but also the consistence and tensile strengths of the visible structures. It is well known that the neural cells grow by absorbing nutrients out of the pia. In other words, they grow by submicroscopical material transport from the outside. The growing cells get pressed to each other and, consequently, become thin and form processes. The first processes are aligned towards the source of nourishment; as they grow they indicate directed metabolic movements which means assimilations in the sense of movements of particles that are directed from the pia mater towards the growing cells. By means of their processes many cells, arranged in several rows, become able to reach the source of their nourishment. The contrary assumption that the neurocoel could be the main source of nourishment should not be taken in to consideration even without experimental investigations.

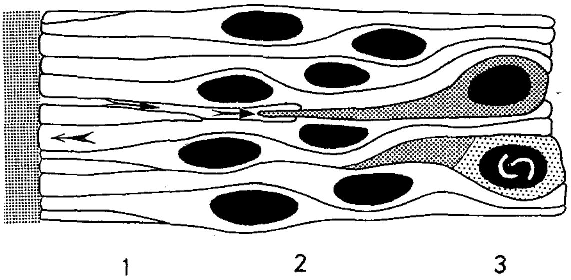

Fig. 1. Wall of the neural tube. On the left side is the pia stippled. *1*, white zone with cell processes; *2*, grey zone with cell processes and nuclei; *3*, black zone (ependyma) with ventricular mitoses, rich in nuclei. The tailed arrows indicate material movements between and within the cells

If we understand the different zones of the neural tube as different metabolic fields, the layering of the wall of the neural tube allows the statement that the outer white zone adjacent to the source of nourishment is a growth zone of neural tube by essential increasing of cytoplasm. The inner dark zone is mainly a zone with multiplicating cell nuclei and the layer between both is a transition zone. Accordingly one should consider the cell processes of the outer zone as being motors which do the work for enlarging the surface area of the growing neural tube against the resistance of the surrounding tissue. Every cell process which grows from the matrix into the so-called mantle layer contributes to the enlargement of the surface of the neural tube circumference.

These findings and our conclusions correspond with the results of Sauer and Chittenden (1959), Sidman et al. (1959), and Langman (1966). Convincing diagrams are shown by Hamilton et al. (1972). Sidman et al. have shown in mice that the primitive ependymal layer is a pseudostratified columnar epithelium within which nuclei of indifferented cells migrate to and fro in relation to the mitotic cycle. Also in mice, the mitoses are found along the ventricular fluid and the assimilation processes obviously occur mainly in the periphery along the vascularized pia. Clearly, it is wrong to derive from similarity of findings in man and mice any identity of the metabolic processes. Microscopic slides of later stages show regularly the cells of the neural tube differentiating into glial cells as well as neurons. The latter are always surrounded by glial cells. Hence it may be concluded that the neurons develop from the primarily uniform cells. Having regard to the cell bodies of the arising neurons showing always concave surface and to the growing glial cells forming no lengthy processes it may be assumed that the arising neurons yield to the pressure of the adjacent growing cells and—in this way—develop their processes. We suppose the growth pressure of the glial cells along the pia becoming regulated by the arising neurons: their cell bodies are impressed by the glial cells and—consequently—form lengthy axons. In other words: the formation of the neurons is resulting from the surface growth of the brain. That will be discussed in a following paper.

After what has been said the following is true for the neural tube: 1) the differentiation of the early embryonic neural tube occurs as a growth function in metabolic fields with spatially ordered metabolic movements; 2) they are the results of assimilations and dissimilations in the course of which the assimilation predominates; 3) no metabolism of the growing embryo is known which eventually would not occur in the scope of forming processes; 4) what is true for the neural tube is also true for the whole nervous system, for the brain as well as for the spinal cord, and for the brain nerves as well as for the spinal nerves.

The Positional-Determined Arising of the Trigeminal Nerve

The arising of the trigeminal nerve and its branches (ophthalmic nerve, maxillary nerve and mandibular nerve) is an ideal example for the *topodynamic differentiation* of nerves. The following can be observed: the wall of the neural tube expands particularly dosally i.e., in the direction of least resistance. The early cutis is very thin dorsally and the growth resistance of the tissue surrounding the neural tube is less dorsally than ventrally. The comparison of developmental

Fig. 2. **a** Spinal cord of a 7 mm human embryo (transverse section) at the beginning of the fifth week. Convergent arrows show the restraining function of the strong (ventral) dura mater. Arrows with base lines indicate the growth direction of spinal cord. The large arrowheads represent expansion pressure of spinal cord, the small arrowheads represent expansion pressure of the arachnoid fluid. Broken line and convergent half-headed arrows show the slight growth resistance of cutis. The tailed arrows indicate the growth of spinal ganglionic cell processes exhibiting efferent metabolic movements. **b** Growth of the afferent and efferent pathways. Neck region of the spinal cord (at the end of the 4th week of development). Arrow with base line represents the growth of the spinal cord. The convergent double arrows in the region of the ventral ectomeninx show the restraining function of the ectomeninx. The convergent double arrows in the region of the cutis show the growth resistance of the cutis. Growth extension of the cutis occurs dorsal to the spinal cord. The simple arrow indicates the restraining function of a dorsal aortic branch. The tailed arrows indicate metabolic movements (direction of fluxions) in the region of the dorsal and ventral roots. A spinal ganglionic cell and a ventral horn cell have been stippled. *1*, thin, expanding ectoderm; *2*, thickened ectoderm; *3*, site of the vertebral column; *4*, site of the dorsal musculature

stages shows that the early dorsal dura is extended in surface and consequently is relatively thin dorsally over the neural tube. In contrast, the ventral part of the dura remains short and thick. As a result of its stronger growth resistance the ventral dura exerts a growth pull onto the neural tube, particularly where the dura is reinforced by the blood vessels which equidistantly flank the neural tube. Thereby, neural tube cells are stripped out off the neural crest in nearly equal distances which are determined by the dorsal branches of the embryonic aortae. That process occurs by means of the relatively strong ventral dura (Figs. 2a and b). Considering these processes as being isolated, they seem to be a migration of separated cells (Johnston, 1966). Theiler (1948) has described in detail the development of the neural crest. The movement of cells begins in the head region and proceeds to the neck region. The first cell group which is stripped off in the head region is the arising trigeminal nerve.

During the first bending of the embryo, characteristic biomechanical pull forces are effective onto the neural tube in the head region. Their existence can

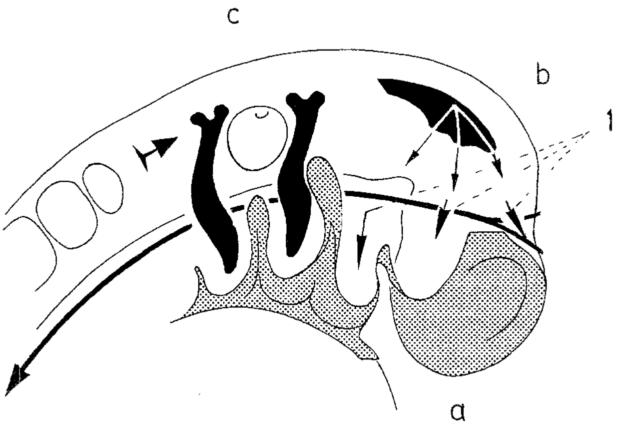

Fig. 3. Arising of the bending folds of a 2.5 mm human embryo at the end of the third week of development. *a, b, c,* prosencephalon, mesencephalon, and opisthencephalon respectively. The thickened ectoderm has been stippled. The stems of the trigeminal nerve, acusticofacial nerve, and glossopharyngeal nerve have been drawn black. The long arrow indicates the restraining function of the right aorta. The arrow with base line represents the lengthening growth of the spinal cord. Large arrowheads near '*l*' represent the alignment of the guiding structure of the trigeminal branches. The small arrowheads indicate the growth directions of the trigeminal branches

easily be concluded from the locally different developmental movements: as known from the human embryology the growing neural tube is longitudinally bridled by the paired aortic anlage from the third week of development (Fig. 3). The aortae remain short relative to the neural tube. The remaining short means biodynamically growth pull. Thus, the mentioned bending in the head region becomes established as a result of bridling. Thereby, particularly located stretches in the tissual bed of the growing brain become evident.

As the paired aorta bridles the neural tube by remaining short (and, consequently, the embryo bends), the known bending folds (visceral arches) of the embryo become formed ventral to the aortae. Between the folds the ectodermal cervical furrows (Fig. 3) and the endodermal pharyngeal pouches become established. As the embryo bends, the intensely growing neural tube displaces from the aortae which remain short. Then, the stroma in the visceral arches becomes stretched circular to the longitudinal axis of the embryo. The stretching of the stroma influences the whole head region in the following manner. As a result of the bending of the embryo, the brain and the cutis are characteristically related in position and shape to each other. In the regions of the crown bending and the forehead the cutis is closely adjacent to the mesencephalon and the arising cerebral hemispheres respectively (Fig. 4). The mentioned portions of the brain act as supports over which the stroma of the embryonic cutis becomes thin and pale and rather free of blood vessels (it is comparable to the skin on the extended side of the finger joint when the fist is strongly clenched). At the end of the first month similarly thin and pale tissue can be ascertained lateral to the optic vesicle, on the corner of the mouth and on the embryonic ear-drum. Those areas

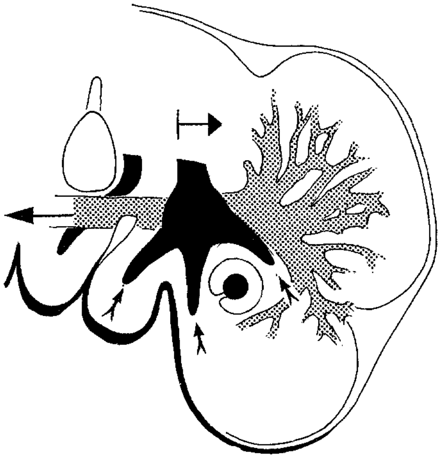

Fig. 4. Part of the serial section reconstruction of a 7.5 mm human embryo. The trigeminal nerve is black. The small tailed arrows show the metabolic movements as a result of the suction effects at the dendritic tips of the trigeminal nerve in the region of the thickened epidermis. The arrow with base line shows the lengthening growth of the spinal cord. The simple arrow represents the restraining function of the large head vein

are well distinguishable from the thick tissual formations of the neighboring zones. Thus, in the region of the upper head and the face the inner tissue is unevenly thick in the various zones. The thick inner tissue forms guiding structures (routes) particularly for the arising trigeminal nerve. The thick tissual formations are evident before nerves appear therein.

The first particularly strong inner tissual route is located between the optic vesicle and the mesencephalon. It is the mesenchymal guiding structure for the arising ophthalmic nerve. The second tissual route occurs between the optic vesicle and the mouth and acts as the guiding structure for the arising maxillary nerve. The third inner tissual band is the guiding structure for the mandibular nerve. The mentioned guiding structures converge towards the relative narrow pons where the trigeminal nerve arises.

Similar distinct guiding structures are demonstrable wherever nerves appear. There they also have an effect as 'programmers.' Because of the alignment of their intercellular substances all cord-like guiding structures are easily distinguishable from the limiting tissues (epithelia). Tissues that are rich in intercellular substances exhibit generally retarded growth in comparison to the limiting tissue. This retarded growth is called 'growth pull.' Thus, the term growth pull is primarily defined morphologically (as resulting in changes of proportions). Those inner tissual structures have spindle-shaped mesenchymal cells and accordingly aligned interstices. The main direction of the interstices is parallel to the spindle-shaped cells. At first, the interstices—filled with intercellular substances—are very small canalization zones. Consequently they initially program only very small bundles of nervous fibers.

The arrangement of the trigeminal nerve with its three branches which diverge from one stem towards the periphery results from the typical straightening of the guiding structures in this region. The biodynamics of the early embryonic brain development determines this straightening. The brain is the motor of the mentioned differentiation. The cell abundance (epithelial character) of the brain has a forming functional importance. The described constructive growth correlations clearly point out that already primarily a connexion exists between the growing nerves and the cutis innervated by the trigeminal nerve.

We remember a rule which states that the establishment of any organic structure generally requires spatial opportunity and dynamical occasion. As we have demonstrated, the positional relationships of the stroma to the thickened cutis of the early face and the brain respectively give opportunity for the arising branches of the trigeminal nerve. But what is the kinetic and biodynamic reason? The morphological investigation of the various stages of differentiation demonstrates the body parts themselves as being the occasion for innervation.

Growth Innervation

The Afferent Growth of Dendrites

The growing nervous fibers generally use evidently narrow canals. Therefore it is not easily comprehensible how they do their work while growing in length. For getting a conclusive description we must postulate particular spatially ordered metabolic movements and ask what sort of metabolic fields the interstices between the cells of the guiding structures are. For a long time (since 1961) we have used the term of metabolic field to describe differentiations and have stated that these generally occur in man as biodynamic processes in spatially ordered metabolic fields. Therefore it is also easy to comprehend the growth of an appearing innervation as such a metabolic process. Barron (1946) has assumed that — in chick — the appearance of neuroblasts is induced by the dendrites of the previously formed neuroblasts: 'neuroblasts possessing growing dendrites have the capacity to induce indifferent cells to differentiate into neuroblasts.'

We see from our investigative materials that the ability of the brain nerves and spinal nerves to grow only in consequence of their position requires the following conditions: the endings of the first sensory nerves are always informed about their location. The sender of the information is the epidermis. Regularly a thickening of the epidermis is found initiating the sensory innervation. Such a thickening becomes established, for example, when the embryo bends in the region of its broad upper trunk end thereby forming the mentioned bending folds (visceral arches, Figs. 5 and 6). The thickening of the epidermis established during the bending is a process of compressing, a compressing which concerns living cells with a metabolism. Those cells react to compression with fluid-release. Other examples for the arising of sensory innervation resulting from the thickening epidermis are the sole of the foot, the palm of the hand, and the whole ectoderm ring (Blechschmidt, 1961, Fig. 352).

We regularly observe that proper sensory nerves grow as the epidermis thickens. They are always straightened perpendicular to the cutis, i.e., the shortest way. That means that they never have any unordered arrangement. With their alignment the growing nerves closely adapt to the given topodynamic situations. The straightening of the connexions between nerves and cutis gradually increases more and more.

An unrelated establishment of nerves on the one hand, and of thickened epidermis on the other hand, can never be observed. Always the stroma of the

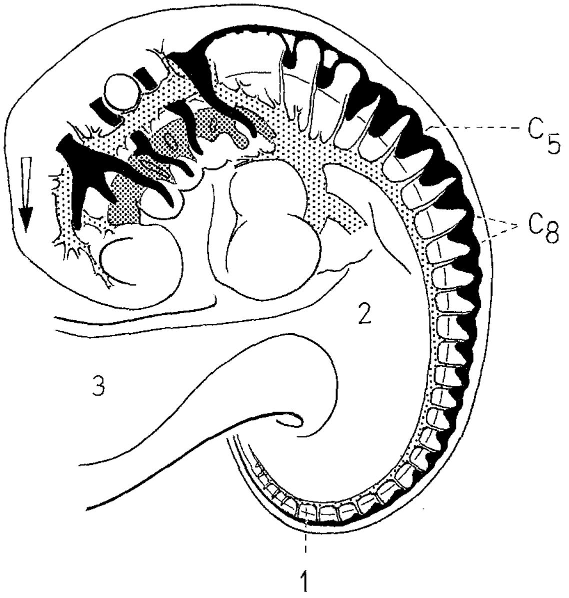

Fig. 5. Serial section reconstruction of a 4.2 mm human embryo at the end of the first month of development. *1*, metameric blood vessels not yet accompanied by metameric nerves; *2*, intraembryonic peritoneum; *3*, extraembryonic peritoneum. The nerves are black, the large veins are coarsely stippled, the head gut is densely stippled. The outlined arrow indicates the lengthening growth of the spinal cord along the large body veins retarded in growth. In the region of the brain nerves the guiding structures of the nerves are located in the continuation of the visceral aortic arches. As these guiding structures are formed the visceral aortic arches grow less in relation to the neural tube

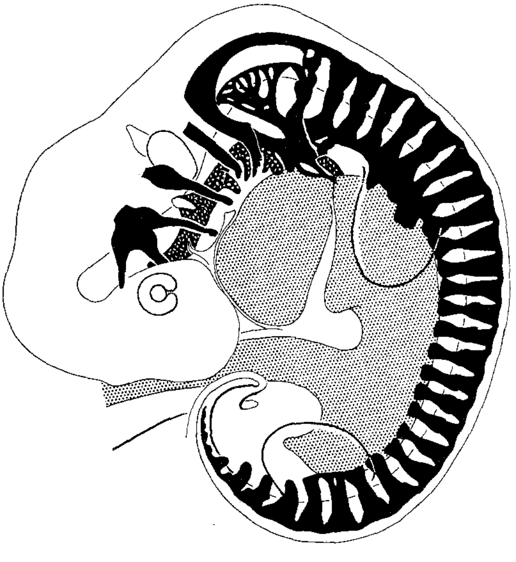

Fig. 6. Serial section reconstruction of a 6.3 mm human embryo. Nerves are black, endoderm and serosa have been stippled. The dorsal and ventral parts of the embryo are connected tensionproofly to each other by the establishing nerves (zone of the ectoderm ring)

thickened epidermis smoothly continues into the bed of the growing nerves. From this flowing continuation we conclude the existence of the mentioned submicroscopically ordered fluxion movements which are named metabolic movements in metabolic fields.

Considering that the growing dendrites (being afferences) are necessarily kinetically correlated to the efferent (karyofugal) growing neurites we learn from the embryonic stages that the dendrites grow appositionally on their tips by

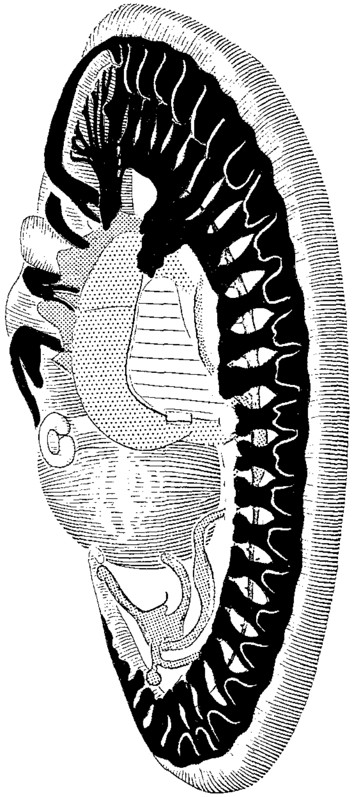

Fig. 7. The same serial section reconstruction of the 6.3 mm human embryo as shown in Figure 6. When the developing nerves are suitably tensionproof they clamp together the dorsal and ventral regions of the embryo. This clamping contributes to the development of the embryo that grows narrow (forming function of the nerves)

absorbing nutritive substances onto their surface from the periphery. They, so to speak, suck themselves onto their innervation zone. The contrary hypothesis that the growing nerves eventually could push into the innervation zone like a bolt under pressure cannot be observed either in experiments with men or with animals, and this, therefore, leads to numerous contradictions. Consequently — in default of other findings — we should comprehend the lengthening of sensory fibers as an afferent growth at the tips of the nerves (Fig. 8 c), i.e., a growth with karyopetal metabolic movements on the surface area of the fibers. The contrast is the efferent growth with karyofugal metabolic movements (fluxion movements).

When we apply this scheme to the establishing trigeminal nerve, Figure 4 results. In this figure the appositional growth of the trigeminal nerve is indicated by arrows. An investigation of microscopical slides under biodynamical viewpoints shows that real suction effect occur at the tips of the trigeminal branches. 'Bow waves' are never visible as would be expected when the nervous endings would grow with pressure. In accordance with the finding that the growing nerve endings cannot be stained with usual colloidal substances in contrast to large molecular structures but instead appear characteristically light, the assumed absorption of fluid at the sensory nerve endings becomes confirmed as the arrows in Figure 8 b and 8 c indicate. The growth of dendrites into the narrow available spaces (against existing resistance) can only occur by means of suction. The suction power explains the orthogonal alignment of the growing dendrites which has been mentioned above.

The strictness and uniformity of this orthogonal straightening of the embryonic nerves, which are rich in sensitive bundles, are shown particularly in Figures 6 and 7. The total reconstruction of a 6.3 mm human embryo (30 days old) demonstrates a spoke-like arrangement of the brain nerves as well as of the spinal nerves and makes clear that the growing nervous system is a very regularly aligned part of the whole embryo.

In regard to the growth pull of the nerve endings, the total reconstructions show the following. All the young nerves are narrowed waist-like between both their ends (Fig. 6). That corresponds with the postulate that the ends of the nerves are sites of biodynamical pull and counterpull and confirms our concept of suction processes. Suction effects cannot be thought of without pull forces. Corresponding to the waist-like shape of the nerves, the interstices between the nerves that succeed one another craniocaudally show a buttonhole shape. These interstices form the sites for the first peripheral skeletization lateral to the vertebral column. Actually skeletization becomes established between the nerves, but the peripheral nerves do not appear intercostally between metameric skeletal pieces.

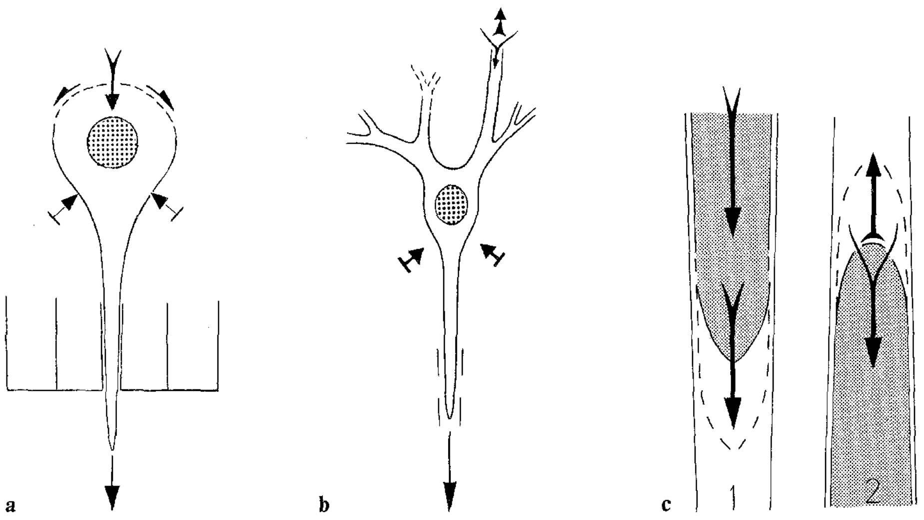

Fig. 8. a Growth dynamics of a ventral horn cell. Simple arrow shows the fluxion direction of the neurite. The divergent half arrows and the broken line represent growth expansion. The tailed arrow indicates material transport. The arrows with base lines indicate growth pressure. **b** The metabolic field of a growing neuron is shown diagrammatically. In situ, the neurons are parts of a mosaic with star-shaped cells. In accordance with the growth fluxion in the neurite a wrinkling of the cell body becomes established resulting in formation of dendrites. The small tailed arrows show the appositional growth of the dendrites occurring in the manner shown in Figure 8c (right). **c** Diagram showing the metabolic movements (tailed arrows) in the regions where motor (left) and sensory (right) processes of a ganglionic cell arise. The tailed arrows (left) represent efferent growth with karyofugal fluxion, the tailed arrows (right) indicate afferent growth with karyopetal fluxion

The Efferent Growth of Neurites

Compared with the dendrites the number of axons is smaller. However, for the sake of completeness we should mention that also the efferences of the nervous system are based on growth processes. These are efferent. Both differentiations cannot be separated from each other during normal development. As the embryonic muscles are in growth dilation lengthening particularly in the direction of the main dilation, the nuclei in the cells move apart from each other after multiplication forming long rows of nuclei within the cells. (These rows of nuclei are a characteristic feature of embryonic muscle cells). By doing this, "suction" spaces become established between the nuclei. These spaces are filled up by material absorption from outside to inside. This is true also without experimental studies. The growing neurons are included into these metabolic movements by building efferent (karyofugal) pathways (neurites, Fig. 8c). The neurites appear so strongly attracted by the muscles that so-called end plates become established at their endings. Such end plates are never found at the tips of dendrites. The mentioned efferent metabolic movements do not exclude a retrograde transport also occuring in the interior of the long portions of adult nervous processes (Kristensson et al., 1971).

From what has been explained, the difference between the appearing motor and sensory nervous pathways—looked at from a kinetic point of view—can be summarized as follows: The sensory fibers are sucking themselves to the cells of their innervation zone by means of absorbing materials in their membranes. On the other hand, the motor fibers are sucked to the growing muscle fibers and thereby grow efferently (Fig. 8c). Consequently the later differences between motor and sensitive pathways which are physiologically evident are based on growth processes with opposite submicroscopic metabolic movements.

As mentioned, our findings testify to the principle that the nervous fibers are *topodynamically programmed.* There is no doubt that the described afferent and efferent growth movements of the nerve fibers exhibit formative functions that are an important prerequisite for the later electrophysiological functions of the nervous system.

The topodynamic differentiation is not only valid for the nervous fibers in the periphery but also for the development of the total central nervous system. This will be demonstrated in a following paper.

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