ABSTRACT: Further argumentation and experimentation is presented to buttress the author's endeavours to extend the cerebrocranial developmental "macroneurotrophic" interrelation, viz., the formative effect of the growing brain upon its bony encasement to the entire developing bony and nervous tissues of the vertebrate body. Even the extracranial skeleton develops in the most intimate interrelation with the actively growing spinal and peripheral nervous structures. Against the petrified belief that the growth of the extracerebral nervous structures is mere passive "innervation follower" of the other tissues to be innervated, the view is defended and experimentally supported that growth in length of the bony skeleton depends upon and is governed by the active co-growth of the nervous skeleton (term by Donaldson 1937). Variable length of the vertebral column as well as of the limb bones in animals and man mirrors the variable growth-in-length potentiality of the spinal and peripheral nervous structures. The nervous skeleton perceives, along exteroceptive and proprioceptive pathways, the conditions prevailing in the environmental niche and provides, by mediation of the more or less extensive neural growth, for the appropriate shape and length of the bony skeleton.

Impairment of the vulnerable neural growth results in "neuroadaptive" deformities of the skeleton consisting in various types of its shortening, i.e. accumulation of the proliferating skeletogenic material along and within the too short nervous skeleton. In a number of instances experimental "osteoneural" findings pattern what happened in the course of evolution and hominization, viz., primary shortening of the nervous skeleton reflected in corresponding transformations of the bony skeleton. Shortening of the human mandible with appearance of the chin is one of the most striking examples of such an (experimentally reproducible) "phylogenetic neuroadaptive deformity".

It is argued that egg and sperm appear to be sources of the two basic growth types of the vertebrate body, the cellular-divisional and the neural-extensive. The possible repercussions of that developmental interrelation upon some problems of general biology are discussed.

KEY WORDS: Bony skeleton — Nervous skeleton — Macroneurotrophism — Neuroadaptive skeletal dysplasias — Neuroadaptive evolution of the skeleton.

Motto: "It is sometimes held that no real progress has been made until a biological mechanism is placed on a firm molecular basis. Such a view denies the existence of different levels of organization at which one can meaningfully investigate biological processes."

INTRODUCTION: MACRONEUROTROPHISM VERSUS MICRONEUROTROPHISM

In spite of innumerable data hitherto piled up the purely "osteological" approach did not yield any acceptable explanation of the developmental anatomy, individual and evolutionary, normal and pathological, of the vertebrate skeleton. Among the extraneous factors, vessels and muscles play a self-evident role in skeletal metabolism and function without, however, any clear-cut contribution to the solution of the major problems of skeletal development.

The undeniable neural influence upon the skeleton, developing and adult, is searched for in "neurotrophism", viz., in that still poorly understood nervous function consisting in some intricate interaction between the utmost neural periphery and the individual cell or group of cells. The term "microneurotrophism" has been coined to designate that cellular-level-effect in contrast to "macroneurotrophism" (Roth 1983) effectuated and dramatically evident, at the organ level, in the neurocranial (cerebrocranial) developmental interrelation. The actively growing bone moulds the shape and size of its skeletogenic envelope which behaves "passively - neuroadaptively" in the course of development, individual as well as phylogenetic. One would hardly subscribe to the idea as though smallness, say, of the canine brain as compared to that of man would depend upon the primarily different size (ampleness) of the neurocranial capsule (Figure 14 B).

In diametral contrast to the highly active and vulnerable growth of the brain, that of the extracranial nervous substance is generally held for an entirely passive process. The embryonic spinal nerve roots, the nerves ingrowing into the limb bud or into the orofacial area are believed to be "taken in tow and dragged along" by the growing non-nervous tissues with the tacitly accepted implication that the definitive adult length of the nerves is determined by and dependent upon the length of the non-nervous tissues, above all of the hard skeleton, attained in the course of development. This widely shared opinion is in diametral contrast, however, to what is self-evidently accepted in connection with the brain and its bony envelope.

The aim of the present report is to overcome that cerebro-extracerebral paradox, viz., to question the "towing" concept and to defend and further buttress the idea (Roth 1987) that the extracerebral nervous substance should share with the brain the "macroneurotrophic" effect upon the skeleton, viz., that the spinal and peripheral neural growth limits the growth of the non-nervous tissues rather than to play a more passive role of innervation follower. The "Leitmotiv" of the author's argumentation is that the cerebrocranial developmental interrelation is just the most striking local manifestation of the universal "osteoneural" relation between the developing nervous and bony tissues throughout the vertebrate body.

IS UNIVERSALIZATION OF THE CEREBROCRANIAL RELATION JUSTIFIED?

It is generally admitted that the delicate central nervous system, i.e. the brain and the spinal cord, is encased by a protective bony envelope with the automatic implication that the shape and size of that envelope is determined by the gross features of the enclosed neural content. In contrast to craniology, vertebrology has disregarded entirely that truism because of the indiscriminate adherence to spinal biomechanics.

It might seem that the spinal cord as a natural "continuation" of the brain should automatically share its moulding effect upon the bony envelope. The converse is true, however, since the brain represents "continuation", evolved by cerebralization, of the spinal cord and as concerns the neurocranial bony envelope manifests what must have been a basic property of the ancient spinal cord and what cannot cease to be a property of the recent spinal cord as well, viz., the ability to mould its vertebral bony envelope.

Muscles are credited with an important effect upon the shape of the skull such as excessive dolichocephalization under the effect of the bulky temporal muscles in Eskimos (Koenigswald 1978). It should be kept in mind, however, that growth of the brain, not so much of the cranial vault, is restrained by the increased mass of temporal muscles so that compensatorily enhanced cerebral growth in sagittal direction accounts for dolichocephalization. With a circular obstacle such as a bandage applied in primitive tribes turricephalia ensues owing to the compensatory vertical direction of brain growth. Flattening of the occiput in bedridden sucklings looking like "passivity" of the brain (seemingly influenced by the flattened impressed occipital squama) is compensated for by enhanced growth of the brain in other directions.

A striking clinical support, not duly appreciated by craniology, is furnished by the deepened gyral imprints on the cranial vault in obstructive hydrocephalus, viz., with increased volume of the otherwise normal brain due to obliteration of the liquor passage e.g. in tumors of the posterior cranial fossa. The enlarging brain is able to erode even the adult cranial bone for the sake of preservation of its indispensable "living space".

THE DISREGARDED "NEUROENVELOPING" FUNCTION OF THE SPINE

The spinal neural content (spinal cord with the nerve roots, the "cord-nerve root-complex", CNRC) is encased by the vertebral column both in the transversal and in the longitudinal direction (Figures 1 - 3). Development and growth of the vertebral column proper involves a number of vertebrogenic processes such as installation of somites, sclerotomes, the heavily discussed "Neugliederung", notochord, chondrification and ossification accomplished and investi-
gated mostly at the cellular level. At the organ level, however, growth in length of the vertebral envelope is inseparably linked with adequate side-by-side growth of the enclosed CNRC. Shorter and broader human vertebræ as compared with the longer and more slender ones in the quadruped animals mirror the different relative length of the CNRC (Figures 1 – 3). Since growth in length of the axial organ proceeds in craniocaudal direction (as evidenced by the obliquity of the spinal nerve roots), shortening of the spine associated with hominization has taken place as though “from below” (Figure 3 A, B) — a feature quite characteristic for the “osteoneural” morphogenesis, normal and pathological, of the skeleton in general. With impairment of the vulnerable spinal neural growth “neuroadaptive” shortening of the vertebral envelope “from below” takes place in form of scoliosis and/or platyspondyly (i.e. exaggerated shortness and broadness of the vertebræ). The developing vertebral column is hindered by the insufficient growth of CNRC from normal growth in the distal direction. The “reins” of the spinal nerve roots are kept “too tight”, the growing spine “rears up” (Figure 5 C, D).

**NEUROPROTECTIVE MECHANISM**
- **THE INDISPENSABLE**
- **OSTEONEURAL BALANCER**

What is going on in the developing axial organ has been specified by O’Rahilly and Benson (1985): “The vertebral canal and intervertebral foramina are specially adapted to contain the structures of the central nervous system... As the nervous system grows, vertebral column grows to accommodate it". The same applies, of course, to the growing cranium as well. The indispensable balance of the two growing structures, the neural-enveloped and the bony-enveloping, viz., adequate “receding”, “giving way” of the skeletogenic envelope to the rapidly enlarging and elongating neural content is provided for by the property of the nervous substance to maintain the surrounding skeletogenic tissues in a “respectful” distance, probably by mediation of some metabolic product released from the neural surface to which precartilage cells react in a negative chemotactic manner (Holtzer 1952). This “neuroprotective mechanism” (NPM — term coined by the present author) may be compared

![Figure 1](image_url)

**FIGURE 1.** A - C. Neuroenveloping function of the vertebral column from the embryo to the adult man and quadruped. (A a-c and B a-c reconstructed according to Serafeg 1949 and Tondury and Thaller 1990). Length of the interganglionic distances arrowed in B d, e. C: Cranial and vertebral envelope of the neural content in a frog tadpole (specimen cleared according to Williams 1943 — the same applies to all subsequent “cleared specimens”). 6 × nat. size.
FIGURE 2. a–m.
Roentgenographic documentation of what is schematized in Fig. 1: 200 mm human fetus (a—cleared specimen, b—roentgenogram). Cervical and lumbar spines: Newborn (c) and adult (d, f) rabbit, man (e, h), dog (g). 25-day duck embryo: Human-like cervical platyspondyly produced by early treatment with the cholinomimetic Carbachol (j, k, i—norm. Cleared specimens). Spinal cord and ganglia drawn in, impairment of neural growth indicated by crosshatching. — Outline of the human pelvis on a rubber stripe (l). With stretching the stripe (= energy requiring extensive neural growth) the pelvis and vertebra attain quadruped-like features: The growing skeleton is "carried with" the growing nervous skeleton (m). (From Roth 1985).

with the "halo" produced around a red-hot wire pushed into a plate of readily melting metal. In this way, as a sort of "instinct of self-preservation", the nervous structure defends its integrity and at the same time moulds the shape of the encasing bony structure. Appearance of the subarachnoid space in the early embryo should be looked upon as the first manifestation of the NPM (Figure 1A b-d, C).

Moss and Salentijn's (1970) postulate of "unloading" of the mandibular nerve, viz., of absence of any tension, compression or shear upon it is related to the NPM of the nerve providing for elaboration of the mandibular canal of adequate cross-sectional size slightly exceeding the thickness of the nerve (for a very instructive picture concerning that process, see Kjaer 1989). What is true for the mandibular nerve, of course, should govern the interrelation of bony and nervous tissues in general, viz., preservation of an "unloaded" condition of any part of the nervous system, central as well as peripheral, including the utmost neural periphery.

SPINAL GANGLIA: PACEMAKERS OF VERTEBRAL GROWTH IN LENGTH

One of the most dramatic manifestations of the NPM is the moulding effect of the spinal ganglia upon
the intervertebral foramina. It should be noted that the primordial vertebral arches are laid down in form of projections of skeletogenic tissue from the frontal side into the narrow embryonic interganglionic spaces (Figures 1 a, 4 B-h). With craniocaudally proceeding growth in length of the axial organ the elongating interganglionic spaces become filled, "casted" with the skeletogenic tissue. Spinal ganglia, rather than being pushed apart passively by the accumulating verteobrogenic tissue, play the role of "pacemakers" of the vertebral growth since definitive length of the vertebral arch, together with that of the vertebral body, depends upon the definitive length of the interganglionic distance, i.e. upon the degree of outgrowth of the CNRC (Figures 1 A,B; 2 f-h; 4 B).

NERVOUS SYSTEM — REPRESENTATIVE OF THE EXTENSIVE TYPE OF GROWTH

Embryonic primordia of the central nervous system are laid down by cellular-divisional proliferation of neuroblasts. Soon, however, the neural primordia shift to the extensive type of growth, otherwise common in the plant kingdom and characterized by sprouting of long (even several decimeters in man, several meters in whales or giant reptiles) branching processes from a single nerve cell body (Figure 7 a). Such a radical transformation of the roughly globular neuroblast into the neuron with all its processes (even as many as several hundred thousands (!) (Winkelmann 1988)) necessitates a rich supply with energy and oxygen and, consequently, means a high vulnerability of that growth type as compared with the cellular-divisio- nal one (Figure 7 a). The vertebrate body (but also that of an insect, for instance) thus consists of products of not one but of two types of growth, the cellular-divisio- nal and the neural-extensive proceeding side-by-side at a different energetic level.

"MACRONEUROTROPHISM" OF THE PERIPHERAL NERVOUS SYSTEM: THE ROLE OF THE "NERVOUS SKELETON"

It may seem hardly feasible to credit the peripheral nerves with the postulated "macroneurotrophic" effect upon the skeleton comparable with that encountered in axial structures since peripheral nerves take their course at a distance from bones, without any direct contact with them. The peripheral nervous system, including the vegetative, represents, however, much more than the individual nervous trunks and branches and various types of nervous endings. In its organ entirety it represents an extremely dense, cotton-wool-like (Figure 6), ubiquitous feltwork of nervous trunks, twigs and fibers, the "nervous skeleton" (Donaldson 1937) which originated by immense amount of extensive growth and permeates diffusely throughout the vertebrate body including the periosteum. Any individual bone is covered, in addition to the con-
nnective tissue of the periosteum, by a feltlike "sac" of the periosteal nervous skeleton (NS). The matter can be compared with digging grassy ground: One perceives a number of thicker and thinner roots without being aware of the finest rootlets diffusely permeating the seemingly pure soil between the thicker roots. What this amounts to is that

1. the relation of the limb bones or jaws to the nervous system is much more intimate than that existing between the central nervous system and its bony envelope separated by the subarachnoid space and the meninges, and

2. the quantity of the nervous tissue present within a limb exceeds significantly that of the bone tissue. With that quantitative ratio in mind one should easily understand the untenability of the "towing" concept demonstrable by means of the cotton-wool-model (Figure 6): To pull out a single fiber does not require any appreciable effort but to do the same with a cluster of fibers means to overcome a rather strong mechanical resistance. Transferred to the NS this means, of course, extensive-growth resistance. An elongating, "growing" plastic rod "thought into" the cotton-wool-model (Figure 6) should be helpful for understanding of what is put forward. Any change of bone shape or length, though proceeding in the explant without any neural influence (this matter will be discussed in the closing paragraph) within the intact living body is inseparably linked with cogrowing NS. Lack of innervation of the bone tissue proper seems to justify the widely shared view that bones are almost independent (except for "microneurotrophism") upon the nervous system. Without any excessive stretch of imagination one is led to the conclusion, however, that individual bones represent something like bony "casts" of correspondingly shaped cavities within the NS. Whereas in the head and spine the moulding nervous substance is enclosed within the moulded bony envelope, in the limbs and jaws the moulding NS is situated around and, in view of the innervated bone marrow, inside the bones. The bony skeleton, including the "centrally moulded" neurocranial and vertebral, is

FIGURE 5. A—D. Physiological "neuroadaptive" shortening of the spine "from below" in the course of hominization (a—quadruped, b—man). With abnormal slowness of the vulnerable neural growth the vertebral envelope attains abnormal features in form of neuroadative kyphoscoliosis (c) and/or platyspondyly (d). (Comp. e.g. Seichert 1988 (his Fig. 64). — Inserts below: Scoliosis, idiopathic in man (C), experimental in osteolathyric rat (D—roentgenograms).
logical neuroskeletal growth differential may be deciphered in the following anatomical features:

In the spine, ascent of the spinal cord is the well-known manifestation of the neurovertebral growth differential (NVGD). What is meant in the given context and what is much more relevant is, however, *lagging behind of the CNRC as a whole*. The gradual onset of the NVGD is manifested in the increasing cranial eccentricity of the embryonic and fetal spinal ganglia “cutting in” (under mediation of the NPM) from below into the primordial vertebral arch and carving the caudal vertebral incisura (*Figures 1, 2, 4*). The cranio-caudal distance between the spinal ganglion and the dorsocaudal border of the vertebral body (amounting to about 10–15 mm in the adult) means that the nervous tissue tract above that level has grown a little less in length than the corresponding portion of the vertebral column (*Figure 1A, B*).

In the limbs the slackened course of the nervous trunks in the neutral posture shifts to a straight one in full extension (*Figure 7g*) so that it becomes surprisingly evident that, as a matter of fact, the nerves are distinctly *shorter* than the slightly angulated limb skeleton in whole. The same may be noted e.g. in digital nerves (*Figure 13*) as a manifestation of the osteoneural growth differential (ONGD).

Hence, there can be little doubt that the elongating vertebrae and limb bones meet with a distinct resistance of the slower neural growth (refer to the cotton-wool-model – *Figure 6*). This physiological neuroskeletal growth differential must be compensated for since otherwise the indispensable “unloading”, i.e. the slackened NS would be compromised. Two types of that “neuroadaptive” compensatory reaction of the skeleton may be deduced from gross skeletal morphology, viz., physiological curvatures and terminal expansions of the individual skeletal elements.

PHYSIOLOGICAL CURVATURES OF THE SPINE AND OF THE LIMB BONES: “BIMETALIC” OSTEONEURAL MECHANISM

Hyperkyphosis of the early embryonic body is attributed to the fast early growth of the dorsally situated central nervous primordia in the still meager and slower growing surroundings. Shift of neuroblasts to the extensive type of growth means a slower neural growth rate as compared with that of the ever faster elongating vertebral column. From now on the slower growing CNRC begins to exert a retarding effect upon the elongating “row of vertebral arches” (“Wirbelbogenreihe” in the German literature) whereas the ventrally situated “row of vertebral bodies” (“Wirbelkörperreihe”) escapes that neural retarding effect, it grows somewhat more in length with resulting lumbo-sacral lordotization (*Figures 2f-h, 4*). In the quadruped animal with its comparatively much longer CNRC the growing spine is less “neurally retarded” so that lordotization is much less pronounced. Cervical lordotization is related to the same neurovertebral

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FIGURE 6. Cotton-wool model of the “nervous skeleton” (Donaldson 1937), viz., of the factual extent and density of the peripheral nervous system. The trunk is not retouched to show that the model is made of cotton-wool. With growth impairment of the nervous skeleton the embedded bones become neuroadaptively shortened “from below” (right — dislocation of the hip, buckling, achondroplasia-like shortening and thickening of bones). Even the human shape of the mandible results from neuroadaptive shortening in the course of hominization (comp. *Fig. 14, 15*).

literally “embedded” within the periosteal and endosteal NS. The growing bones, instead of towing and dragging along the nerves, have rather to obey the dictates of growth-in-length potentiality, normal or impaired, of the NS they are embedded within. The skeletal growth, not the neural, behaves passively “neuroadaptively” even in the limbs and in the orofaciun.

The truism “the individual survives as long as his neurons” (Donaldson 1937, p. 8) may be paraphrased as “the individual grows up so long as his neurons”. The vertebrate body, be it a sparrow, man or whale (but also an insect) may be conceived as a correspondingly shaped tangle of the NS “stuffed” with non-nervous tissues (*Figure 21b*) that are exploited by the nervous substance for its own survival. In case of a visually or acoustically perceived dangerous event a nervous escape-impulse is sent out to the musculature. The “stuffing” non-nervous tissues and organs being “carried with” are rescued together with the NS.

THE PHYSIOLOGICAL NEUROVERTEBRAL AND OSTEONEURAL GROWTH DIFFERENTIAL

The extensive neural growth proceeding at a higher energetic level lags to a distinct degree behind the cellular-divisional bone growth. This physio-
growth mechanism whereas thoracic and coccygeal kyphosis represent remnants of the original embryonic condition. There cannot be emphasized enough that no mechanical pull of the nerve roots upon the growing spine is anticipated. The free space spared between the spinal ganglion and the roof of the intervertebral foramen (Figure 1 A, B) due to the NPM implies a slackened, "unloaded" course of the spinal nerve roots in spite of their retarding effect upon the growing spine. The NPM works in the longitudinal direction as well.

In the limb skeleton physiological neuroadaptive curvatures comprise partly angular posture of the joints such as that at the knee or elbow (to be discussed below) or inflexion of the fingers, partly incursions of the individual long bones (Figure 7 g, k) attributable to what may be illustrated by means of a bimetallic stripe (Figure 9): It can be bowed either by a direct mechanical force (the factor insistently resorted to by osteology) or by heating, viz., by eliciting elongation differential of its two components.

**TERMINAL EXPANSIONS ("WAISTING") OF VERTEBRAE AND LIMB BONES: ANOTHER OSTEONEURAL COMPENSATION**

Terminal expansions of the developing vertebral bodies (i.e., exuberations at their cranial and caudal end resulting in "waisting") as well as of the limb bones (most conspicuously in the phalanges) appearing almost simultaneously in the 10-week human embryo represent another manifestation of the physiological NVGD and ONGD (Figures 8 f, g; 10 A, B). The accumulating bone tissue begins to be somewhat "short of space" along and/or within the slower growing NS. Products of skeletal growth cannot be fully realized in length since this would result in undue stretch of the nervous structures. This is the reason why accumulating skeletogenic material is dissipated partly in transversal direction—a basic feature governing the entire field of osteoneural growth relations, both normal and pathological.
Muscles are generally credited with an important morphogenetic effect upon the skeleton. Elusiveness of that effect upon the overall shape of the cranial vault has been already alluded to (p. 2). Processes, protuberances and/or crests, though sometimes very prominent, are just surface modifications of the osteonurally evolved skeletal parts (Figure 3 c, d) associated with muscular functions performed according to the immediate needs of the individual concerning locomotion, feeding, defense, etc. The role of muscles in respect to the skeleton is "immediately functional" rather than developmental, their effect upon the morphogenesis of the skeleton is, in the present author's view, far less than is generally believed. Klatt's (1949) insistence to distinguish strictly the relative merits of muscular and neural effects upon cranio genesis should be universalized, viz., applied to the entire neuroskeletal development. Last but not least, it should be borne in mind that even the insertional prominences are embedded, together with muscles and tendons, within the NS (Figure 12 a).

OSTEONEURAL GROWTH DIFFERENTIAL: SUPPORTING INDIRECT EVIDENCE FROM PALAEOOSTEOLOGY

"Addition" of the NS to palaeoosteological findings yields a fair piece of support to the advocated concept. The rounded appearance of the individual bony elements encountered in the fin-like limbs of Pessopteryx, their squareness in Ichthyosaurus and a fairly common shape (with terminal expansions) of the phalangae as well as of the radius and ulna in Mixosaurus (Figure 8 a-c) suggest absence of any appreciable ONGD in (a), comparable with the initial appearance of the vertebral bodies in Streeter's (1919) diagram (f). In Figure 8 b the increasing quantity of bone tissue was not "allowed" to grow adequately in length because of incapacity of the NS to grow so that the accumulating bone tissue could not but dissipate in transversal direction, a distinct "neuroadaptive crowding" of bone tissue has taken place. With enhancement of neural growth during the further course of evolution, elongation of bones has been "neurally permitted" to take place (Figure 8 c-e); terminal epimetaphyseal expansions reflect the physiological ONGD. The sequence of events indicated in Figure 8 a-e may be read from left to right in the sense of evolutionary history of the elongated terrestrial tetrapod limb but when reading it from right to left, the change of a terrestrial limb into the fin-like one, appropriate for aquatic way of life, may be envisaged.

FIGURE 8 a – g. Emergence of the osteoneural growth differential (reflected in terminal expansions of bones) in the forelimbs of Pessopteryx (a), Ichthyosaurus (b) and Mixosaurus (c) (redrawn from Müller 1985 — Bd. III, Teil 2, Abb. 140, 141), fully established in a fossil reptile and amphibian (redrawn according to Romer 1976 (Abb. 131, 132). In addition to the nervous skeleton, vessels and muscles (providing for skeletal metabolism and motion) are sketched as well. — Lower left (f, g): Emergence of the neurovertebral growth differential (i.e. of terminal widenings of the vertebral bodies in (g) in the diagram by Streeter (1919). — Right above — variable length of reptilian vertebrae dependent upon the variable length of interganglionic distances.
FIGURE 9. a — b. Bimetallic stripe, a model of the two diametrically different approaches to the formative effects upon the skeleton: The stripe can be bent either by a directly applied mechanical force (a) or by heating, viz., by eliciting elongation differential of its two components (b).

FIGURE 10. A - B. Growth-dynamic diagrams should illustrate dependence of skeletal growth (including the longitudinal extent of ossification) upon the neural co-growth, normal (A — left) or impaired (B — right). In the latter instance the accumulating skeletogenic tissue dissipates, extends more in the transversal direction with terminal or general thickening of bones and with more or less impaired ossification (right above — "anosteogenesis" and thanatophoric nanism (Roth 1994). — A — left above: First appearance of terminal expansions of the originally cylindrical bone primordium (see any communication concerning development, above all of the phalanges (e.g. Pauwels 1975, 1976, Kieny 1973 a.o.). Transversal dissipation of bone tissue as an neuroadaptive answer to the physiological osteoneural growth differential (comp. Fig. 8). — X, Y, Z: Syndactyly (or polydactyly) (x) related to a fault in establishment of the individual digital nervous skeletons in the developing limb bud (y,z).

OSTEONEURAL GROWTH PATHOLOGY

This paragraph treating a topic seemingly remote from the current interests of anthropology is of utmost importance since it indicates the natural "osteoneural" link between the normal and pathological (teratogenic) skeletal morphogenesis. Some pathological findings seem to point to what underlies the evolutionary transformations of the skeleton (Vorobyeva and Slipka 1969, Slipka and Slaby 1989 a.o.). The experimentation partly reported here (for technical and other particulars see Roth 1985, 1991) has been based on the following working hypothesis: Im-
Neuroadaptive deformities of the hind limbs in the chick (a) and duck (b) embryos and in frog tadpoles (c-f, 6 x nat. size) producible by a host of most heterogeneous "skeletal" teratogens and characterized by "shortening from below": Buckling, dislocation, achondroplasia-like shortening with thickening. d — osteological view (cleared according to Miller 1921). Primary impairment of neural growth is manifested in the straight course of the nerves in cleared specimens in contrast to the angulated (i.e., longer) bones. (Technique and details see Roth 1985, 1991). — The same pathomechanism indicated in human "achondroplasia" (g) characterized by tissular oxidative deficiency (Mackler et al. 1973), a factor injurious above all to the vulnerable neural growth. — Physiological "achondroplastic" features of horse's humerus (i) as compared with that of man (h). (Roentgenograms reproduced to unit length). (Comp. Fig. 19 A).

A skeletal deformity, is the very biological purpose of neuroadaptive deformities (Figure 10).

Experimental "skeletal" teratogens, mostly respiratory inhibitors, neurotoxicants or antimetabolites (to quote just a few) appear to interfere primarily with the vulnerable neural growth and this is sufficient to jolt the bone growth out of its accustomed groove. Even the most bizarre deformities just reflect the exaggerated osteoneural growth differential, viz., display exaggerated features of what is normal in physiological ONGD. Accentuated curvatures of the limb bones, exaggerated terminal splaying or flexion "contractures" of the fingers ("curled toes" in experimental animals) (Figures 10, 11, 13) are the most frequently encountered examples of the "osteoneural growth pathology". Dislocated hind limb bones in osteolathytic tadpole had to "crowd" (by shifting over of the bone ends) along too short nervous trunks.
FIGURE 12. a–k. Diagrams (a, b) showing the longer course of the radial (single arrowhead), ulnar (double arrowhead) and fibular nerve accounting for their distinct "shortness" at the level of the wrist and ankle (indicated by crosshatching) in respect to the straightly coursing median and tibial nerves. Neutral joint postures are "neuroadaptive" compensations for that neural shortness. — Insert in (b): Crosssection at the knee with fibular lodgement of both big nervous trunks, tibial and fibular (from Corning 1942) — Hind limb of the rat with the sciatic nerve exposed in flexion (c) and full extension (d, e). — Turtle (Chrysemis scripta elegans) (cleared specimen): Forelimb in full extension (f), hindlimb in neutral posture (g) and in semiextension (h) with physiological hyperadduction of the foot. Note straighter course (i.e. shortness) of a number of nerves as compared with the bones. — Forced adduction (i) and abduction (j) of the foot (detail from (g), 5 X nat. size) with slackening (i) and stretching (j) of the arrowed nerve, the "limiter" of abduction. — Cleared hind limbs of a frog tadpole in neutral posture (k). Note the longer way of the fibular (single arrowed) as compared with the tibial (double arrowed) nerve.
There is hardly any room for doubt that clinical skeletal “dysplasias” characterized by dwarfing “from below” and reproduced in the teratogenic experiment are related to the same osteoneural mechanism though the causative inhibitor of neural growth is not so clearly defined (Figures 5 C, 11 g). Endogenous and often hereditarily transmitted disturbance of neural growth appears to be primarily involved.

**NEUTRAL JOINT POSTURE**

**OSTEONEURLY EVOLVED**

In combination with the neuroadaptive skeletal deformities, changed joint posture is another mechanism how to preserve “unloading” of the growth insufficient, too short nerves, viz., how to compensate for the exaggerated ONGD. Its physiological degree appears to be responsible for the normal joint anulation such as, for instance, slight inflexion of the fingers or of the knee joint (Figures 7 g, 13). The slight physiological abduction of the human hand in neutral posture may serve as the object of the following deliberation: Though a rather fair degree of excusibility at the radiocarpal joint including, for instance, forced adduction is possible and indispensable for the manifold hand functions, permanent adoption of the forced posture would be perceived uncomfortably since the pertaining nerves with the corresponding portion of the capsular NS would persist in a state of distinct though still physiological stretch. Neutral posture, i.e. slight ulnar abduction of the hand, semiflextion of the fingers, valgosity at the elbow and at the knee, adduction at the hip joint a.o. means the optimal “neural comfort” since the entire articualr NS (i.e. its flexion-, extension-, adduction- and abduction-sided portions) is entirely slackened. Forced joint excursion such as hyperextension elicits pain which sets definitive limit to the overshot excursion: *Neutral limitation is superior to the biomechanical one* (Figure 12).

The “limiting shortness” of the nervous trunks in full extension as compared with their slackenedness in flexion is shown in the hind limb of the rat (Figures 7 g, 12 c – e) and in the limbs of a turtle (Figure 12 f – j). Especially in the latter instance the exaggerated physiological adduction of the foot (a mirror image of pathological hyperabduction of the human hand (“main en coup de vent”) in rheumatoid arthritis and in some skeletal dysplasias) appears to represent a clear-cut neuroadaptive posture due to limiting shortness of the accompanying thin nervous trunk representing, naturally, the entire dense NS of the area.

The characteristic neutral joint postures should be thus viewed upon as musculoskeletal adaptations to the “phylogenetically intentional”, because “bio-mechanically advantageous” in the given environment, lagging behind of the neural growth in respect to that of the skeleton.

Physiological valgosity at the knee in man appears to reflect, not unlike the anteflected knee in the frog (Figure 7 g), a distinct shortness of the tibial and

**Figure 13.** a – e. Sharp buckling of the tarsometatarsus with “curled toes” in a thallium-treated duck embryo along the shorter nervous trunks as compared with physiological hyperextension of a normal digit “permitted” by the digital nerve of normal length (a). Note “neuroadaptive” interphalangeal subluxation in (d). Experimental deformity yields a teratogenic model of neuroadaptive homization of the foot and of its exaggerated vaulting (pes cavus) (e) in a number of neurological disorders.

(Figure 11 e, comp. Figure 16 a). Osteological approach alone (d) does not yield any acceptable explanation.
FIGURE 14. A—F. Neuroadaptive features of the jaws. A a, b: Lateral dissection of the head of an 18 mm and 35 mm pig embryo (from Arey 1940, Fig. 582, 586, by permission of W. B. Saunders Comp., Philadelphia). Growth of the trigeminal nerve is considered a “limiter” rather than passive “follower” of the viscerocranial growth. — Diagram of Weidenreich’s truism “Large brain yields small jaws, small brain yields large jaws”. The truism concerns “reciprocity” of neural growth. — C a–c. Two-growth-types morphogenesis of the beak (normal stages a–c) according to Hamburger and Hamilton 1951). Every couple should be viewed upon superimposed. — D a–c. Examples of neuroadaptive deformities of the beak in duck embryos (a: osteolathyrism, b, c: thallium-induced. (Comp. Barica 1992). — E: Various degrees of growth impairment of the orofacial nervous skeleton producible by all possible teratogens or encountered as genetic defects, with or without exencephaly, sketched in a generalized vertebrate head. Lower left — the lingual nervous skeleton has been less interfered with than that of the jaws. — F. Chin-effect in a mouse embryo exposed to hypervitaminosis A (redrawn from Kalter 1968 (his Fig. 6a) by permission of the University of Chicago Press). Orofacial nervous skeleton with anticipated growth impairments of the mandibular nerve indicated by the present author (comp. Fig. 15 d, e). Deformities of the limb bones of the “shortening-from-below” type are producible by hypervitaminosis A as well (Love and Vickers 1971 a. o.).


**FIGURE 15.** a–h. Experimental-teratogenic deformities of the jaws in 25-day duck embryos (cleared specimens). a–c: Normal beak: lateral view (a), lower (b) and upper (c) beak. d–f: Osteolathryic deformities with chin-like appearances in (d, e), g: Thallium induced shortening. (Cca 2 × nat.size). h: “Chin” in the elephant or mammoth referable to shortness of the mandibular nerve, “reciprocal” to the extensive innervation field of the maxillary nerve supplying, among others, the trunk and the pulpal cavity of the tusk.

fibular nervous trunks as compared with the length of the skeleton: In cross-section both are situated behind the fibular femoral condyle, viz., in a site favouring the neuroadaptive valgosity (Figure 12 b).

Concerning the other abovenamed joints it should be noticed that the ulnar, radial and fibular nerves, owing to their winding around the ulnar epicondyle, along the humeral shaft and around the head of the fibula have to pass a longer distance to reach the periphery of the limb than the much straighter median and tibial nerves. At the level of the wrist the ulnar nerve is somewhat “shorter” than the median. For the sake of ulnar “unloading” that shortness is compensated for by a slight ulnar abduction of the hand as the basic neutral posture. Similar osteoneural mechanism appears responsible for valgosity at the elbow (“radial shortness”) and for fibular abduction of the foot. Moreover, since fibular nerve is significantly “shorter” than the tibial at the ankle level and terminates for the most part on the dorsum of the foot, it appears responsible for the neutral orientation of the human foot at a right angle to the tibia whereas the tibial nerve accounts for evolutionary shortening and vaulting of the human foot (Figures 12 b, 13 e) – a mechanism in essence identical with that involved in shortening of the human mandible (Figures 14, 15). In connection with the similar neutral posture of the foot in the frog tadpole (Figure 12 k) the distinctly longer course of the fibular as compared with the tibial nerve should be noticed.

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FIGURE 16.
A - C. Neuroadaptive joint dislocation patterns and tooth retention. a: The dislocated tibia "hangs" on the too short (in respect to the length of femur) sciatic nerve (osteolathyric frog tadpole, cleared — comp. Fig. 11 d, e). b: Retention of the upper canine interpreted as neuroadaptive dislocation. c: Multiple retentions and obliquity of the teeth in a chimpanzee (below — redrawn by permission from Schumacher 1965) with indication of a "chin".

FIGURE 17.
A - D. Neuro-atrophogenic changes of the senile mandible. A: "Degenerative" narrowing (i.e. shortening) of the intervertebral discs interpreted as neuroadaptive answer to atrophogenic shortening of the spinal nerve roots (from Roth 1989). B: a, b: Pointed chin in the aged referable to atrophogenic shortening of the mandibular nerve. (Shape of the mandible redrawn with permission from Schumacher and Schmidt 1972, their Fig. 339, 340). C: Pointed chin in acromegaly (according to Geddes 1911) due to enhanced bone growth without adequate neural co-growth. D: a, b. Reduction of the pulpal cavity in the aged related to atrophogenic impairment of the neuroprotective mechanism of the pulpal nervous skeleton (b). (Shape and size of the pulpal cavity redrawn by permission from Schumacher and Schmidt 1972, their Fig. 346).
MACRONEUROTROPHIC FEATURES OF THE JAWS

In schematic drawings of the neurocranium and viscerocranium the former is consistently depicted and considered in close association with the brain whereas the latter is reproduced as though entirely "nerveless". This mode of illustration mirrors the prevailing opinion, viz, acceptance of the important craniogenetic ("macroneurotrophic") role of the brain and denial of any similar role, except for "micro-neurotrophism", on the part of the viscerocranial nerves. In analogy with the osteoneural events in the limbs the author would tend to regard it as self-evident that the length of the jaws is determined by the phylogenetically established, more or less evolved growth-in-length potentiality of their NS. With impairment of the latter, neuroadaptive deformities of the jaws consisting in their "shortening from below" (i.e. from the periphery), chin-like buckling and/or bowing would ensue (Figure 14). Straight chord-like (in geometric sense) course of the mandibular (lower alveolar) nerve in respect to the angulated (i.e. longer) mandible or its concave-sided eccentricity in smoothly curved lower jaw appears to reflect abnormal slowness of the neural growth (Figure 15 d-g).

TERATOCIONIC MODELS OF PHYLOGENETIC TRANSFORMATIONS OF THE JAWS

Teratogenic experiments covering the individual ontogenesis yield a model of homization of the jaws, viz., of the gradual shortening of the maxillo-mandibular NS having taken place in the course of evolution parallel with increasing size of the brain (Figure 14 B). The hypothetical dorsally directed pull exerted upon the frontal portion of the mandible postulated by Schuricht (1952) to explain production of the human chin appears thus to be related to the physiological slowness of neural growth: Periosteal NS covering the mental portion of the mandible "cuts in" from in front, under mediation of the NPM, into the slightly faster growing mandible in the course of the individual as well as phylogenetic development (teratogenic models see Figure 15 d, e). Shortness of the mandible with a distinct "chin" in the elephant and mammoth is hardly related to any other mechanism than the osteoneural one (Figure 15 h).

Explanation of the "undersized" human viscerocranium as persistence of the condition found in newborn anthropoids ("fetalization") means, as a matter of fact, persistence up to adulthood of the comparatively undersized viscerocranial NS in man which offers a limited amount of space only for proliferation of the orofacial non-nervous tissues.
DEVELOPMENTAL JOINT DISLOCATION AND TOOTH RETENTION: A COMMON OSTNEURAL PATHOMECHANISM

Experimental-teratogenic and clinical congenital dislocation of joints may be readily explained as a “neuroadaptive” deformity of the “shortening-from-below” type brought about by abnormal growth slowness of the nervous trunks supplying the limb. With involvement of the knee in the frog tadpole, the dislocated tibia literally “hangs” on the too short sciatic nerve (Figure 16 a). Tooth retention may be related to the same cause, viz., to growth insufficiency of the nerves supplying the tooth germ which then “hangs” on the too short nerves and comes to occupy a more or less proximal site within the jaw (Figure 16 b). Not unlike in joint dislocation, preservation of “unloading” of the involved dental nerves is the very “purpose” of the retention. Obliquity of the teeth in multiple retention reported in a chimpanzee (Schumacher 1963) (Figure 16 c) fits very well with the proposed “too-short-nerves” mechanism. Moreover, the slight concavity of the ventral outline of the involved mandible, i.e., indication of a chin points to a distinct chin-producing slowness of the mandibular NS in whole.

INVOLUTIONAL ATROPHOGENIC SHORTENING OF THE NERVOUS SKELETON: ITS ROLE IN SENILE TRANSFORMATION OF THE MANDIBLE

Involutional atrophy of the brain, i.e. a distinct decrease of its mass with advancing age is a condition which even laymen are familiar with. Extracerebral nervous substance can hardly escape that widespread process. Owing to its elongated shape, atrophic loss should be manifested in a distinct degree of shortening of the CNRC and/or of the peripheral nerves. Not unlike that taking place in the course of development, atrophogenic neural shortening in the adult should be compensated for by neuroadaptive shortening of the adult skeleton. There exists a fair piece of evidence that “degenerative” narrowing (i.e., shortening) of the intervertebral disc and/or of the joint cartilage represents such a neuroadaptive or “neuroprotective” answer to atrophogenic shortening of the corresponding nervous structures (Roth 1989) (Figure 17 A).

In the given context the accentuated retroversion of the mental portion and pointed prominence of the chin in the senile mandible (Figure 17 B) appear to be due, in all probability, to atrophogenic shortening of the mandibular NS. This interpretation is indirectly buttressed by the strikingly similar shape of the mandible in acromegaly (Geddes 1911, Dokládal 1969) where neuromandibular length disproportion results from stimulation of mandibular bone growth by STH released in excess. “Unloading” of the mandibular nerve unresponsive to STH is maintained by gradually increasing retroversion (Figure 17 C).

PULPAL CAVITY — A PRODUCT OF THE NEUROPROTECTIVE PROPERTIES OF THE PULPAL NERVOUS SKELETON

A striking feature of gerontostomatology is reduction of the pulpal cavity with advancing age. The rich supply of the pulp with nerves represents in its entirety a fairly dense pulpal NS with additional local enhancement beneath the crown (Raschkow’s plexus). One should not hesitate to consider the pulpal NS as determiner of the shape and size of the pulpal

FIGURE 19.
A - B. A: Diagram of “reciprocity” of the gross neural growth and of its bearing upon the length proportions of the jaws, spine and limbs. Decreasing relative length of the spinal cord (from left to right: Limbless snake, reptile, rat, man) confronted with increasing length of the forelimbs (of their nervous skeleton). — Insert to the right: Reciprocal length proportions of the hindlimb in man, rat and horse. — Below: Extensive nervous skeleton of the hand in the bat (comp. Kouton 1985) accounting for presence of elongated bones and associated with relative shortness of the spinal cord. B: Duplication of the hand or foot is usually associated with “neuroadaptive” radoulnar or tibiofibular shortening and/or bowing. b: Note similar features of the limb skeleton in an extinct reptile (Plesiosaurus pterygius (from Müller 1985, Bd. III, Teil 2, Abb. 208).
The "macroneurotrophic" morphogenesis of the jaws is just a special instance of what might be termed "reciprocity" of the gross neural growth and what appears to be a fairly common attribute of the growing nervous system. To author's knowledge this phenomenon has been first alluded to by Naegeli (1897) who found a compensatory hypergenesis of the spinal cord associated with a severe congenital defect of the brain "as though a part of the growth energy lost in development of the brain would be handed over to the spinal portion of the neural tube" (translation from German by the author). Bardeen (1906/07) pointed out that nerves grow as plants grow and that extensive growth of one nerve tends to retard its neighbours, lack of development tends to excite them to more active growth (p. 298). With reference to Figure 21 a, it is strongly suspected that behind the progressive relative shortening of the spine associated with lengthening of the limbs and shortening of the jaws one should disclose a primary plus or minus change of growth of the NS. "Reciprocal" length of the limb nerves such as the long sciatic and femoral as compared with the short foot nerves in man and the converse proportion in quadrupeds and birds (Figures 18, 19) appear to be responsible for the "reciprocal" length of the enclosed skeleton, viz., for the changes of limb proportions with change of function (Gregory 1928). Significantly increased number of vertebrae in all species where limbs are reduced or absent (Gans 1975) reflect the excessive elongation of the spinal cord associated with "reciprocal" stunting of the appendicular NS (Figure 19). Talpid and other similar mutants represent another examples of neural growth "reciprocity" (Figure 20).

Duplication of the limbs, spontaneous or experimental, above all in chick embryos are mostly associated with "achondroplasia-like" shortening, bowing and/or thickening of the radio-ulnar or tibio-fibular portion of the limb skeleton (Abbott 1959, Amprino and Camosso 1959, Landauer 1956, Zwilling 1956 a.o.), viz., with features pointing to involvement of the osteoneural mechanism. Hamburger (1939) has shown that the extent of the peripheral innervation field of a nerve is a fairly constant parameter which cannot be enlarged but in rather narrow limits. There seems to exist a factor intrinsic in the nerve which sets a definite limit to the neural growth stimulating activity of the peripheral innervation field. Radical enlargement of that field resulting from duplication leads to "reciprocal" (compensatory) reduction of the nervous skeleton of the radio-ulnar or tibio-fibular area with a "micromelic" effect upon the embedded skeleton: The increased overall quantity of the limb skeleton must "accomodate", at the cost of a deformity, within the roughly unchanged overall extent of the NS (Figure 19 B).
Palaeozoological literature yields many striking examples of a similar neural growth reciprocity in extinct reptiles (Figure 19 C). Hyperphalangeal hand or foot makes up more than half length of the limb with a vast digital innervation field and reciprocal shortness of the proximally located NS accounting for the stunted appearance of the long bones.

PERIOSTEAL NERVOUS SKELETON
- A DIFFUSE GROWTH CENTER

The advocated universalization of the cerebrocranial developmental interrelation should imply universality of the NPM including the utmost neural periphery. Even that feltlike nervous structure and, after all, every individual nervous fiber should be incessantly "unloaded", viz., should be able to impose restraint upon the nearby skeletogenic tissue proliferating in undesirable sites and directions. In this respect particular importance should be ascribed to the periosteum as a "growth center" (Schumacher 1985) represented, in the present author's view, by the periosteal NS. The feltlike "sa" of the latter is responsible for or at least contributes to remodelling processes, above all to those carving the surface relief of the viscerocranium, viz., makes the bone tissue to "recede" at resorptive sites (Hoyte and Enlow 1966) with production of the most variable degrees, normal and pathological, of shortened viscerocranium. Identical "neuroprotective" mechanism underlies, in all probability, the postulated pressure effect of the periosteum in "modeling" of the limb bones (Heft 1972, Warrell and Taylor 1979). Should the limb bone represent a cast of the cavity within the NS (p. 4) then periosteal NS would be immediately engaged in shaping of the enclosed bony contents. The different cross-sectional shape of long bones in terrestrial and aquatic mammals (Figure 18) is a striking example of what is advocated: The water resistance is neurally perceived and so is also the way how the appropriate "hydrodynamic" shape of bones is achieved.

INTERDIGITAL NERVOUS SKELETON
PROVIDES FOR INTERDIGITAL WEBBING

The advocated "leading" role of the NS in morphogenesis applies to the soft parts as well since its surface sets an insurmountable limit to proliferation.

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**FIGURE 21.** A. B. Phylogenetic development of the vertebrate skeleton (reproduced from Gregory 1974 by permission of the American Museum of Natural History, New York). Head profiles and nervous skeleton of the right hindlimbs indicated by the present author. Note the relative "reciprocal" shortening of the spine associated with elongation of the limbs as well as shortening of the viscerocranium with increasing size of the brain. The bony skeleton just mirrors the changing features of the nervous skeleton.
B. Egg and sperm (center) as sources of the two growth opes, cellular-divisional and neural-extensive. The latter, in form of the nervous skeleton (lower left) is "stuffed" with the products of the former (lower right) and determines the shape of the body. Extensive plant growth originates from the plane seed and provides for the shape of the plant but the substance necessary for outgrowth is supplied by the "mother earth". In the animal the "substance" is supplied by mother's womb (Aristotle's concept). Even the "homunculus" within the sperm suggests the idea of paternal responsibility for the shape of the body and material for its outgrowth. — Insert below: Schematic cross-section of the human embryonic spinal cord with individual neuroblasts (redrawn with permission from Villiger and Ludwig 1946, Fig. 26).
of the “stuffing” non-nervous tissues. Within the originally compact embryonic hand or foot plate the prospective individual digits are provided with their own individual nervous skeletons. Cells situated outside the confines of the digital NS are “doomed to death” since they are not allowed to lead a “one-growth-type” way of life; interdigital cell death ensues (Figure 10 x, y). Where interdigital webbing appears indispensable in the given environment, however, the NS purposefully permeates also the interdigital spaces so that interdigital cellular population remains viable since two-growth-types composition is preserved (Figure 18). Accordingly, syndactyly would reflect abnormal extension of the digital NS into the interdigital space, polydactyly would be related to installation of individual digital nervous skeletons in excess (Figures 10 z, 20).

NERVOUS SUBSTANCE:
FUNCTIONAL MEDIATOR
AND MORPHOGENETIC REALIZER
IN SKELETAL DEVELOPMENT

Two ways are acknowledged how information from the environment can enter the organism (Lorenz 1965, quotation from G. Roth 1982): “Either it is the species which gathers “information” by means of the “method” of mutation and selection and stores this information in the genes; or it is the individual which, through interaction with the environment, gathers and stores information in the nervous system, which results in adaptive modification of behaviour, or learning”. It seems most likely and even inevitable, however, that the species-way is accomplished also along neural pathways since changes in the environment requiring corresponding adaptive changes of the organism are neurally perceived, above all by exteroception and proprioception. This complex information is “translated” into different growth-in-length potentiality of various portions of the NS with resulting appropriate shape (length) of the bony skeleton. Nervous substance thus has the privilege to mediate between what is going on in the environment and what should be adequately changed in the bodily morphology and, consequently, to provide for the unity of form and function. In addition to the instantaneous reflexoric reaction to acute, potentially injurious effects from the environment such as thermal or mechanical insults there should also exist extremely protracted neuroadaptive reactions working throughout eons of evolution and resulting in appropriate and (phylo)genetically anchored neuroadaptive transformations of the vertebrate skeleton.

OSTEONEURAL CONCEPT
AND SKELETAL GENETICS

It is self-evident that the shape of the skeleton is genetically anchored. Grüneberg (1975) pointed out, however, that “rather few genes can be regarded as “skeletal”... Most of them involve the skeleton in a somewhat round about way...” (a similar viewpoint see in Alberch 1982). It seems that the “round about way” of the gene effect is a “macroneurotrophic” way. Gross neural growth rather than bone growth proper seems to represent what is genetically established. Hubbard (1974) is probably right in his statement (p. 341) “the nerve not only stimulates protein synthesis nonspecifically but also exerts a qualitative influence on the type of protein synthesized; this has led to the suggestion of a neural influence on gene expression as being one of the major aspects of neurotrophic function”.

GOETHE’S “ÖKONOMIE DER NATUR”
LINKED WITH THE NERVOUS SKELETON

The osteoneural concept with its phylogenetic aspects should be taken in consideration in connection with what was commented since Aristotle, what has been termed “Ökonomie der Natur” (Goethe 1795) or “balancement des organes” (G. de St. Hilaire 1831 — quotations by Brednow 1965) and what Kant (1790 — quoted by Langenbeck 1969) called “admirable simplicity of the ground plan” (“eine bewunderungswürdige Einfachheit des Grundrisses”) of the animal body which, “by elongation of some parts and shortening of others resulted in such a great variety of species”. Needless to say that “elongation and shortening” appear to concern primarily the NS and its growth.

There is strong reason to suspect that the coordinate system applied to explain Cartesian transformations of the animal body (Thompson 1961) as well as “functional matrices” of Moss (1972) are identical with the NS.

THE TWO GROWTH TYPES,
CELLULAR-DIVISIONAL
AND NEURAL-EXTENSIVE,
RELATED TO THE EGG AND SPERM

The adduced argumentation is based on the existence of two growth types within the vertebrate body, the cellular-divisional and the neural-extensive. Would we try to examine when the two growth types appeared in the course of individual ontogenesis, viz., would we revert “stream up” to the ever earlier developmental stages, we would reach at last the egg and the sperm as the sources of the two growth types with the implication that the sperm should have something in common with the origin of the nervous system. Resemblance of the sperm cell to the young neoblast is striking (Figure 21 b). Moreover, a remarkable analogy between the egg-sperm interaction and that between the embryonic nervous fiber and the cell to be innervated has been pointed out by the
pioneers of neurobiology (Harrison 1907, Cajal 1919): The embryonic cell, once innervated, loses the potentiality for or acquires resistance to further innervation just as, in a not dissimilar fashion, the entrance of one single sperm into the egg renders impossible the penetration of others. The sprouting nerve fibers pass along the cells already innervated towards other hitherto not innervated cells. The sperm would be thus the source of the extensive neural growth and of the NS whereas the rest of the bodily tissues the NS is “stuffed with” would originate from the egg by cellular-divisional proliferation. Disappearance of the sperm within the fertilized egg would be a transient event indispensable for genetic interaction since the sperm would “reappear” and continue its existence in form of neuroblasts and of the NS responsible for the general shape of the body (Figure 21 B).

Harris’ statement (1981) that “the phylogeny an animal recapitulated in its ontogeny extends back to the egg and thus to the age of primitive unicellular organisms” should concern also the sperm, viz., extension back to the age of primitive flagellate organisms. Moreover, the egg has been said to be “a storage place of immense treasure of experiences gathered in the course of evolution enabling the individual to survive in the ever changing world” (Duspiva 1989, also Horder 1989). In the light of the presented evidence it appears more probable, however, that what is ascribed to the egg applies rather to the sperm. The sperm is equally “immortal” like the egg: The latter in cellular populations originating from it, the former in neuroblasts and in the NS which, stuffed with the egg-products, is the “realizer of experiences” stored in the sperm.

That grossly provocative idea throws peculiar light on the Aristotelian and “naturphilosophical” concepts concerning the origin of animals. It is self-evident that the plant seed provides for the constant shape of the individual plant originating from it but the matter for its development and growth is furnished by the “mother earth”. In the origin of animals the maternal body plays the role of the earth, it supplies the substance for development and growth of the body whereas the male semen supplies the bodily form (quotation from Moore 1987), i.e. by mediation of the NS originating from the sperm. Also the idea of “spermists” who believed the tiny preformed body (homunculus) to reside in sperm (Moore 1987) seems to imply inevitable maternal contribution of substance for the subsequent development and growth of the “paternally” established bodily form.

Still another conclusion seems warranted as concerns the common features of neural growth and plant growth. In both instances the stage of embryonic cellular-divisional proliferation is followed by that of extensive growth. Though resulting in products so different as contemporaneous plants and animals, the identical sequence of the two growth types points to some ancient relationship extending back to the very beginnings of the two kingdoms on this planet.

**Pros and Cons**

Concluding, still several aspects of the proposed concept and possible objections should be briefly discussed.

1. Lack of innervation of the bone tissue proper has led us to think of bones as something outside the nervous system what is governed almost exclusively (except for the vague “microneurotrophism”) by the laws of biomechanics and genetics. Every bone is embedded, however, within the periosteal and endosteal NS which governs its biomechanical parameters. It seems most likely, without much exaggeration, that the complicated mathematical, physical and geometrical calculations associated with modern biomechanics are “performed” in the higher nervous centers and “applied” at the level of the local NS.

2. Faced with the hard adult bone tissue and the delicate nerves one is naturally reluctant to admit any gross effect of the latter upon the former. Development of a bone should be viewed upon, however, as gradual hardening by chondrification and ossification of the originally very soft bone primordium easily pliable by the NS, a process comparable with what is going on in glass-blowing: Blow of air and a gentle touch are enough to shape the mass of molten glass (“primordial bone”) which then hardens by cooling (“ossification”). The moulding effect of the brain upon its skeletogenic envelope is the most striking example of that “glass-effect” in osteology.

3. Denervation and explantation experiments seem to speak against the concept since even the denervated bone primordium does not cease to grow and develop. The osteoneural interrelation does not work, however, but in situ, under normal conditions within the intact living body. Denervation is a gross artifact and to deduce from its results neural independence of bone is not far from the conclusion that continuing normality of a dog released from its lead would indicate independence of the animal upon the lead. Spinal nerve roots and peripheral nerves demonstrated or schematized in the presented documentation represent normal or too short “leads” by which the growing bones are “curbed”.

4. Successful operative lengthening of the limbs in human dwarfism seems to confirm subdivision of “passive” neural growth to “active” bone growth. Is the artificial procedure protracted enough and supply with energy adequate, the nerves elongate (grow up) since, as any other living matter, they have to cope even with unusual circumstances. Would osteotomy and distraction be applied, however, to the short limbs e.g. of some extinct or recent reptiles (Figures 8, 19 c) or of mammals (Figure 11 i), human-like elongation of the skeleton would be achieved. Similarly, distraction of a normal human humerus or femur would result in their elongation and thinning resembling the limb skeleton of some birds or primates (Figure 18). Hence, operative lengthening of the limbs is a gross artifact which has nothing to do with the natural osteoneural developmental events.
5. Central nervous system is treated usually in the 3rd volume of anatomical handbooks, the skull with the rest of the skeleton in the 1st volume. In spite of that unavoidable separation, everyone is aware of the fact that, as concerns growth and development, the brain and the skull "belong together." Exactly the same mental operation of "putting together" should be practiced, at the macroneurotrophic level, as concerns the vertebral column and the limb skeleton from the 1st volume and the spinal cord and peripheral nerves from the 3rd volume.

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