

# Analysis of the structure of the brain stem of mammals by means of a modified D’Arcy Thompson procedure

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**Abstract** In his famous book, ‘On Growth and Form’, D’Arcy Thompson demonstrated that the shapes of related animals, or parts thereof, can be transformed into each other by a simple graphical procedure, called the method of coordinates. In this procedure, an object is inscribed in a net of Cartesian coordinates. It appeared that the shape of related objects could be characterized by means of simple, harmonious deformations of the initial orthogonal system of coordinates. Here, I demonstrate that: (1) the central nervous system contains a built-in, natural coordinate system; (2) differences in shape and proportion of cross sections through the brain stem of various mammals can be easily analyzed with the aid of this coordinate system, and (3) sets of structures in the mammalian brain stem, which are closely related to the neocortex, but form part of entirely different functional systems, form spatially constrained complexes, and have the capacity to expand jointly and harmoniously within these complexes.

**Keywords** Brain stem · Coordinate systems · Neocortex · Transformations

## Introduction

In the most celebrated chapter of his famous book, ‘On Growth and Form’, D’Arcy W. Thompson (1942)

demonstrated that the shapes of related animals (crustaceans, teleosts), or parts thereof (carapaces, skulls), can be transformed into each other by means of a simple graphic procedure, called the method of coordinates. The procedure begins with the inscription of the outline of a particular biological object A in a net of rectangular, equidistant (Cartesian) coordinates, and with marking the intersections of the coordinates on the surface of the object. Next, points corresponding to the intersections in object A are plotted on the outline of a related object B. It quite often appears that these corresponding points may be linked up by smoothly curved lines of intersection, revealing that object B is a harmoniously transformed as a representation of A. Thus, in Fig. 1, a human skull is ‘transformed’ into the skull of a chimpanzee, which in turn is ‘transformed’ into the skull of a baboon.

In what follows, I indicate how transverse sections through the brain stem of mammals can be analyzed with the aid of a modified version of the ‘D’Arcy Thompson procedure’ outlined above, in which advantage is taken from the fact that the brain stem (and the vertebrate neuraxis in general) contains a (non-Cartesian) built-in, natural coordinate system.

## Selection of material, histological techniques, the natural coordinate system and the modified ‘D’Arcy Thompson procedure’

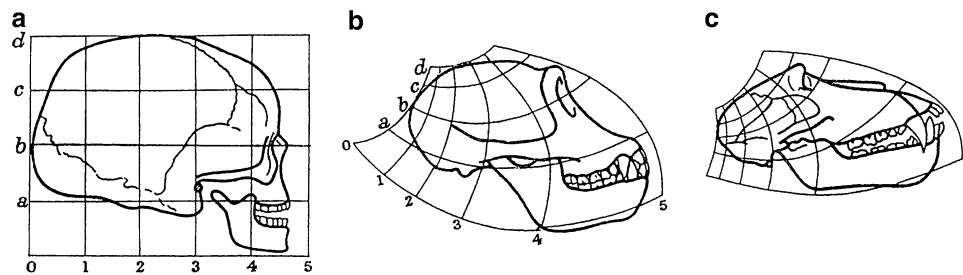
### Selection of material

The central nervous system of mammals distinguishes itself from that of other vertebrates by the presence of a neocortex, i.e. an ultracomplex, multilayered structure, which occupies a superficial position in the dorsal part of

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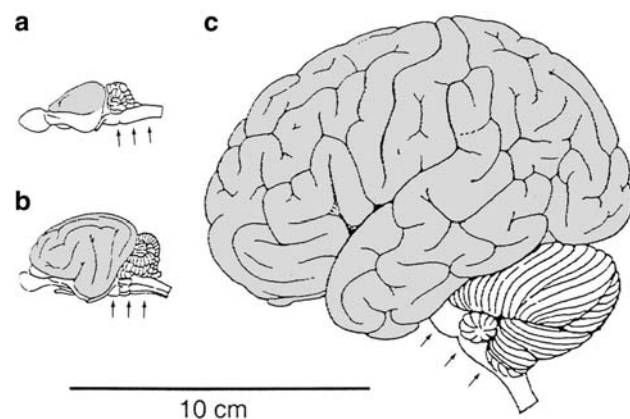
**Fig. 1** Thompson's coordinate transformations on the skulls of the human (a); the chimpanzee (b), and the baboon (c). Reproduced from Thompson (1942)



the cerebral hemispheres. Quantitative studies have shown that the size of the neocortex (surface area, volume) shows enormous differences among mammals, and that this size is positively correlated with the size of the cerebellar cortex and with that of some subcortical structures, such as the striatum, the pons, and the inferior olive (Hofman 1982, 1985a, b; Stephan et al. 1981; Sultan 2002; Sultan and Braitenberg 1993). Three mammalian species, the North American opossum *Didelphis virginiana*, the cat, *Felis catus* and the human *Homo sapiens*, were selected for the present inquiry. These species have been selected because they form a morphocline of increasing neocortical size (Fig. 2).

#### Histological techniques

The analysis discussed below has been carried out on transverse sections through the midbrain and the hindbrain of the three species mentioned. The sections were selected from histological series, stained with the Nissl-, Klüver-Barrera- and Weigert-Pal techniques. Their levels are indicated in Fig. 3. The cell masses and fibre bundles observed in the sections are represented semidiagrammatically in the left halves of Figs. 6 and 7.



**Fig. 2** Lateral views of the brains of the opossum (a); the cat (b), and the human (c). The neocortex is shaded. The brain stem is indicated by arrows

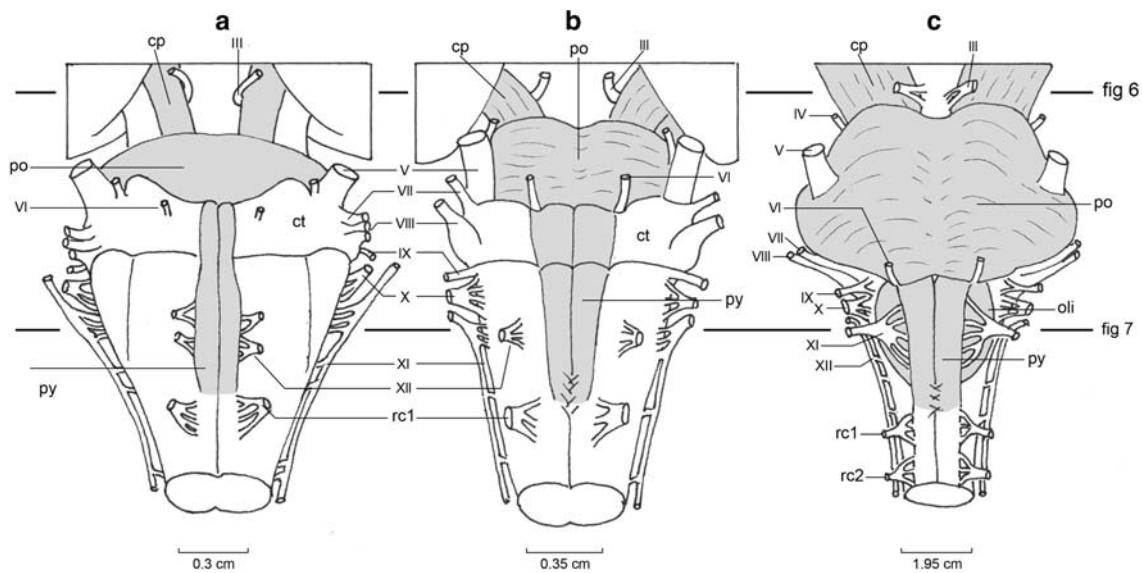
#### The natural coordinate system

As detailed in previous publications (Nieuwenhuys 1994, 1998a, b), the vertebrate central nervous system contains its own, built-in, natural coordinate system (NCS). This system consists of sets of radially and tangentially oriented curves. The radial curves manifest themselves during early development in the direction and orientation of the matrix cells and of the ependymal gliocytes (Fig. 4a). It is important to note that the processes of these elements play an important role as guidelines during the migration of neuroblasts and their precursors. This implies that many developing neurons shift in a simple way within the NCS. The neuroblasts are the product of mitoses, which take place in the immediate vicinity of the ventricular surface; consequently, this surface can be considered as the 'starting plane' or 'zero plane' of neurogenesis. The tangential component of the NCS manifests itself in the course of 'arcuate fibres', i.e. axonal processes which during early development pass dorsoventrally, directly peripheral to the matrix layer (Fig. 4b). Numerous additional arcuate fibres come about during further development. These fibres form, just like the processes of the matrix cells and of the ependymal elements, an important substrate for the migration of neuroblasts.

The NCS, which may be considerably deformed during ontogenesis, reveals the general morphology and the basic organization of the central nervous system. In transverse sections through the brain stem of adult mammals, it can be read off from: (1) the direction of the central fibres of cranial nerves (see the fibres of the oculomotor nerve in Fig. 6, and those of vagus and hypoglossus nerves in Fig. 7); (2) the course of arcuate fibres; (3) the course of blood vessels, and (4) the 'lattice pattern' formed by the interstices between the bundles of longitudinally running fibres (Fig. 4c).

#### The modified 'D'Arcy Thompson' procedure

The procedure devised by D'Arcy Thompson starts with the inscription of an outline of the object to be analyzed into a net of rectangular, equidistant coordinates (Fig. 1a). The author mentioned presents no particulars on



**Fig. 3** Basal views of the brain stems of the opossum (a); the cat (b), and the human (c). The coarse interrupted horizontal lines indicate the levels of Figs. 6 and 7. The cerebral peduncles (*cp*), pons (*po*),

pyramids (*py*), and olivary eminences (*oli*) are shaded. *III–XII* cranial nerves III to XII, *ct* corpus trapezoideum, *rc1*, *rc2*, roots of spinal nerves

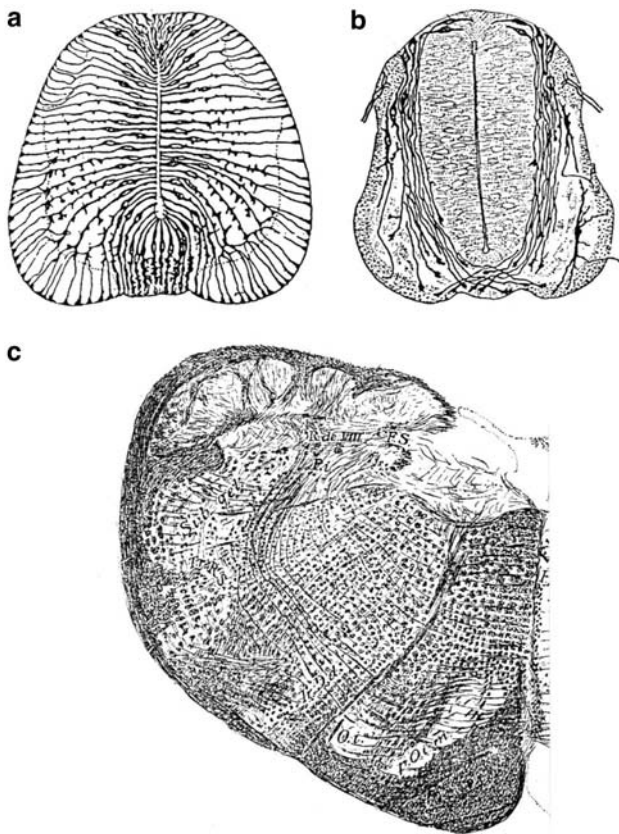
the size of the meshes of the net, but it is clear from his figures that this size is selected in relation to the complexity of the object. I followed this procedure, with the exception that advantage is taken from the presence of a natural coordinate system in the central nervous system of vertebrates. The ventricular surface and the meningeal surface of the right half of the section through the midbrain of the opossum were divided into eight equal parts and the corresponding points on these two surfaces were connected by radial curves. Next, each of these radial curves and the dorsal and ventral midlines of the section were divided into four equal parts and the corresponding points on these radial lines and curves were connected by tangential curves. Thus, the surface of the hemisection in question was subdivided into 32 ‘rectangular’ patches: a1–d8 (Fig. 6a). It appeared readily possible to plot points, corresponding to the intersections of the radial and tangential curves in the hemisection through the midbrain of the opossum, in hemisections through the midbrain of the cat and the human, which indicates that the three hemisections analyzed are topologically equivalent. The points plotted in the hemisections of the cat and the human were connected by best fitting radial and tangential curves (Fig. 6b,c). The procedure just outlined was repeated for the sections through the rhombencephalon of the species selected; however, because the wall of this brain part tapers dorso-laterally into a thin ependymal membrane, the length of the lateral sides of the patches a8–d8 is zero in these sections (Fig. 7a-c). The surface area of some sets of patches was determined with an Ott planimeter. The results of these

measurements were expressed as percentages of the total surface area of the corresponding hemisection.

## Results and discussion

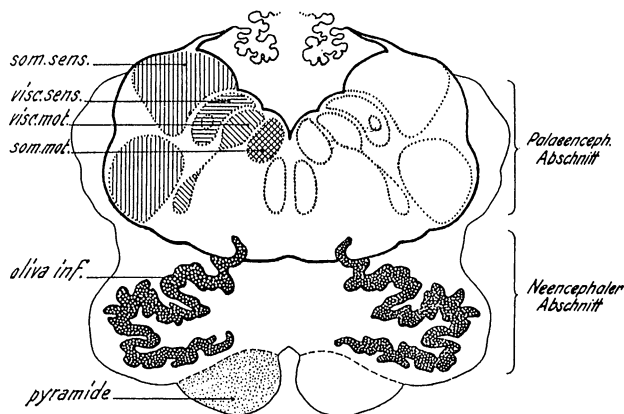
The networks of coordinates inscribed in the sections through the mesencephalon (Fig. 6) and the rhombencephalon (Fig. 7) of the three species selected, reveal superficially situated local deformations, accompanied by considerable differences in relative size. The most conspicuous of these include a mesencephalic region consisting of the patches d2 and d3 and a rhombencephalic region formed by the patches d1 and d2. As indicated in Figs. 6 and 7, the surface area of the mesencephalic region d2–d3 increases in the series of animals selected from 15%, via 24%, to 45% of the total surface area of the corresponding hemisections, whereas the surface area of the rhombencephalic region d1–d2 increases from 11%, via 21%, to 52%.

The mesencephalic region d2–d3 encompasses two structures, the cerebral peduncle and the substantia nigra (Fig. 6). The cerebral peduncle consists entirely of fibres descending from the neocortex which descend, via the peduncle, to the basal pontine nuclei, and to sensory and motor centres in the lower brain stem and spinal cord. In primates, the corticopontine fibres form the medial and lateral parts of the peduncle, whereas the corticobulbar and corticospinal fibres occupy an intermediate position (Fig. 6c). The most salient hodological feature of the substantia nigra is that it entertains strong, reciprocal



**Fig. 6** Transverse sections through the mesencephalon of the opossum (a); the cat (b), and the human (c), at the levels indicated in Fig. 3. In the right halves of the sections, the cell masses and the location of the fibre connections are indicated; the right halves are subdivided into 32 corresponding ‘rectangular’ patches, according to a methodology described in the text. It is indicated that a region in the basal midbrain, formed by the patches d2–d3, increases in relative size from 15% in the opossum, via 24% in the cat, to 45% in the human. *bic* brachium of inferior colliculus, *cbst* corticobulbospatial tract, *cp* cerebral peduncle, *EW* nucleus of Edingger–Westphal, *fpt* frontopontine tract, *ip* interpeduncular nucleus, *mcs* mesencephalic central gray, *mesV* mesencephalic trigeminal nucleus, *ml* medial lemniscus, *mlf* medial longitudinal fasciculus, *pbn* parabigeminal nucleus, *ptpt* parietotemporo-pontine tract, *rf* reticular formation, *rn* red nucleus, *sc* superior colliculus, *sn* substantia nigra, *III* oculomotor nucleus, *III<sub>n</sub>* oculomotor nerve, *a, b* etc. and *I, 2* etc., are indicators of the ‘rectangular’ patches in which the sections are subdivided

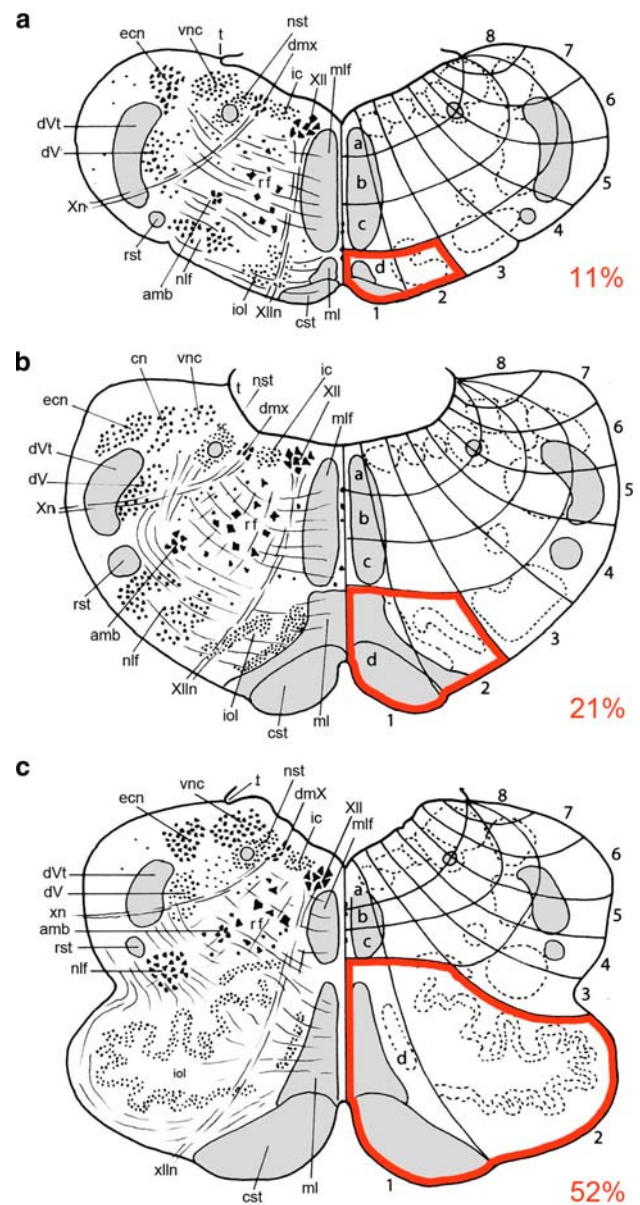
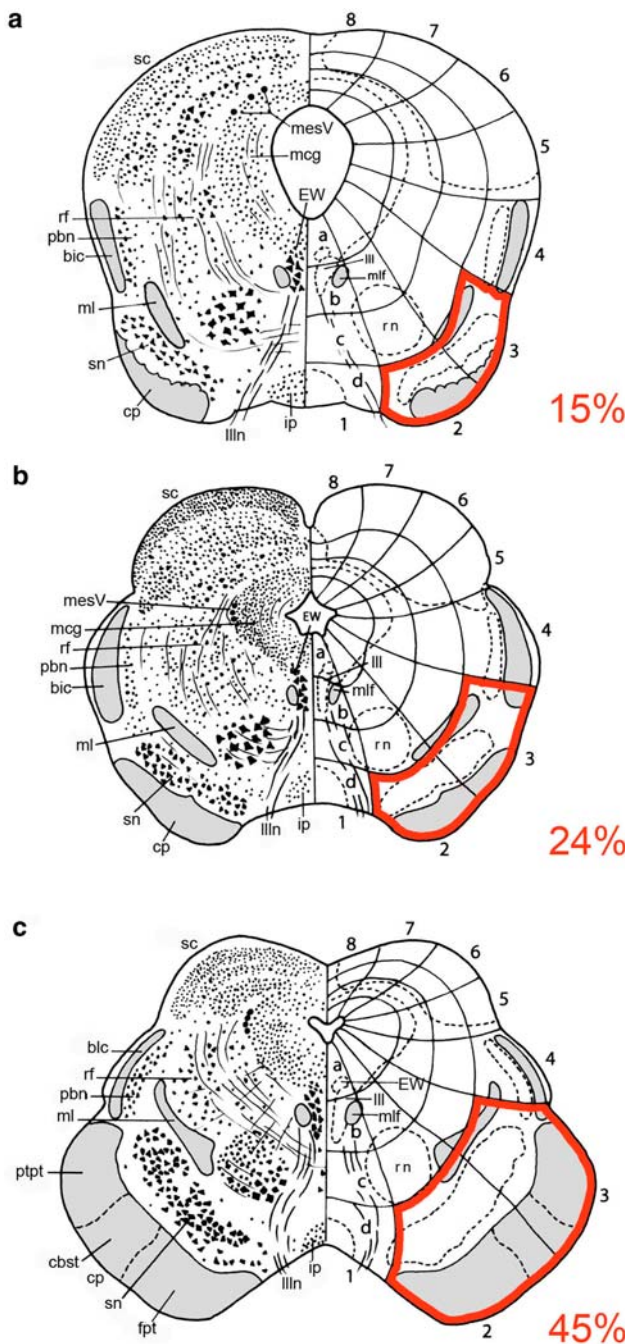
**Fig. 4** Transverse sections through the central nervous system, showing elements of the natural coordinate system. **a** Radially arranged neuroepithelial cells in the spinal cord of a 5-day-old chick embryo. **b** Primordial dorsal-horn neurons giving rise to ventrally coursing arcuate fibres in the spinal cord of a 4-day-old chick embryo. **c** Arcuate fibres and the typical ‘lattice pattern’, formed by the interstices between longitudinally oriented fibres, in the lower rhombencephalon of an adult cat. **a, b** are reproduced from Ramon y Cajal (1909); **c** is reproduced from Winkler and Potter (1914)



**Fig. 5** Superimposed transverse sections through the rhombencephalon of a kangaroo, *Macropus* (heavy outline) and of man (thin outline), intended to show that in the course of evolution a ventral, neencephalic portion has been added to a dorsal palaeencephalic portion. Reproduced from Haller von Hallerstein (1934)

connections with a very large cell mass, situated in the subpallial part of the telencephalon, known as the striatum or the caudatus–putamen complex. This complex forms part of a still larger entity: the basal ganglia. Classically, the striatum has been regarded as a part of the motor system, particularly because disturbances of its functions can lead to severe movement disorders. During the first half of the last century, it was generally believed that the striatum influences motor activity quite independently from the control exerted by the motor regions of the neocortex via the pyramidal tract (hence the term: *extrapyramidal motor system*). Later, it became clear that the basal ganglia do not operate independently from the cortex. It appeared that the striatum receives a massive projection from the entire neocortex and that this cell mass, via the globus pallidus (another basal ganglion) and the ventral lateral thalamic nucleus, projects back to the motor and premotor regions of the neocortex (Voogd et al. 1998). The volume of the striatum is strongly correlated with the volume as well as the surface area of the neocortex (Hofman 1985a, b; Stephan et al. 1981). Hence, because of its strong reciprocal connections with the striatum, the substantia nigra may be considered as a neocortical dependency.

The rhombencephalic region d1–d2 harbors three structures, the pyramis, the medial lemniscus, and the inferior olivary nucleus (Fig. 7). The *pyramis* consists of neocortical efferents, passing to sensory and motor centres in the lower rhombencephalon and spinal cord. The *medial lemniscus* forms part of a sensory projection known as the dorsal column—medial lemniscus system. The first order neurons of this system are located in the spinal ganglia. Peripherally, these neurons contact low-threshold cutaneous mechanoreceptors. Their axons enter the spinal cord, ascend in the dorsal column of that structure and terminate in two large cell masses, the gracile and cuneate nuclei. These nuclei are situated dorsally in the most caudal part of the brain stem. Secondary sensory fibres arising from these nuclei pass ventromedially as internal arcuate



**Fig. 7** Transverse sections through the rhombencephalon of the opossum (**a**); the cat (**b**), and the human (**c**), at the levels indicated in Fig. 3. The filling in of the sections corresponds to that in Fig. 6. It is indicated that a basal region formed by the patches d1–d2, increases in relative size from 11% in the opossum, via 21% in the cat, to 52% in the human. *amb* ambiguus nucleus, *cn* cuneate nucleus, *cst* corticospinal tract, *dmX* dorsal motor vagus nucleus, *dV* nucleus of the descending tract of the trigeminal nerve, *dVt* descending tract of the trigeminal nerve, *ecn* external cuneate nucleus, *ic* intercalate nucleus, *iol* inferior olivary nucleus, *nlf* nucleus of lateral funiculus, *nst* nucleus of the solitary tract, *rst* rubrospinal tract, *t* taenia, *vnc* vestibular nuclear complex, *XII* hypoglossal nucleus, *Xn* vagus nerve, *XIIln* hypoglossal nerve. For remaining abbreviations and symbols, see legend Fig. 6. A preliminary version of **c** has been published previously (Nieuwenhuys 1998a, b)

fibres, decussate to the opposite side, and enter the medial lemniscus. Within this compact fibre bundle, they pass up to the diencephalon, to terminate in the ventral posterior nucleus of the thalamus. Initially, the medial lemniscus is situated adjacent to the median plane (Fig. 7), but in the rostral hindbrain, it shifts laterally and in the midbrain, it occupies a ventrolateral or lateral position (Fig. 6). Fibres, passing from the ventral posterior thalamic nucleus to the somatosensory region of the neocortex, form the third and final link in this epicritic somatosensory projection.

The *inferior olivary nucleus* projects to the contralateral cerebellar cortex. The afferents to this nucleus stem from small cells in the red nucleus and from a group of nuclei

in the border zone of the mesencephalon and the dien-cephalon, which includes the zona incerta, the nucleus of the optic tract, and the nucleus of Darkschewitsch. All of these nuclei serve as links in neocortico–olivary projections (Voogd et al. 1998; Voogd 2004). In primates, the small cells in the red nucleus are abundant and concentrated in a distinct rostral part of the nucleus. The neocortical afferents to this parvocellular red nucleus originate principally from the motor, premotor, and supplementary motor cortical areas. The efferents from the parvocellular red nucleus to the inferior olive are concentrated in a compact central tegmental tract, which is extremely large in the human brain (Verhaart 1970; Voogd et al. 1998).

It can be concluded that the constituents of the mesencephalic region d2–d3 and the rhombencephalic region d1–d2 are either direct neocortical efferents, or structures (cell masses, fibre paths), which are so closely associated with the neocortex that they can be characterized as neocortical dependencies. This salient similarity notwithstanding, the various components of the two regions under discussion form part of widely different functional systems and are accordingly not connected with each other. Their relationships are spatial rather than functional.

There are several other sets of patches showing considerable differences in size among the species studied. Thus, the region formed by the mesencephalic patches c5–8 + d5–8 decreases in relative size from 36% in the opossum, via 29% in the cat, to 13% in the human (Fig. 6), and the region formed by the rhombencephalic patches 1a–c decreases from 10% in the opossum, via 7% in the cat, to 3% in the human (Fig. 7). An important difference between these two regions on the one hand and those discussed above on the other hand is, however, that the former, contrary to the latter, are occupied by structures related to a single functional system.

Mesencephalic region c5–8 + d5–8 is occupied by the superior colliculus. The homologue of this structure represents in all non-mammalian vertebrates the principal visual centre ('tectum opticum'). In mammals, it is gradually superseded by the geniculo-cortical system and reduced to a centre for the control of reflex movements of the eyes and the head.

Rhombencephalic region 1a–c is occupied by the medial longitudinal fasciculus, a conspicuous, coarse-fibred bundle, which may be characterized as the 'primeval system of motor control'. It is composed of fibres originating from the nucleus interstitialis of Cajal, i.e. a small cell mass situated in the mesodiencephalic transition zone, the superior colliculus, the vestibular nuclear complex, and the reticular formation. Most of its fibres descend through the brain stem and a certain proportion enters the anterior funiculus of the spinal cord. It is concerned with the

coordination of eye movements as well as with those of head and trunk.

Haller von Hallerstein (1934) compared transverse sections through the rhombencephalon of a marsupial (*Macropus*) and the human. He concluded that in the course of the evolution of mammals, a ventral *neencephalic* portion has been added to a dorsal *palaencephalic* portion (Fig. 5). Comparison with the corresponding sections shown in Figure 7a–c shows clearly that the differences between these two sections cannot be explained by the addition of any new parts, but rather by the conjoint expansion of the pyramid, the medial lemniscus and the inferior olive.

## Conclusions

Sets of structures in the brain stem of mammals, which are closely related to the neocortex, but form part of entirely different functional systems, form spatially constrained complexes, and have the capacity to expand jointly and harmoniously within the confines of these complexes. The mechanisms involved in these remarkable spatial regulations are entirely unknown.

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