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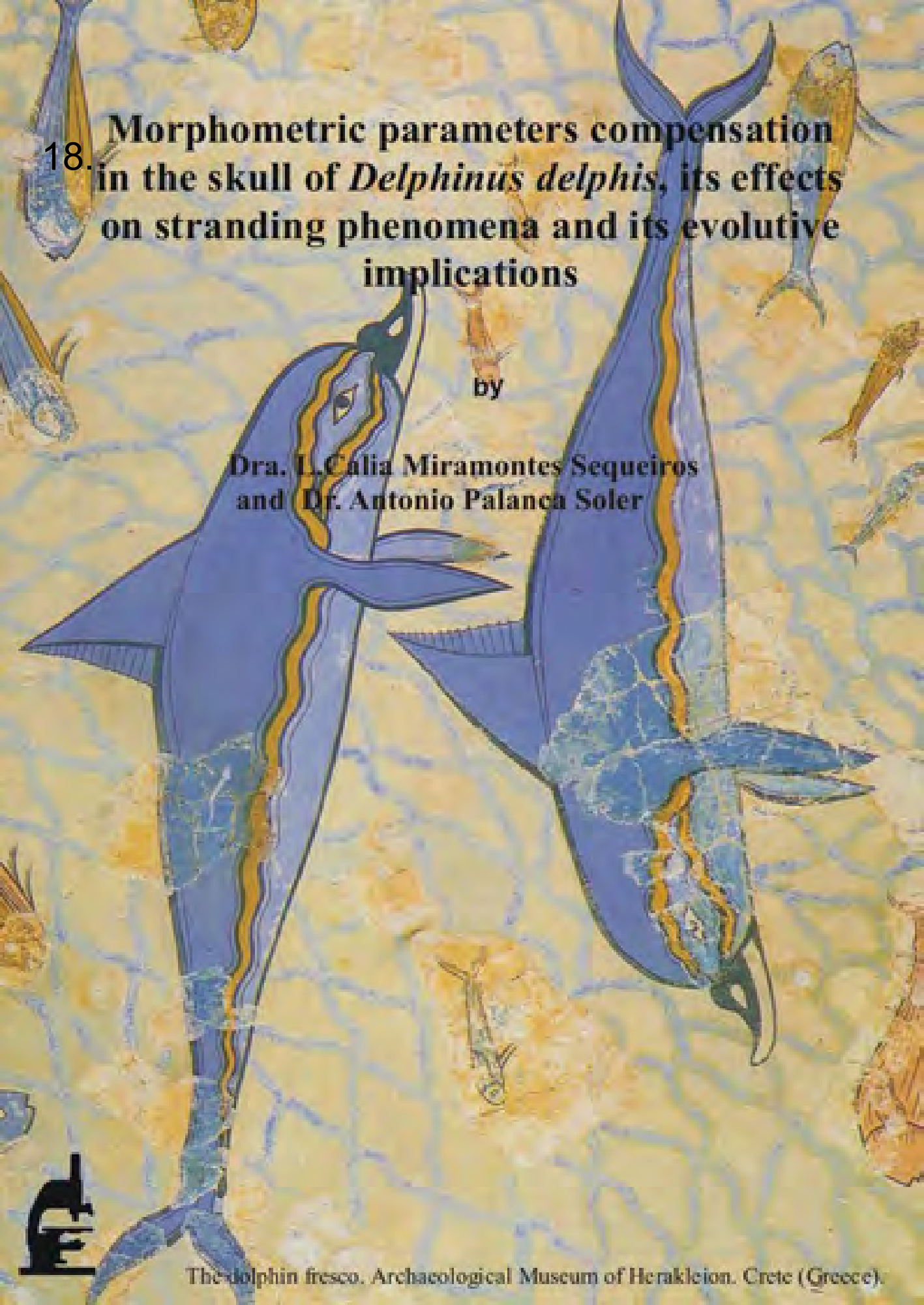
Morphometric parameters compensation in the skull of *Delphinus delphis*, its effects on stranding phenomena and its evolutive implications

by

Dra. Lª Cália Miramontes Sequeiros
and Dr. Antonio Palanca Soler



The dolphin fresco. Archaeological Museum of Herakleion. Crete (Greece).

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Acknowledgements

Dra. L. Calia Miramontes Sequeiros:

I would really like to thank Professor Dr. Antonio Palanca Soler for his human quality, his scientific shrewdness and for his great tenacity. Without all of that this work would never see the light.

Also I am in debt with the Animal Anatomy Laboratory Foundation for acceptting me as a patrono member and making possible all the financial activity of this investigation.

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A mis Padres, mi familia, a Gonzalo y a mis amigos por su apoyo incondicional a la libertad.

A Nicolás Palanca Castán, Fernando Miramontes Reinoso y Adam McKay por su ayuda en la tradución del manuscrito.

Y así es cómo los que nos iluminan son los ciegos.Y así es cómo alguien, sin saberlo, llega a mostrar irrefutablemente el camino que por su parte sería incapaz de seguir (Cortázar, J. 1984).

Part of this work was held as a Doctoral Thesis which obtained the maximum degree conceded by an international tribunal composed by five reputed Scientific Members.

Professor Dr. Antonio Palanca Soler, as Team leader of Animal Anatomy Laboratory:

Dedicated to all the official organisms and people that did not beleave in my personal management and supervising capacity because that forced me to make a serie of anatomical monographs. Also to all who help me to do it, where the co-author can be find.

Preface

The occipital bone of the craniovertebral region has been considered an unstable, “ontogenetically restless” skull zone and thus susceptible to the parameters variation that alter the occipital caudal fossae depth. This alteration can affect the cerebellum and the trigeminal nerve causing problems in *Delphinus delphis* aquatic adaptations. The morphometric parameters compensation could be addressed by an Anatomical Index. However, the variation of the occipital caudal fossae depth remains unclear. Here we show the occipital bone morphometric parameters compensation explained by a new morphometric index (Kalya Index). This is the first Anatomical Index that can be considered as a constant in *Delphinus delphis* species. Our results show the morphological genes harmony activity, contributing to the evolution laws comprehension and clarifying their understanding.

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Chapter 1

Study of *Delphinus delphis* skull: generalities

Diversity in the Mammalian Skull

When we review in detail the diversity morphology in the mammalian species skull we realize how the cetacean skull represents a homogeneity and different group within the class.

The order Cetacea includes whales, dolphins and porpoises, is divided into two suborders, Mysticeti (baleen whales) and Odontoceti (toothed whales, which includes dolphins and porpoises). Here we will study the skull of the common dolphin *Delphinus delphis* (family Delphinidae).

Distribution

Delphinus delphis is well distributed in warm temperate, subtropical, and tropical waters worldwide (Figure 1).

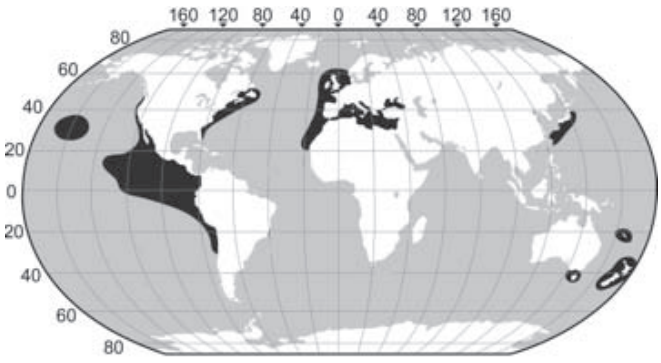


Figure 1. Map of Geographical Distribution of *Delphinus delphis.*

Factors that concentrate or disperse prey may secondarily affect the distribution and abundance of cetaceans. Therefore, it may be difficult to discriminate between the effects of environmental shifts due to climate change, whether ‘natural’ or a result of the greenhouse effect and other factors affecting the availability of dolphin prey, such as overfishing and habitat degradation.

Stranding phenomenon

Strandings occur when marine mammals swim or float into shore and become "beached" or stuck in shallow water. In most stranding cases, the cause of the stranding is unknown, but some identified causes have included disease, parasite infestation, harmful algal blooms, injuries due to ship strikes or fishery entanglements, pollution exposure, trauma, and starvation.

Once a cetacean comes ashore, a cascade of physiological changes occurs, often resulting in shock and death. Because the species typically involved are extremely social, the bonds that hold groups together are perhaps strong enough to supercede the survival instincts of individual animals. Although we don't know what specifically might set off a mass stranding event, we know that once animals start coming ashore, it's extremely difficult to stop the process from continuing and escalating. Affected animals will relentlessly follow one another ashore, as if crippled by widespread panic, even when there is clear access to open water.

Gregarious offshore species such as Atlantic white-sided dolphins (*Lagenorhynchus acutus*) and long-finned pilot whales (*Globicephala melaena*) are particularly known to mass strand in New England, mainly on Cape Cod.

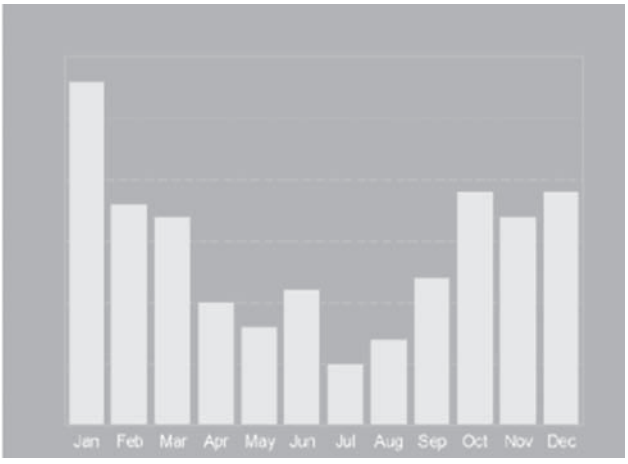
Some authors have studied the spatial and temporal links between some mass strandings of cetaceans - predominantly beaked whales - and the deployment of military sonar. They

present evidence of acute and chronic tissue damage in stranded cetaceans that results from the formation *in vivo* of gas bubbles, challenging the view that these mammals do not suffer decompression sickness.

The incidence of such cases during a naval sonar exercise indicates that acoustic factors could be important in the aetiology of bubble-related disease and may call for further environmental regulation of such activity.

The interest of this phenomenon has led us to study the differences in skull anatomy of the stranded *versus* non stranded specimens of *Delphinus delphis*, as a first step beginning with isolated or reduced groups' strandings leaving mass strandings for further studies.

In Graphic1 are represented the cumulative monthly frequencies of *Delphinus delphis* strandings for 24 years, from 1966 to 1990 (The Natural History Museum of London), where we can see the winter influence.



Graphic1. Cumulative monthly frequencies of *Delphinus delphis* strandings.

Phylogenetic hypothesis

Variation in the morphology of the cetacean body is almost certainly narrowly constrained by selection. The locomotor organs of all modern cetaceans are relatively similar, because the locomotor modes are similar. Hind-limb locomotion has been eliminated in favor of locomotion by movements of the vertebral column. Feeding variation is also limited within each of the suborders. Modern odontocetes have a large (polydonty), single (monophyodonty) series of repeated similar (homodonty) elements: simple peg-like teeth. There are no teeth in mysticetes, but food procurement in these forms also occurs by a large series of repeated, similar elements: the baleen plates.

Eocene cetaceans were very different; they had a wide variety of swimming modes and morphologies, from quadrupedal paddling in pakicetids to caudal oscillation in dorudontids. Similarly, feeding morphologies are different; all Eocene cetaceans were heterodont and diphyodont and had a stable number of teeth (10 or 11, depending on species, per jaw half).

In cetaceans there is a historical correlation between hind limb reduction and homogenization of the vertebral column. Both may be underlain by the same genetic changes, as they are in snakes. Furthermore, the similarities in genetic cassettes that are used in both limb and tooth development make it tempting to speculate that the similarities in historical pattern (loss of regionalization, repetition of elements) in locomotor system and dentition are underlain by the similar developmental patterns.

It is clear that selection played a pivotal role in identifying morphologies useful for the survival of Eocene cetaceans in their new, watery, environment, but development is at the root of producing the morphologies available for sorting. Studying the interaction of development and evolution is one of the most exciting challenges in evolutionary biology and one in which historical patterns in cetaceans may play a pivotal role.

In this phylogenetic hypothesis are shown the relations among all Eocene genera of cetaceans:

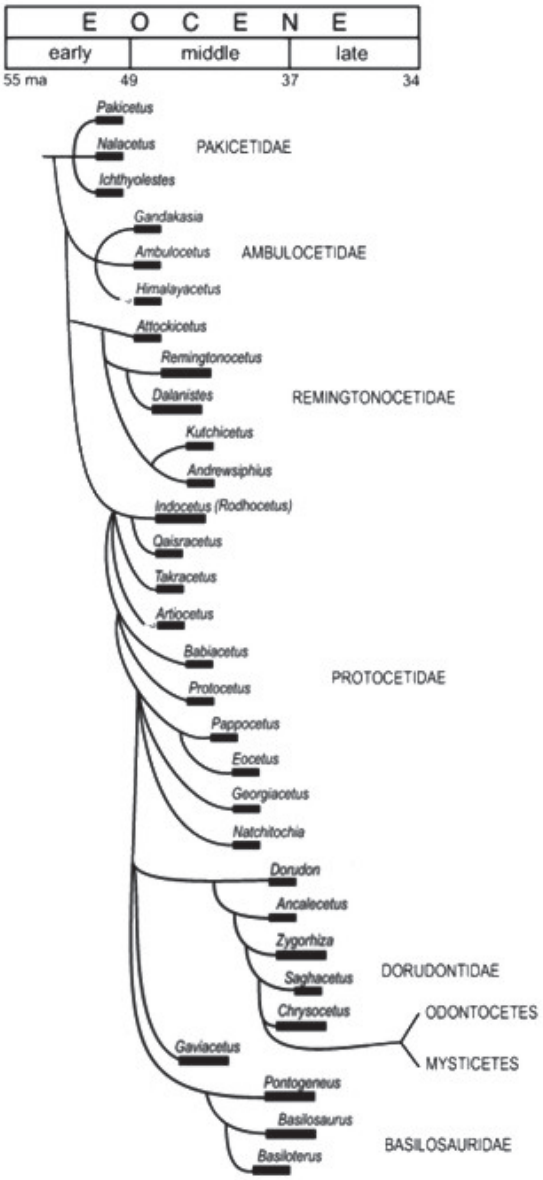


Figure 2. Phylogenetic hypothesis showing the relations among all Eocene genera of cetaceans. (Uhen 1998, 1999; Geisler 2001; Gatesy & O'Leary 2001; Thewissen & Hussain 2000; Thewissen et al. 2001a).

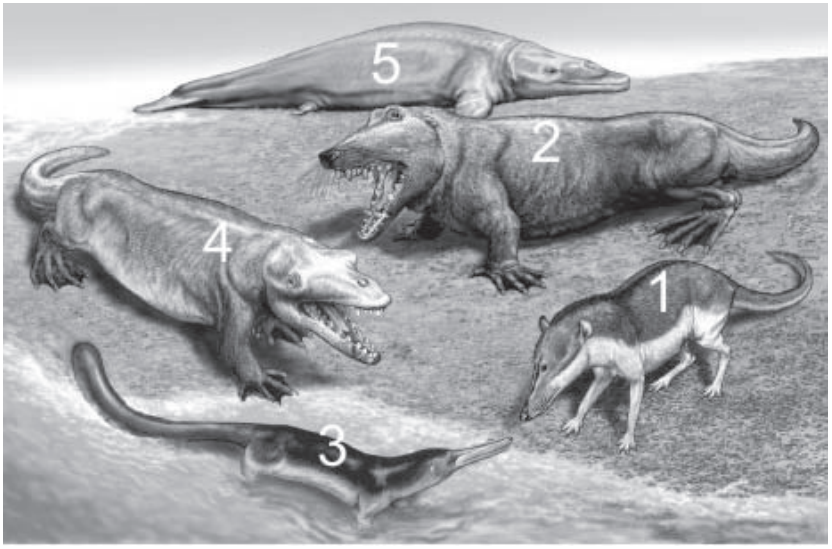


Figure 3. Drawing showing all Eocene genera of cetaceans. *Pakicetidae* 1; A*mbulocetidae* 2; *Remingtonocetidae* 3; *Protocetidae* 4; *Dorudontidae* 5. (Carl Buell, Annu. Rev. Ecol. Syst. 2002.33:73-90).

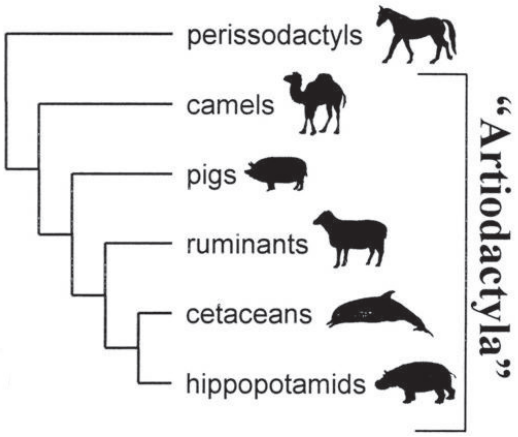


Figure 4. Cladogram depicting competing phylogenetic hypotheses for the position of cetaceans among ungulates. Cladogram supported by molecular data (*e.g.*, Gatesy *et al.*, 1999*a*), "Artiodactyla" is paraphyletic. Molecular sequence data alone cannot inform on the position of the wholly extinct clade Mesonychia. (O'Leary, M. A. *Integr. Comp. Biol*. 2001 41:487-506).

Cetacean evolution is one of several transitions across the land-water barrier documented in the history of vertebrate evolution. Through the fossil record and the living biota we can observe the hypothesized extremes of the continuum: a pig-sized, four-footed, mesonychid or artiodactylan, and an immense, hairless baleen or toothed whale with no functional hind limbs. These extremes beg the questions: when did such a transition happen, how long did it take, what character systems changed first, what did the intermediate forms look like, how did they move, what did they eat, and how were they distributed throughout the globe? Answers to these questions rely on having a highly corroborated hypothesis of phylogenetic relationships that becomes the building block or pattern upon which we base specific hypotheses of descent with modification. The diagnosis of clades through synapomorphy becomes the starting point for the investigation of functional, temporal, adaptive and biogeographic questions.

The position of cetaceans among mammals is currently unresolved. Many types of data still need to be collected for taxa relevant to this problem including osteology, soft tissues, behavior and molecular sequences.

Chiari Malformation

Chiari malformations (CMs) are structural defects in the cerebellum, the part of the brain that controls balance. When the indented bony space at the lower rear of the skull is smaller than normal, the cerebellum and brainstem can be pushed downward. The resulting pressure on the cerebellum can block the flow of cerebrospinal fluid (the liquid that surrounds and protects the brain and spinal cord) and can cause a range of symptoms including dizziness, muscle weakness, numbness, vision problems, headache, and problems with balance and coordination. There are three primary types of CM. The most common is Type I, which may not cause symptoms and is often found by accident during an examination for another condition. Type II (also called Arnold-Chiari malformation) is usually accompanied by a myelomeningocele -a form of spina bifida that occurs when the spinal canal and backbone do not close before birth, causing the spinal cord to protrude through an opening in the back. This can cause partial or complete paralysis below the spinal opening. Type III is the most serious form of CM, and causes severe neurological defects. Other conditions sometimes associated with CM include hydrocephalus, syringomyelia, and spinal curvature.

Chiari type I (CM1)

It is the congenital downward displacement of the cerebellar tonsils through the foramen magnum into the cervical canal; it is also associated with syringomyelia in up to 80% of cases.

In table 1 are shown some genetic disorders in which Chiari Type I malformation can co-occur.

Table 1. Summary of Genetic Disorders in Which Chiari Type I Malformation Can Co-Occur.

Disorder or syndrome	Known loci	OMIM reference numbers	CMI/disorder reference
Achondroplasia	4p16.3, fibroblast growth factor receptor-3 gene (*FGFR3*)	# 100800	(Nakai *et al.*, 1995; Orioli *et al.*, 1986)
Blepharophimosis (BPES)	3q23, (*FOXL2* gene)	#110100	(Paquis *et al.*, 1998)
Cleidocranial dysplasia	6p21, or core binding factor, runt domain, alpha subunit 1 (CBFA1, plays a role in osteogenesis)	#119600 #600211	(Yari *et al.*, 1996)
Crouzon syndrome	10q26 fibroblast growth factor receptor-2	#123500	(Cohen and Kreiberg, 1992; Fujisawa *et al.*, 2002)
Cystic fibrosis	7q31.2	#219700	(Needleman *et al.*, 2000; Steinberg and Brown, 1960)
Empty sella turcica, primary, with generalized dysplasia	One child with duplication of Xq13.3-q21.2	#130720	(Yokoyama *et al.*, 1992)
Growth hormone deficiency	17q22-q24, or growth hormone (GH1)	*139250 #173100	(Hamilton *et al.*, 1998; Lindsay *et al.*, 1994)
Hajdu–Cheney syndrome	No known linkage	#102500	(Sawin and Menezes, 1997)
Goldenhar syndrome (Hemifacial Microsomia) (HFM)	14q32	*164210	(Mesiwala *et al.*, 2001; Morrison *et al.*, 1992)
Hyperhidrosis	No known linkage	144110	(Stovner and Sjaastad, 1995)
Hypophosphatemic rickets	Xp22.2-p22.1	#307800	(Caldemeyer *et al.*, 1995)
Kabuki syndrome	No known linkage	147920	(McGaughran *et al.*, 2001; Niikawa *et al.*, 1988)
Klippel-Feil sequence	reported inversion (8) (q22.2), possibly segmentation syndrome 1 (SGM1)	#148900	(Ritterbusch *et al.*, 1991; Goldberg, 1987)
Neurofibromatosis type I	17q11.2	*162200	(Afifi *et al.*, 1988; Dooley *et al.*, 1993; Lazaro *et al.*, 1994; Parkinson *et al.*, 1986)
Paget's disease of bone	Genetically heterogeneous with mutations located at 18q22.1.	#602080	(Iglesias-Osma *et al.*, 1997)

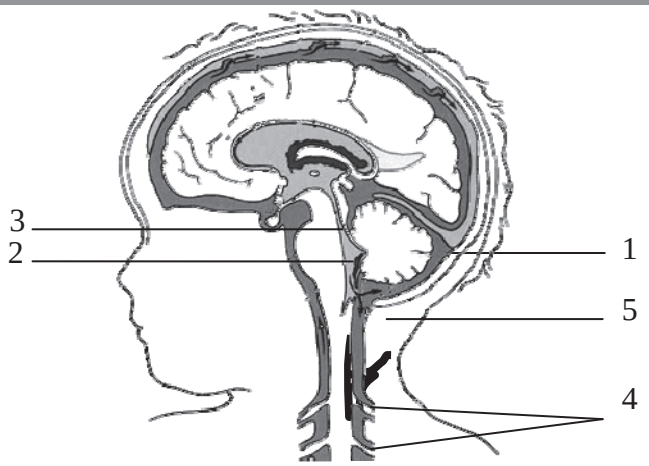


Figure 5. Example of Chiari type I in a child: 1: normal cerebellum; 2: fourth ventricle; 3: aqueduct of Sylvius;4: spinal nerves; 5: black outline shows CM1-cerebellar tonsils extending through foramen magnum.(Pediatric Section of the American Association of Neurological Surgeons and Congress of Neurological Surgeons, 2001).

In individuals with CM1, the malformation can cause:

- Headaches
- Ocular disturbances
- Lower cranial nerve signs
- Cerebellar ataxia
- Spasticity
- Primary cough headache (PCH)
- Otoneurologic disturbances
- Posterior fossa crowdedness
- Cerebellar spinal fluid space decrease
- Obstruction of the CSF flow at foramen magnum
- Smaller bony posterior fossa

Chiari type II (CM2)

Also known as the Arnold-Chiari malformation consists of elongation and descent of the inferior cerebellar vermis, cerebellar hemispheres, pons, medulla, and fourth ventricle through the foramen magnum into the spinal canal.

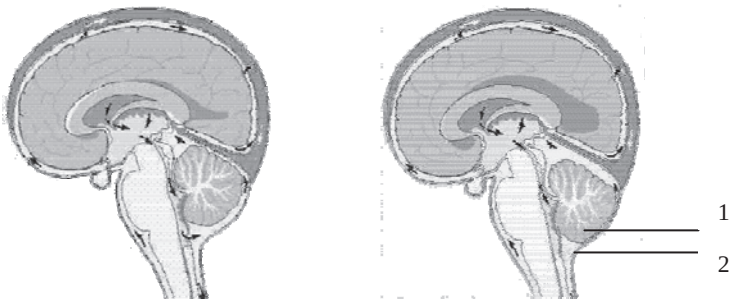


Figure 6. Pictures showing Chiari type II in an adult human. 1: obliteration of cisterna magna; 2: downward displacement and hypoplasia of the cerebellum.

In individuals with CM2, the malformation can cause:

- Spinal myelomeningocele
- Cerebellar hypoplasia
- Displacement of the tonsils
- Polygyria
- Elongated distal brainstem through enlarged foramen magnum
- Displacement of the tonsils
- Agenesis of the corpus callosum
- Ventricular abnormalities
- Subnormal intelligence
- Spina bifida
- Hydrocephalus
- Syringomyelia

Chiari type III (CM3)

It is characterized by caudal displacement of the medulla and herniation of part of the cerebellum in an occipital or cervical meningocele. Part of the hindbrain may also be herniated. Hydrocephalus is associated in 50% of cases.

In individuals with CM3, the malformation can cause:

- Encephalocele contained varying amounts of brain
- Hypoplasia of the low and midline aspects of the parietal bones
- Petrous and clivus scalloping
- Cerebellar hemisphere overgrowth
- Cerebellar tonsillar herniation
- Deformed midbrain
- Hydrocephalus
- Dysgenesis of the corpus callosum
- Posterior cervical vertebral agenesis
- Spinal cord syrinxes
- Occipito Cervical bony defect

Chiari type IV (CM4)

It refers to hypoplasia of the cerebellar hemipheres and alterations of the pons with marked dilatation of the fourth ventricle, cisterna magna, and basal cisterns.

In individuals with CM4, the malformation can cause:

- Hypoplasia of the cerebellar hemispheres
- Alterations of the pons
- Marked dilatation of the fourth ventricle
- Marked dilatation of the cisterna magna
- Marked dilatation of the basal cisterns
- A normal sized posterior fossa

Whereas Chiari types II, III, and IV are considered to be primarily neural in origin resulting from neuroectodermal anomalies, Chiari type I is considered to result from a mesodermal defect.

Methodology

Material

We reviewed 652 *Delphinus delphis* skulls deposited in marine mammal collections of the NMNH and NHM. All specimens were examined in detail, and all the morphometric measurements were taken with a digital calliper to the nearest 0.1 mm.

Catalogue number of Marine Mammal Collections from NMNH of Washington and NHM of Los Angeles will give the opportunity to other researches to repeat our measures.

Some information complementary to our measurements was recorded from the museums databases: X-Ray images; morphometric data; soft-tissues information; infestation, and other diseases and special conditions.

Mass strandings involving several hundred of animals have not been studied in this work.

Table 2. Catalogue number of *Delphinus delphis* Collections from NMNH of Washington and NHM of Los Angeles.

NMNH	**NMNH**	**NMNH**	**NHM**	**NHM**	**NHM**
A0000021917	572776	487834	31491	72407	91919
A0000021918	572859	487835	52320	72413	91917
A0000021919	572777	487836	54071	72414	91914
267478	572871	487837	54068	72412	91912
267968	572872	487821	54073	72411	91921
267969	572877	487822	54565	72417	91920
300191	572875	487823	54568	72418	91922
395120	572890	487826	54621	72416	91944
395121	572885	487825	54622	72415	91943
395768	572893	487828	54626	72420	91932
395773	572894	487829	54625	72419	91931
395858	572895	487850	54627	72425	91949
395859	572900	487849	54628	72423	91947
395860	572901	487853	54631	72426	91946
395861	572911	500047	54629	72428	91945
395862	572927	500048	54632	72495	91957
395863	572950	500049	54633	84067	91955
395865	572930	487840	54634	84134	91953
395923	572972	487839	54635	84171	91952
470545	572973	487843	54636	84155	91963
484902	572974	487847	54640	84172	91964
500272	572975		54641	84178	91961
500273	572977		54642	84208	91960
550261	572978		54643	84209	91968
550262	572979		54644	84207	91969
550450	572981		54732	84222	91967
550470	572980		54736	84224	91974
550475	482780		54738	84229	91973
550476	482779		54741	84226	91971
550478	482783		54743	84225	91970
550755	482784		54744	84255	91979
504107	482785		54745	84231	91980
504138	482786		54746	84257	95678
504202	482797		54748	84279	95675
504219	482798		72121	84283	95692
504240	482787		72120	85953	95691
504241	482788		72119	84280	95693
504263	482796		72126	86048	95695
504262	482795		72125	86003	95702
504264	482790		72124	86067	95697
504266	482789		72123	86070	95736
504268	482791		72130	86069	95723
504269	482792		72128	86068	95714

NMNH	NMNH	NMNH	NHM	NHM	NHM
504270	482794		72127	86075	95704
504271	482799		72133	86076	95744
504272	482800		72131	86077	95740
504276	482801		72138	86082	95739
504277	500081		72136	86083	95825
504278	500084		72142	86081	95829
504280	500083		72141	86080	95831
504281	500086		72139	86086	95830
504283	500085		72181	86087	95832
504284	500088		72144	86085	95833
504285	500087		72293	86084	95957
504407	500073		72304	88926	95965
504421	500074		72299	88945	95964
504616	500075		72333	91304	95966
504631	500076		72308	91318	95978
504838	500077		72307	91315	96431
504840	500078		72306	91317	96433
504839	500079		72336	91368	96435
504846	500080		72337	91369	96437
504878	487848		72335	91370	96438
504958	500066		72334	91373	96440
550003	500067		72340	91372	96442
550004	500068		72341	91371	96444
550006	500070		72339	91377	91981
550005	500069		72338	91378	91985
550007	500071		72345	91375	91982
550014	500072		72344	91376	91983
550041	500050		72343	91381	91987
550015	500060		72342	91382	91988
550206	500062		72348	91380	91990
550065	500061		72347	91379	92003
550211	500065		72346	91385	92001
550207	500063		72353	91386	92000
550205	500082		72352	91384	92008
550192	500099		72351	91383	92004
550201	500097		72350	91389	92007
550239	500129		72357	91390	92006
550240	500131		72355	91388	92012
550841	500089		72354	91387	92009
550819	500092		72361	91391	92011
550846	500091		72358	91394	92026
550849	500095		72359	91392	92025
550847	500096		72364	91397	92023
550875	500142		72365	91398	92015
550916	500141		72363	91396	92013
550938	500144		72362	91395	92028

NMNH	NMNH	NMNH	NHM	NHM	NHM
571232	500143		72368	91751	92029
571233	500146		72369	91752	92035
571234	500148		72367	91400	92037
571235	500147		72366	91399	92038
500269	500133		72372	91763	92055
504877	500134		72373	91764	92064
504849	500135		72370	91754	92075
504654	500136		72376	91753	92076
504820	500137		72377	91775	92090
504614	500138		72375	91776	92089
504323	500139		72374	91765	92078
571438	500140		72380	91783	92097
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571598	500263		72379	91778	92096
571620	500264		72378	91777	92092
571491	500266		72385	91859	92094
571621	500267		72382	91860	95669
571635	500256		72383	91853	
571655	487766		72388	91866	
572039	487767		72389	91867	
572110	487768		75387	91865	
572175	487769		72386	91861	
572128	487774		72392	91873	
572176	487773		72393	91872	
572256	487776		72391	91871	
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572617	487782		72400	91882	
572618	487791		72401	91891	
572619	487806		72402	91880	
572640	487807		72405	91896	
572632	487809		72406	91904	
572650	487810		72404	91893	
572652	487811		72403	91892	
572655	487830		72409	91909	
572714	487831		72410	91906	
572775	487833		72408	91905	

Occipital Area

The occipital bone forms the back part of the skull and the base of the cranium. It joins with the parietal and temporal bones. In the center, underside (inferior) portion of the cranium, there is a large opening called the foramen magnum, through which nerve fibers from the brain pass and enter into the spinal cord.

In figure 7 we can see the measures used in *Delphinus delphis* occipital bone to study this area. The measures were chosen in function of their anatomical and embryological origins; in this case only the related with a paraxial mesoderm origin (see Chapter 1).

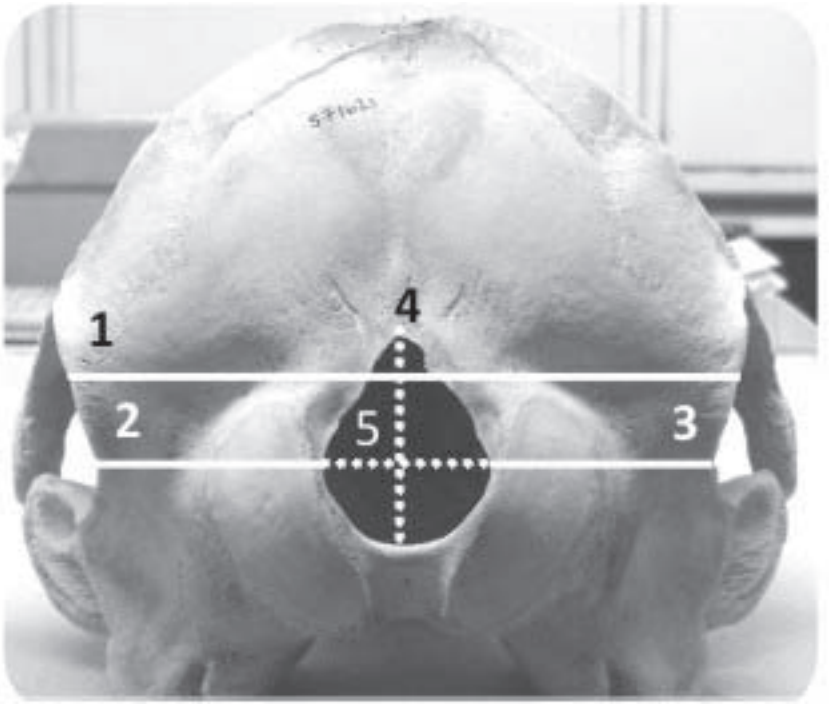


Figure 7. Measures taken in the occipital bone of *Delphinus delphis* for our study. 1: Maximum width of the Occipital bone; 2: Left width of the Occipital bone; 3: Right width of the Occipital bone; 4: Anteroposterior diameter of the Foramen Magnum; 5: Transversal diameter of the Foramen Magnum.

Premaxillary foramina

To find a relation between ectomesenchymal and paraxial mesoderm bones we studied the premaxillary foramina ossification in the course of Trigeminal nerve, from Foramen magnum to Premaxillary foramina:

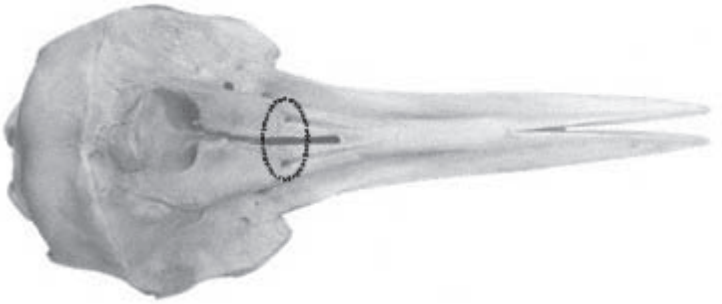
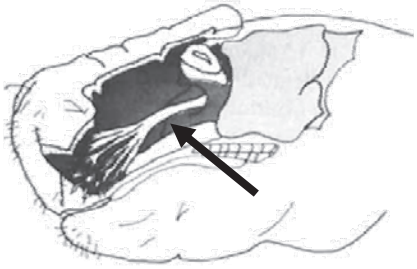
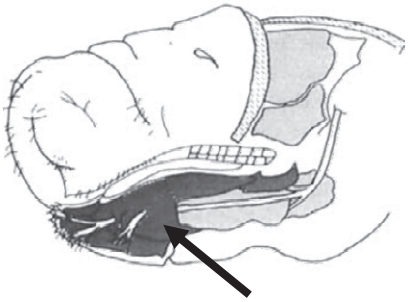


Figure 8. *Delphinus delphis* skull in dorsal view, inside the circle we can see the premaxillary foramina.

- Infraorbital branches: Ophtalmic and Maxillary

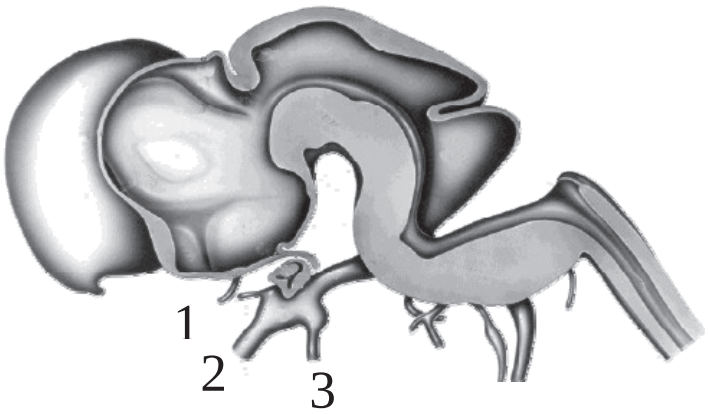


- Inferior alveolar branches: Mandibular



Mediosagittal view of a sperm whale brain graphic reconstruction:

- Infraorbital branches: Ophtalmic 1 and Maxillary 2
- Inferior alveolar branches: Mandibular 3



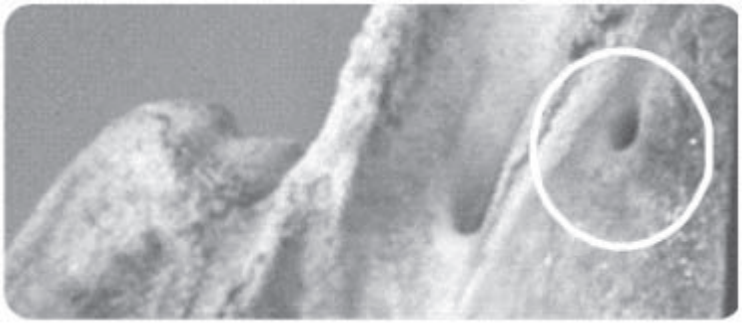
Graphic 2. Graphic reconstruction in mediosagittal view of a sperm whale brain, where the main trigeminal nerve ganglia is showed with the three ramifications: 1:Infraorbital Ophtalmic branch; 2: Infraorbital Maxillary branch; 3:Inferior Alveolar Mandibular branch.

These foramina of the premaxilla serve as apertures for infraorbital branches of the trigeminal nerve. This nerve exits the maxilla in all other mammals, including mysticetes.

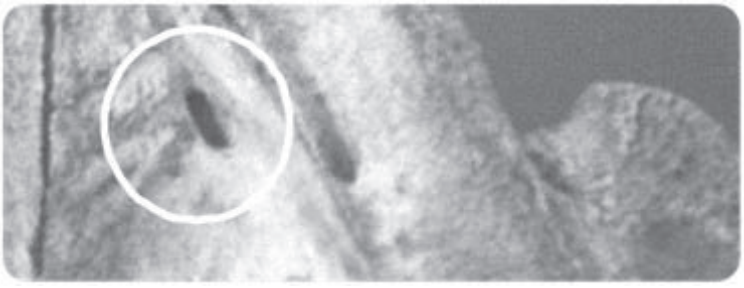
In function of their shape we have found three main different types of Ossification Degree of the Premaxillary foramina: round-shaped, elliptic-shaped and two-hole-shaped.

The round-shaped is defined as a ”high ossification degree”, because we can see one hole; the elliptic-shaped is defined as an “intermediate ossification degree”; and finally, the two-hole-shaped is defined as a “low ossification degree” in this case we can see two holes in each side of the premaxillary foramina:

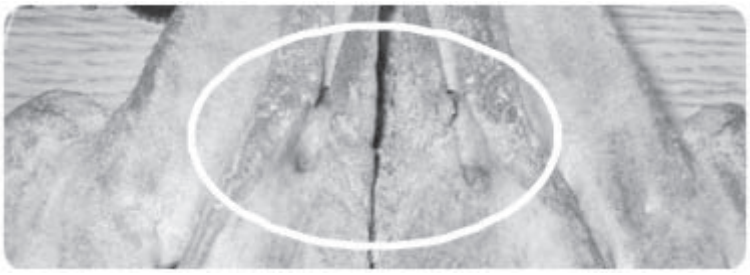
High



Intermediate



Low



General Anatomy of *Delphinus delphis* occiput derived from paraxial mesoderm:

Basic principles of *Delphinus delphis* skull anatomy

Skull bones have two different anatomical and embryological origins:

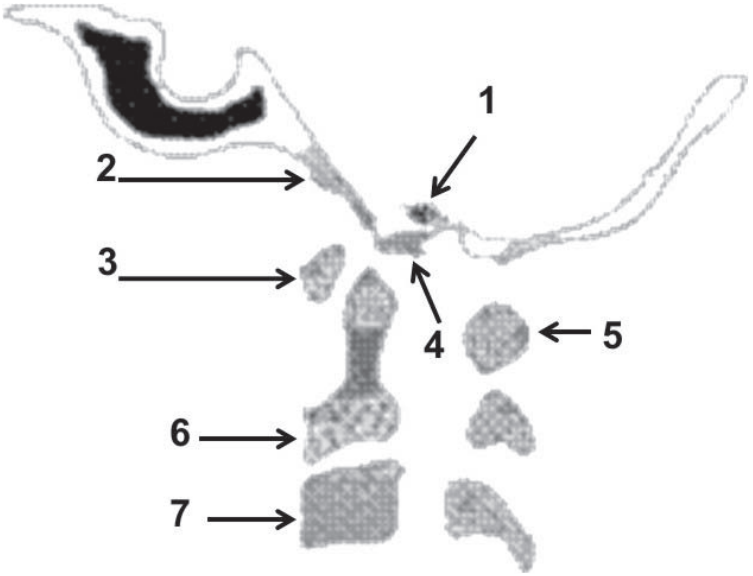
- Skull bones originated from ectomesenchyme:
  - Supraoccipital

- Skull bones originated from paraxial mesoderm:
  - Basioccipital
  - Exoccipital
  - Occipital condyles
  - Foramen magnum

Craniovertebral region

Head (occipital) somites which have a metameric origin develop from proliferation of local mesenchyme lateral to the cranial end of the notochord. The definitive structures formed by the sclerotome segments are:

1. Hypoglossal canal
2. Basiocciput
3. Anterior arch of the atlas
4. Occipital condyles
5. Posterior arch
6. Axis
7. Third cervical vertebra



In humans the cervico-occipital junction develops between the last occipital and first cervical sclerotomic segments. Normally, the less cellular, loose cranial part of the fourth occipital sclerotome with the remaining three occipital sclerotomes located rostral to it forms the basiocciput. The more cellular dense caudal part of the fourth occipital sclerotome segment, differentiates into exoccipital and also participates in the formation of occipital condyles laterally. It also contributes to the formation of the basiocciput medially.

Occipital region variability

Occipital bone Dysplasia:

One abnormality of the development of the canine occipital bone is the occipital dysplasia where there is an incomplete ossification of the supraoccipital bone, resulting in the widening of the foramen magnum.

Syringomyelia:

It consists in an irregularly shaped cavitation of the cord centred upon the spinal canal and extending as fissures into adjacent grey and white matter the cavitation extends to the dorsal and ventral subdural space. It is associated with an abnormality at the foramen magnum, particularly the Chiari malformation type I (CM1), as well as other malformations.

Occipital bone hypoplasia:

Occipital hypoplasia in dogs results in reduced volume of the caudal fossa, leading to overcrowding of the neural structures and, in severe cases, development of syringomyelia.

Occipitalization of the atlas:

The total occipitalization of the atlas results in a bilateral obliteration of the atlanto-occipital joints.

Occipital bone

It forms from fusion of the mesenchyme of at least three occipital somites. In human fetuses the mesenchyme forms cartilage which in turn undergoes the process of endochondral ossification to form bone.

Foramen Magnum

It is a ring of bone formed from four occipital bone centres:

- supraoccipital bone dorsally,
- basilar part ventrally,
- both exoccipitals that bear the occipital condyles laterally.

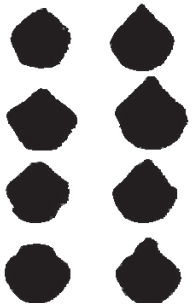
Dorsal notch of the foramen magnum

It is the variation in the degree of ossification of the ventro-medial part of the supraoccipital bone.

Morphological Variability of the Foramen magnum due to the dorsal notch:

Without dorsal notch

With dorsal notch



The caudal fossa

It is part of the intracranial cavity, located between the foramen magnum and tentorium cerebelli. This is the most inferior of the fossa. It houses the cerebellum, medulla and pons. Anteriorly it extends to the apex of the petrous temporal. Posteriorly it is enclosed by the occipital bone. Laterally portions of the squamous temporal and mastoid part of the temporal bone form its walls. It contains critical motor and sensory areas and houses cranial nerves III through XII.

Chapter 2

Anatomical Laws in the Species Evolution and Patterns of development in the Occipital region of *Delphinus delphis*

In the Developmental Anatomical Laws studies many biometrical indexes are used. All of them employ two variables and the variables proportion is maintained. Our Index (Kalya Index), with four variables, is constant in this species and allows the study of different morphotypes. In this Index, there is the possibility of compensating the variation of a first variable, with the variation of a second one, to maintain the same proportion but not the shape.

In our Index the variables can have different correlation degree in function of the studied species. If different morphotypes occur in the same species in function of Sex, Geographical distribution, Stranding, etc…, different means and variances are supposed to be found at least in two of the four variables studied.

The Kalya Index is constant in all the specimens of *Delphinus delphis* and allows us to make a comparative base to study the other variables involved in the Occipital bone. It compensates the other variables fluctuation converting them in one constant that could be interpreted as a first Anatomic Concordance Law (Kalya Index variables: Width of the Right + Left Occipital bone, excluding the FM, Transverse Diameter of the Foramen Magnum, and the Width Occipital bone) .

Two groups of dolphins are observed with significant different means. One group is composed by the stranded dolphins with a caudal fossa depth smaller than the second group composed by the non stranded dolphins.

The Degree of Ossification of the Premaxillary Foramina, as a synonym of osteopetrosis, is one of the principal variables that discriminates the Stranded and Captured dolphins. Taking into account that almost 99% of the anomalities described in Stranded dolphins can be associated with a typical clinical expression of the Chiari's disease, and that osteopetrosis is a typical symptom of Chiari's disease, we can conclude that at least the 50% of the Stranded dolphins of our study are due to suffer from this disease.

Biometrical Indexes Used by other authors:

1.-The “Area of the Foramen Magnum” by using the formula: 1/4 WH, where W = width and H = height of the foramen magnum.

2.-The “Index of the Foramen Magnum” was calculated by dividing the AP diameter of the FM by the transverse diameter.

3.-The “Actual Area of the Foramen Magnum” of the occipital bone using the formula of Radinsky (1967): Area = $\pi \times 1/4 \times W \times H$. Where W is the maximum width of the foramen magnum and H is its maximum anteroposterior diameter in the median plane.

4.-The “Relative Index of the Foramen Magnum” width/height x 100.

5.-The “Inverse Index of the Foramen magnum”, defined as the ratio between the maximal width and the total height of the foramen.

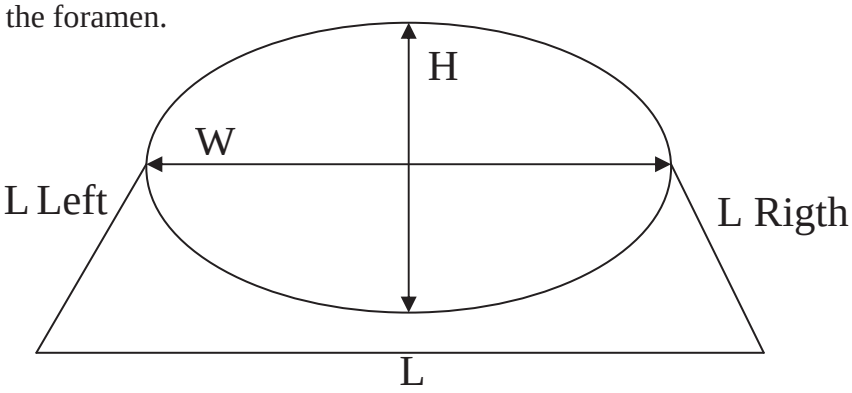


Figure 9. This Picture represents dolphins Foramen magnum; W: Width of the Foramen Magnum; H: High of the Foramen Magnum; L Left: Left width of the Occipital bone; L Right: Right width of the Occipital bone.

We did not find any interesting scientific conclusions after this indexes calculation.

Kalya Index

The Kalya Index is the percentage of the addition of the Width of the Right and Left Occipital bone and Transverse Diameter of the Foramen Magnum divided by the Maximum Width of the Occipital bone.

To compensate the fluctuant asymmetry both lateral widths of the occipital bone were taken into account, excluding the variability due to the dorsal notch (H). So we can optimize most variables of the Occipital bone area of the skull.

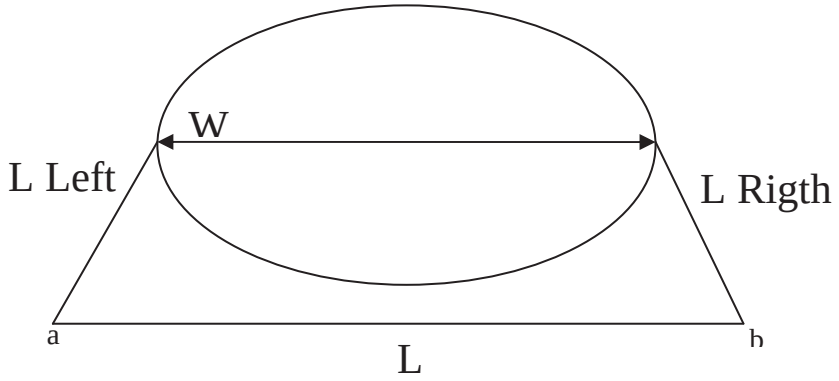


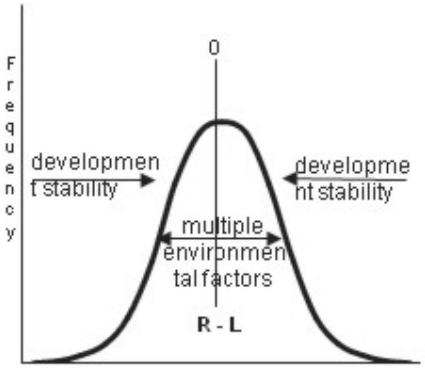
Figure 10. This Picture represents dolphins' Foramen magnum; W: Width of the Foramen Magnum; L Left: Left width of the Occipital bone; L Right: Right width of the Occipital bone.

Kalya index calculation:

$$L\ right + L\ left + W / ab * 100$$

This Index does not take into account the High of the Foramen Magnum because it can be an anatomical expression of the dorsal notch morphological variability.

Random deviation from the perfect symmetry of normally symmetrical characters for an individual with a given genotype occurs during individual development due to the influence of multiple environmental factors, named Fluctuant Asymmetry (FA).



Graphic 2. Fluctuant Asymmetry.

In the following quantitative genetic model of occipital region it is possible to explain the relationships between the multiple environmental factors that increase the Fluctuant Asymmetry values, which includes the specimens own's genome as well as other effects like uterine effects, postnatal nursing effects and non-maternal environment.

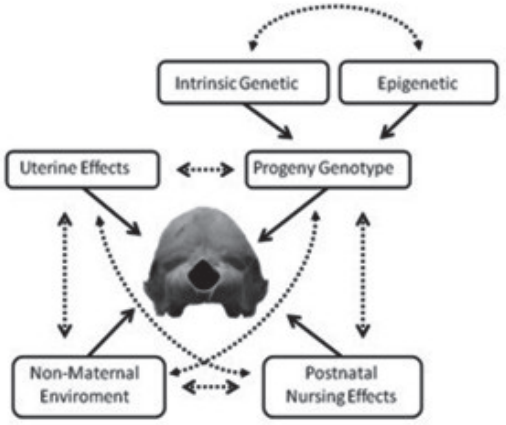


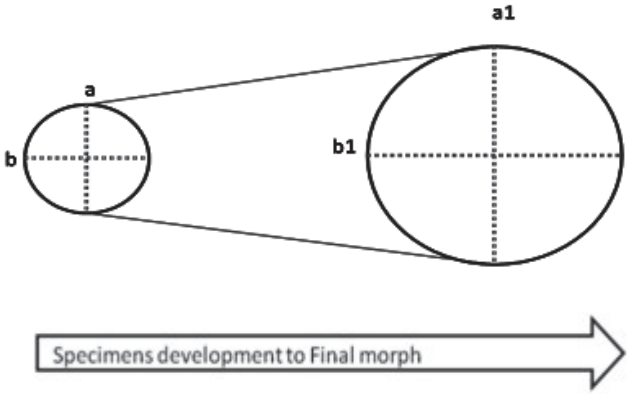
Figure 11. Environmental and genetic effects model of occipital region. Solid lines with single-headed arrows represent the action of causal factors; dashed lines with double-headed arrows represent interactions between causal factors.

2008 (4), Miramontes Sequeiros L.C., Palanca Soler, A., Morphometric parameters compensation in the skull of Delphinus delphis, its effects on stranding phenomena and its evolutive implications, Rev. Fenol. Anat (https://anatolab.net/fundacion/FENOMICA/1998-2018.html)

Index with two variables

In another indexes, the variables proportion is maintained:

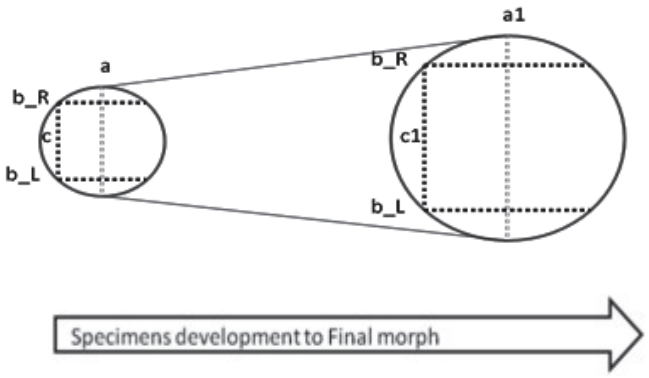
$$b/a = b1/a1$$



Index with four variables (Kalya Index)

In the Kalya Index, there is the possibility of compensating the variation of variable b, with the variation of variable c, to maintain the same proportion but not the shape.

$$b\_L + b\_R + c/a = b\_L1 + b\_R1 + c1/a1$$

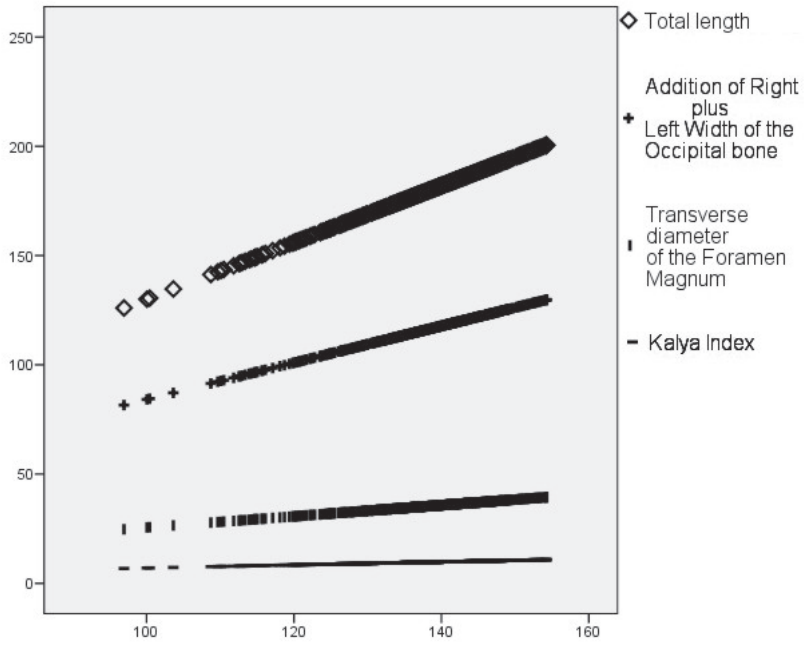


Pearson's correlation coefficient among the variables and the Kalya Index was calculated. Correlation is significative at the level 0,01 (bilateral). Total Length shows a great correlation with all the occipital bone variables, the Kalya Index is constant in all the specimens measured of *Delphinus delphis*, compensating all the variables used to calculate it. Due to this compensation, this index allows us to make a comparative base to study the other Occipital bone morphotypes.

Table 3. Pearson's correlation coefficient between the total length and width of the occipital bone, sum of the left and rigth width of the occipital bone (S_LR_occ), transverse diameter of the foramen magnum and Kalya index. ** Correlation is significative at the level 0,01 (bilateral).

		Total Length
Width of the Occipital bone	Pearson's correlation	,798(**)
	Sig. (bilateral)	,000
	N	563
S_LR_occ	Pearson's correlation	,709(**)
	Sig. (bilateral)	,000
	N	548
Transverse Diameter of the Foramen Magnum	Pearson's correlation	,591(**)
	Sig. (bilateral)	,000
	N	559
Kalya Index	Pearson's correlation	,128(**)
	Sig. (bilateral)	,003
	N	543

In our index the variables fluctuation is compensated (Width of the Right + Left Occipital bone, excluding the FM + Transverse Diameter of the Foramen Magnum, and the Width Occipital bone) converting them in one constant that could be interpreted as a first Anatomic Concordance Law (see Graphic 3).



Graphic 3. Linear correlation among the variables and the Kalya Index.

The last position is the Index that stays constant, and characterizes the studied species.

Study of the differences in occipital bone anatomy of the stranded *versus* non stranded specimens of *Delphinus delphis:*

Testing possible morphotypes

To test the normality of all variables studied in our data we used the Kolmogorov-Smirnov Test among Stranded and Captured specimens of *Delphinus delphis,* in all the cases, the variables studied fit the normal distribution.

Stranding

As we can see in table 4, the Kalya Index and the Transverse Diameter of the Foramen Magnum have a homogeneous variance among stranded and captured specimens.

Table 4. Showing the homogeneity of Variance of the variables among the Stranded and Captured specimens of *Delphinus delphis.*

	Levene's test	gl1	gl2	Sig.
Total Length	6,833	1	568	,009
Width of the Occipital bone	9,348	1	638	,002
S_LR_occ	17,457	1	621	,000
Transverse Diameter of the Foramen Magnum	,198	1	633	,656
Kalya Index	,088	1	616	,766

Table 5. Fisher's ANOVA of the variables among the Stranded and Captured specimens of *Delphinus delphis*:

		Sum of squares	gl	Quadratic mean	F	Sig.
Total Length	Inter-groups	49994,99	1	49994,99	70,7	,000
	Intra-groups	401302,06	568	706,51		
	Total	451297,05	569			
Width of the Occipital bone	Inter-groups	2499,85	1	2499,85	32,3	,000
	Intra-groups	49291,05	638	77,25		
	Total	51790,90	639			
S_LR_occ	Inter-groups	1162,58	1	1162,58	13,9	,000
	Intra-groups	51640,17	621	83,15		
	Total	52802,76	622			
Transverse Diameter of the Foramen Magnum	Inter-groups	229,37	1	229,37	23,1	,000
	Intra-groups	6274,10	633	9,91		
	Total	6503,47	634			
Kalya Index	Inter-groups	,023	1	,023	,002	,962
	Intra-groups	6361,16	616	10,32		
	Total	6361,19	617			

The ANOVA study (Table 5) reported significant results for mean differences in all the variables, except in the Kalya Index which stays constant, among Stranded and Captured specimens of *Delphinus delphis.*

We conclude that the Stranded and Captured specimens of *Delphinus delphis* have a different anatomical skull structure.

The anatomical skull studies should consider the stranding condition as the first and most important variable.

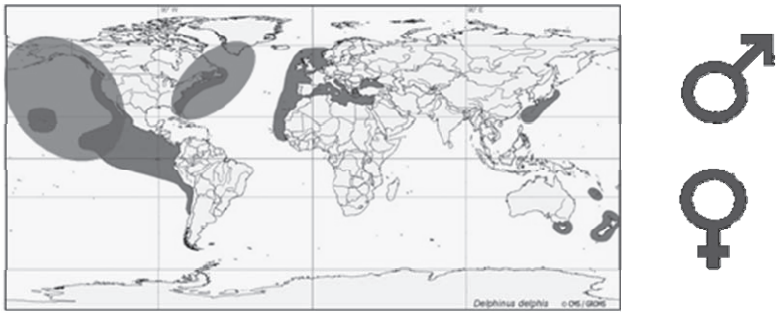
Geographical distribution of the studied specimens of Delphinus delphis

The Captured specimens from the North Atlantic Ocean have a low valid number so they were not included in any analysis.

Table 6. Geographical distribution of the studied specimens of *Delphinus delphis.*

		N valid
North Atlantic	Stranded	82
	Captured	11
North Pacific	Stranded	122
	Captured	403
Unknown		30

Figure 12. Distribution map of the studied specimens of *Delphinus delphis*: Stranded specimens from North Atlantic Ocean and stranded and captured specimens from North Pacific Ocean.



These tables below show the matrix of correlation comparing values for the three Principal Components of the measures taken in the Stranded specimens of *Delphinus delphis* from the North Atlantic and North Pacific Ocean.

In function of this statistical analysis the variables studied show a similar behaviour in Stranded specimens from the North Atlantic and North Pacific Ocean; as a result the stranded populations studied are similar.

It can be concluded that the Geographical distribution does not have a significant effect in the occipital proportions of the stranded populations studied.

Table 7. Matrix of correlation comparing values of the three Principal Components of the measures taken in the Stranded specimens of *Delphinus delphis* from the North Atlantic Ocean.

	Principal Components		
	1	2	3
Width of the Occipital bone	,905		
Width of the Left Occipital bone, excluding the FM	,902		
Width of the Right Occipital bone, excluding the FM	,862		
Degree of Ossification of the Right Premaxillary Foramina	-,441	,789	
Degree of Ossification of the Left Premaxillary Foramina	-,528	,664	
Anteroposterior Diameter of the Foramen Magnum		,601	-,552
Transverse Diameter of the Foramen Magnum		,511	-,667

Table 8. Matrix of correlation comparing values of the three Principal Components of the measures taken in the Stranded specimens of *Delphinus delphis* from the North Pacific Ocean.

	Principal Components		
	1	2	3
Width of the Left Occipital bone, excluding the FM	,953		
Width of the Right Occipital bone, excluding the FM	,934		
Width of the Occipital bone	,879		
Degree of Ossification of the Left Premaxillary Foramina		,883	
Degree of Ossification of the Right Premaxillary Foramina		,874	
Anteroposterior Diameter of the Foramen Magnum			,847
Transverse Diameter of the Foramen Magnum			,807

These tables below show the matrix of correlation comparing values for the three Principal Components of the measures taken in the Captured and Stranded specimens of *Delphinus delphis* from the North Atlantic and North Pacific Ocean.

In function of this statistical analysis the variables studied show a different behaviour in the Captured and Stranded specimens from both Oceans; as a result the stranded and captured populations studied are not similar.

It can be concluded that the Geographical distribution does not have a significant effect in the occipital proportions of the stranded and captured populations studied, thus their differences are based on their anatomical design, particularly in the Transverse Diameter of the Foramen Magnum.

Table 9. Matrix of correlation values of the three Principal Components of the measures taken in the captured specimens of *Delphinus delphis* from North Pacific and North Atlantic Ocean.

Captured specimens of both Oceans	Principal Components		
	1	2	3
Width of the Occipital bone	,959		
Width of the Left Occipital bone, excluding the FM	,907		
Width of the Right Occipital bone, excluding the FM	,890		
Transverse Diameter of the Foramen Magnum	,716		
Degree of Ossification of the Left Premaxillary Foramina		,952	
Degree of Ossification of the Right Premaxillary Foramina		,950	
Anteroposterior Diameter of the Foramen Magnum			,790

Table 10. Matrix of correlation values of the three Principal Components of the measures taken in the stranded specimens of *Delphinus delphis* from North Pacific and North Atlantic Ocean.

Stranded specimens of both Oceans	Principal Components		
	1	2	3
Width of the Left Occipital bone, excluding the FM	,924		
Width of the Right Occipital bone, excluding the FM	,904		
Width of the Occipital bone	,895		
Degree of Ossification of the Left Premaxillary Foramina		,809	
Degree of Ossification of the Right Premaxillary Foramina		,802	
Anteroposterior Diameter of the Foramen Magnum		,520	-,674
Transverse Diameter of the Foramen Magnum		,571	-,666

Sex

Table 11. Descriptive Statistics of the Geographical Distribution and Sex among the Stranded and Captured studied specimens of *Delphinus delphis.*

		Sex	N
North Atlantic	Stranded	Female	27
		Male	43
	Captured	Female	5
		Male	5
North Pacific	Stranded	Female	45
		Male	58
	Captured	Female	194
		Male	207

In this case, differences due to sex are not statistical significant.

Other authors reported the existence of morphometric characters related to sexual dimorphism but our measures do not support their results, may be due to our selected morphometric characters.

Total Length

Table 12. Descriptive Statistics of the Total Length in our data.

		Sex	N	Mean	SE	Variance
North Atlantic Ocean	Stranded	Female	25	206,3	4,7	556,3
		Male	43	214,6	2,2	225,3
	Captured	Female	3			
		Male	2			
North Pacific Ocean	Stranded	Female	44	174,9	2,7	335,4
		Male	52	186,1	2,2	260,1
	Captured	Female	187	168,6	1,9	696,4
		Male	199	175,1	2,0	798,8

Geographical differences in the means of the Total Length were found, as it was reported in the literature.

Significant differences within the same Ocean between Stranded and Captured specimens of *Delphinus delphis* were also found.

Total Length effect in Stranded versus Captured specimens from North Pacific Ocean

Significant differences in stranded versus captured specimens of *Delphinus delphis* from North Pacific Ocean were found.

Table 13. Homogeneity of Variance of the Total Length measured in the Stranded and Captured specimens of *Delphinus delphis* from the North Pacific Ocean.

Levene's test	gl1	gl2	Sig.
25,634	1	485	,000

Table 14. Fisher's ANOVA of the Total Length measured in the Stranded and Captured specimens of *Delphinus delphis* from the North Pacific Ocean.

	Sum of squares	gl	Quadratic mean	F	Sig.
Inter-groups	6292,211	1	6292,211	9,416	,002
Intra-groups	324100,964	485	668,249		
Total	330393,175	486			

Total Length effects in Male Stranded versus Male Captured in North Pacific Ocean

Significant differences in Total Length between male stranded versus male captured specimens from the North Pacific Ocean were found.

Table 15. Homogeneity of Variance of the Total Length measured in the female Stranded versus female Captured specimens of *Delphinus delphis* from the North Pacific Ocean.

Levene's test	gl1	gl2	Sig.
18,823	1	249	,000

Table 16. Fisher's ANOVA of the Total Length measured in male Stranded versus male Captured specimens of *Delphinus delphis* from the North Pacific Ocean.

	Sum of squares	gl	Quadratic mean	F	Sig.
Inter- groups	4962,541	1	4962,541	7,208	,008
Intra- groups	171438,482	249	688,508		
Total	176401,023	250			

Despite the significant means difference the variances do not have it in the following analysis:

- Total Length effect in North Pacific Stranded versus North Atlantic Stranded specimens.
- Total Length effects in Female Stranded versus Female Captured in North Pacific Ocean.
- Total Length effects in Male from North Pacific Stranded versus Male North Atlantic Stranded.
- Total Length effects in Stranded Female from North Pacific versus Stranded Female from North Atlantic.

Premaxillary foramina

The stranded specimens have a bigger percentage of high ossification degree of the premaxillary foramina in relation to the captured specimens.

Table 17. Descriptive Statistics of the Degree of Ossification of the Premaxillary Foramina in the measured Stranded and Captured specimens of *Delphinus delphis.*

	Degree of ossification	% of population	N
Stranded	High	49,0 %	81
	Low	43,6%	72
	Intermediate	7,4%	12
Captured	High	27,1%	106
	Low	65,8%	257
	Intermediate	7,1%	28

Table 18. Contingency table of the Degree of Ossification of the Premaxillary Foramina in the measured Stranded and Captured specimens of *Delphinus delphis.*

	Degree of ossification			Total
	High	Low	Intermediate	
Stranded	105	102	18	225
Captured	117	269	31	417
Total	222	371	49	642

Table 19. χ- square tests of the Degree of Cacification of the Premaxillary Foramina in the Stranded and Captured specimens of *Delphinus delphis.*

	Value	gl	Asympt. Sig. (bilateral)
Pearson's χ -square test	23,996(a)	2	,000
Maximum Likelihood	23,773	2	,000
Linear by Linear Association	13,592	1	,000
N valid	642		

The Degree of Ossification of the Premaxillary Foramina is a character with significant differences between Stranded and Captured specimens of *Delphinus delphis.*

“Ni son todos los que están ni están todos los que son” “Not all those present should be here, nor are all those which should be here present".

So, as it was impossible to know the number of captured dolphins that were not going to strand in either data, and we do not know if within the stranded specimens we have some dead due to other diseases, infestations or antropic traumatisms.

First we tried to discriminate between Stranded and Captured dolphins taking into account the following variables: Total Length, Width of the Occipital bone, S_LR_occ, Degree of Ossification of the Premaxillary Foramina, Transverse Diameter of the Foramen Magnum (Tables 20 and 21).

Table 20. Wilks' lambda distribution corresponding to the analysis made in the Table 21.

Contrast of Functions	Wilks’ Lambda	χ-Square	gl	Sig.
1	,880	68,687	5	,000

Table 21. Matrix of structure showing the combined intra-group correlations among the discriminant variables (Total Length, Width of the Occipital bone and Sum of the Left and Right Width of the Occipital bone (S_LR_occ), Degree of Ossification of the Premaxillary Foramina, Transverse Diameter of the Foramen Magnum) and the typificated canonical discriminant functions. These variables were arranged by their correlation with the function.

	Function 1
Total Length	,853
Width of the Occipital bone	,556
S_LR_occ	,446
Degree of Ossification of the Foramina	-,394
Transverse Diameter of the Foramen Magnum	,313

But the problem is that the discriminating distribution is not good (Wilks' Lambda, 0,880).

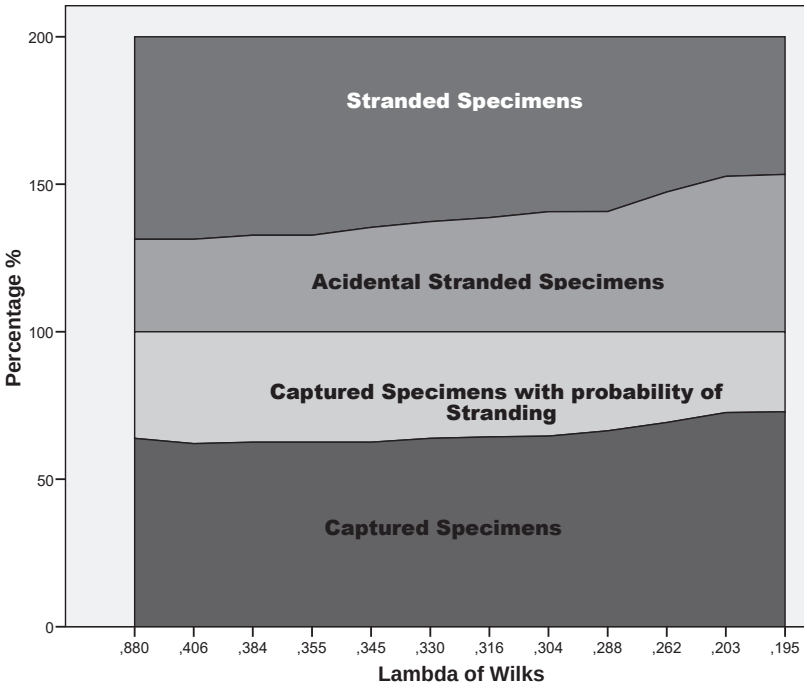
The forecast of the belonging group values have been used with success as a gathering variable until the Wilks' lambda distribution was minimized (Tables 22 and 23).

Table 22. Wilks' lambda distribution corresponding to the analysis made in the Table 23.

Contrast of Functions	Wilks' Lambda	χ-Square	gl	Sig.
1	,195	875,509	5	,000

Table 23. Matrix of structure showing the combined intra-group correlations among the discriminant variables (Total Length, Width of the Occipital bone, Sum of the Left and Right Width of the Occipital bone (S_LR_occ), Degree of Ossification of the Premaxillary Foramina, Transverse Diameter of the Foramen Magnum) and the typification of the canonical discriminant functions. The variables were arranged according to their correlation with the function.

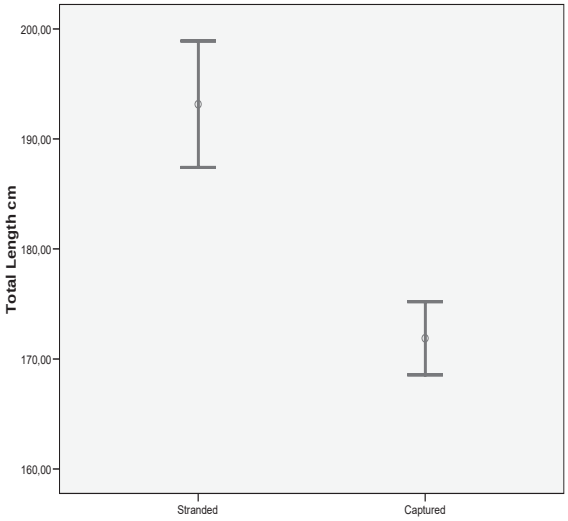
	Function 1
Degree of Ossification of the Premaxillary Foramina	,997
Transverse Diameter of the Foramen Magnum	-,059
Total Length	-,049
Width of the Occipital bone	-,039
S_LR_occ	-,029



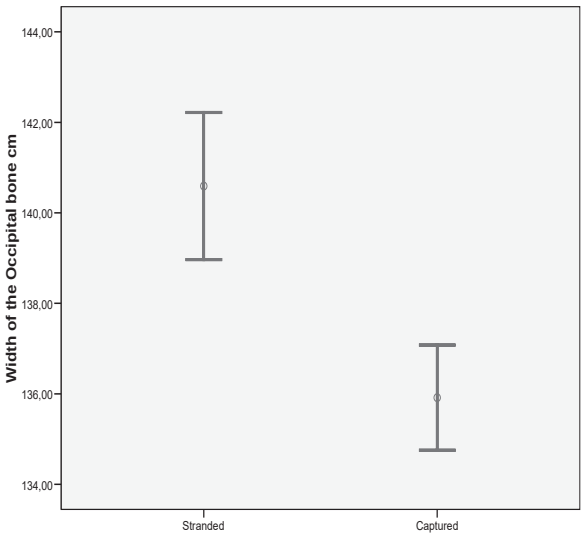
Graphic 4. Results in percentage of the canonical discriminant functions employed in the analysis of the foretold Stranded and Captured specimens as the successive gathering variables, and as the independent variables: Total Length, Width of the Occipital bone, S_LR_occ, Degree of Ossification of the Foramina and Transverse Diameter of the Foramen Magnum

The Degree of Ossification of the Premaxillary Foramina, as a synonym of osteopetrosis, is the principal variable that discriminates the Stranded and Captured dolphins. Taking into account that almost 99% of the abnormalities described in Stranded dolphins can be associated with a typical clinical expression of the Chiari's disease, and that osteopetrosis is a typical symptom of Chiari's disease, we can conclude that at least the 50% of the Stranded dolphins in our data are due to suffer from this disease.

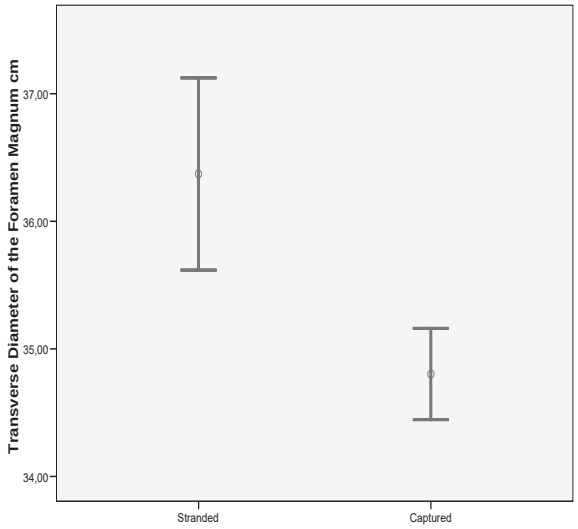
Once we get the data optimized we can see the great differences between the Stranded and Captured dolphins in relation to the studied variables:



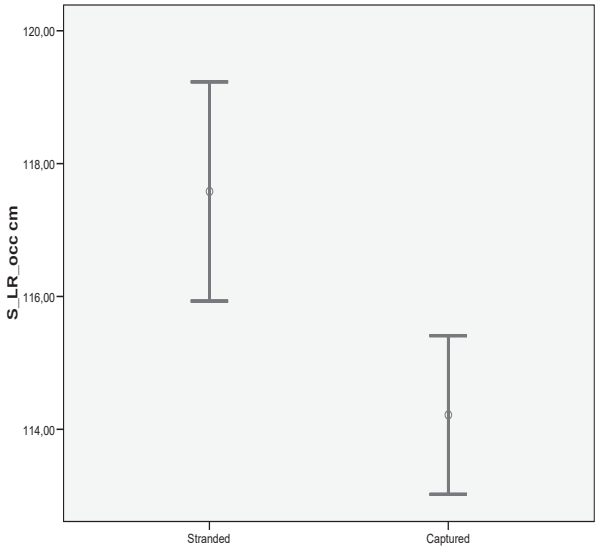
Graphic 5. Mean and Variance of the Total Length in the foretold Stranded and Captured specimens of *Delphinus delphis.*



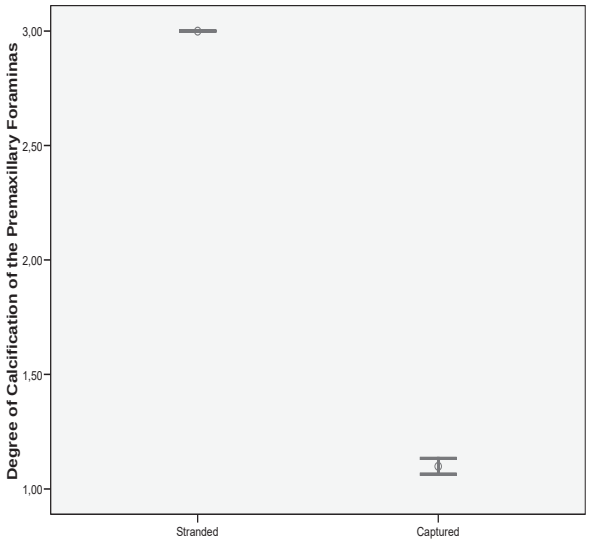
Graphic 6. Mean and Variance of the Width of the Occipital bone in the foretold Stranded and Captured specimens of *Delphinus delphis.*



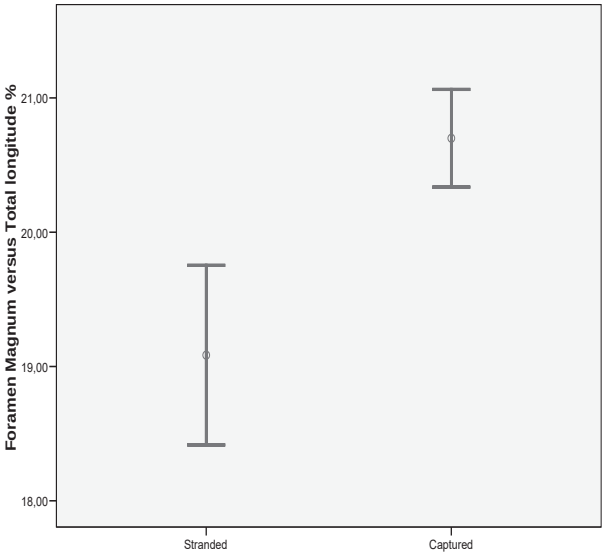
Graphic 7. Mean and Variance of the Transverse Diameter of the Foramen Magnum in the foretold Stranded and Captured specimens of *Delphinus delphis.*



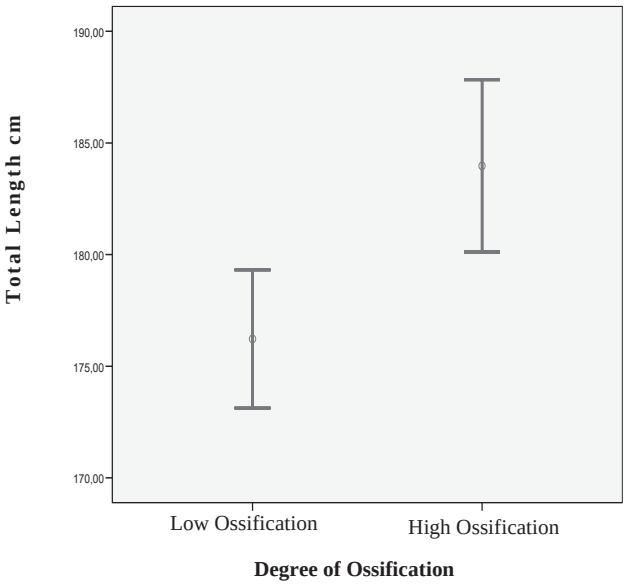
Graphic 8. Mean and Variance of the S_LR_occ in the foretold Stranded and Captured specimens of *Delphinus delphis*.



Graphic 9. Mean and Variance of the Degree of Ossification of the Premaxillary foramina in the foretold Stranded and Captured specimens of *Delphinus delphis.*

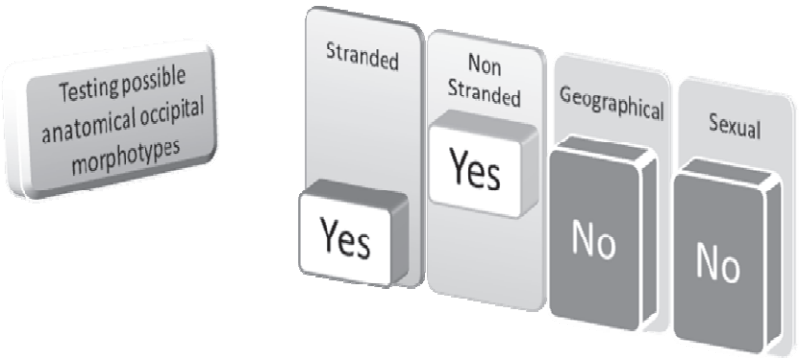


Graphic 10. Mean and Variance of the proportional ratio of the Transverse Diameter of the Foramen Magnum and the Total Length in the foretold Stranded and Captured specimens of *Delphinus delphis.*



Graphic 11. Mean and Variance of the relation between the Degree of Ossification of the Premaxillary Foramina and the Total Length in the specimens of *Delphinus delphis.*

In some studies for the existence of two divergent lineages that have evolved independently, the possibility is discussed as separate subspecies or as events of introgressive hybridization. One possibility for this apparent non-supporting in their results may be due to the fact that Chiari's diseases, as they are genetic malformations, were not taken into account in the recent genetic studies in the *Delphinus sp*.



Fluctuant Asymmetry

FA is the difference among Right and Left width of the occipital bone in absolute value (the mean is the Fluctuant Asymmetry of a population of species).

Table 24. Descriptive Statistics of the Fluctuant Asymmetry of the Width of the Occipital bone (FA_occ) measured in the Stranded and Captured specimens of *Delphinus delphis.*

	N valid	AF_occ
Stranded	208	2,1988
Captured	415	2,0375

Table 25. Homogeneity of Variance of the Fluctuant Asymmetry of the Width of the Occipital bone among the Stranded and Captured specimens of *Delphinus delphis.*

Levene's test	gl1	gl2	Sig.
,593	1	621	,441

Table 26. Fisher's ANOVA of the Fluctuant Asymmetry of the Width of the Occipital bone measured among the Stranded and Captured specimens of *Delphinus Delphis.*

	Sum of squares	gl	Quadratic mean	F	Sig.
Inter-groups	3,603	1	3,603	1,191	,276
Intra- groups	1878,885	621	3,026		
Total	1882,488	622			

There are no significant differences in the results of Fluctuant Asymmetry calculated in the Width of the Occipital bone between Stranded and Captured specimens of *Delphinus delphis.* Therefore, the stranding condition in our dataset does not depend on the environmental stress.

Stranding Condition

The 99% of the abnormalities described in Stranded dolphins previously reported can be associated with a typical clinical expression of the Chiari's disease.

Some recurrent anomalies reported in many works that study the stranding condition among cetaceans are:

Amyloidosis: the association of Budd-Chiari's syndrome with amyloidosis may be related to the increased risk of thrombosis (Paliard, P. et al. 1983). Amyloidosis in cystic fibrosis has been also reported by Mc. Laughlin, A. M. et al. (2006).

Angyomatosis: cystic angiomatosis of the craniocervical junction associated with Chiari I malformation has been reported by Pavanello, M. et al. (2007).

Corticomedullary differentiation: X-ray of long bones revealed increased bone density with loss of corticomedullary differentiation. Osteopetrosis has been associated with an Arnold Chiari malformation, neurological complications like spastic quadriparesis, IX, X and XII cranial neuropathies and cerebellar signs. The neurological effects of osteopetrosis result from a restriction of growth of the foramina, through which cranial nerves, spinal cord and major blood vessels traverse the skull. Skull also showed increased bone density and osteosclerosis more so in the base of skull with non pneumatisation of frontal sinuses and sclerosis of mastoid bones. Sclerosis was also noticed in the vertebral bodies and pelvis (Kulkarni, M.L. et al. 2007).

Degeneration eighth cranial nerve: pathological changes in the cerebello-pontine angle region and right side deafness revealed cochleovestibular nerve compression syndrome on the same side. Arnold-Chiari malformation type I,

right side deafness and left side sensorineural hearing loss occurred at high frequencies, as well as, episodes of vertigo with nausea and vomit. Arnold-Chiari malformation type I and degeneration eighth cranial nerve occurring simultaneously might be responsible for deafness in the right ear (Urban, I. et al. 2004).

Cystic Fibrosis (CF): suggest that Chiari type I malformation is more common in CF than in the general population. The possibility of Chiari type I malformation should be included in the differential diagnosis of unexplained neurologic complaints in patients with CF (Needleman, J. P. et al. 2000).

Flabby and pale right ventricle: as a possible result of the tricuspid atresia associate to Chiari malformations. It is a heart lesion. (Bhatnagar, K. P. 2005; Gibson, J. B. 2005; Ragland, M. M. 2006).

Heart failure: the most common cause of edema of the legs and dyspnea is congestive heart failure. Further differential diagnosis such as renal or hepatic failure have to be considered. Imaging studies showed a thrombosis of the inferior vena cava (IVC) caused by a tumor between the right kidney and the IVC. Histological examination revealed a leiomyosarcoma of the IVC. Hepatic failure due to venous outflow obstruction (Budd-Chiari syndrome, BCS) was diagnosed (Eckel, F. et al. 2002).

Hepatic changes: hepatic parenchymal changes associated with Budd-Chiari syndrome (BCS) have been tentatively explained by combined arterial and portal perfusion disturbances in addition to the complete occlusion of hepatic veins (Cazals-Hatem, D. et al. 2003).

Osteomyelitis: has been reported in ssociation with Arnold-Chiari type II (Aristizábal, A. 2002).

Peeling skin: there is a few reports of skin ulcers and Budd–Chiari syndrome associated with PS deficiency (Dillmon, M. S.et al. 2005).

Salivary gland: histology of a liver biopsy sample revealed findings of chronic nonsuppurative destructive cholangitis consistent with PBC. In addition, decreased salivation was observed and sialography showed points and spotty pooling in the right salivary gland. Based on the clinical and histological findings, the diagnosed was a PBC with Sjögren's syndrome complicated by syringomyelia and Chiari I malformation (Ohira, H. et al. 2003).

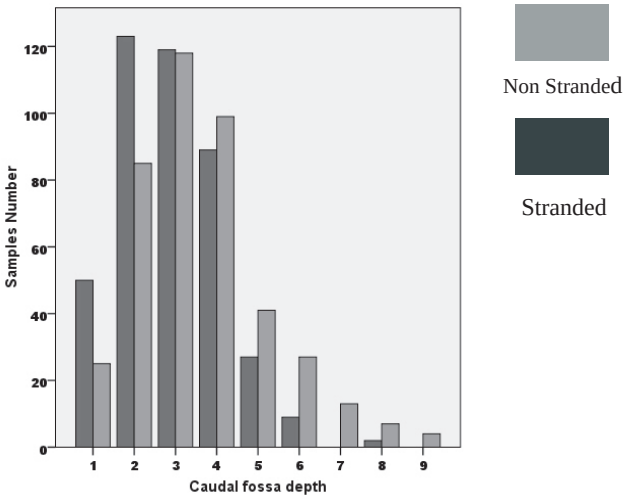
Thyroid gland: Orguc, S. et al. (2004) hypothesized that the occurrence of C2 malformation and a thyroglossal cyst is not totally independent; their association shown may be related to incomplete embryonic development.

Caudal fossa depth

The Caudal fossa depth is calculated by:

$$FM\%=FMx100/L$$

$$\text{Caudal fossa depth}=KI-FM\%$$



Graphic 12. Caudal fossa depth calculation in our data.

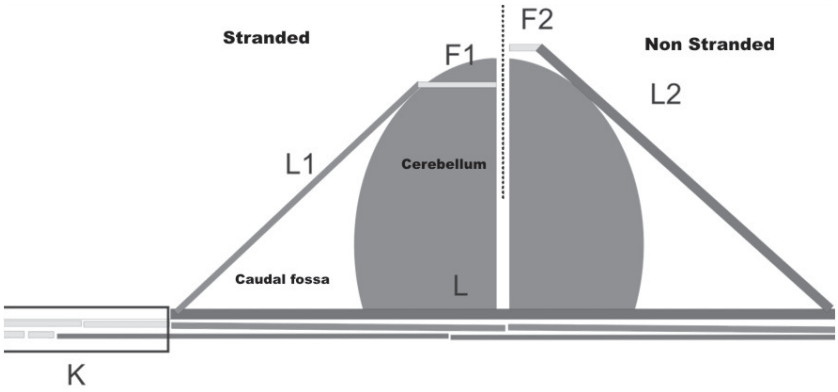
Two groups of dolphins are observed with significant different means.

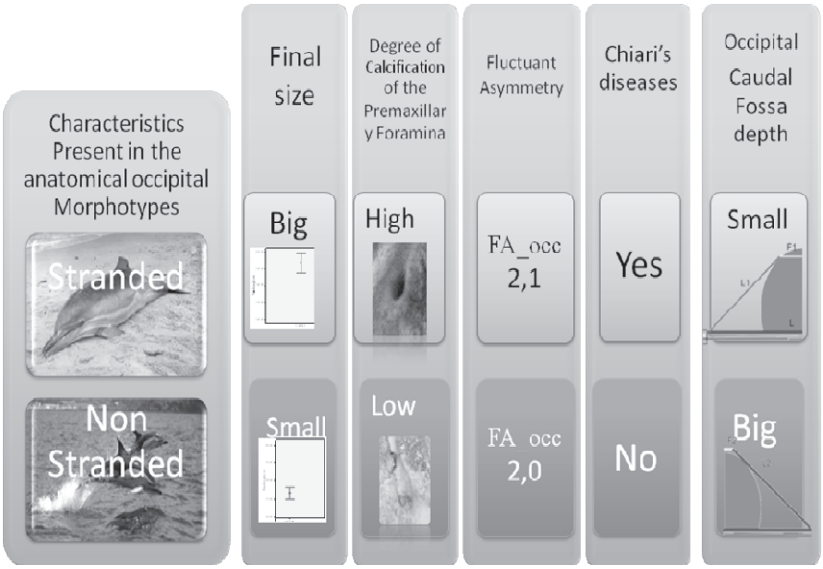
One group is composed by the stranded dolphins with a caudal fossa depth smaller than the second group composed by the non stranded dolphins.

The variation of the Width of the Foramen Magnum (case F1: Foramen magnum of a Stranded specimen, bigger foramen magnum; or case F2: Foramen magnum of a Non Stranded specimen, smaller foramen magnum) do not alter the

Kalya Index (K), being compensated by the Left and Right Width of the Occipital bone (case L1 or L2).

The variation occurs at the level of the caudal fossa depth, producing the extrusion of the cerebellum through the Foramen Magnum, which is enlarged.




Characteristics Present in the anatomical occipital Morphotypes
Stranded
Non Stranded
Final size
Big
Small
Degree of Calcification of the Premaxillar y Foramina
High
Low
Fluctuant Asymmetry
FA_occ 2,1
FA_occ 2,0
Chiari's diseases
Yes
No
Occipital Caudal Fossa depth
Small
Big

Chapter 3

Vestigial Achondroplastic characteristics in actual dolphins

The aim of this part of the study is to try to demonstrate that actual dolphins could have evolved through a process of Achondroplasia that affected their ancestors. Therefore the problems derived from Achondroplasia should remain, although with mitigated effects, in actual dolphins.

Heterozygous achondroplasia is the prototypical and most common rhizomelic (proximal shortening) dwarfism syndrome. Although the disease is autosomal dominant in transmission, approximately 80 - 90 % of cases are sporadic, reflecting mutations. The genetic defect lies at the fibroblast growth factor-3 gen. Females are affected more than males.

Literally "shortened extremities", as an example, some types of equine achondroplastic dwarfism have specific physical characteristics such as short limbs and small ears with a normal head, neck and torso. These deformities do not adversely affect the intelligence or lifespan of the horse.

Also we have compared Dolphin’s anatomy similarities with achondroplast mammals’ and other anatomies related to achondroplasia.

Achondroplasia (ACH)

Heterozygous achondroplasia is the prototypical and most common rhizomelic (proximal shortening) dwarfism syndrome. Although the disease is autosomal dominant in transmission, approximately 80 - 90 % of cases are sporadic, reflecting mutations. The genetic defect lies at the fibroblast growth factor-3 gen. Females are affected more than males.

Literally "shortened extremities", some types of equine achondroplastic dwarfism have specific physical characteristics such as short limbs and small ears with a normal head, neck and torso. These deformities do not adversely affect the intelligence or lifespan of the horse (See Appendix I).

Dolphin's anatomy similarities with achondroplast mammals

1. - Significantly smaller frontal lobe depths.

2. - Significantly smaller foramen magnum diameters.

3. - Achondroplastic subjects experience dynamic changes in brain morphometry resulting in a rostral displacement of the brainstem with gradual compression of the frontal lobes due to enlargement of the supratentorial ventricular spaces commensurate.

4. - Foramen magnum stenosis. The achondroplastic foramen magnum is small at birth, and during the first year, it has a severely impaired rate of growth especially in the transverse dimension.

5. - Osseus overgrowth with foraminal obstruction problems.

6. - Micromelic: entire limb shortened.

7. - The limb bones are short with abnormally wide ends.

8. - Extension and rotation are limited at the elbow.

9. - A thoraco-lumbar gibbus is typically present, but usually gives way to exaggerated lumbar lordosis.

10. - The characteristic "trident" deformity is present, consisting of separation of the first and second as well as the third and fourth digits. Notice the shortened tubular bones of the hand, particularly the proximal phalanges.

11. - Frequent features of Achondroplasia are coexistent with Chiari malformation.

12. - Sackett, J.F. et al. 1997, reported patients (human) with coexistence of Chiari disease and Achondroplasia.

Other anatomies related to achondroplasia

In humans dwarfism syndromes are complex, heterogeneous, and generally rare. Achondroplasia is the most common short-limbed dwarfism syndrome.

The offspring of two achondroplasts may produce a hereditary form of the disease known as homozygous achondroplasia. This is a lethal form of the disease in the neonatal period.

Some authors found that achondroplasts had significantly smaller frontal lobe depths, optic tract angles, foramen magnum diameters and sinojugular transition zones. Furthermore, with respect to age, frontal lobe depth was smaller when compared to

controls and the descending sigmoid sinus area became increasingly larger. This study concluded that achondroplastic subjects experience dynamic changes in brain morphometry resulting in a rostral displacement of the brainstem with gradual compression of the frontal lobes due to enlargement of the supratentorial ventricular spaces commensurate.

Disproportion between the base of the skull and the brain results in internal hydrocephalus in some cases. The hydrocephalus may be caused by increased intracranial venous pressure due to stenosis of the sigmoid sinus at the level of the narrowed jugular foramina. Other outhors pointed out that the large head of the achondroplastic fetus creates an increased risk of intracranial bleeding during delivery. Some studies concluded that brainstem compression is common in achondroplasia and may account in part for the abnormal respiratory function.

Foramen magnum stenosis consists in a smaller than average foramen magnum is present in all children with achondroplasia.

The achondroplastic foramen magnum is small at birth, and during the first year, it has a severely impaired rate of growth especially in the transverse dimension**.** This markedly diminished growth results not only from abnormal endochondral bone growth but also because of abnormal placement and premature fusion of the synchondroses.

The size of the foramen magnum in patients with achondroplasia was small at all ages, particularly in those with serious neurologic problems. The data suggest that measurement of the foramen magnum may identify achondroplastic individuals at high risk of developing neurologic complications.

Other study reported a case of achondroplasia with downward displacement of the brain stem. Although upward displacement and anterior angular deformity of the brain stem are common findings in achondroplasia, they were not observed in this case, because of a coexistent Chiari malformation.

The association between sudden death and cervicomedullary compression in infants with achondroplasia has been well described. Craniocervical magnetic resonance imaging (MRI) findings included narrowing of the foramen magnum, effacement of the subarachnoid spaces at the cervicomedullary junction, abnormal intrinsic cord signal intensity and mild to moderate ventriculomegaly.

In a lateral skull radiograph it is possible to identify the typical enlarged skull of a patient with achondroplasia. The base of the skull and the facial bones are somewhat small. Due to the small skull base, the foramen magnum may be small, resulting in hydrocephalus. The spinal cord and posterior fossa structures may be compressed as well. Ten percent of patients have respiratory difficulties due to the midface hypoplasia or spinal cord compression.

Some authors reviewed the neurologic abnormalities in the skeletal dysplasias from a clinical and radiologic perspective. Three important major groups were identified: a) achondroplasia (cranio-cervical junction problems in infancy, spinal stenosis, and neurogenic claudication in adulthood); b) type II collagenopathies (upper cervical spine anatomic and functional problems); and c) craniotubular and sclerosing bone dysplasias (osseous overgrowth with foraminal obstruction problems).

The genetic defect of achondroplasia lies at the fibroblast growth factor-3 gen. This results in defective endochondral bone formation with resultant shortening of tubular bones. The shaft caliber is less affected because periosteal intramembraneous bone formation is not affected. True megalencephaly occurs in achondroplasia and has been speculated to indicate effects of the gene other than those on the skeleton alone.

In fact, dwarfism as an entity is a type of skeletal dysplasia - a term used to refer to syndromes with abnormal bone growth and development-.

Several terms are used when describing which bone within a limb is most shortened: a) Rhizomelic: proximal shortening (humerus or femur); b) Mesomelic: middle shortening (tibia/fibula or radius /ulna); c) Acromelic: distal shortening (hand) and d) Micromelic: entire limb shortened.

Achondroplasic limb bones are short, with abnormally wide ends. The patient has a head and trunk of normal size, and disproportionately short but well-muscled arms and legs. The face usually has a large forehead, prominent supraorbital ridges, and deepset root of the nose. Sexuality is generally normal, and intelligence is distributed as for the general population, with many well above-averages.

Other characteristics are hyperextensibility of most joints, especially the knees, is common, but extension and rotation are limited at the elbow. A thoraco-lumbar gibbus is typically present at birth, but usually gives way to exaggerated lumbar lordosis.

The characteristic "trident" deformity is present, consisting of separation of the first and second as well as the third and fourth digits. Notice the shortened tubular bones of the hand, particularly the proximal phalanges. Identified are the short tubular bones with a gracile distal ulna, characteristic of achondroplasia.

The X-Ray studies illustrated that although achondroplasia is primarily a rhizomelic dwarfism (proximal segment), the intermediate segments are also affected to a lesser degree. The characteristic "ball-in-socket" deformity of the knee consisting of a broad indented metaphysis with a rounded femoral epiphysis can be seen; also characteristic is the greater shortening of the tibia relative to the fibula.

A typical radiograph of the humerus shows the classic metaphyseal flaring of the distal humerus with bowing of the

shaft. We can notice that the shaft thickness is preserved, due to preserved periosteal intramembraneous bone formation.

Some studies reviewed the subject of obesity in achondroplasia, concluding that it is a major problem which, whatever its underlying cause, aggravates the morbidity associated with lumbar stenosis and contributes to the nonspecific joint problems and to the possible early cardiovascular mortality in this condition. Other authors developed weight for height (W/H) curves for these patients. They showed that to a height of about 75 cm, the mean W/H curves are virtually identical for normal and achondroplastic children. After this height, the W/H curves for achondroplastic patients rise above those for the general population.

Homozygosity for the achondroplasia gene results in a severe disorder of the skeleton with radiologic changes qualitatively somewhat different from those of the usual heterozygous achondroplasia; early death results from respiratory embarrassment or difficulty from the small thoracic cage and neurologic deficit from hydrocephalus. Other studies reported upper cervical myelopathy in a homozygote.

Orthodontic problems were found in 53.8% of individuals; only 3.2% of these individuals presented within the first 10 years of life. Apnea was reported in 10.9% of individuals by age 4 years and 16.1% of individuals overall.

Some studies characterized cardiorespiratory and sleep dysfunction in 17 patients with achondroplasia referred to Great Ormond Street Hospital for Children, London. Three distinct etiologic groups were identified: group 1 had a mild degree of midfacial hypoplasia resulting in relative adenotonsillar hypertrophy; group 2 had jugular foramen stenosis resulting in muscular upper airway obstruction and progressive hydrocephalus due to jugular venous hypertension; and group 3 had muscular upper airway obstruction without hydrocephalus resulting from hypoglossal canal stenosis with or without

foramen magnum compression. In addition, gastroesophageal reflux, which tended to occur in group 3 patients, was identified as a significant factor in the development of airway disease.

Other authors reported to find abnormality of the type II collagen gene in achondroplasia. If such a defect is present, one might expect ocular abnormality in achondroplasia in as much as type II collagen is present in vitreous.

Patients with achondroplasia are of normal intelligence but may have delay in reaching pediatric milestones. Hearing problems may result from multiple ear infections in childhood due to skull abnormalities. Hypochondroplasia is a milder form of achondroplasia which presents in late childhood.

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Animal Anatomy Atlas Skull of *Delphinus delphis*	Abril 2008

Glossary

Achondroplasia: is the most common short-limbed dwarfism syndrome.

Acromelic dwarfism: distal shortening (hand).

Adenotonsillar hypertrophy: hypertrophy of the adenoid tonsil (the mat of lymphoid tissue is called adenoids) is the unusual growth of the tonsils (lymphoepithelial organs at the opening of the upper aerodigestive tract).

Amyloidosis: amyloid refers to a particular insoluble form that many different proteins can take, due to an alteration in their secondary structure. This characteristic alteration in the protein shape is called the beta-pleated sheet. Amyloidosis refers to a variety of conditions in which amyloid proteins are abnormally deposited in organs and/or tissues, causing disease. Approximately 25 different proteins are known that can form amyloid in humans, most of them are constituents of the plasma. Different amyloidoses can be systemic-affecting many different organ systems, or organ specific. Some are inherited, due to mutations in the precursor protein. Other, secondary forms are due to different diseases causing overabundant or abnormal protein production-such as with over production of immunoglobulin light chains in multiple myeloma (termed AL amyloid), or with continuous overproduction of acute phase proteins in chronic inflammation (which can lead to AA amyloid).

Angiomatosis: is a general term employed to describe a spectrum of rare benign conditions characterized by thinwalled ectatic vascular channels, lined with banal endothelial cells and filled with lymph or blood. Jacobs and Kimmelstiel were the first to describe cystic angiomatosis in 1953.

Ankylosing spondylitis: also known as Bechterew's disease; Bechterew syndrome; Marie Strümpell disease / Marie Struempell disease / Spondyloarthritis) is a chronic, painful, degenerative inflammatory arthritis primarily affecting spine and sacroiliac joints, causing eventual fusion of the spine; it is a member of the group of the autoimmune spondyloarthropathies with a probable genetic predisposition. Complete fusion results in a complete rigidity of the spine, a condition known as bamboo spine.

Ball-in-socket deformity of the knee: consisting of a broad indented metaphysis with a rounded femoral epiphysis and the greater shortening of the tibia relative to the fibula (Fig.11).

Brain stem compression: consisits in an increased intracranial pressure may include headaches, vomiting, nausea, papilledema, sleepiness, or coma, or death. Elevated intracranial pressure may result in uncal and/or cerebellar tonsill herniation.

Budd-Chiari syndrome: consists in the obstruction of intrahepatic veins leads to congestive hepatopathy. This results from obstruction of either large- or small-caliber veins, which leads to hepatic congestion as blood flows into, but not out of, the liver. Hepatocellular injury results from microvascular ischemia due to congestion. Portal hypertension and liver insufficiency result.

Cerebellar tonsill herniation: in tonsillar herniation, the cerebellar tonsils herniate downward through the foramen magnum.

Chiari malformation: is a complex abnormality consisting of various combinations of brainstem and cerebellar malformations usually associated with spinal defects.

Dorsal notch of the foramen magnum: variation in the degree of ossification of the ventromedial part of the supraoccipital bone, Fig.2.

Embryonic development: organs originating from neuroectodermal tissues may show dysgenesis resulting from the same or simultaneous insult during

development. During the 4th week of gestation, a process of folding called neurulation converts the neural plate to a hollow neural tube, and then the neural tube begins to differentiate into the brain and spinal cord. Neurulation begins in the occipitocervical region as the neural folds fuse and the fused neural tube detaches from the surface ectoderm. This fusion continues towards the cranial and caudal regions. The abnormal development of the neural tube in the 3rd and 4th weeks may result in arachnoid, pia, vertebra and calvarium malformations. During this period, neural crest cells detach from the neural plate or neural tube and migrate to many specific locations in the body, where they differentiate into a remarkable variety of structures. Neural crest cells from the mesencephalon and rhombencephalon regions give rise to structures in the eveloping pharyngeal arches of the head and neck. These structures include the dermis, smooth muscle and fat of face and ventral neck, the odontoblasts of developing teeth and C cells of the thyroid. Abnormal development of the pharyngeal arches causes head and neck abnormalities. During embryogenesis, the thyroglossal cyst may occur during thyroid gland migration. The thyroid gland primordium first appears in the late 4th week as a small, solid mass of the endoderm proliferating at the apex of the foramen cecum of the developing tongue. The thyroid primordium descends through the tissues of the neck at the end of the slender thyroglossal duct. The thyroglossal duct starts to close at the end of the 5th week and closes completely by the 7th week. Normally, the only remnant of the thyroglossal duct is the foramen cecum itself. Thyroglossal cysts may occur anywhere along the thyroglossal duct from the base of the tongue to the anterior part of the neck. In the neck, they may be symptomatic, gradually enlarging, round, midline or off-midline masses that move with swallowing because of their attachment to the hyoid bone. Sinuses or fistulae that drain clear or purulent fluid may be associated with the anterior part of the neck. These cysts, their typical location and cystic signal

characteristics can be demonstrated using MRI. Neural crest cells from the mesencephalon and rhombencephalon regions give rise to structures in the developing phayrngeal arches of the head and neck. Hence, it may be assumed that the neural tube and pharyngeal arch development may be affected by the same or simultaneous insult, which may result in abnormal induction of the notochord on the ectoderm and mesoderm.

Fibrosis: is the formation or development of excess fibrous connective tissue in an organ or tissue as a reparative or reactive process, as opposed to a formation of fibrous tissue as a normal constituent of an organ or tissue.

Foramen magnum stenosis: consists in a smaller than average foramen magnum Fig.7.

Hydrocephalus: abnormal accumulation of cerebrospinal fluid (CSF) in the ventricles, or cavities, of the brain. This may cause increased intracranial pressure inside the skull and progressive enlargement of the head, convulsion, and mental retardation.

Hypochondroplasia: is a milder form of achondroplasia which presents in late childhood.

Lymphangiomyomatosis (LAM): a rare disease characterized by progressive proliferation of spindle cells, resembling immature smooth muscle, in the lung parenchyma and along lymphatic vessels in the chest and abdomen. Proliferation of spindle cells along the bronchioles leads to air trapping and the development of thin-walled cysts. Rupture of these cysts can result in pneumothorax. The spindle cell proliferation can also involve the hilar, mediastinal and extrathoracic lymph nodes, sometimes resulting in dilatation of intrapulmonary lymphatics. Involvement of the lymphatics can lead to chylous pleural effusion.

Megaencephalia: is a type of cephalic disorder. It is a condition in which there is an abnormally large, heavy, and usually malfunctioning brain. By definition, the brain weight is greater than average. Head enlargement may be evident

at birth or the head may become abnormally large in the early years of life.

Mesenteric lymph nodes: are present near mesenteric vessels and between bowel loops. They normally appear flattened, ovoid, or disc-shaped, and they have a characteristic fatty central hilum and a solid peripheral cortex. Vessels enter and exit the node at the hilum and branch within the node in a fashion similar to that of the kidney. The normal mesenteric lymph node vary in size, but, in general, the short-axis diameter is 4 mm or shorter.

Mesomelic dwarfism: middle shortening (tibia/fibula or radius /ulna).

Micromelic dwarfism: entire limb shortened.

Midface hypoplasia: the midfacial bones are somewhat small Fig.8.

Myelopathy: is a disturbance of the spinal cord that results in loss of sensation and/or mobility.

Occipital bone dysplasia: is an incomplete ossification of the supraoccipital bone, resulting in the widening of the foramen magnum, Fig.3.

Occipital bone hypoplasia: results in reduced volume of the caudal fossa, leading to overcrowding of the neural structures and, in severe cases, development of syringomyelia.

Occipitalization of the atlas: is the result of a bilateral obliteration of the atlanto-occipital joints and the stability of the asymmetrical atlanto-axial joints is ensured by the additional articular area and the configuration of the facets as seen in Fig.5.

Osteomyelitis: is an infection of bone or bone marrow, usually caused by pyogenic bacteria or mycobacteria. It can be usefully subclassifed on the basis of the causative organism, the route, duration and anatomic location of the infection.

Osteopetrosis: is a collective term for a range of sclerosing bone diseases resulting from an absence or defective function of osteoclasts. The clinical expression is variable and includes skeletal, hematological and

neurological manifestations. The common neurological manifestation includes cranial neuropathies involving optic, cochlear, facial and trigeminal nerves. Type 1 Arnold Chiari malformation can be associated with osteopetrosis resulting in brain stem compression syndrome.

Peeling skin syndrome: is an extremely rare inherited disorder characterized by continual, spontaneous skin peeling (exfoliation). Other findings may include reddening of the skin (erythema) and itching (pruritus). Based on its occurrence peeling skin syndrome is likely to be transmitted as an autosomal recessive genetic trait.

Rhizomelic dwarfism: proximal shortening (humerus or femur).

Right ventricle: is one of four chambers (two atria and two ventricles) in the human heart. It receives de-oxygenated blood from the right atrium via the tricuspid valve, and pumps it into the pulmonary artery via the pulmonary valve. It is triangular in form, and extends from the right atrium to near the apex of the heart.

Skeletal dysplasias: are bone and cartilage disorders that affect the growth and development of the skeleton and result in short stature and dwarfism. Most of these are genetic conditions.

Syringomyelia: is a tubular cavity in the spinal cord, Fig.4.

The caudal fossa: is part of the intracranial cavity, located between the foramen magnum and tentorium cerebelli. It contains the brainstem and cerebellum. This is the most inferior of the fossa. It houses the cerebellum, medulla and pons. Anteriorly it extends to the apex of the petrous temporal. Posteriorly it is enclosed by the occipital bone. Laterally portions of the squamous temporal and mastoid part of the temporal bone form its walls. It contains critical motor and sensory areas and houses cranial nerves III through XII.

The mediastinum: is a non-delineated group of structures in the thorax, surrounded by loose connective tissue. It is the central compartment of the thoracic cavity. It contains

the heart, the great vessels of the heart, esophagus, trachea, thymus, and lymph nodes of the central chest.

Tricuspid atresia: in this condition, there's no tricuspid valve so no blood can flow from the right atrium to the right ventricle. As a result, the right ventricle is small and not fully developed.

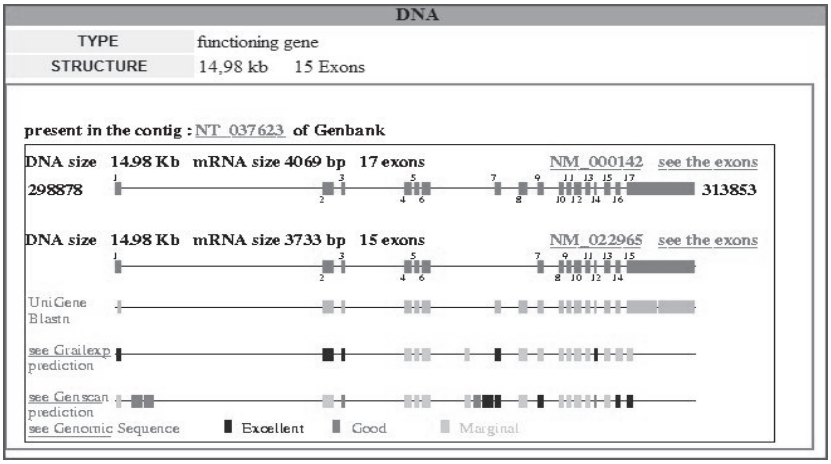
Trident deformity: separation of the first and second as well as the third and fourth digits (Fig.9).

Ventricular shunt: is a tube that is surgically placed in one of the fluid-filled chambers inside the brain (ventricles). The fluid around the brain and the spinal column is called cerebrospinal fluid (CSF). When infection or disease causes an excess of CSF in the ventricles, the shunt is placed to drain it and thereby relieve excess pressure.

Vestibulocochlear nerve: also known as the auditory or acoustic nerve is the eighth of twelve cranial nerves, and is responsible for transmitting sound and equilibrium (balance) information from the inner ear to the brain.

Appendix I

Achondroplasia genetic information:



FLASH GENE		
Symbol	FGFR3	*last update* : 03/07/2006
HGNC name	fibroblast growth factor receptor 3 (achondroplasia, thanatophoric dwarfism)	
HGNC id	3690	
Corresponding disease	ACH , CRS10 , CRS5B , CRSCNS , CRS8 , SADDAN , TNTP1 , TNTP2 , HCH , BSCGS2 , LADD2 , CATSHL	
Location	4p16.3	
Synonym name	tyrosine kinase JTK4	
Synonym symbol(s)	ACH, CEK2, JTK4	

ASSOCIATED DISORDERS

corresponding disease (s)	ACH , CRS10 , CRS5B , CRSCNS , CRS8 , SADDAN , TNTP1 , TNTP2 , HCH , BSCGS2 , LADD2 , CATSHL				
Other morbid association(s)	**Type**	**Gene Modification**	**Chromosome rearrangement**	**Protein expression**	**Protein Function**
	tumoral		LOH		
	in transitional cell carcinomas				
	tumoral	somatic mutation			
	in superficial urothelial cell carcinoma (UCC), in bladder carcinomas (superficial or low-grade)				
	constitutional	somatic mutation			gain of function
	somatic activating mutations in acanthosis nigricans and seborrheic keratosis				
	tumoral			other	
	dysregulated in multiple myeloma with t(4;14)(p16.3;q32)				

EXPRESSION/SUBCELLULAR LOCATION

EXPRESSION (based on Unigene)	63 libraries where FGFR3 expressed	2.13 average number of ESTs/Library	0.17 average percent of ESTs/Library	See detail

EXPRESSION (based on citations)

expressed in

organ(s)

System	Organ	S_Organ	Ss_Organ	level
blood / hematopoietic	spleen			lowly
Cardiovascular	heart			lowly
Nervous	brain			
Reproductive	male system	testis		
Skeleton	axial	skull		
Urinary	bladder			
	kidney			

System	Tissue	S_Tissue	Ss_Tissue
Connective	cartilage		
Lymphoid			

cells

System	Cell	S_Cell	Ss_Cell
	chondrocyte		

1. **OMIA 65/000004 Achondroplasia** in *Felis catus* (cat)
2. **OMIA 66/000004 Achondroplasia** in *Bos taurus* (cow)
3. **OMIA 67/000004 Achondroplasia** in *Canis familiaris* (dog)
4. **OMIA 68/000004 Achondroplasia** in *Oryctolagus cuniculus* (rabbit)
5. **OMIA 2058/000004 Achondroplasia** in *Bubalus bubalis* (water buffalo)
6. **OMIA 2196/000004 Achondroplasia** in *Ovis aries* (sheep)
7. **OMIA 70/000005 Achondroplasia foetalis** in *Capra hircus* (goat)
8. **OMIA 2184/000005 Achondroplasia foetalis** in *Bos taurus* (cow)
9. **OMIA 71/000006 Achondroplasia, creeper** in *Gallus gallus* (chicken)

Morphometric parameters compensation in the skull of *Delphinus delphis*, its effects on stranding phenomena and its evolutive implications, by L.Calia Miramontes Sequeiros & Antonio Palanca Soler, is part of the Animal Anatomy Laboratory Foundation series, which offers quality editions at affordable prices to the student and the general reader, including new scholarship, thoughtful design, and pages of carefully crafted extras. The Animal Anatomy Laboratory Foundation series are published in two different Scientific Journals: Animal Anatomy Atlas and Journal of Anatomy and Phenology.