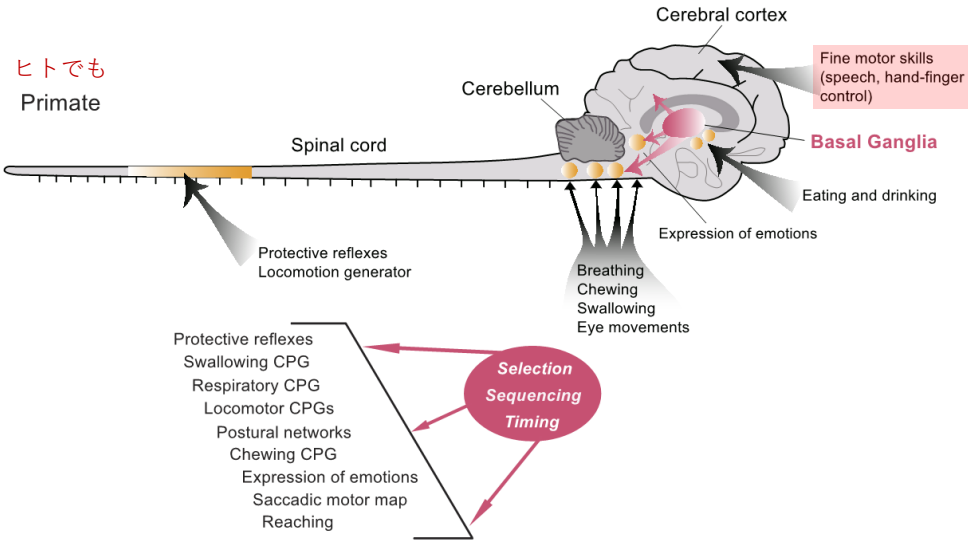
運動神経系の系統発生

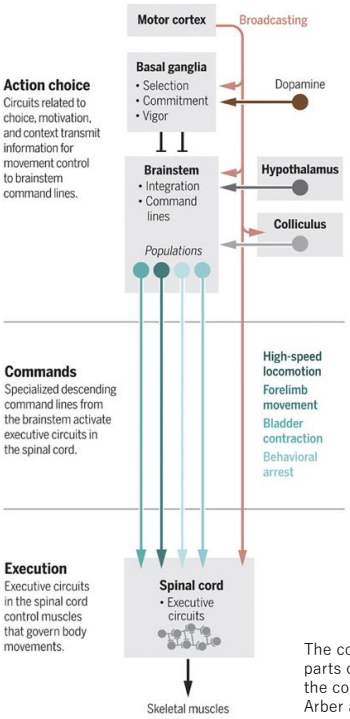
1

運動神経系の系統発生

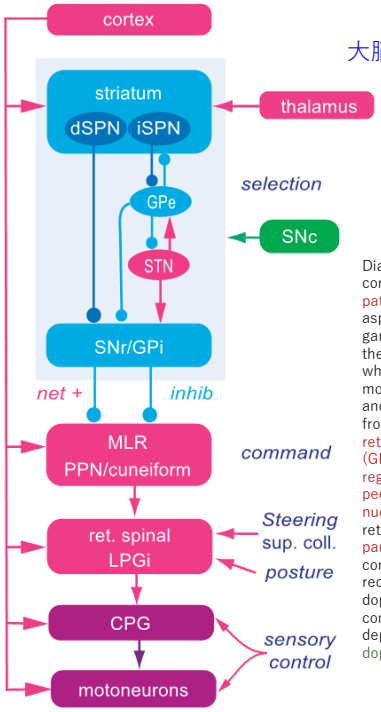


Grillner S, El Manira A. Current Principles of Motor Control, with Special Reference to Vertebrate Locomotion. Physiol Rev. 2020;100:271-320.

2



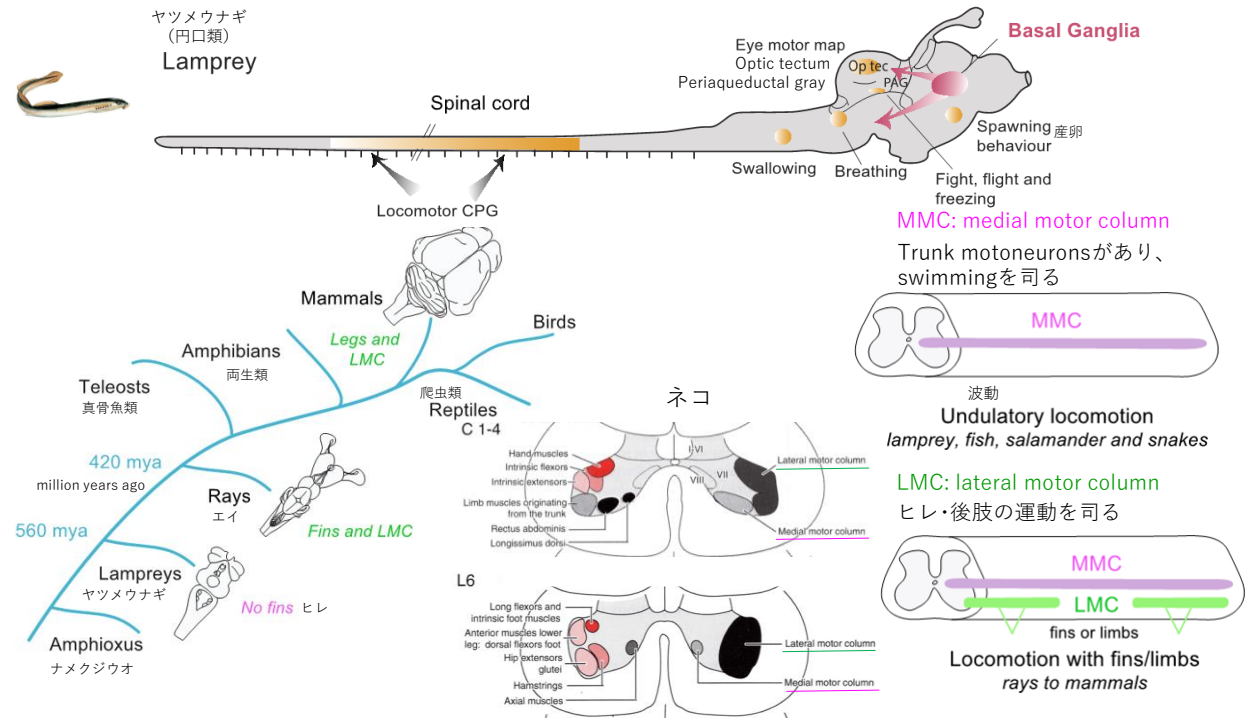
The contribution of different parts of the nervous system in the control of movement. [From Arber and Costa]



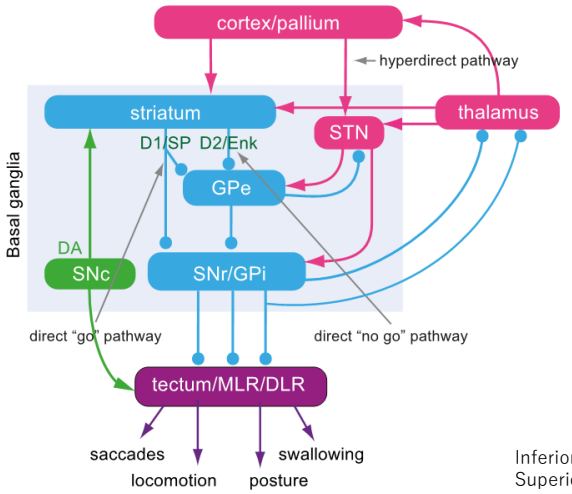
哺乳類では
大脳から脊髄への直接投射あり

Diagram of the different components from cortex and basal ganglia to spinal central pattern generators (CPGs) regulating basic aspects of locomotor propulsion. The basal ganglia and the striatal projection neurons of the direct pathway (dSPN) initiate locomotion, while the indirect pathway (iSPN) inhibits movement via globus pallidus externa (GPe) and the subthalamic nucleus (STN).The output from the basal ganglia [substantia nigra, pars reticulata(SNr), and globus pallidus interna (GPi)] acts on the mesencephalic locomotor region (MLR) consisting of the pedunculopontine (PPN)and cuneiform nucleus, which in turn impinge on reticulospinal neurons in the lateral paragigantocellular nucleus (LPGi) that controls the spinal CPGs. The basal ganglia receive input from cortex, thalamus, and dopamine neurons in substantia nigra, pars compacta(SNc). Inhibitory structures are depicted in blue, excitatory in red, and dopamine in green.

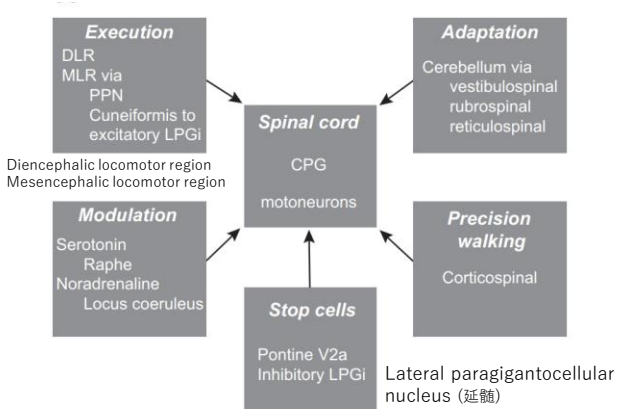
3

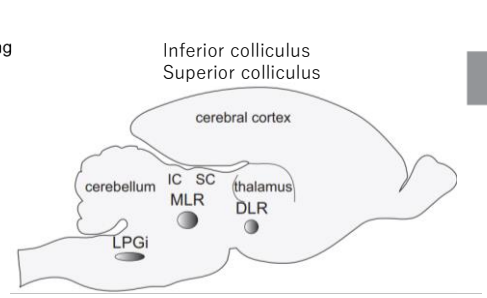


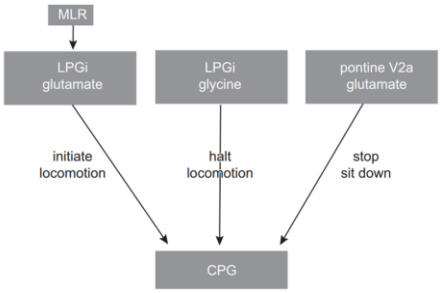
4



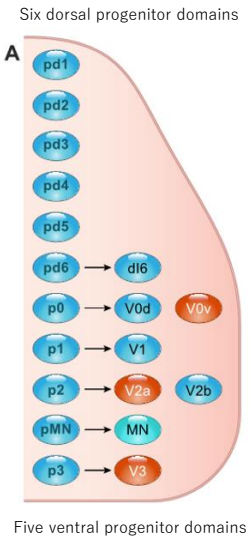
ヤツメウナギからあり

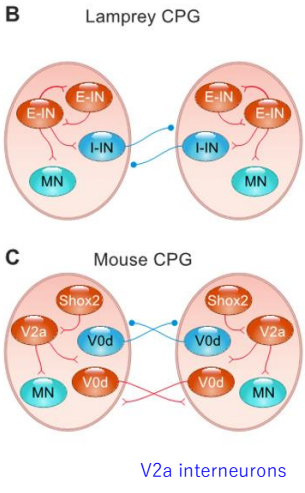


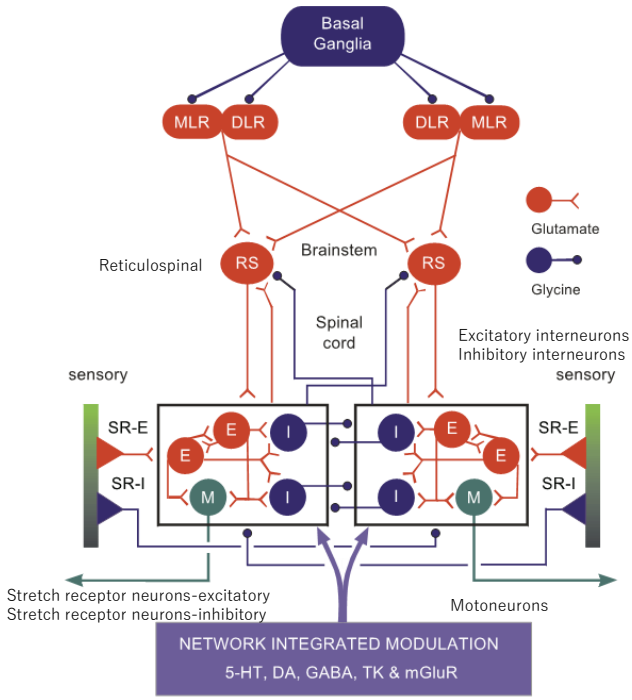




5

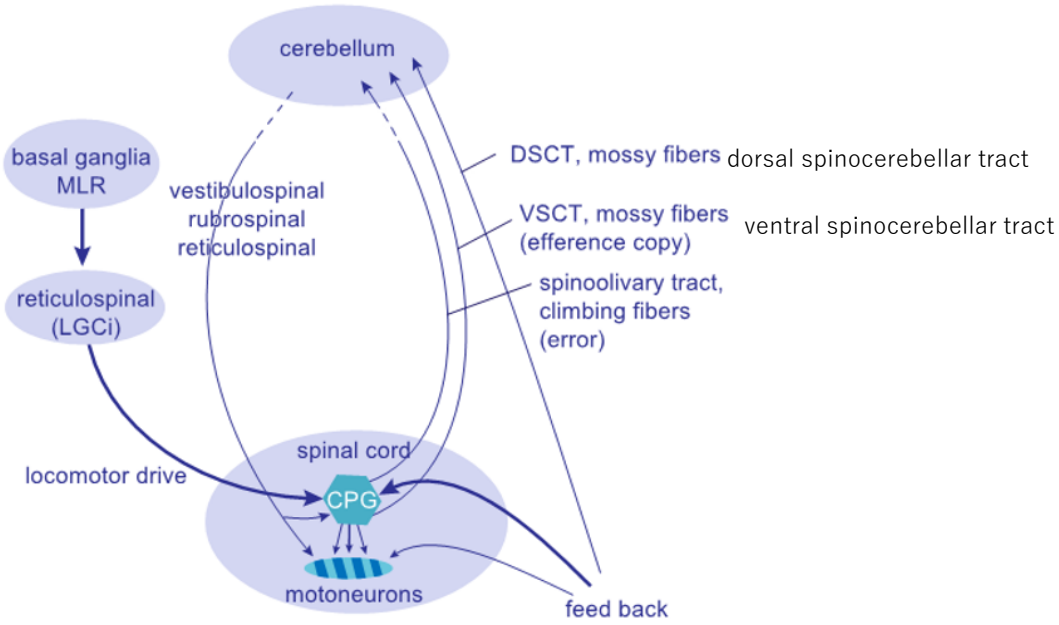






6

Role of cerebellum: fine tuning of the locomotor movements



7

Ferreira-Pinto MJ, et al. Connecting Circuits for Supraspinal Control of Locomotion. Neuron 2018;100:361-374.

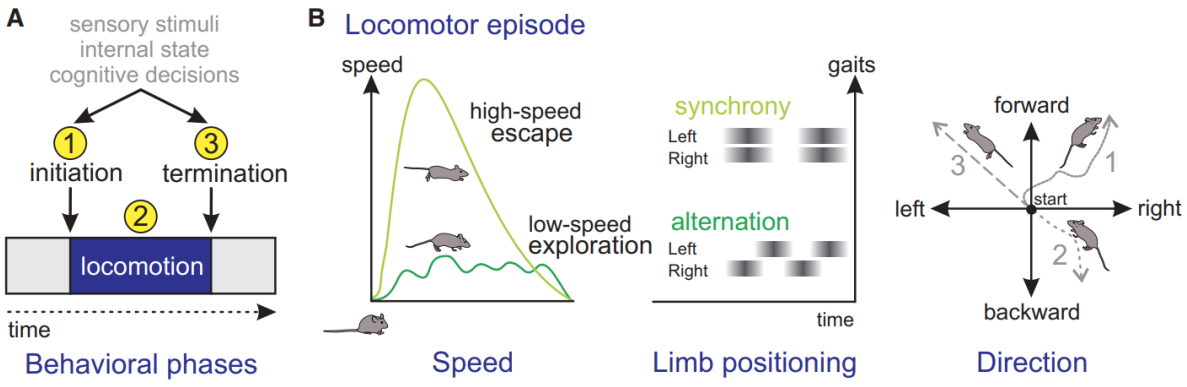


Figure 1. **Temporal and Regulatory Categories of Locomotion**
(A) Division of the locomotor process in three behavioral phases (initiation, locomotion, and termination).
(B) A locomotor episode can range from low-speed exploration to high-speed escaping, during which different locomotor speeds align with alternating or synchronous gait and patterns, and can have different directions of the chosen trajectory (illustrated by three example mice; (1) low-speed exploration, (2) backward walking, and (3) high-speed locomotion).

8

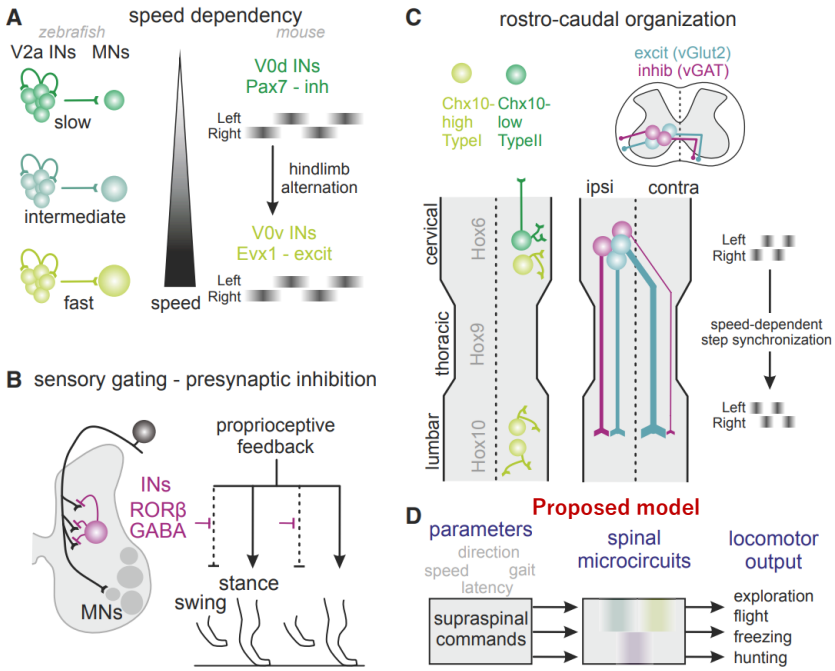


Figure 2. **Diversity and Specificity in Spinal Circuits for Execution of Locomotion**
(A) Summary diagram of spinal circuits in zebrafish (left) and mice (right) implicated in the regulation of speed-linked locomotor parameters.
(B) Schematic summary of the role of RORb-expressing spinal GABAergic neurons in sensory gating through presynaptic inhibition and influence on behavior.
(C) Rostro-caudal organization of spinal circuits based on Chx10-expression levels, Hox transcription factor expression (left), or the organization of descending projections from the cervical to the lumbar spinal cord and their influence on fore- and hindlimb coordination during locomotion (right).
(D) Proposed model of how supraspinal commands may signal locomotor parameters, including speed, gait, latency, or direction, to spinal executive microcircuits that in turn regulate locomotor output.

9

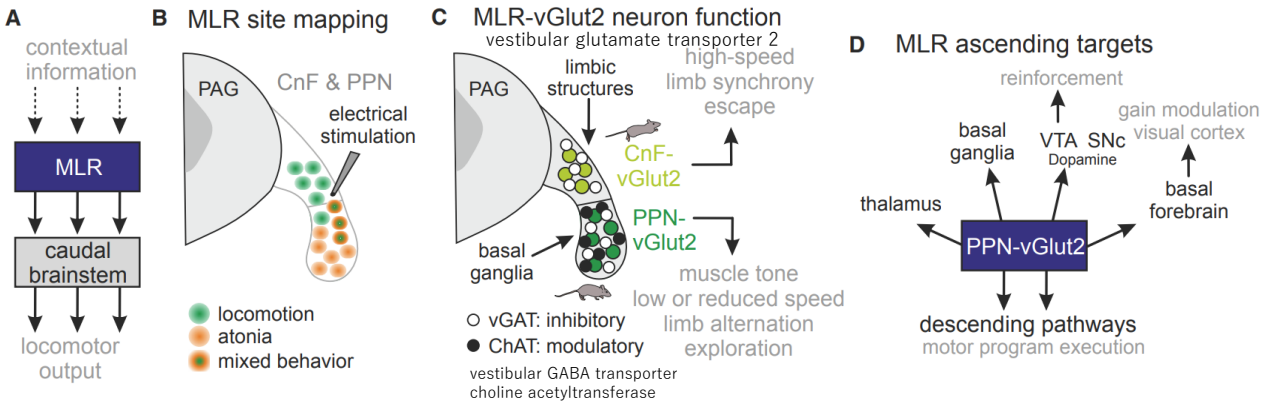


Figure 3. **Functional and Cellular Diversity of the Mouse MLR**
(A) MLR processes contextual information and its descending pathways signal to caudal brainstem neurons to influence locomotor output.
(B) Summary diagram of historical electrical site-mapping experiments in the cat CnF and PPN to define locations influencing locomotion (see Takakusaki et al., 2016, for review).
(C) Schematic diagram summarizing recent findings on the role of mouse MLR-vGlut2 neurons subdivided by location within CnF (cuneiform nucleus) and PPN (pedunculopontine nucleus). Both CnF and PPN also contain vGAT neurons, but only PPN contains cholinergic neurons.
(D) Summary diagram of PPN-vGlut2 neuron projections to ascending targets and known implicated functions.

10

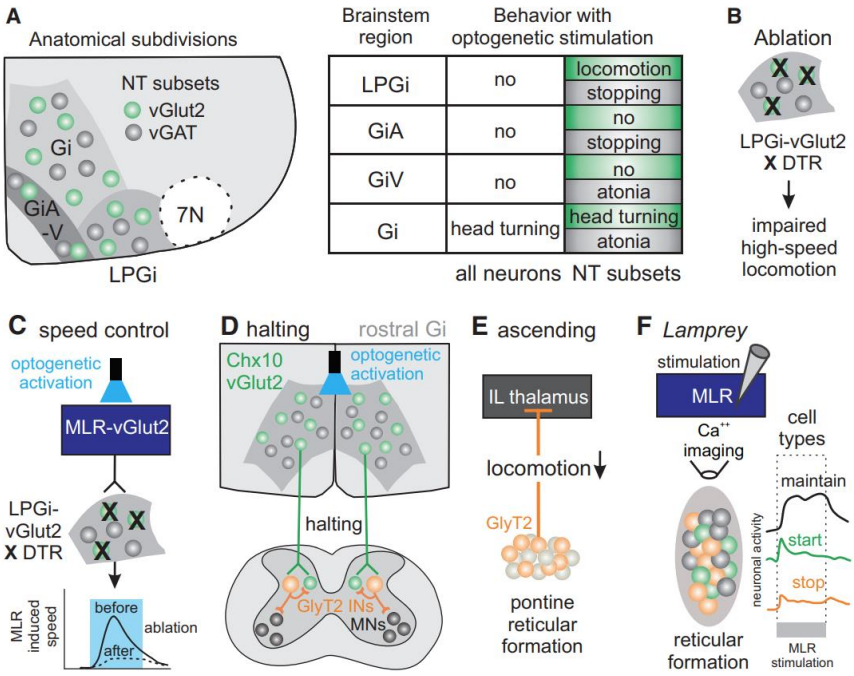


Figure 4. **Brainstem Cell Types Regulating Locomotion**
(A) Subdivision of ventral medulla into four regions (LPGi, lateral paragigantocellular nucleus; GiA, gigantocellular nucleus alpha; GiV, gigantocellular nucleus ventral; Gi, gigantocellular nucleus) all containing intermingled neurotransmitter (NT)- stratified (vGlut2/vGAT) neurons (7N demarcates facial motor nucleus). Table (right) summarizes behavioral findings from optogenetic activation experiments of different neuronal subpopulations.
(B and C) Ablation of LPGi-vGlut2 neurons impairs high-speed locomotion (B) and attenuates speed of locomotion induced by optogenetic stimulation of MLR-vGlut2 neurons (C).
(D) vGlut2 neurons expressing the transcription factor Chx10 in the rostral gigantocellular nucleus (Gi) implicated in halting by signaling through locomotion-inhibiting circuits in the spinal cord.
(E) Glycinergic neurons in the pontine reticular formation project ascendingly to the intralaminar nucleus of the thalamus (IL) to attenuate locomotion.
(F) Summary of firing properties of three populations of neurons in the lamprey reticular formation implicated in locomotor control.

11

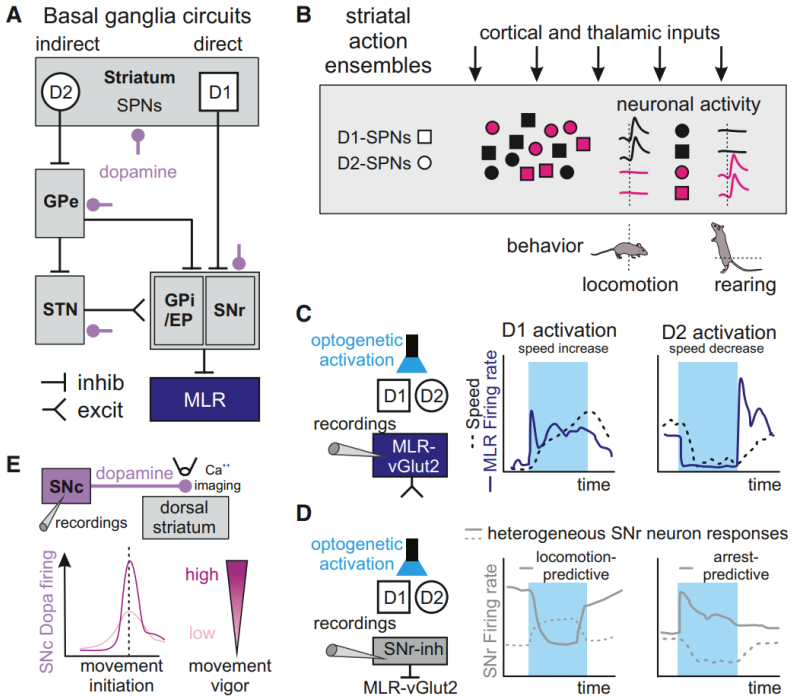


Figure 5. Basal Ganglia Circuit Control of Locomotion
(A) Schematic diagram of the main feedforward connectivity by indirect (D2) and direct (D1) striatal spiny projection neurons (SPNs) within the basal ganglia, as well as their dopaminergic inputs.
(B) D1- and D2-SPNs containing striatal functional ensembles exhibit a proximity-biased spatial distribution, according to different behaviors (e.g., locomotion or rearing). Summary of their neuronal activity patterns is depicted on the right.
(C and D) Recording of MLR-vGlut2 (C) or SNr-inhibitory (D) neurons upon optogenetic stimulation of D1- or D2-SPNs. Note that not all SNr neurons are predictive of locomotor behavior, likely a reflection of further neuronal diversity yet to be identified.
(E) SNc-derived dopamine signaling to the dorsal striatum before movement initiation (e.g., locomotion) determines the vigor of the future executed action.

12

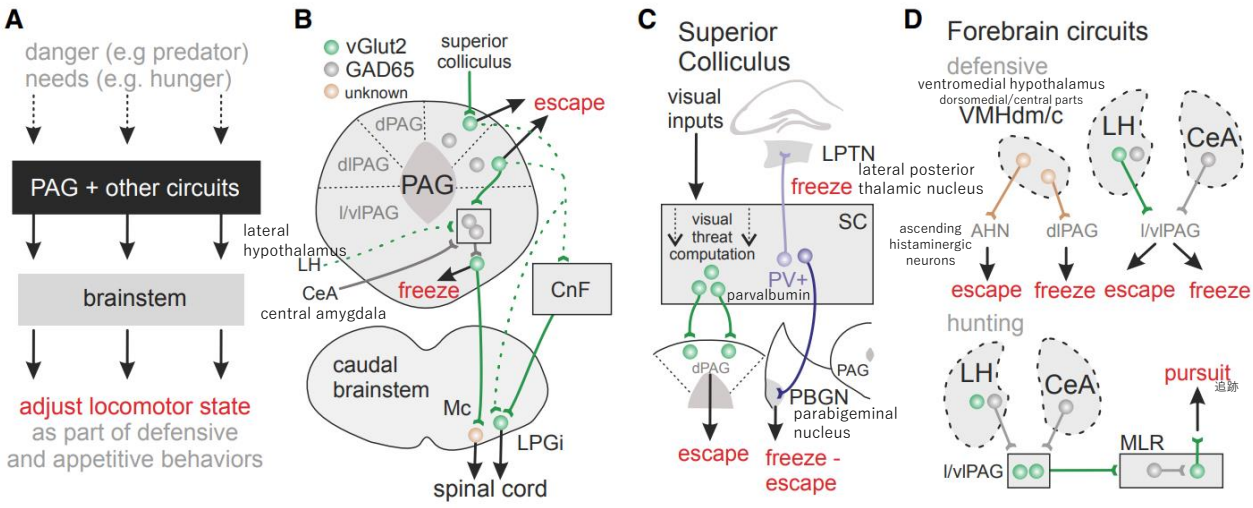
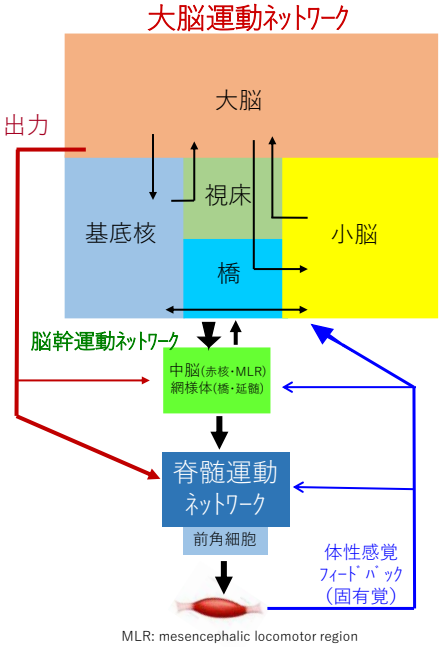


Figure 6. **Circuits for Behavioral Need and Context Influencing Locomotion**
(A) Periaqueductal gray (PAG) and associated structures are central in processing information about danger and needs in order to then signal through brainstem circuits to adjust locomotor state as part of numerous defensive and appetitive behaviors.
(B–D) Summary of functionally known (solid) and inferred (dashed) circuit organization for the PAG (B), superior colliculus (C), and forebrain circuits implicated in defensive and hunting behaviors (D). Neurons shown in boxes implies that there might be multiple neuronal subpopulations processing the shown inputs.

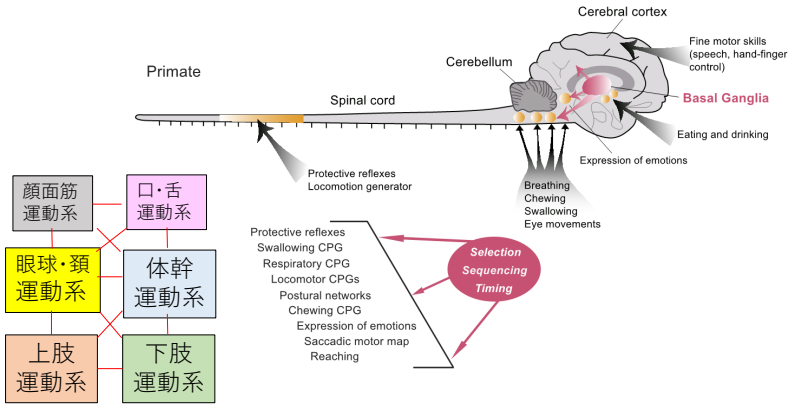
13

成熟運動神経系(私案)



- 脊髄運動ネットワークは自律性が高い
- 自動運動の遂行に大脳はほとんど関与しない
  →上位運動ニューロンは存在しない
- 哺乳類では大脳から脊髄への直接投射あり
  →随意運動に関与　*特に上肢

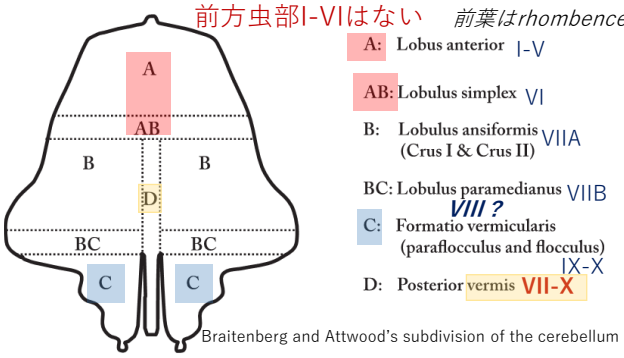
✓発達期脳性運動障害の症候は、常時筋収縮状態を含めて、大脳障害による脊髄運動ネットワークの変容によるのであろう



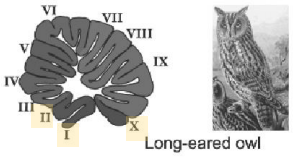
14

Sultan F, Glickstein M. The cerebellum: Comparative and animal studies. Cerebellum 2007;6:168-76.

前方虫部I-VIはない　*前葉はrhombencephalosynapsis様にみえる*

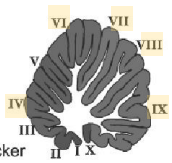


Braitenberg and Attwood's subdivision of the cerebellum



Long-eared owl

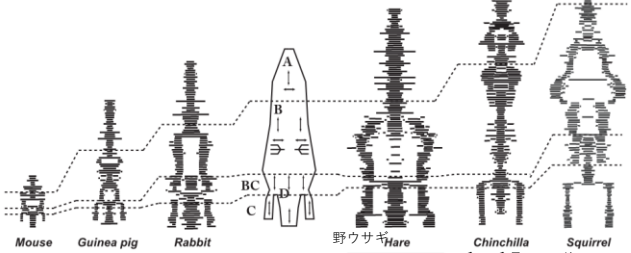
ヨーロッパアオゲラ
（キツツキ）



Green woodpecker

IX: tonsil(paraflocculus)-uvula
X: flocculus-nodulus
の小脳半球と虫部は独立である

excellent climbers
・岩山に棲む
・夜行性-非視覚
・後肢からの固有覚に頼る



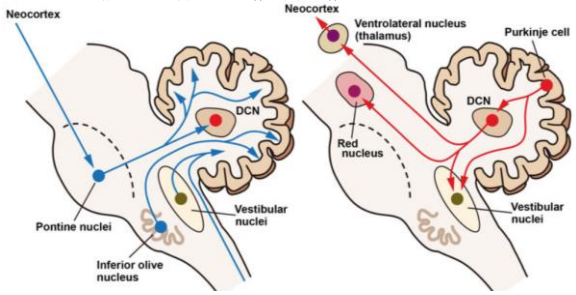
・木登り
・昼行性-視覚
・前肢の把握が発達
⇒VIIa(anisoform lobe)の発達

- フクロウはI･II･Xが大きい
- オウム･カラス･キツツキはIV･VI-IXが大きい

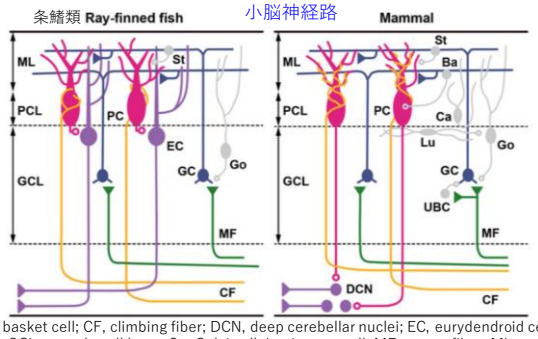
15

Hibi M, et al. Evolutionary mechanisms that generate morphology and neural-circuit diversity of the cerebellum. Dev Growth Differ 2017;59:228-243.

哺乳類小脳の入力路と出力路

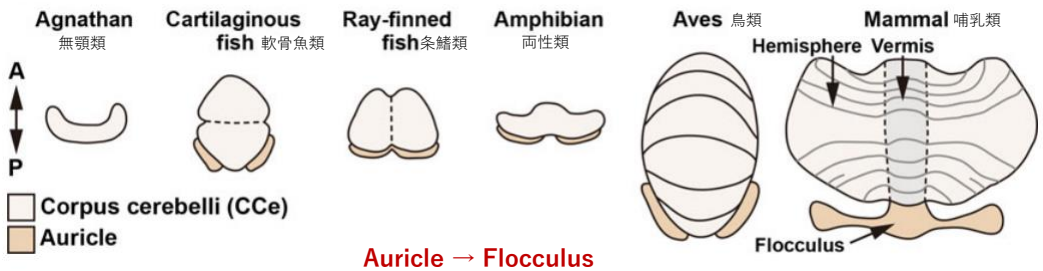


小脳神経路



Ba, basket cell; CF, climbing fiber; DCN, deep cerebellar nuclei; EC, eurydendroid cell; GC, granule cell; GCL, granule cell layer; Go, Golgi cell; Lu, Lugaro cell; MF, mossy fiber; ML, molecular layer; PC, Purkinje cell; PCL, Purkinje cell layer; St, stellate cell; UBC, unipolar brush cell.

脊椎動物の小脳

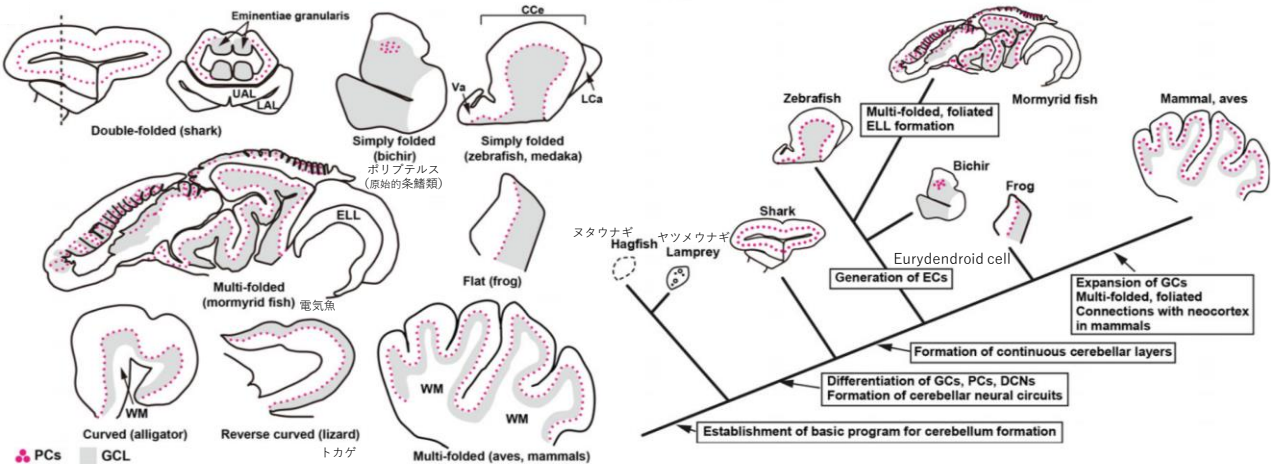


Auricle → Flocculus

16

Diversity of cerebellum structures

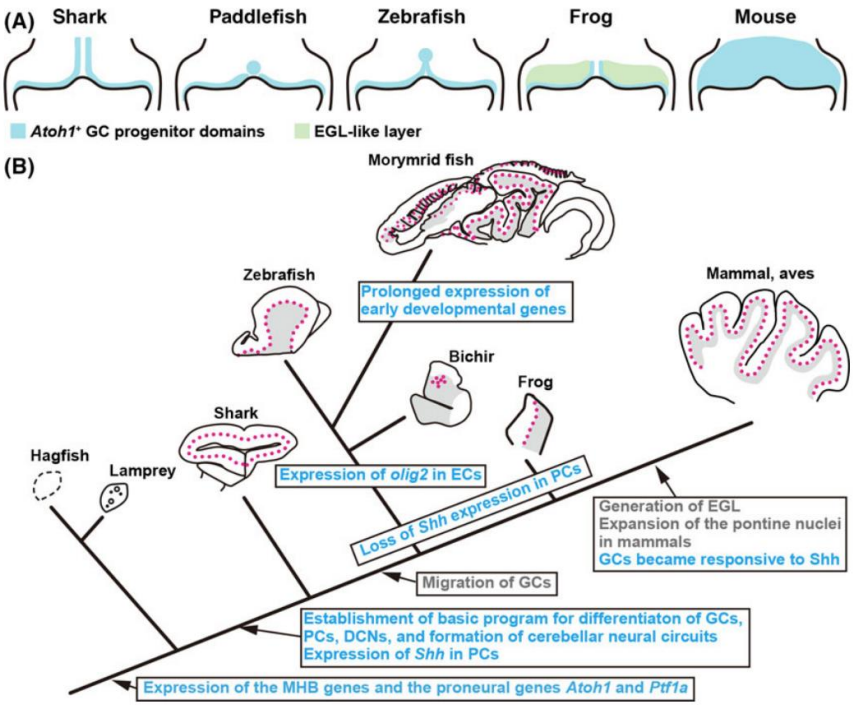
Structures of vertebrate cerebella



The GCLs are marked by shading. PCs are marked by magenta dots.

ELL, electrosensory lateral line lobe; LAL, lower auricular leaf; UAL, upper auricular leaf; WM, white matter, CCe, corpus cerebelli; Va, valvula 小脳弁; LCa, lobus caudalis.

17

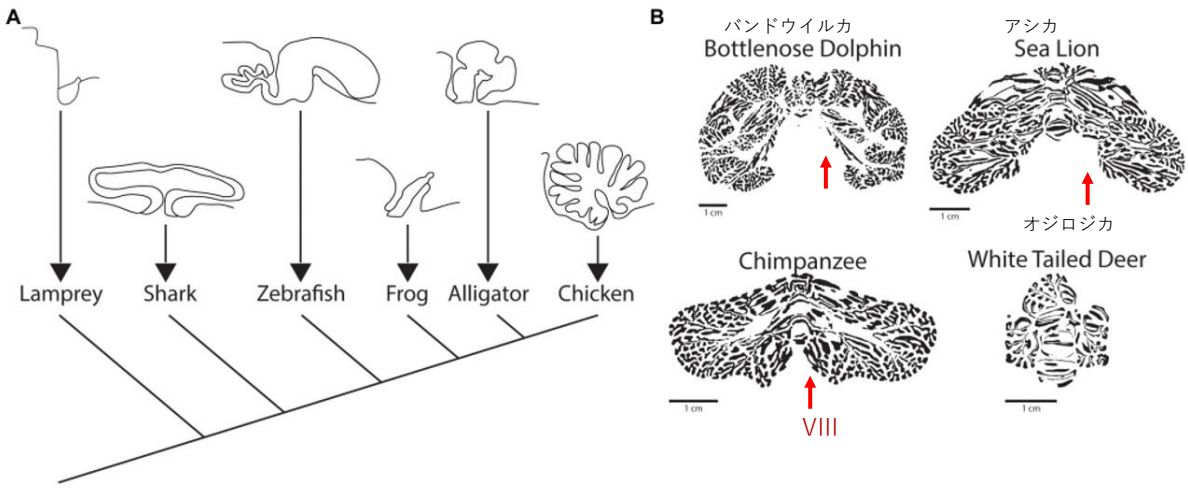


Mechanisms that generate diversity in the cerebellum

(A) Variations in cerebellum morphology during development. Dorsal views of the cerebellum. Atoh1+ GC progenitor domains are marked by blue shading. The proliferating GC progenitors are located in the medial and caudal regions, which are derived from the URL, in shark, paddlefish, and zebrafish. In the frog cerebellum, non-proliferating Atoh1+ GCs expand to transiently form an EGL-like layer (green shading) at metamorphosis. In the mouse cerebellum, proliferating Atoh1+ GC progenitors expand to form the EGL.
(B) Changes in cellular (gray text) and genetic (blue text) programs that generated diversity in the cerebellum during evolution.

18

Gill JS, Sillitoe RV. Functional Outcomes of Cerebellar Malformations. Front Cell Neurosci 2019:13:441.



19

Butts T, et al. Development of the cerebellum: simple steps to make a 'little brain'. Development 2014;141:4031-41.

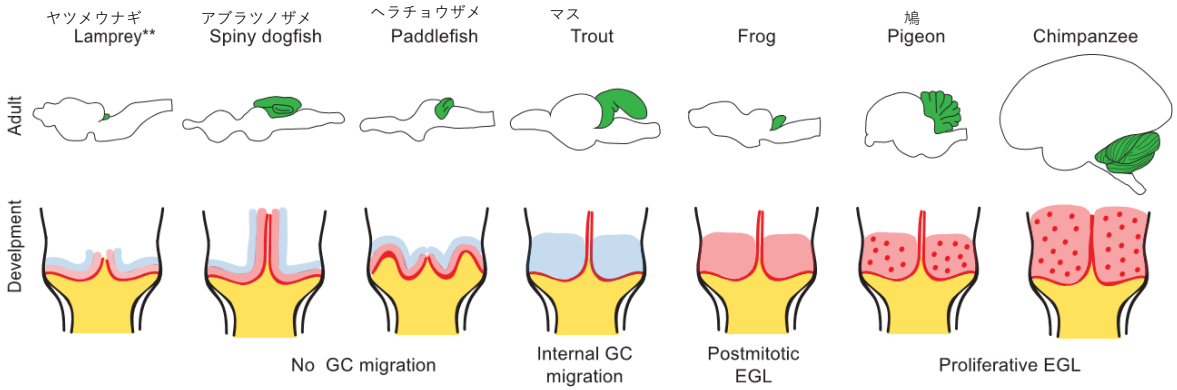
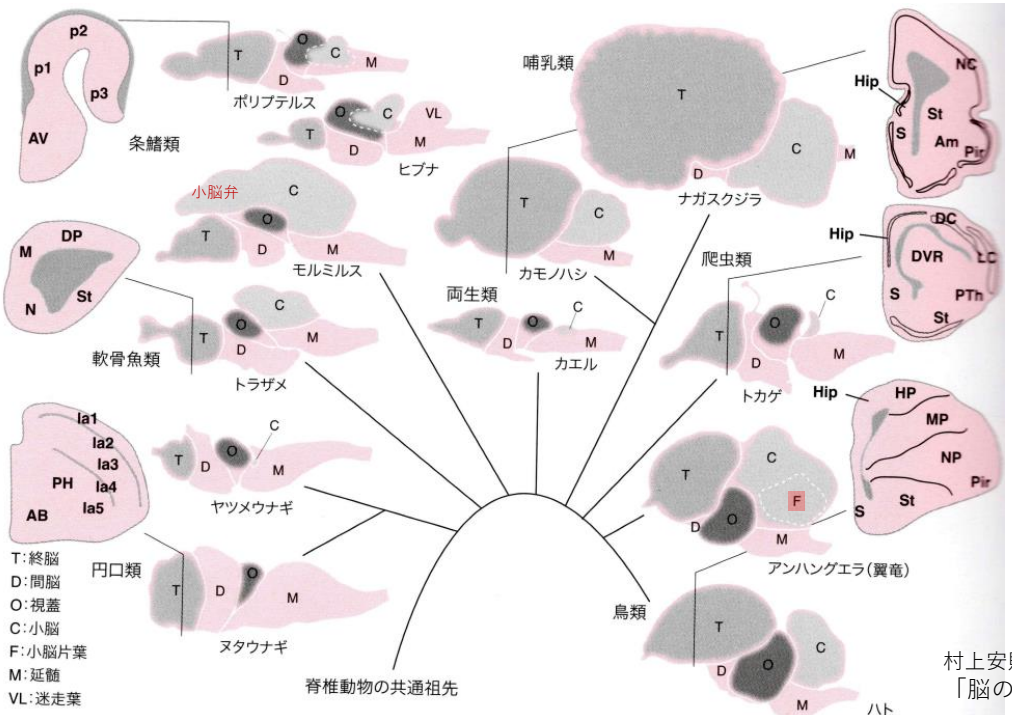


Fig. 2. Variations in cerebellar morphology. Variation in the morphology and of the adult cerebellum (green) across vertebrates is reflected in developmental adaptations of the granule cell precursor pool (red). Cerebellar expansion in basal fish corresponds to linear extensions of the rhombic lip axially (spiny dogfish)or medially (paddlefish). In other clades, granule cells (pink shaded area) are distributed in an internal layer that is co-extensive with the overlying Purkinje cells (blue). To achieve this, granule cells migrate internal to (teleosts and tadpoles) or external to (metamorphic amphibians, birds and mammals) and then through the Purkinje cell layer. Only in birds and mammals do granule cell precursors themselves migrate in substantial numbers to form a transient external germinal layer. **A theoretical model of the as yet uncharacterised embryonic lamprey.

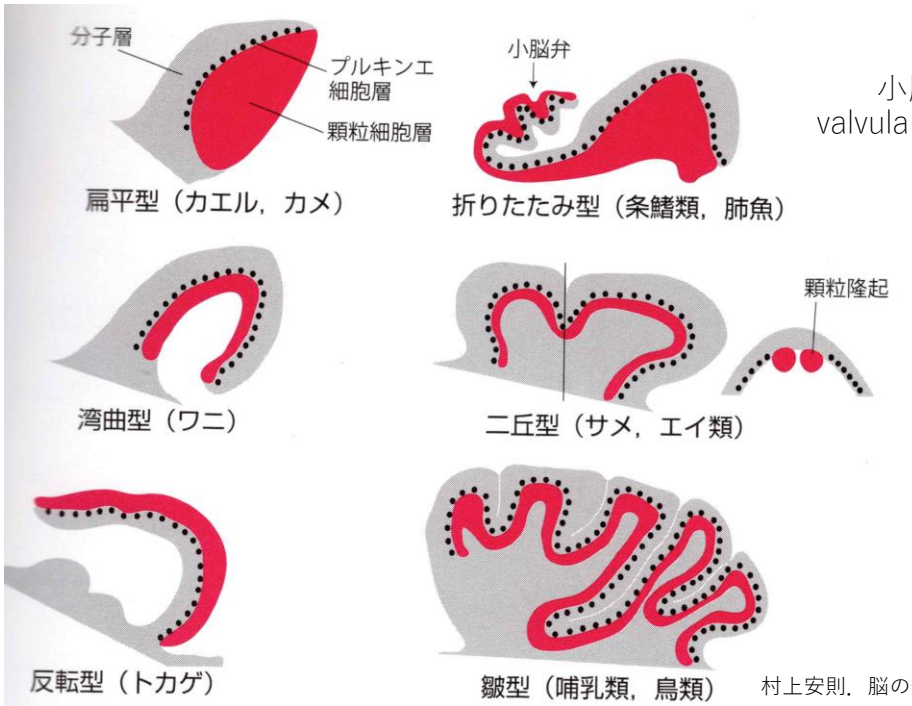
20



条鰭類
小脳対-小脳耳
auricle
↓
片葉
flocculus

村上安則．脊椎動物の脳の進化．「脳の発生学」2013.

21



小脳弁
valvula cerebelli

村上安則．脳の進化形態学．2015.

22

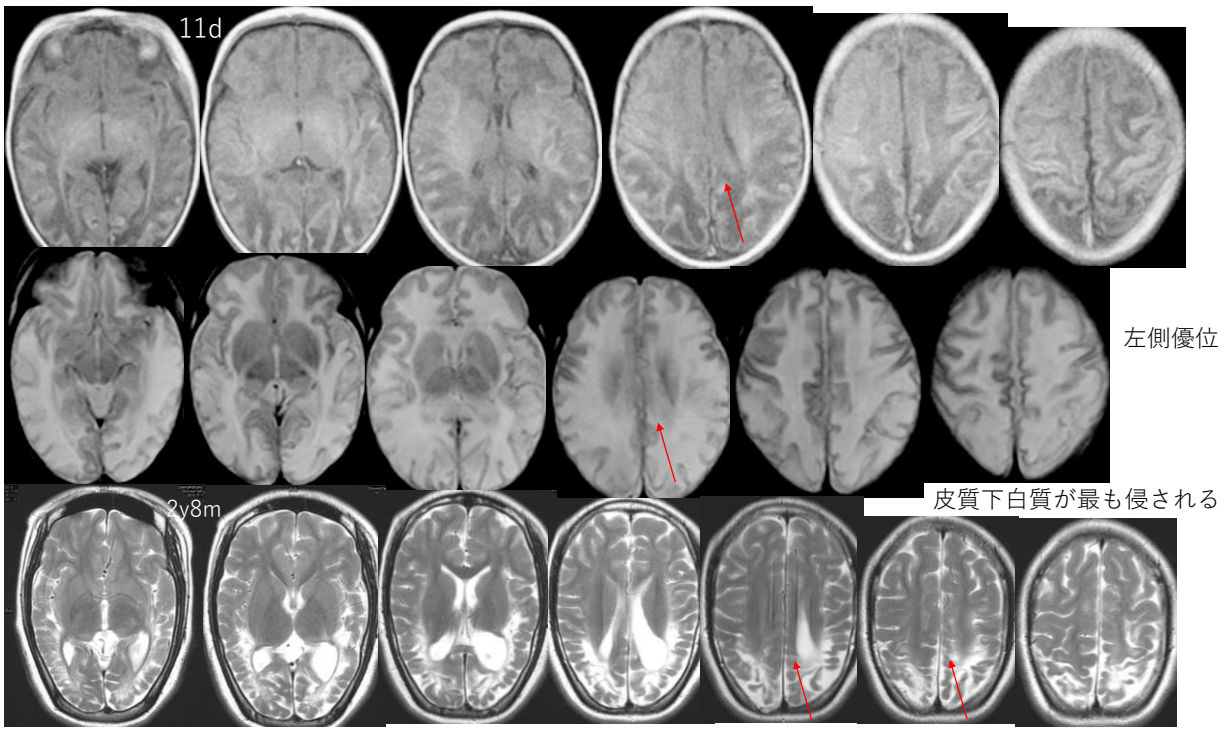
・39w　HIE　・独歩2y10m　・重度ID

股屈曲過活動
・股伸展荷重制限

周生期脳低血流障害-外表後方型は どうして知的障害が重いのか

Precuneus 楔前部

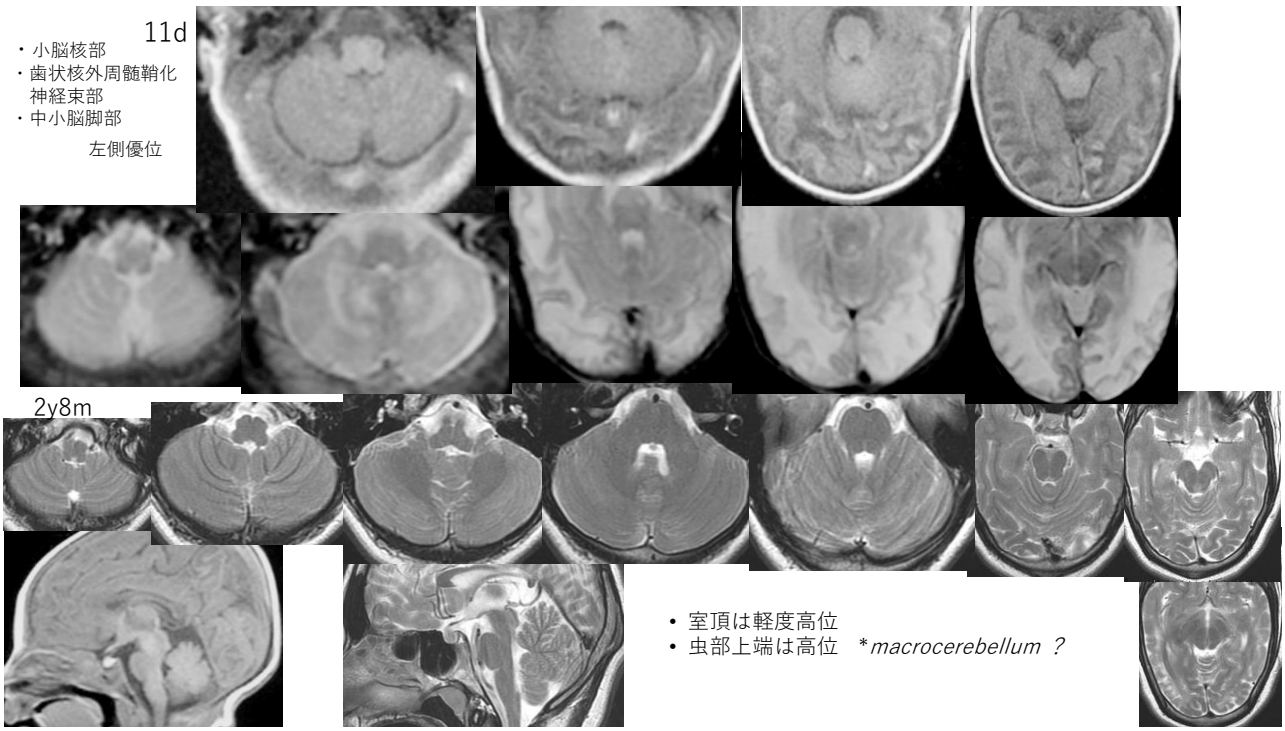
23



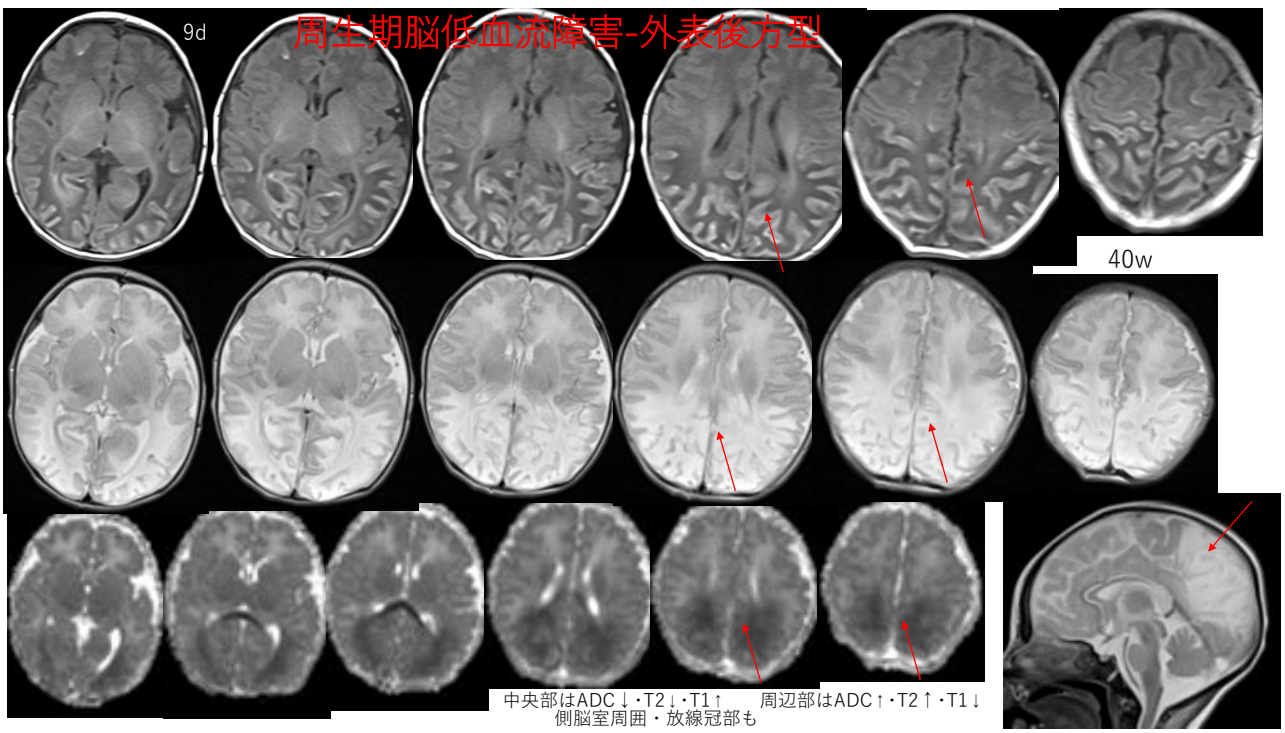
左側優位

皮質下白質が最も侵される

24

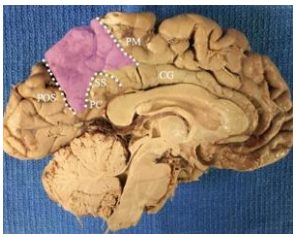

11d
・小脳核部
・歯状核外周髄鞘化
神経束部
・中小脳脚部
左側優位
2y8m
• 室頂は軽度高位
• 虫部上端は高位 *macrocerebellum ?

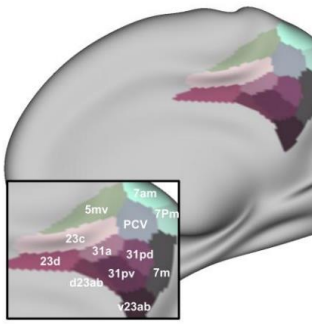
25


9d
周生期脳低血流障害-外表後方型
40w
中央部はADC↓・T2↓・T1↑
側脳室周囲・放線冠部も
周辺部はADC↑・T2↑・T1↓

26

Precuneus 楔前部（けつぜん）



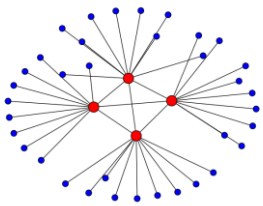


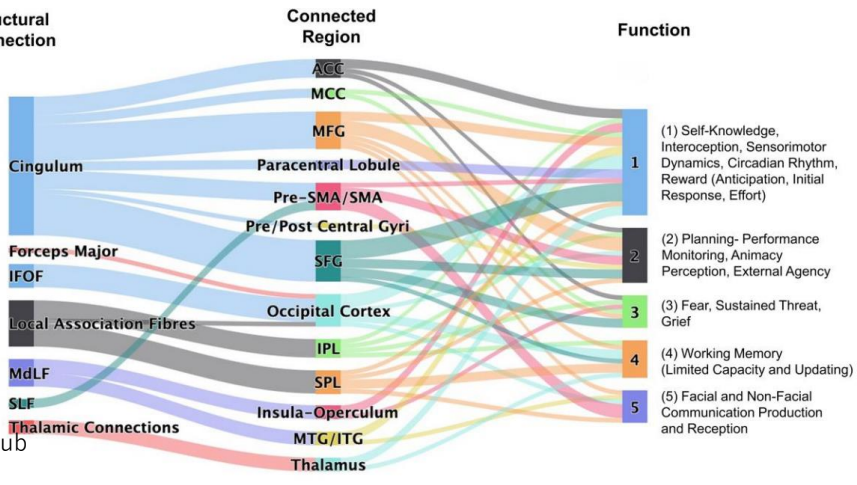
Functions identified	Para-cingulate network	Default mode network
Animacy perception	PCV, 7Pm, 23c	–
Circadian rhythm	7Pm	–
External agency	POS2, 7Pm	7m
Facial communication-production	33pr, 23d, 23c	–
Fear	RSC	v23ab
Grief	RSC, POS2, PCV, 7Pm, 23d	d23ab, v23ab
Initial response to reward	PCV	–
Interoception	PCV, 23d, 23c	31pv, 7m, d23ab
Non-facial communication-production	RSC, 23d	–
Non-facial communication-reception	RSC	d23ab
Planning-performance monitoring	POS2, 23c	7m
Reward anticipation	POS2, 7Pm, 33pr	POS2, 7Pm, 23d, 23c
Reward effort	POS2, 7Pm, 33pr	7m
Self-knowledge	RSC	31pv, d23ab, v23ab
Sensorimotor dynamics	POS2, PCV, 7Pm	31pd, 7m
Sustained threat	RSC, 33pr, 23d	d23ab
Working memory-limited capacity	POS2, PCV, 7Pm	31pd, 7m
Working memory-updating	POS2, 7Pm, 23d, 23c	31pd, 7m, v23ab

Dadario NB, Sughrue ME. The functional role of the precuneus. Brain 2023;146:3598-3607.

27

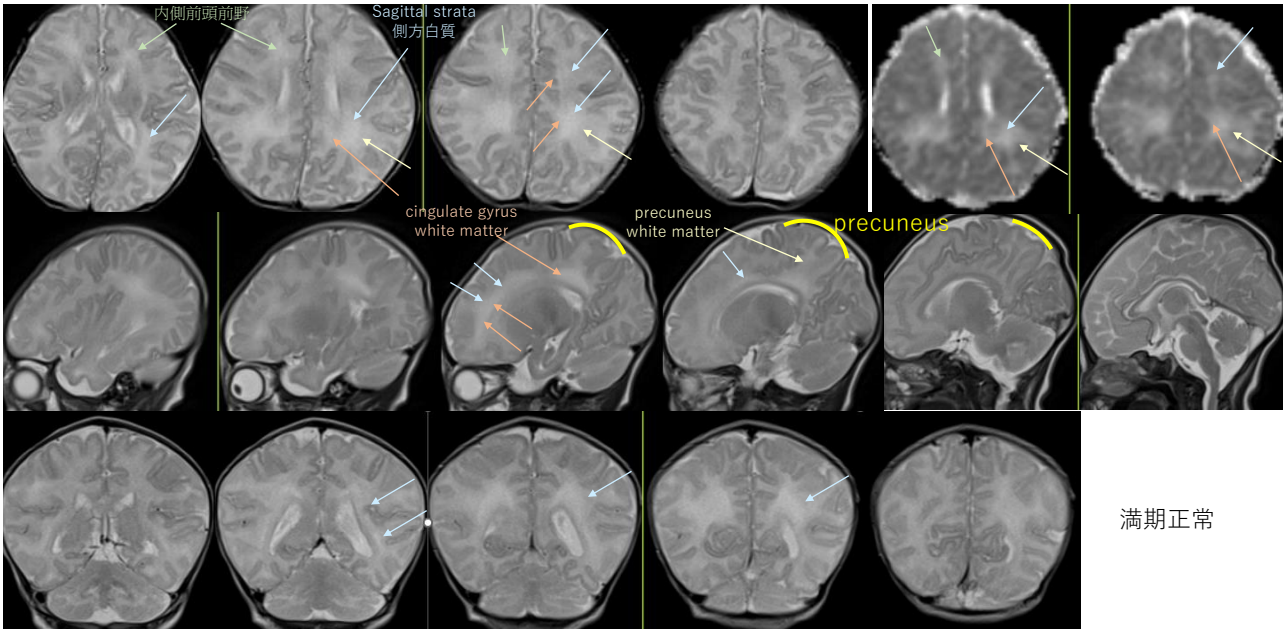
Messina A, et al. Clinical anatomy of the precuneus and pathogenesis of the schizophrenia. Anat Sci Int 2023;98:473-481.





- 脳ネットワークのrich club
- Default mode networkの基本的なhub
- 大脳皮質の系統発生上の進化型
- 3部に分けられる
  - ・Dorsal-anterior: frontal-parietal cortexと連絡し、mental representation of space、object-body relations、visual guided movementに関与する
  - ・Dorsal-posterior: occipital-parietal lobesとhippocampusに連絡し、visual-spatial information、deductive reasoning 演繹的推論、spatial navigation、motor imageryを処理すること、cognitive and abstract reasoning processesに使われるspatial mental modelsを作り直すことを可能とする
  - ・Ventral: cingulate, temporal, and limbic lobeと連絡し、emotional and episodic memory processingに関与する。autobiographic eventsを収集するための時と空間に及ぶepisodic memory retrievalの際に活性化される。visuospatial informationはここでコード化された後海馬に貯蔵される

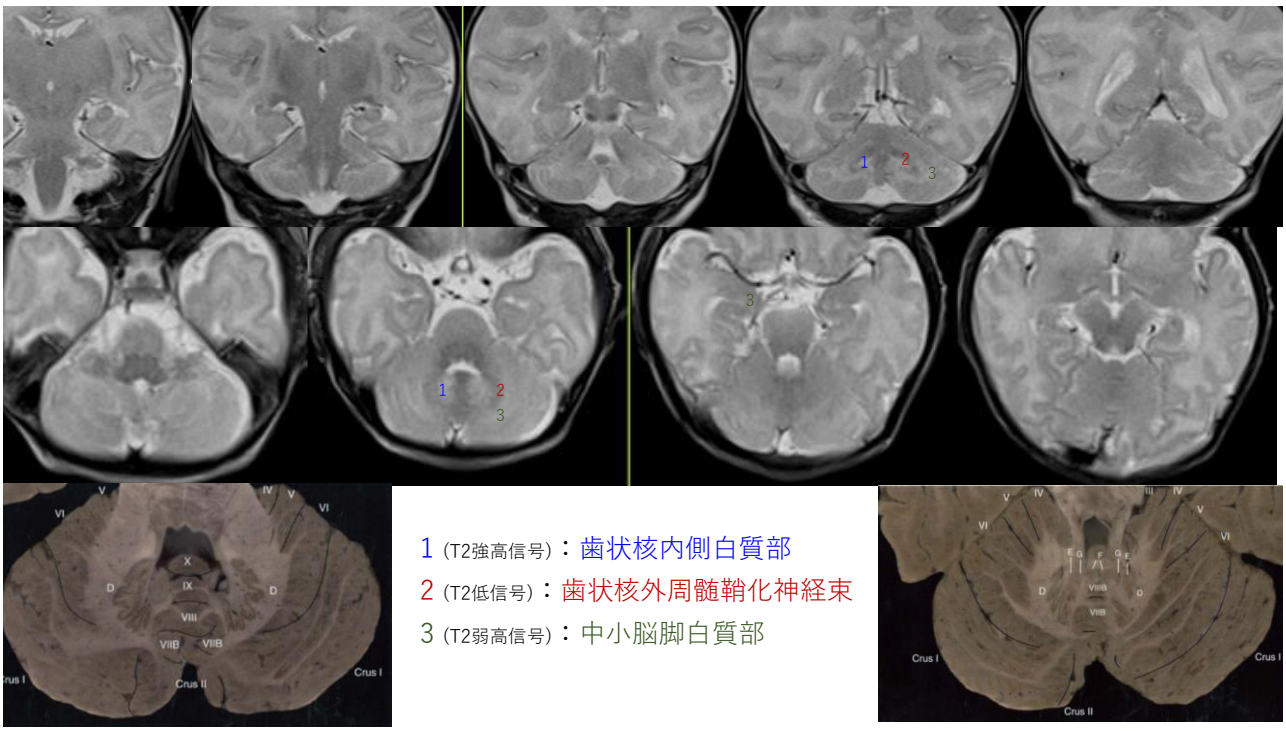
28



満期正常

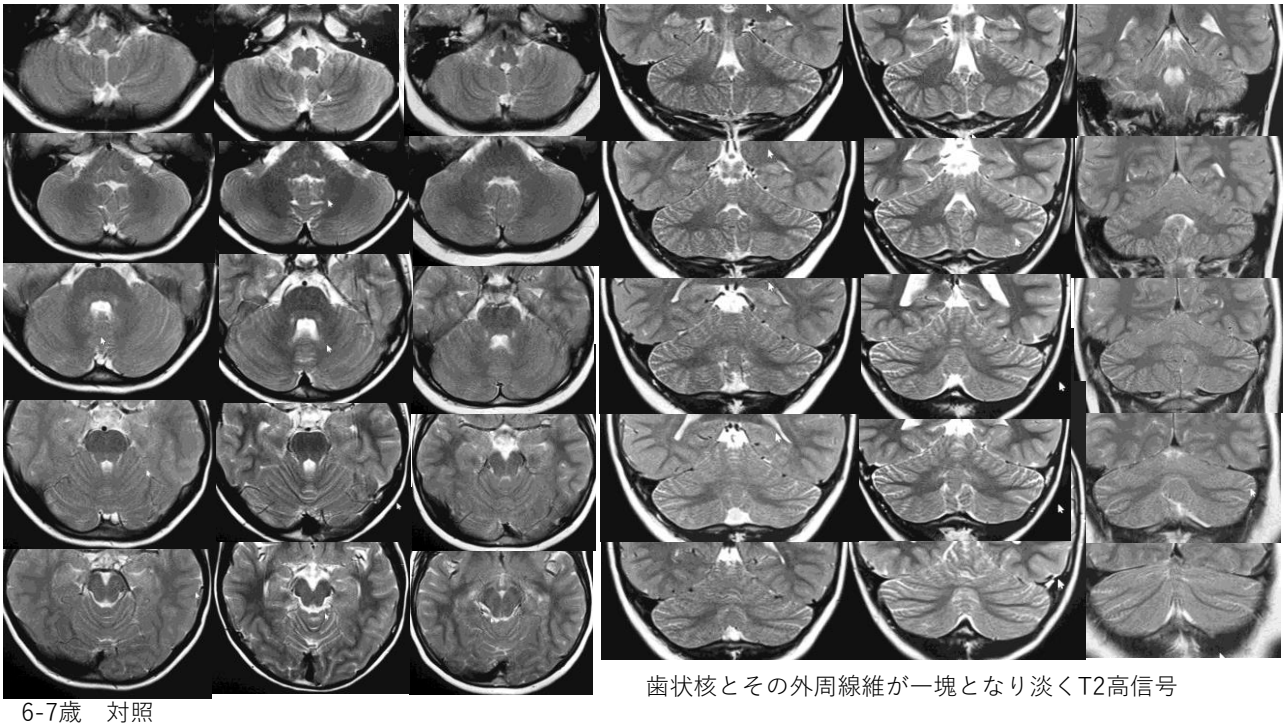
T2高信号部は水溶性神経伝達物質の多い神経路発達急な部位
（Kostovicのcrossroads）

29



1（T2強高信号）：歯状核内側白質部
2（T2低信号）：歯状核外周髄鞘化神経束
3（T2弱高信号）：中小脳脚白質部

30



6-7歳　対照

歯状核とその外周線維が一塊となり淡くT2高信号

31