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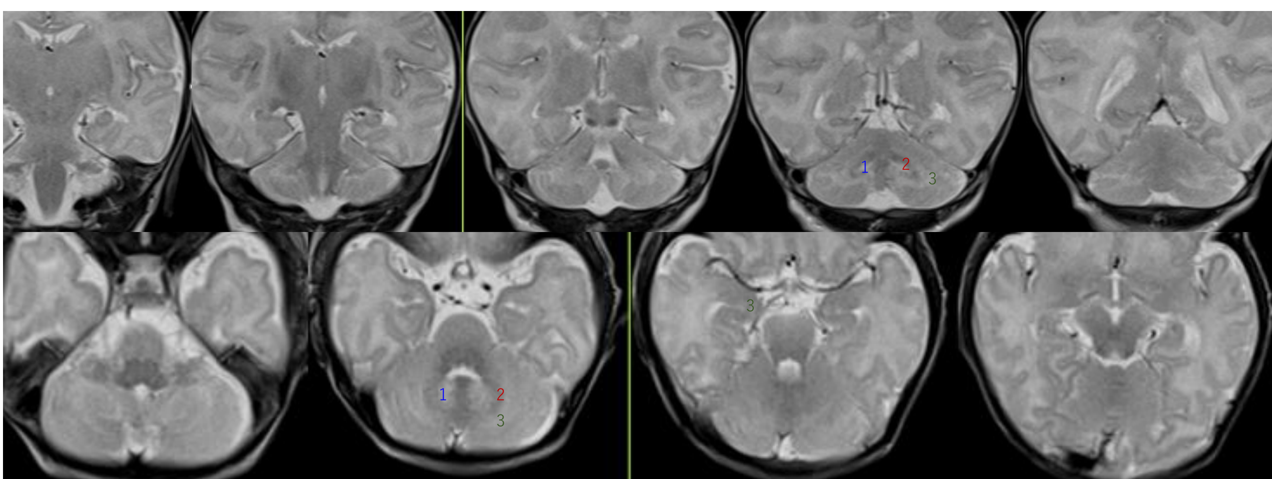
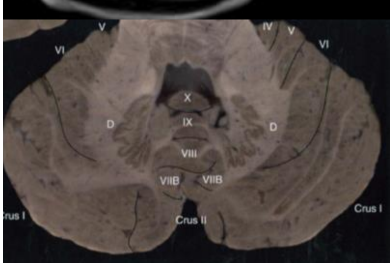




これは何か

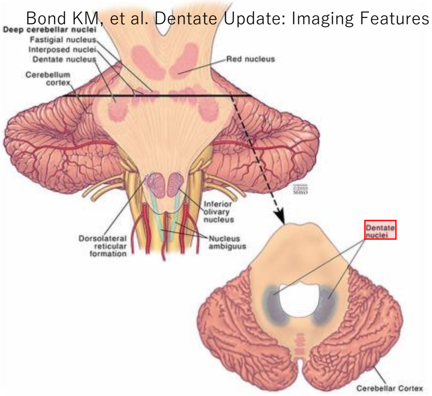
1 (T2強高信号)：歯状核内側白質部

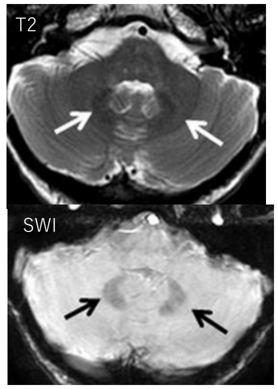
2 (T2低信号)：歯状核外周髄鞘化神経束

3 (T2弱高信号)：中小脳脚白質部

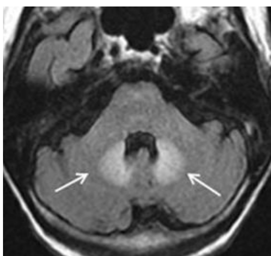
2

Bond KM, et al. Dentate Update: Imaging Features of Entities That Affect the Dentate Nucleus. AJNR Am J Neuroradiol 2017;38:1467-1474.





Neuro degenerative iron accumulation

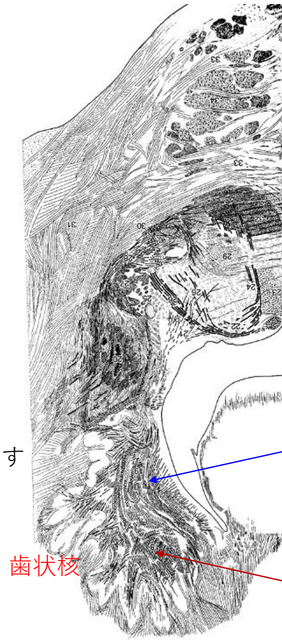


Metronidazole toxicity

Gadolinium deposition

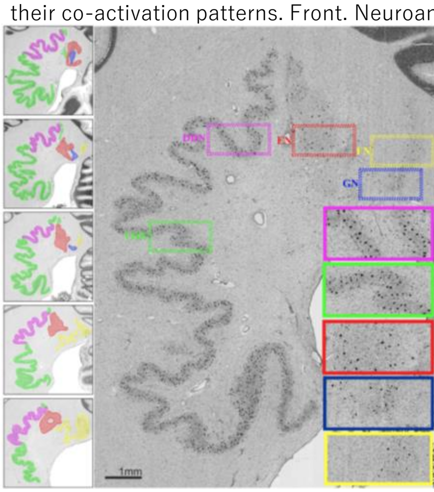
画像上の歯状核は
神経細胞集団と内側線維束を指す

歯状核内側白質部の主体は
歯状核から出力する上小脳脚
髄鞘化前の高度分化途上



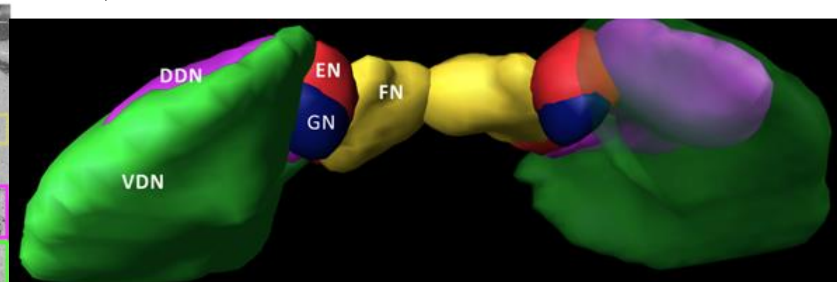
3

Tellmann S, et al. Cytoarchitectonic mapping of the human brain cerebellar nuclei in stereotaxic space and delineation of their co-activation patterns. Front. Neuroanat 2015:9;54.



(Left) Localization and extent of cerebellar nuclei in a rostro-caudal sequence of histological sections of a post mortem brain; distance between sections 60 µm.

(Right) Cytoarchitecture of each cerebellar nucleus and the two parts of the dentate nucleus. Magenta: dorsal **dentate nucleus** (DDN); green: ventral **dentate nucleus** (VDN); red: emboliform nucleus (EN); blue: globose nucleus (GN); yellow: **fastigial nucleus** (FN).

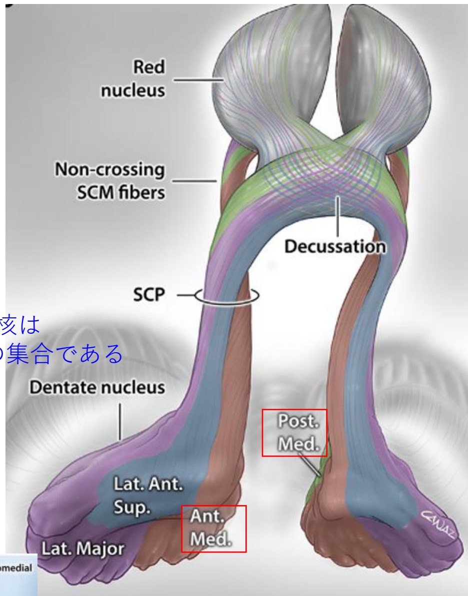


3D model of the deep cerebellar nuclei (posterior to anterior view) of an individual brain (post mortem brain10); visualization by Amira 5.6.0 (www.amira.com). Dorsal **dentate nucleus** (DDN; magenta); ventral **dentate nucleus** (VDN; green); emboliform nucleus (EN; red); globose nucleus (GN; blue); **fastigial nucleus** (FN; yellow). Due to the smoothing, the dentate appears less denticulated than it is. The transparency of the right ventral dentate nucleus clarifies the partly covered extend of the DDN.

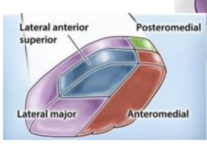
神経放射線上の歯状核は
神経細胞集団とその出力部(上小脳脚)を含んだものを指す

4

Tacyildiz AE, et al. Dentate Nucleus: Connectivity-Based Anatomic Parcellation Based on Superior Cerebellar Peduncle Projections. World Neurosurg 2021:152:e408-e428.



歯状核は
多様な機能の集合である



Anteromedial: ほぼすべて非交差　nonmotor
Posteromedial: 半分は非交差　motor

Table 1. Connectivity-Based Anatomic Parcellation of the Dentate Nucleus and Their Presumptive Functions

Dentate Nucleus Compartments	SCP Origin	Course	Involvement in Decussation	Presumptive Function[10]
Lateral anterosuperior	Most ventral (anterosuperior) part	Most ventral fibers within the decussation, initial SCP fibers entering the decussation after first turn	Most of its fibers participate in the SCP decussation	Nonmotor functions
Lateral major	Inferior, middle, superior parts of lateral DN; occupies the largest surface area along DN surface; dorsal to fibers originating from lateral anterosuperior part	Forms middle part of the decussation with a twist of 150° turn	Most of its fibers participate in the SCP decussation; some of its noncrossing fibers ascend ipsilaterally	Motor and nonmotor functions
Anteromedial	Most medial and anterior part	Fibers arise from medial anterior part; pass posterolateral to fibers of posteromedial compartment during its climb	Almost all fibers are noncrossing; fibers do not participate in the SCP decussation and ascend ipsilaterally	Nonmotor functions
Posteromedial	Medial posterior part; dorsal to anteromedial compartment	Fibers course anterior to the anterior medial fibers at the highest levels	Half of the fibers ascend ipsilaterally as part of the noncrossing dentatorubrothalamic tract and the other half join the decussation	Motor functions

SCP, superior cerebellar peduncle; DN, dentate nucleus.

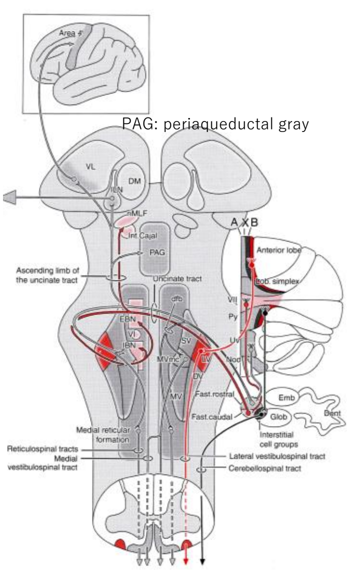
Table 2. Functions of the Dentate Nucleus Summarized

Reference	Dorsal	Ventral	Dorsorostral	Dorsocaudal	Ventrocaudal	Ventrorostral
Dum and Strick, 2003[4] (monkeys) (retrograde transneural transport of neurotropic virus)	Motor functions show rostrocaudal arrangement (leg-arm-face); connected with primary motor and premotor areas	Nonmotor functions; associated with prefrontal and posterior parietal areas				
Küper et al., 2012[15] (human) (functional magnetic resonance imaging)			Motor functions	Visuospatial (bilateral)	Verbal working memory	
Thurling et al., 2011[11] (human) (7-T MRI)		Aloud reading (bilateral)	Aloud reading (bilateral)		Verb generation (bilateral)	Silent reading (left predominant); verb generation (bilateral)
Küper et al., 2012[15] (human) (7-T MRI)			Motor functions, mostly ipsilateral dorsorostral dentate nucleus; finger caudal; foot rostral			

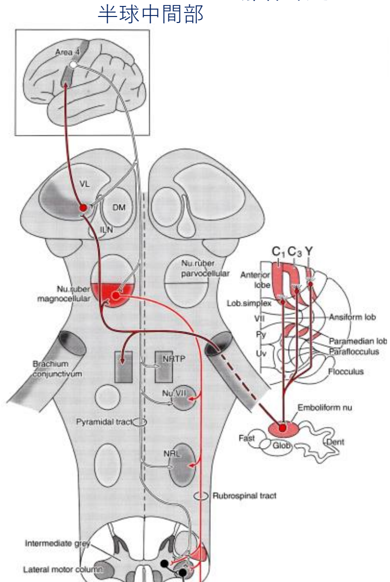
5

小脳出力

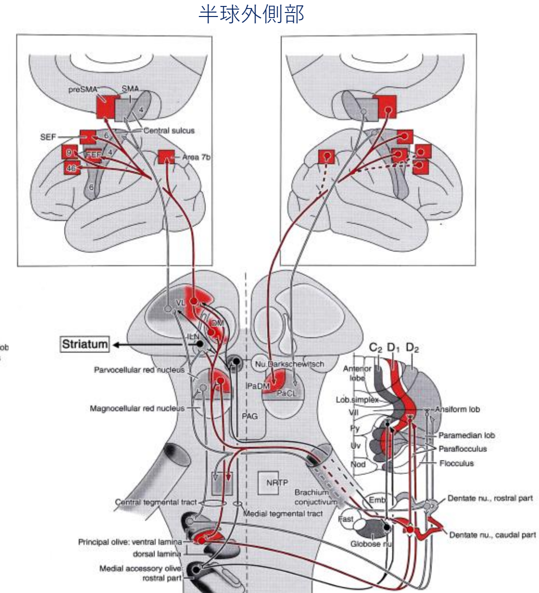
虫部とその側方部



半球中間部



半球外側部

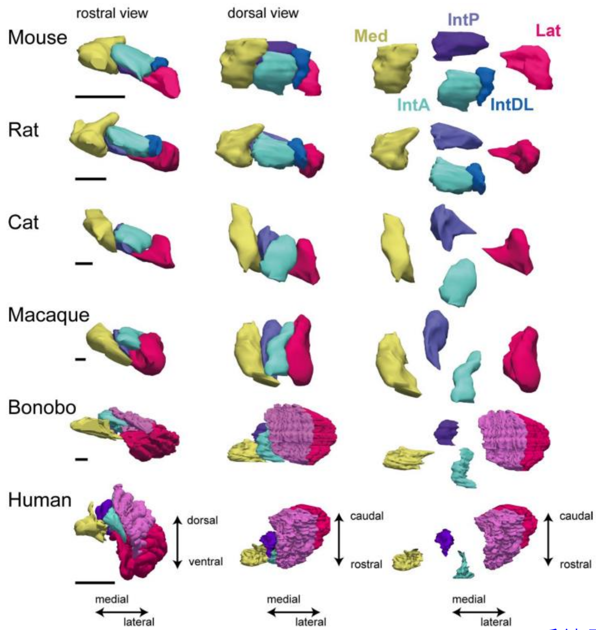


VIIからはemboliform nucleusに出力しない

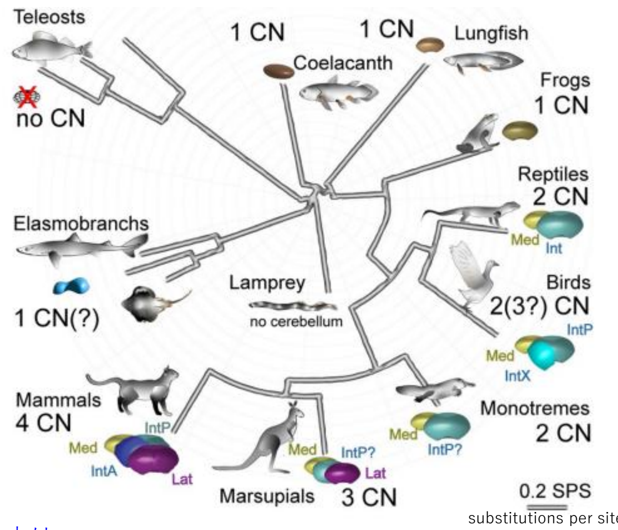
満期時の上小脳脚髄鞘化線維はfastigial・globose・emboliform nucleus由来であろう
Dentate nucleusの出力線維は髄鞘化未達だが機能レベルは高い

6

Kebschull JM, et al. Cerebellum Lecture: the Cerebellar Nuclei-Core of the Cerebellum. Cerebellum 2023: 10.1007/s12311-022-01506-0.



Medial cerebellar nucleus (Med): Fastigial nucleus
Posterior interposed nucleus (IntP): Globose nucleus
Anterior interposed nucleus (IntA): Emboliform nucleus *IntDLを含む
Lateral cerebellar nucleus (Lat): Dentate nucleus

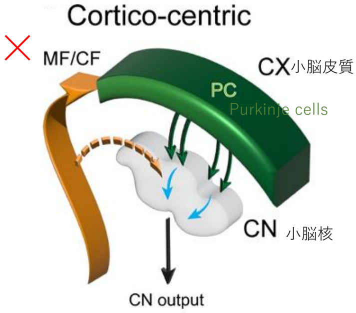


系統発生上は
Fastigial nucleus → Globose nucleus → Emboliform nucleus → Dentate nucleus

7

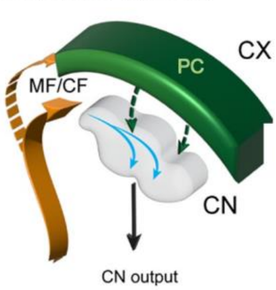
古典的皮質機能局在

Cortico-centric

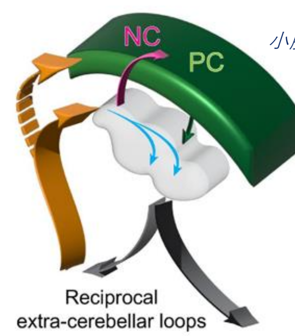


CF: climbing fibers
MF: mossy fibers

Nucleo-centric

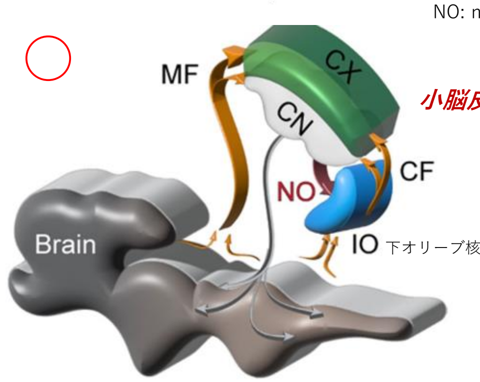


→



小脳皮質と小脳核は独立機能単位

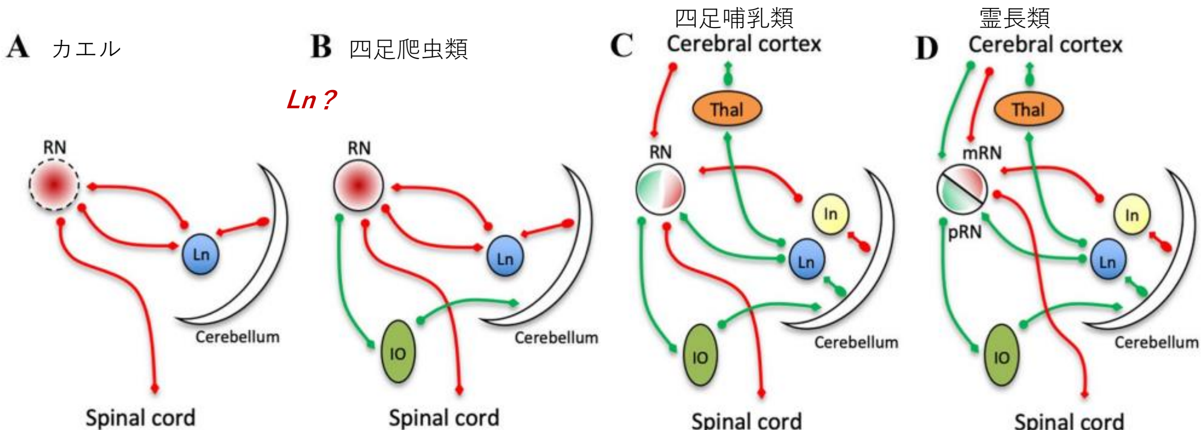
NC: nucleocortical pathway
NO: nucleo-olivery pathway



小脳皮質と小脳核は一体

8

Basile GA, et al. Red nucleus structure and function: from anatomy to clinical neurosciences. Brain Struct Funct 2021;226:69-91.



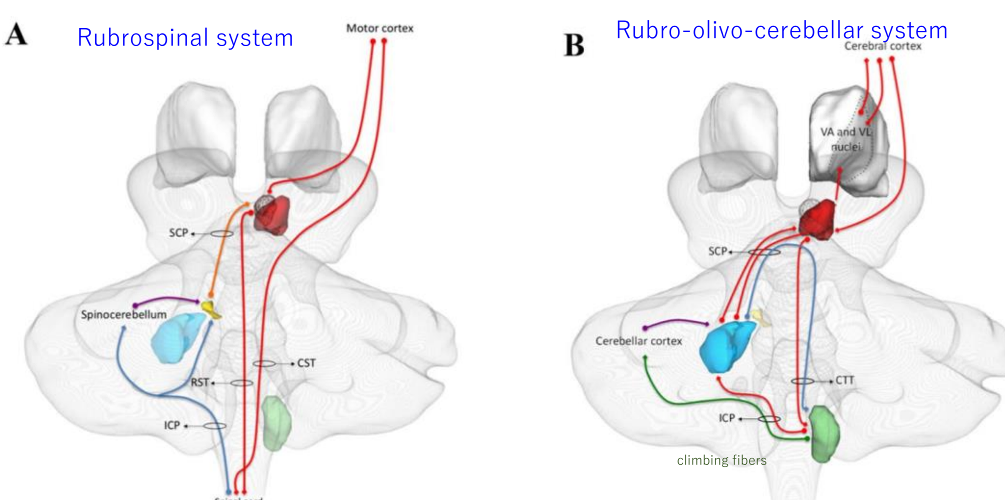
・Rubro-olivary pathwayの出現

・Rubrospinalとrubro-olivo-cerebellar systemの部分的な分離
・小脳出力の進化
・pRNとmRNの分化の始まり

・Rubrospinalとrubro-olivo-cerebellar systemの完全な分離

mRN: magnocellular red nucleus, pRN: parvocellular red nucleus, Ln: lateral nucleus (dentate), In: interposed nucleus, IO: inferior olive, Thal: thalamus.

9



mRN (edges), pRN (red), dentate nucleus (light blue), interposed nucleus (yellow), inferior olive (green) and thalamus (white)
RST rubro-spinal tract, **CST** cortico-spinal tract, **CTT** central tegmental tract, **ICP** inferior cerebellar peduncle, **SCP** superior cerebellar peduncle, **VA** ventral anterior, **VL** ventral lateral

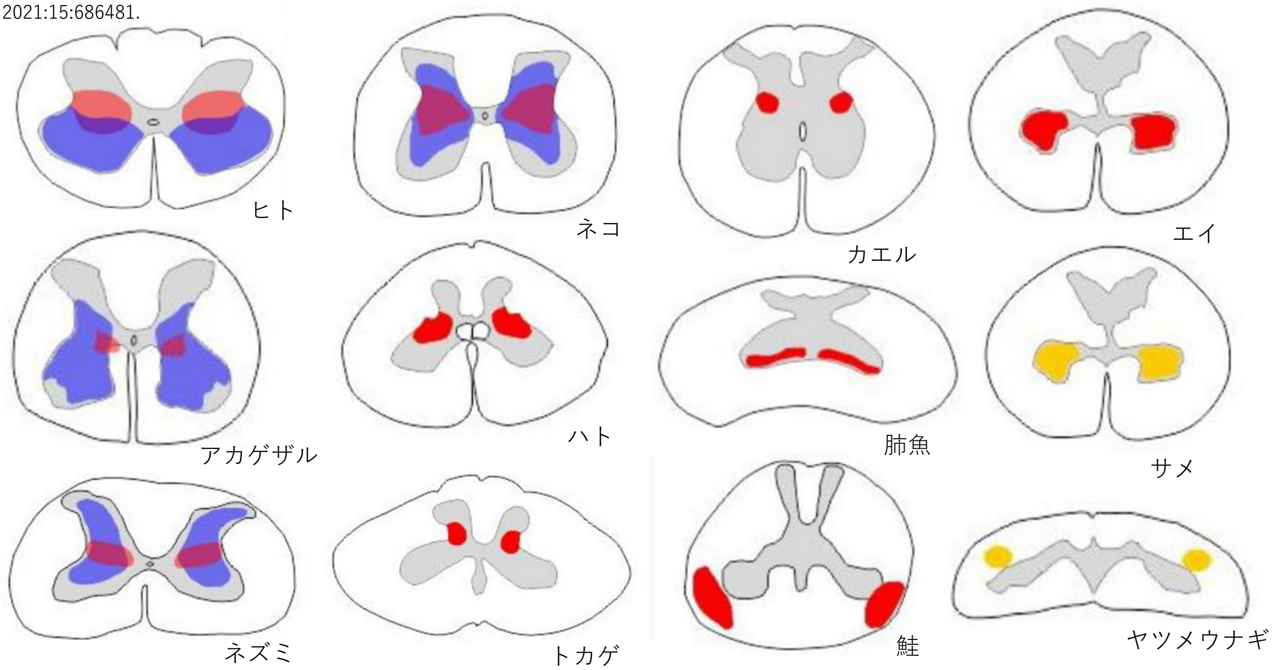
- 赤核は系統発生上はlimbまたはlimb様構造の出現に対応しており、水中から地上への移行に重要な役割を負っている
- 原始的赤核はmRN(magnocellular red nucleus)に対応しており、単純な移動運動と常同的運動の遂行に関与している。pRN(parvocellular red nucleus)は遅れて発達し、さらに複雑な行動に関与している
- ヒトではmRNは退行している意味は不明。pRNの動物での意義は不明
- 赤核が抗侵害受容反応に関与している証拠がある

赤核とMLRとの関連は？

10

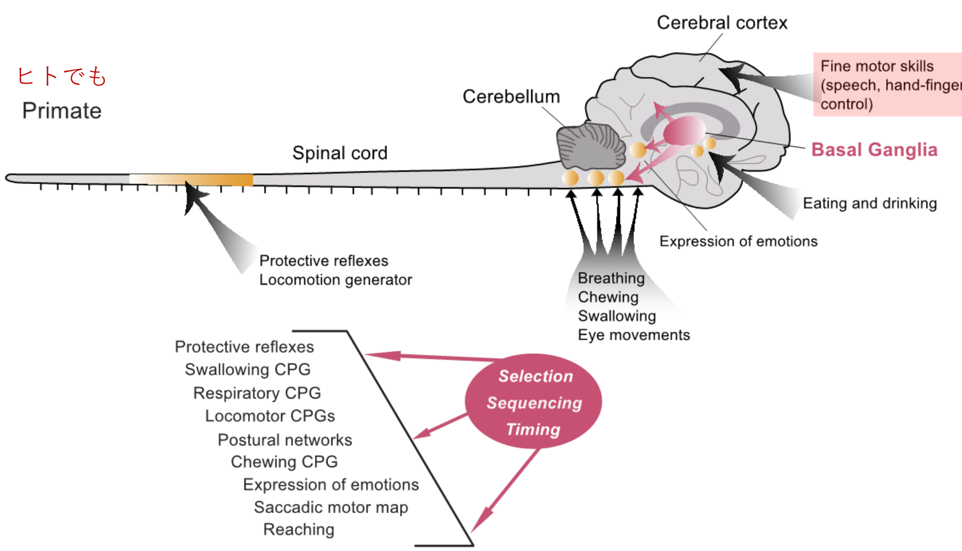
Olivares-Moreno R, et al. Corticospinal vs Rubrospinal Revisited: An Evolutionary Perspective for Sensorimotor Integration. Front Neurosci 2021:15:686481.

corticospinal rubrospinal reticulospinal



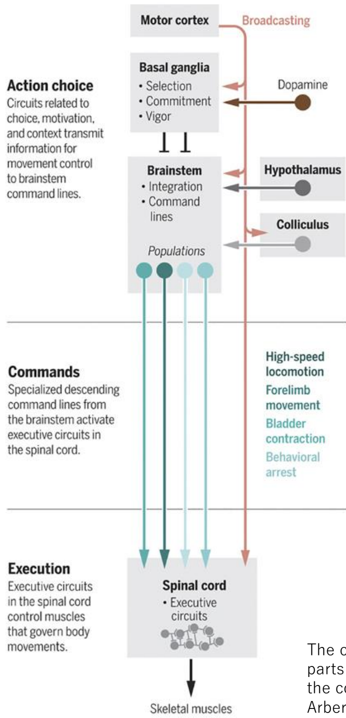
11

運動神経系の系統発生

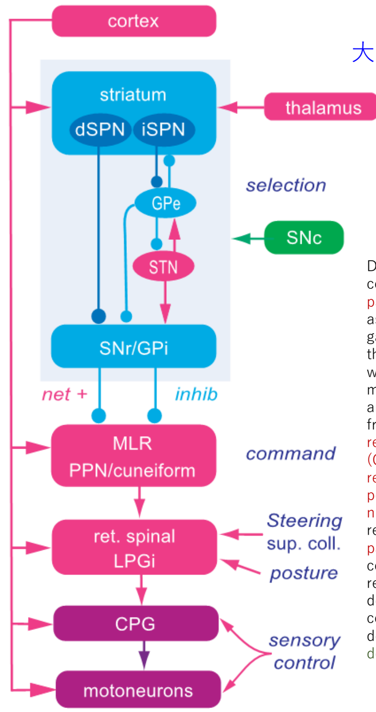


Grillner S, El Manira A. Current Principles of Motor Control, with Special Reference to Vertebrate Locomotion. Physiol Rev. 2020;100:271-320.

12



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

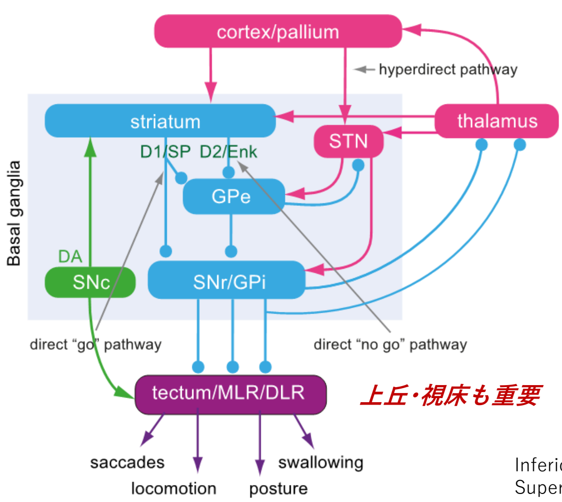


哺乳類では
大脳から脊髄への直接投射あり

赤核は？

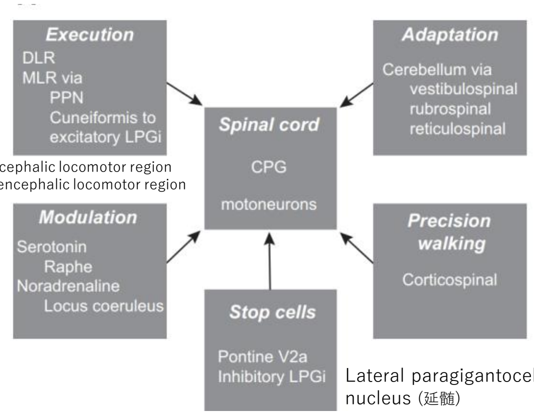
Diagram of the different components from cortex and basal ganglia to spinal central pattern generators (CPGs) regulating basic aspects of locomotor propulsion. The basal ganglia and the striatal projection neurons of the direct pathway (dSPN) initiate locomotion, while the indirect pathway (iSPN) inhibits 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.

13



上丘・視床も重要

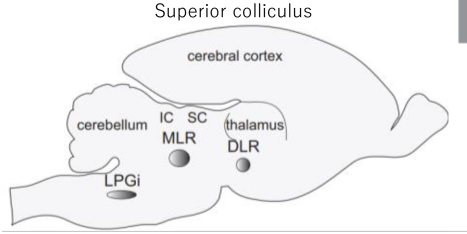
ヤツメウナギからあり

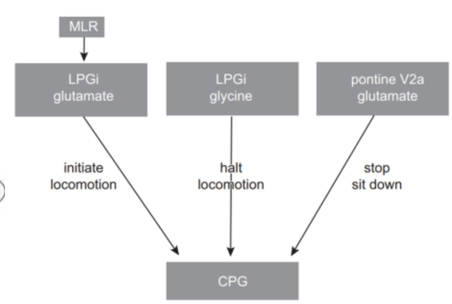


Diencephalic locomotor region
Mesencephalic locomotor region

Lateral paragigantocellular nucleus (延髄)

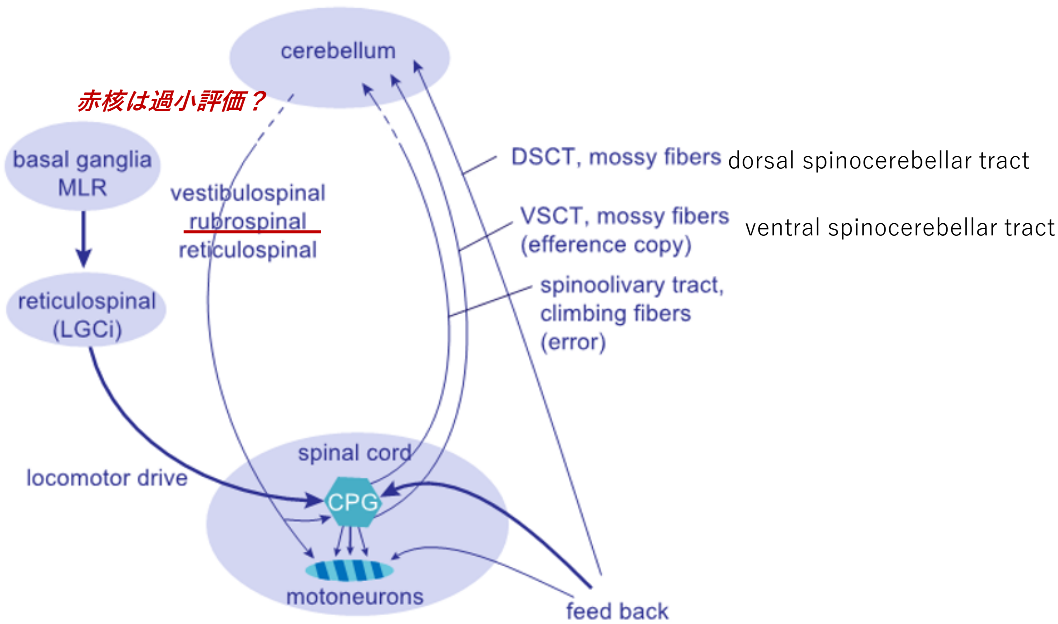
Inferior colliculus
Superior colliculus





14

Role of cerebellum: fine tuning of the locomotor movements



15

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

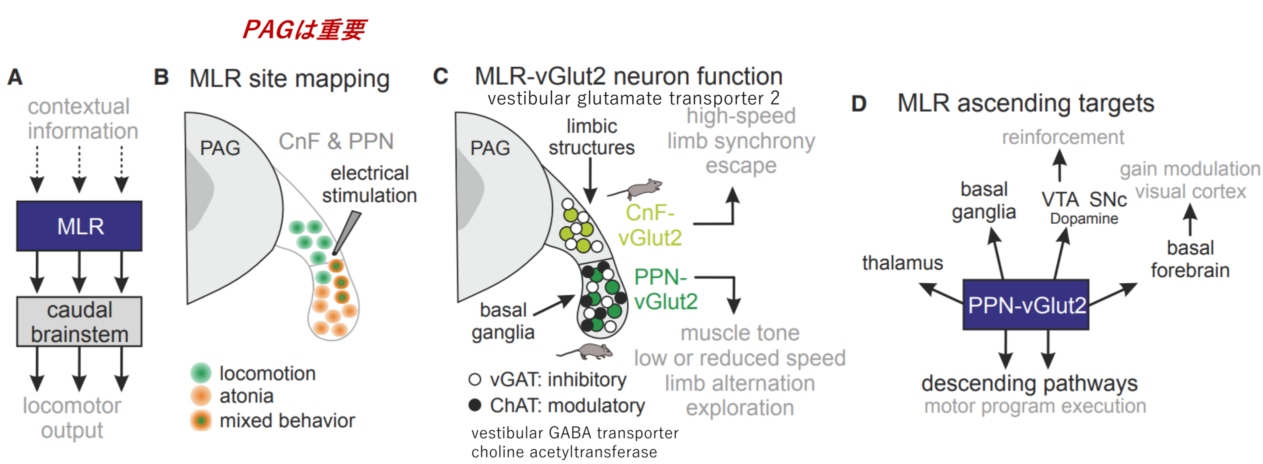


Figure 3. **Functional and Cellular Diversity of the Mouse MLR**
(A) MLR processes contextual information and its descending pathways signal to caudal brainstem neurons to influence locomotor output.
(B) Summary diagram of historical electrical site-mapping experiments in the cat CnF and PPN to define 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.

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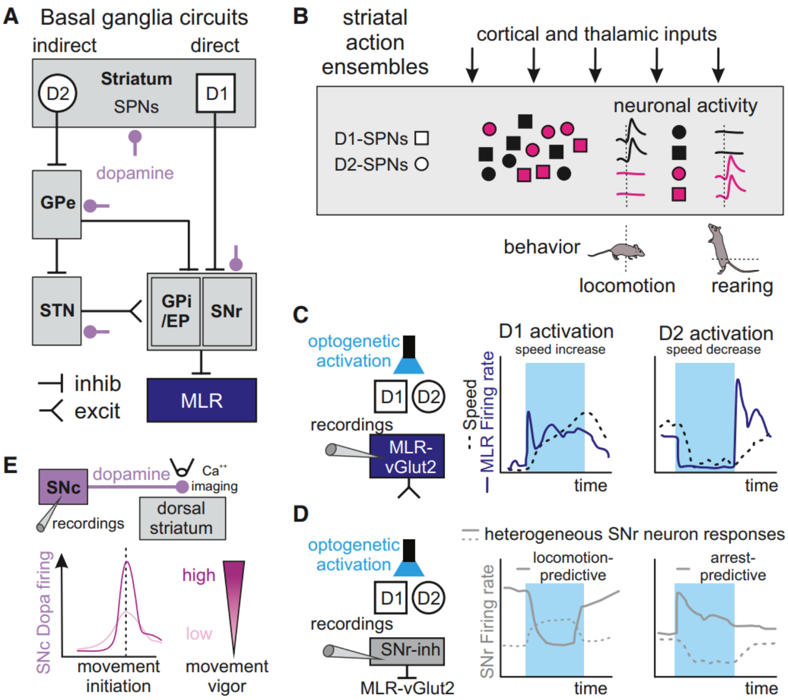


基底核が運動を選択する

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.

17

上丘・視床も重要

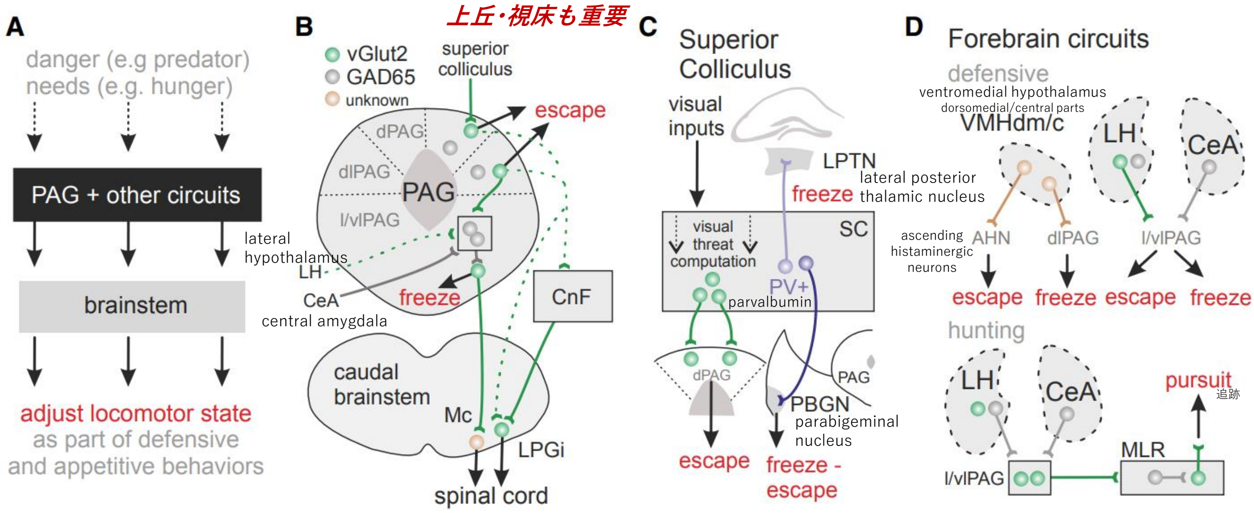
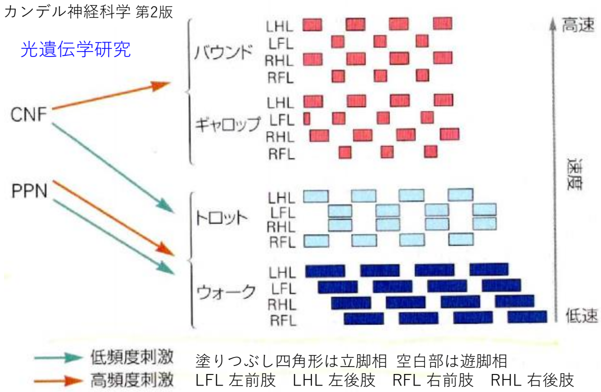


Figure 6. **Circuits for Behavioral Need and Context Influencing Locomotion**
(A) Periaqueductal gray (PAG) and associated structures are central in processing information about danger and needs in order to then signal through brainstem circuits to adjust locomotor state as part of numerous defensive 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.

18

Caggiano V, et al. Midbrain circuits that set locomotor speed and gait selection. Nature 2018;553:455-460.

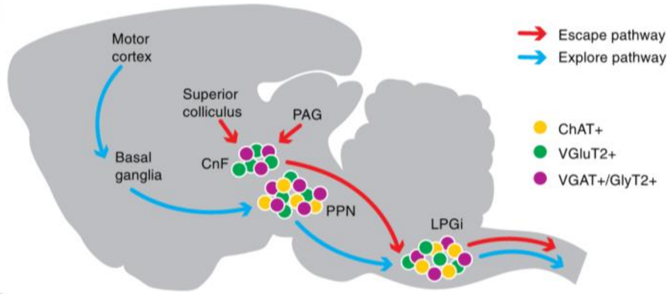
カンデル神経科学 第2版



Walk：3~4本の脚で同時に支える
Trot：対角線上の前肢と後肢が同時に活動する
Gallop：前肢がわずかにずれて動き、後肢がほぼ同時に活動する
Bound：後肢と前肢が同時に働き、前肢と後肢の活動する位相がずれている

MLRが運動パターンを決める

Gatto G, Goulding M. Locomotion Control: Brainstem Circuits Satisfy the Need for Speed. Curr Biol 2018;28:R256-R259.



Anatomical and functional characterization of a bimodal circuit for speed.
The mesencephalic motor region comprises two areas: the pedunculopontine nucleus (PPN) and cuneiform nucleus (CnF).
The pedunculopontine nucleus has at least three neurochemically distinct populations: glutamatergic (purple), cholinergic (yellow) and inhibitory neurons (green).
The cuneiform nucleus is a mix of glutamatergic and inhibitory interneurons.
The lateral paragigantocellular nucleus (LPGi) resides in the medulla and is as heterogeneous as the pedunculopontine nucleus.
The midbrain areas, like the superior colliculus and periaqueductal grey, initiate fast escape responses, which are relayed to the effector circuits in the spinal cord via the cuneiform nucleus–lateral paragigantocellular nucleus pathway (red arrows).
Conversely, motor cortex and basal ganglia promote a series of goal-directed movements that are translated into slow-paced exploratory motor behavior via the pedunculopontine nucleus-induced activation of probably lateral paragigantocellular nucleus and other medullary and spinal nuclei (blue arrows).

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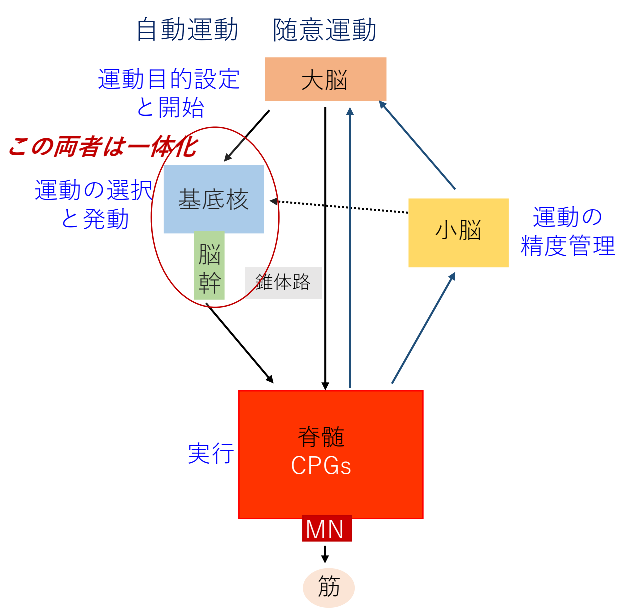
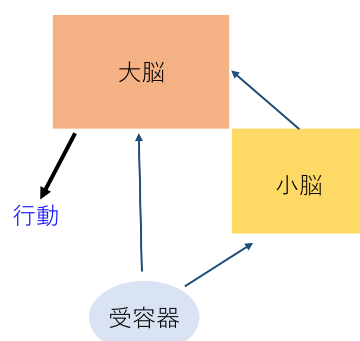
運動神経機構

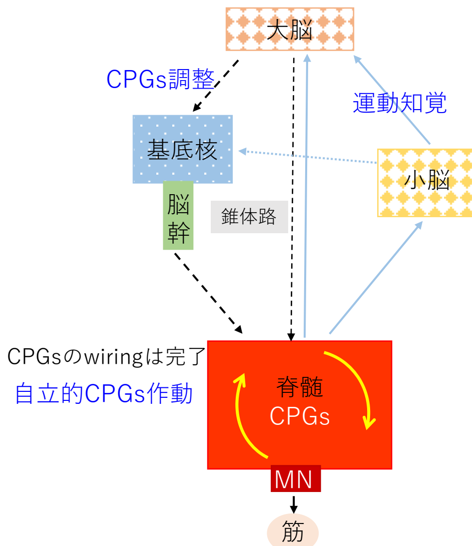


外界内界認知と行動決定



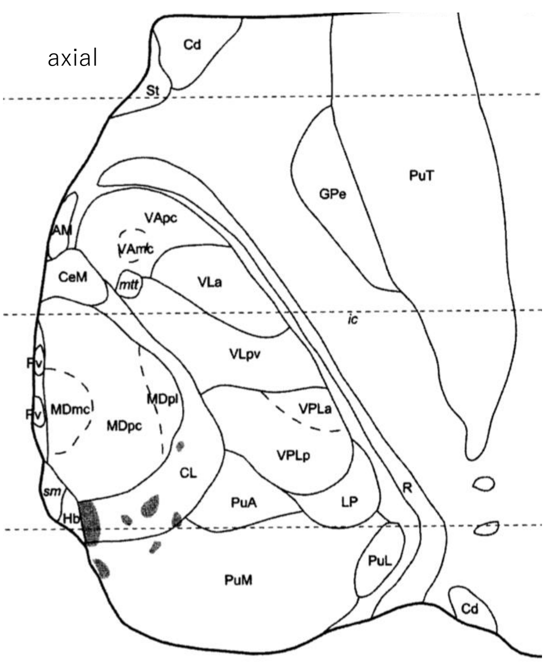
20

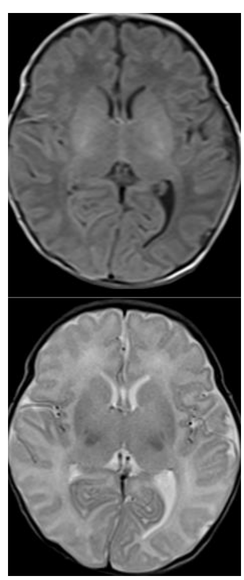
Writhing期の運動神経機構

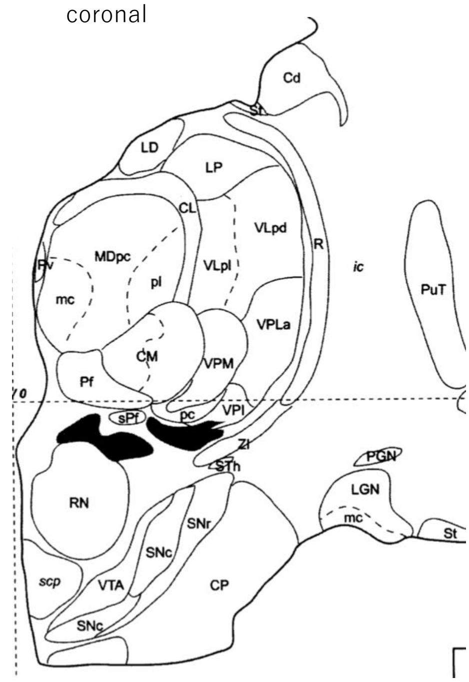


- ✓ 新生児期にも大脳･基底核の脊髄運動ネットワークへの出力はあり、同部の病変はwrithingの変容をきたしうる
  脳性麻痺のlucid intervalは存在しない
- ✓ 周生期の大脳脳変により、自動運動･随意運動の発動･調整の機能成熟は損なわれる。その成熟段階に応じた運動症候をとる

21



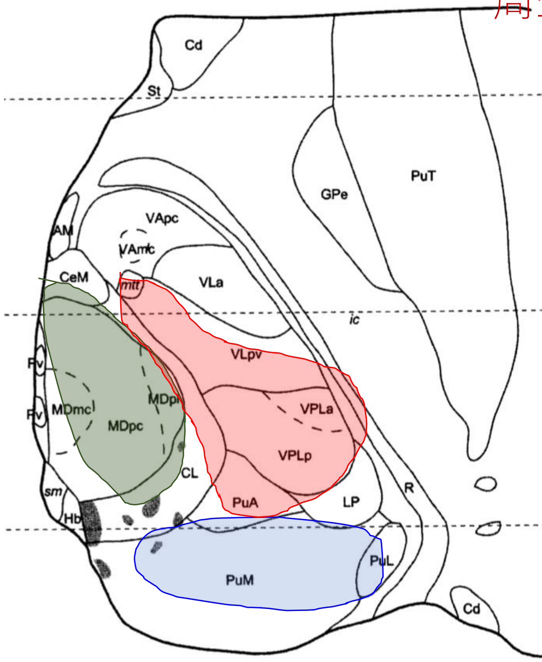




Morel A. Stereotactic Atlas of the Human Thalamus and Basal Ganglia. 2007.

22

周生期低酸素性脳症の易侵襲性視床部



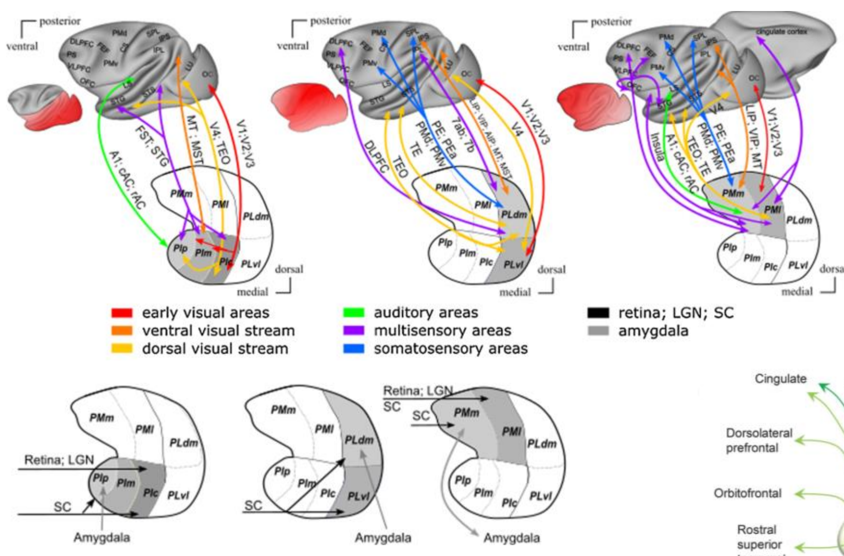
- VL核
  小脳核と大脳運動野皮質VI層と連絡
- PuA
  ・somatosensory cortexとconnection
  ・動物では認知されていない
- VPL核・VPM核
  ・固有覚　→内側毛帯系

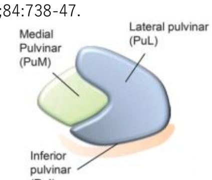
23

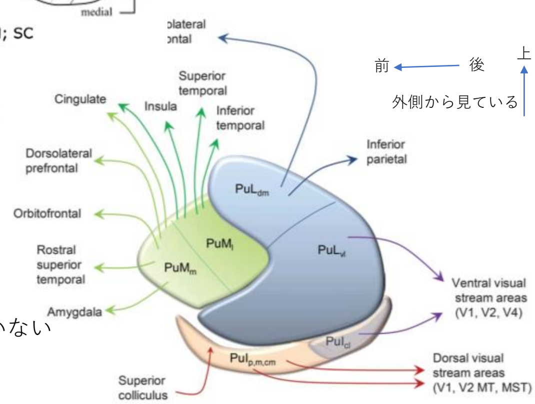
Froesel M et al. A multisensory perspective onto primate pulvinar functions. Neurosci Biobehav Rev 2021;125:231-243.

Pulvinar

Benarroch EE. Pulvinar: associative role in cortical function and clinical correlations. Neurology 2015;84:738-47.



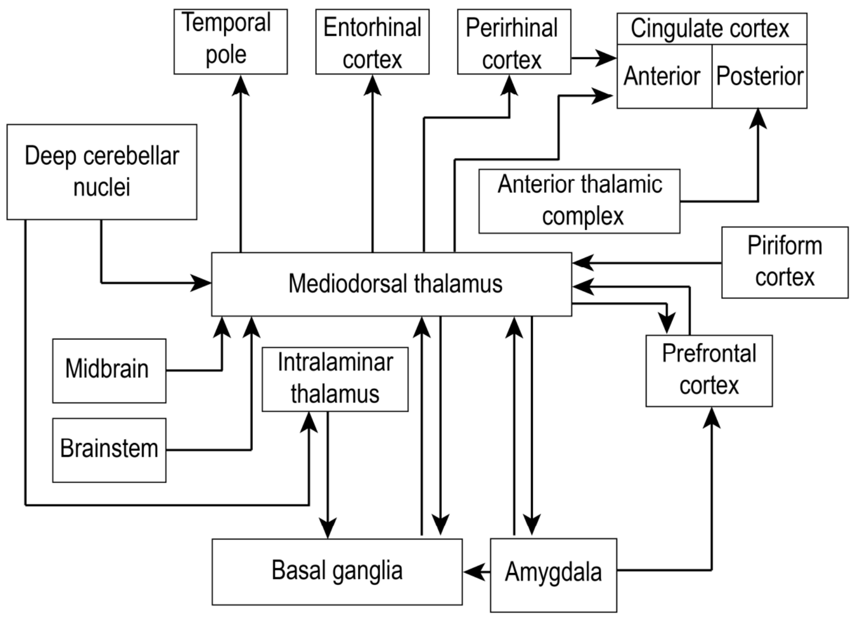




PuAはsomatosensory cortexとconnection　動物では認知されていない
dm:dorsomededial vl:ventrolateral cl:centrolateral cm:centromedial

24

Georgescu IA, et al. The Anatomical and Functional Heterogeneity of the Mediodorsal Thalamus. Brain Sci 2020;10:624.



Centromedian (CM) nucleus
非特異核

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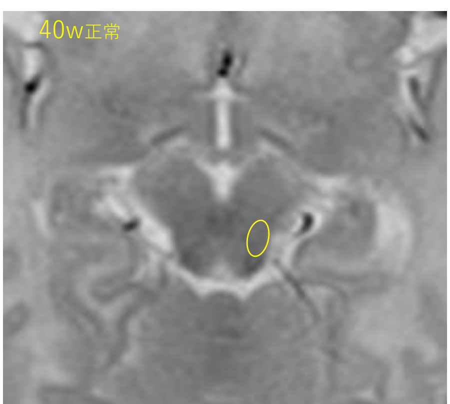
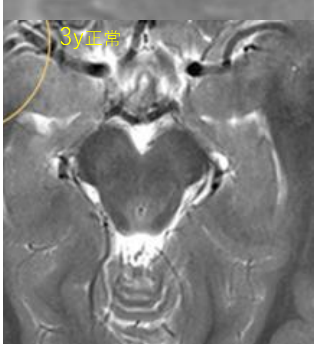
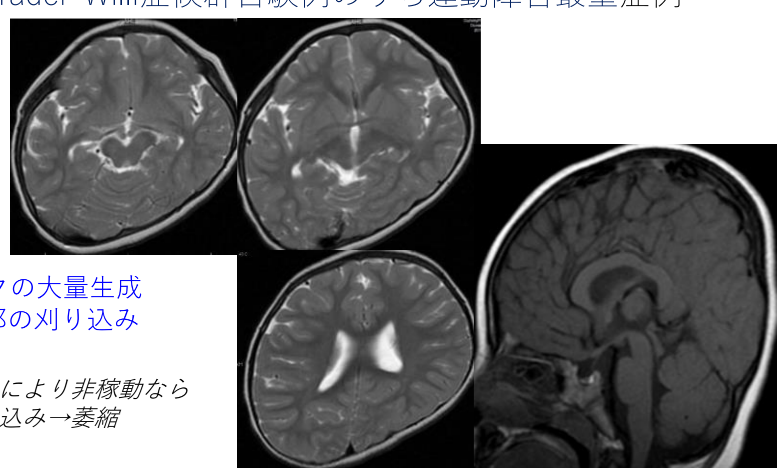




中脳低形成となる部位

- Parabigeminal nucleus 上丘と連絡
- Cuneiform nucleus
- Pedunclopontine nucleus *橋との境界部*

Prader-Willi症候群自験例のうち運動障害最重症例



ネットワークの大量生成
→非稼動部の刈り込み

遺伝子変異により非稼動なら
大量刈り込み→萎縮

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発達期脳性運動症候

- 基底核･脳幹･大脳･小脳の運動ネットワークの発達障害には以下の2ベクトルがある

  股屈曲過活動　*四足歩行ネットワークの屈筋過活動*

  股伸展荷重制限　*直立二足歩行の荷重筋力動員の未達*

- 大脳運動出力が途絶すると共同運動を越えた運動ができない

  分離運動制限　*脊髄運動ネットワークの脱抑制*

- 基底核が損なわれると、拮抗筋･連動筋の筋活動調整ができなくなり、運動の開始と静止が不調となり、過剰な連合運動が出現する

  共収縮制御障害

- 中脳が損なわれると、運動パターンを選別遂行することができなくなる。そのため、極端な関節位で固まることになる

  中脳性運動発現障害（中脳性無動）

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