NEUROPATHOLOGY BRAIN CUTTING MANUAL

LAST UPDATED ON 6/22/2015

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1. Brain Processing protocol

Autopsy neuropathology will have two major objectives:
a) Provide a high quality neuropathologic diagnosis in a timely manner and
b) Train house officers in neuropathology.

This protocol further clarifies how examinations should proceed.

CLASSIFICATION OF BRAINS:
Brains are classified at the time of autopsy by the house officer and attending staff, with consultation by the neuropathologist on call for surgical neuropathology if needed.

Normal brains are those brains that have a negative neurologic history, absent or negative radiographs, and are grossly normal.

Abnormal brains are those brains from patients with pathology or symptoms directly related to the brain. Examples would include patients with any of these: significant neurologic symptoms, abnormal CT or MRTI, patients with possible brain metastases or those brains that are grossly abnormal.

WORKFLOW:
After a decision has been made regarding the classification of the brain, the examination continues as described below for each type. All brains and spinal cords are to be removed by the house officer, with assistance by the dieners. Neuropathology staff does not need to be in attendance for brain harvesting unless the house officer requests their presence.

A. ***Normal brains:***
These brains are processed completely by the house officer and attending staff.

Harvesting and cutting: The brains may be cut fresh, or fixed and cut alone at a later date. The house officer sections the brain and takes sections for routine H&E staining as directed by the attending pathologist. House officers are encouraged to cut as many as possible of these brains fresh, since this will (1) increase their familiarity with fresh neuroanatomy, (2) decrease the amount of time needed to process the entire case.
Slides: The sections are submitted by the house officer, for routine H&E sections. It is recommended that the CNS sections are fixed independently and in good amount of formalin for proper fixation prior processing. Slides are reviewed by the house officer with the regular attending staff. If questions arise, the attending neuropathologist on call for surgical neuropathology can be consulted. It should be stressed that house officers are expected to quickly learn how to process and sample a normal brain by themselves.

B. ***Abnormal brains:***
Consultation with neuropathologist on call for surgical neuropathology may be done concerning the initial processing of these brains.

Harvesting: In most cases, the brain and pituitary gland and in some occasions spinal cord will be removed and fixed in formalin.
Clinical History: From the patient's chart, the house officer should come prepare with clear short summary of events leading to death and major neurologic issues that require further evaluation for the neuropathology team. These brains will be cut at the Brain Cutting Conference by the neuropathologist on call for surgical neuropathology.
Scheduling Brain Cutting: A maximum of 3 cases per session will be scheduled, cases will be chosen by the oldest harvested brain on the shelf. Diana French will keep track of fixing times and communicate next brain to be cut with neuropathology assistant. The resident of the general autopsy is expected to attend brain cutting and provide Neuropathology assistant a short 2-3 sentences summary of major clinical history and relevant neurologic questions for neuropathologist by the Friday before brain cutting. If there is an extenuating circumstance that the resident cannot be in attendance, this house officer should arrange backup by the house officer on UH autopsy duty or another house officer who will be available for that brain cutting. If there is a neuropathology fellow, the resident should communicate with the fellow in a timely manner and share details of the case and neurology related question. It is expected that the assigned resident follow up with the slides and preview the slides by him/herself, with fellow and/or neuropathology attending.

BRAIN CUTTING CONFERENCE (for hospital cases or "brain only"):
House officers will cut the abnormal brains of their cases with the help of the neuropathologist on call for surgical neuropathology at the weekly brain cutting conference in the morgue. Maximal involvement of each house officer as described below is essential to their training. The house officer will present the patient's history and systemic autopsy findings in brief 1-5 minute verbal summary, and record the macroscopic observations. The neuropathology attending will lead discussion of the neuropathology.
The **dieners** will wash the scheduled brains thoroughly, set up the appropriate instruments for cutting the brains, forward the morgue phone to an answering machine, make every attempt to curtail use of the bone saw during Tuesday Brain Cutting Conference, and clean up after brain cutting.

Tissue Blocking:
Sections will be taken by the house officer, under the guidance of the attending neuropathologist (who may also check the house officer's macroscopic description).
The house officer should record laterality (left or right) and region of cerebrum (frontal, parietal, thalamus, etc.) in the block description. The sections will be given to a histologist after brain cutting and fixing in cassettes. A decision will be made at the time of selecting sections which stains should be performed. Section and stain selection, and description are important components of the house officer's training, and house officers should be actively involved in the macroscopic description and selection of the neuroanatomic areas for study and the stains that will be used for this examination. For example, brains with metastatic or ischemic disease are best viewed with H&E stains, while Luxol fast blue is preferred for demyelinating disease, and Bielschowsky silver and ubiquitin for dementia. Microscopic sections of abnormal brains are reviewed with the neuropathologist who was present at gross brain cutting.

The House Office and neuropath fellow prepare the gross report incorporated into the autopsy report under additional dissection.

Slides:
Slides stained with H&E and the special stain slides will be returned directly to the house officer's mailbox. If a brain is cut at brain cutting conference with a neuropathologist, then it is expected that the house officer will review and sign out the CNS autopsy slides with that neuropathologist and neuropathology fellow if applicable.

Completion of the UMMC hospital case:
The house officer writes the microscopic description. If the case was reviewed were reviewed with a neuropathologist, put their name as a Consulting Pathologist on the first page of the final autopsy report. If a neuropathologist is consulted it is expected that the house officer shows final report to the attending to assure accuracy of diagnosis and description.

FLOW CHART FOR HANDLING AUTOPSY BRAINS

	A. Normal	**B. Abnormal**
Consultation prior to harvesting (day 1)	Attending staff Pathologist; Neuropathologist, if needed	Neuropathologist on call for surgical neuropathology, if needed
	↓	↓
Harvesting (day 1 if fresh or day 15 if fixed)	House officer (HO) cuts fresh, or fix	Fix in formalin Freeze 1 cc of frontal lobe if infection, toxic, metabolic, CJD, or degenerative disease is suspected If suspected infection, harvest 1 cm and put in media to send to microbiology.
	↓	↓
Sections (day 1 if fresh or day 15 if fixed)	HO takes	HO takes at brain cutting, with supervision by neuropathologist or fellow
Special Stains	Ordered by HO, if needed	Ordered by HO in consultation with neuropathologist
	↓	↓
Processing (within 3 days after sectioning the brain)	Histology CNS cassettes should fix in sufficient formalin for at least 2 days before processing CNS blocks should fix separate and in sufficient formalin for proper processing	Histology CNS cassettes should fix in sufficient formalin for at least 2 days before processing. CNS blocks should fix separate and in sufficient formalin for proper processing

	↓	↓
Slides returned	To House officer	To House Officer or neuropath fellow
	↓	↓
Review Slides (Within 1 week of sectioning the brain)	Autopsy attending staff pathologist	Neuropathologist who cut the brain
Final Report (Within two weeks of sectioning the brain	Autopsy attending staff pathologist or if consultation was requested to a neuropathologist he/she should review the report	Neuropathologist who reviews the slides

2. Suggested Sections for brain cutting

1. Include a section of any abnormal brain regions identified at brain cutting.

2. In hypoperfusion/ischemic events, include appropriate watershed areas (2-4 cassettes).

3. If history of alcohol abuse, include a section of superior and inferior cerebellar vermis, mammillary bodies and periaqueductal grey matter.

4. Brains without gross pathology and additional sections for the above mentioned cases:
   A. Cerebral cortex (frontal, temporal, parietal OR occipital).
   B. Basal ganglia.
   C. Hippocampus at the level of the lateral geniculate (LGN) a.k.a. Napoleon's hat
   D. A section of brain stem (midbrain, pons and /or medulla)

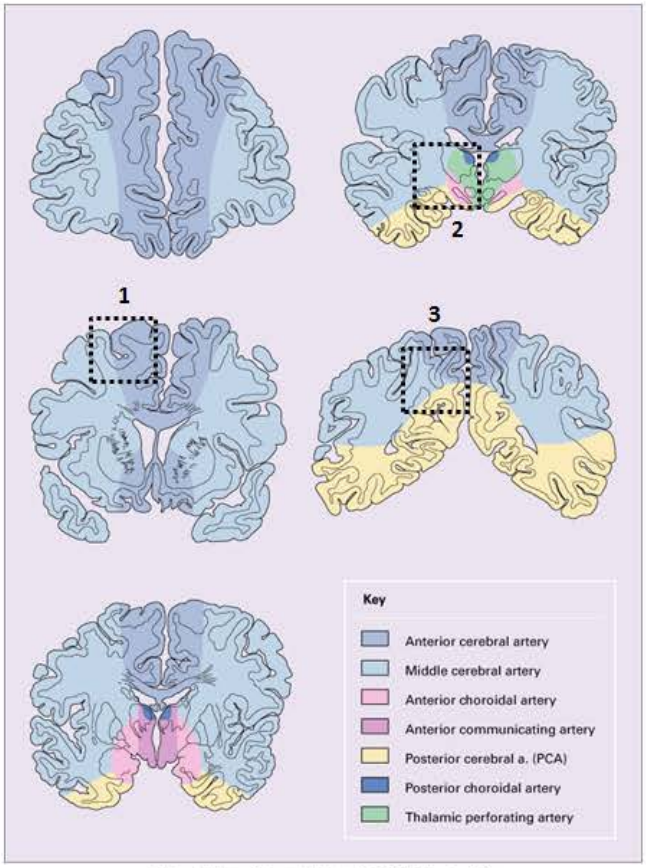
3. Brain Gross Description Template

Case # _____ Gross description:

The brain weighs _____ g fixed (normal range: 1200-1400 g). Both the external and internal surfaces of the dural leaflets are smooth and free from nodules. The superior sagittal sinus is patent. There _____evidence of cingulate, uncal, or cerebellar tonsilar herniation. The leptomeninges are _____(thin, translucent, and free from exudates or cloudy). Examination of the arteries of the circle of Willis and their major branches reveals they are patent with _____ atherosclerosis. Aneurisms are _____seen. The superficial veins of the brain and cranial nerves are unremarkable. There is _____ atrophy primarily affecting the _____ lobes. After coronal sectioning, the cerebral hemisphere reveals a cortex of _____mm at the level of the genu of the corpus callosum. The lateral ventricle is _____ dilated. There is no deviation of the septum pellucidum. The centrum ovale is free from hemorrhage and tumor mass. The central nuclei of the brain including caudate, lentiform, thalami, lateral geniculate bodies and subthalamic nuclei all are unremarkable. The hippocampus and amygdala are _____. The substantia nigra and locus ceruleus are _____. The remainder of the midbrain, pons, medulla, cerebellar hemispheres, vermis and cerebellar nuclei are_____. The spinal cord is _____.

4. CNS Watershed Areas

CNS WATERSHED AREAS (SICP sections)



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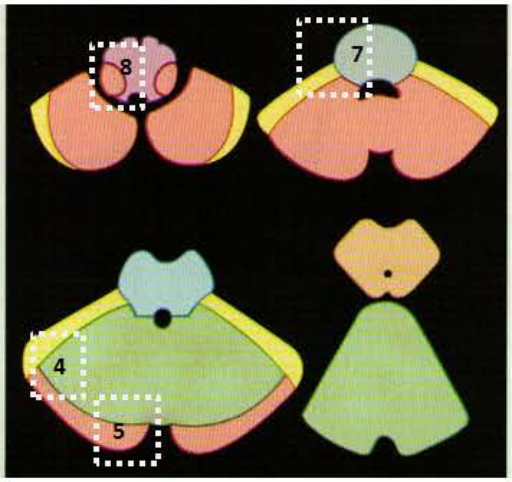
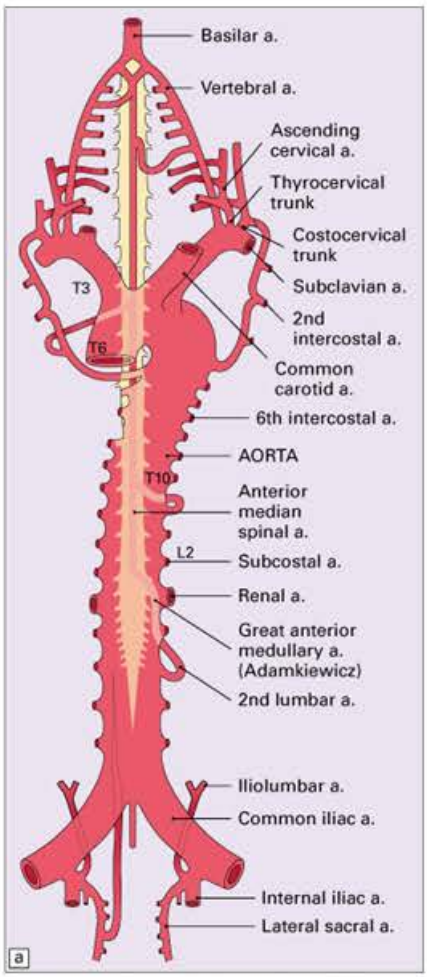


- Pontine perforating arteries
- Sup Cerebellar Art
- Antero Inferior Cerebellar artery
- Postero Inferior Cerebellar artery
- Medullary Perforating arteries

1. Superior and Middle Frontal gyrus at the level of CAP
2. Thalamus, Red nucleus, SN and LGN
3. Medial Parieto-Occipital cortex
4. Cerebellar hemispheres
5. Cerebellar vermis
6. Pons
7. Medulla

CNS WATERSHED AREAS (SICP sections)



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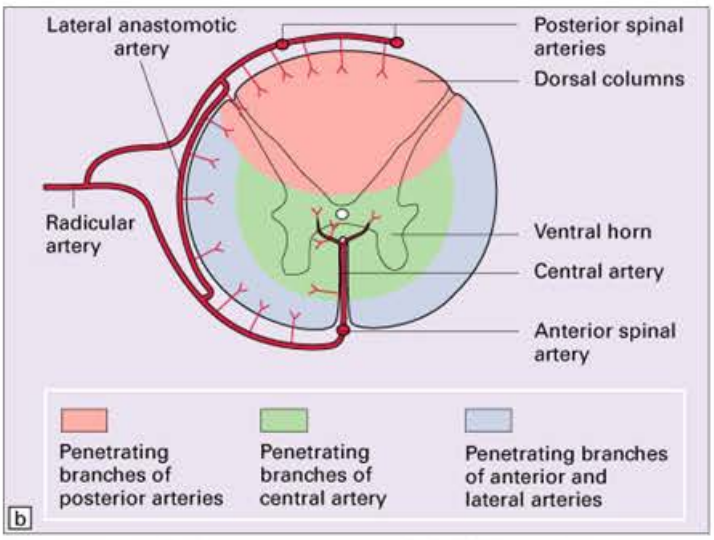

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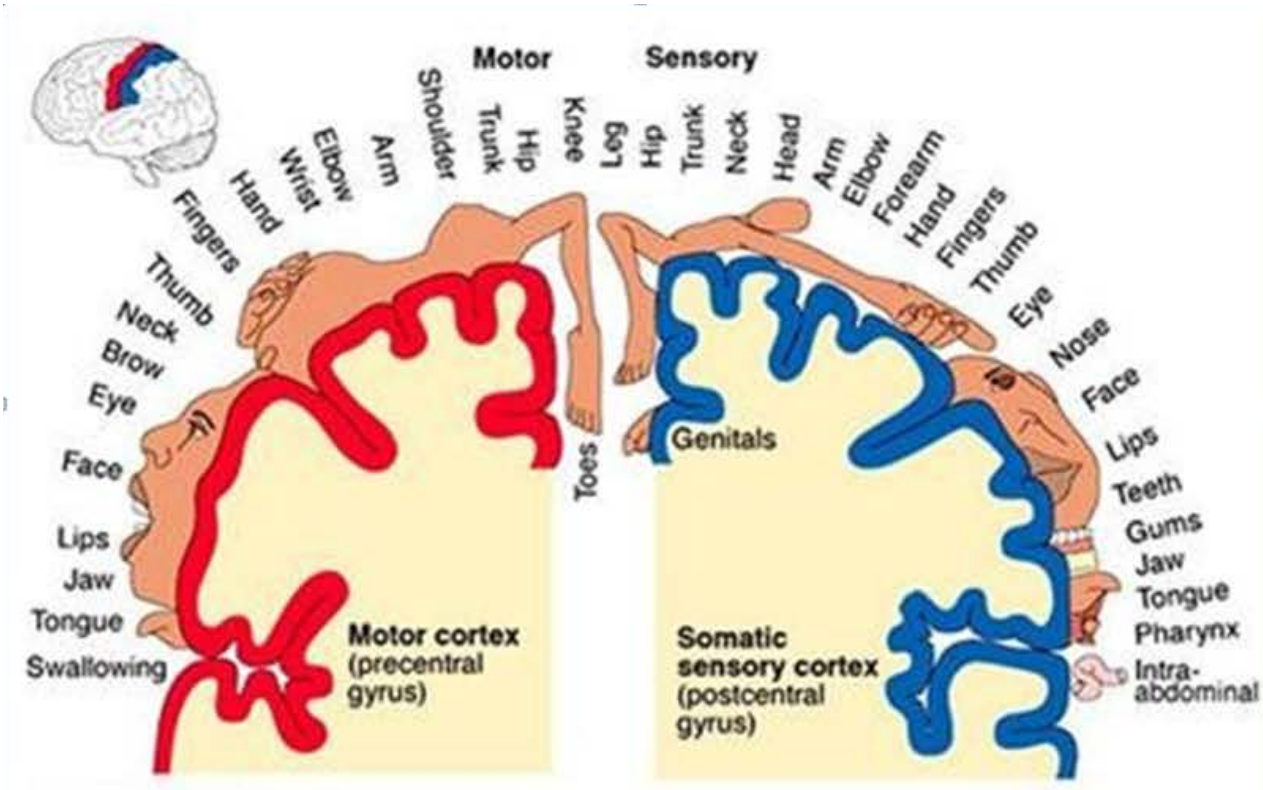
Infarction in the distribution of AnteriorSpinal Art:

- Anterior grey matter
- Anterior tracts
- T4 is the most vulnerable watershed area

HOMUNCULUS


Motor
Sensory
Shoulder
Arm
Elbow
Wrist
Hand
Fingers
Thumb
Neck
Brow
Eye
Face
Lips
Jaw
Tongue
Swallowing
Trunk
Hip
Knee
Leg
Toes
Hip
Trunk
Neck
Head
Arm
Elbow
Forearm
Hand
Fingers
Thumb
Eye
Nose
Face
Lips
Teeth
Gums
Jaw
Tongue
Pharynx
Intra-abdominal
Genitals
Motor cortex (precentral gyrus)
Somatic sensory cortex (postcentral gyrus)

5. Fetal and infant brain weights ranges

Table 4.2 Fresh brain weight, fixed brain weight, infratentorial weight and percentage of infratentorial weight/total brain weight in relation to age

Age (weeks)	Fresh brain weight (g) (n = 175)	Fixed brain weight (g) (n = 298)	Infratentorial weight (g) (n = 114)	% Infratentorial/total brain weight (n = 113)
8–9	–	0.80 (1)	–	–
10–11	–	1.20 (1)	–	–
12–13	–	5.87 (1)	–	–
14–15	15.45 ± 1.20 (2)	14.40 ± 3.34 (6)	0.76 ± 0.14 (4)	5.91 ± 0.62 (4)
16–17	21.17 ± 1.05 (3)	21.49 ± 5.34 (10)	1.21 ± 0.19 (8)	5.37 ± 0.78 (8)
18–19	37.33 ± 8.17 (10)	38.75 ± 9.52 (22)	2.19 ± 0.7 (16)	4.88 ± 0.50 (16)
20–21	52.19 ± 7.23 (15)	55.38 ± 10.18 (22)	2.81 ± 0.42 (10)	4.98 ± 0.49 (10)
22–23	75.01 ± 17.76 (9)	78.15 ± 14.37 (30)	3.71 ± 0.74 (14)	4.54 ± 4.41 (13)
24–25	101.53 ± 18.75 (9)	111.97 ± 17.30 (22)	5.23 ± 0.70 (12)	4.61 ± 0.29 (12)
26–27	130.62 ± 17.38 (21)	146.21 ± 21.69 (31)	6.95 ± 1.41 (8)	4.52 ± 0.32 (8)
28–29	169.22 ± 19.11 (18)	184.62 ± 26.40 (29)	7.63 ± 0.79 (6)	4.76 ± 0.46 (6)
30–31	203.02 ± 25.99 (21)	229.54 ± 29.84 (26)	12.25 ± 2.02 (4)	5.24 ± 0.35 (4)
32–33	234.98 ± 28.24 (13)	266.00 ± 32.78 (13)	14.00 (1)	5.18 (1)
34–35	280.3 ± 28.19 (14)	309.32 ± 47.04 (19)	15.75 ± 3.18 (2)	5.58 ± 0.41 (2)
36–37	325.83 ± 40.75 (6)	366.00 ± 50.27 (11)	21.43 ± 3.36 (6)	6.07 ± 0.66 (6)
38–39	391.69 ± 41.39 (10)	433.30 ± 56.89 (20)	26.93 ± 4.70 (10)	6.27 ± 0.56 (10)
40–41	409.63 ± 37.55 (17)	455.27 ± 53.66 (33)	29.05 ± 4.04 (13)	6.68 ± 0.65 (13)

Data given as mean ± standard deviation (SD), with number of cases in parentheses.
Data from Guihard-Costa and Larroche (1990).[229]

Table 4.3 Percentiles of brain weights in relation to gestational age

Gestational age (weeks)	Percentile				
	10	25	50	75	90
26–27	94	102	110	120	120
28–29	125	135	147	160	170
30–31	170	180	190	203	217
32–33	190	201	210	234	252
34–35	226	240	251	280	287
36–37	280	295	311	328	346
38–37	317	332	356	328	346
40–41	370	400	420	440	463

Adapted from Larroche (1977).[327]

Table 4.4 Brain weight in infants in relation to age and length

Age	Body length (cm)	Brain weight		
		Mean (g)	SD (g)	*n*
Newborn	N/A	325	158	13
1 week	N/A	370	78	2
2 weeks	N/A	456	54	7
3 weeks	N/A	430	120	6
1 month	N/A	492	120	26
2 months	N/A	608	248	22
3 months	N/A	672	274	15
4 months	N/A	734	240	13
5 months	N/A	687	290	9
6 months	N/A	839	290	8
7 months	N/A	880	86	5
8 months	N/A	845	280	4
9 months	N/A	905	238	7
10 months	N/A	988	280	10
11 months	N/A	893	186	6
12 months	N/A	980	156	3
14 months	74	944		
16 months	77	1010		
18 months	78	1042		
20 months	79	1050		
22 months	82	1059		
24 months	84	1064		

N/A, not applicable; SD, standard deviation.

Data from newborn to 12 months adapted from Thompson and Cohle (2004).[586]

Data from 14 to 24 months adapted from Sanderman and Boerner (1949).[518]

6. ADRC brain cutting

6.1. Blocking List for Neurodegenerative Diseases (ADRC)

(See next page)

Blocking list for Neurodegenerative diseases *(modified 6-23-15 by SCP)*

Sections	**R /L**	**For Every Dementia Case (AD and FTD-Picks)**	**For other FTD**	**For PSP or CBD**	**If Synuclein Positive in either 5 or 12**	**MSA**	**ALS**
1 Middle Frontal Gyrus		H&E, Biel, Beta-amyloid, Tau, GFAP	Tau, Ubiquitin, TDP-43		Synuclein		TDP-43
2 Superior and Middle Temporal Gyrus		H&E, Biel, Beta-amyloid, Tau, GFAP	Tau, Ubiquitin, TDP-43	Tau	Synuclein		
3 Inferior Parietal Cortex		H&E, Biel, Beta-amyloid, Tau			Synuclein		
4 Primary Visual Cortex		H&E, Biel, Beta-amyloid, Tau					
5 Anterior cingulate with corpus callosum		H&E, Biel, Beta-amyloid, Tau, Synuclein		Tau	X		
6 Amygdala		H&E, Biel, Beta-amyloid, Tau,		Tau	Synuclein		
7 Nucleus basalis at the level of anterior commissure. Include Basal Ganglia GP and Putamen		H&E, Biel, Beta-amyloid, Tau,		Tau	Synuclein	Tau, Synuclein	
8 Hippocampus at the level of the lateral geniculate		H&E, Biel, Beta-amyloid, Tau,	Tau, Ubiquitin, TDP-43	Tau	Synuclein		TDP-43
9 Subthalamic nucleuses and Thalamus		H&E, Biel, Beta-amyloid, Tau		Tau		Tau, Synuclein	
10 Superior cerebellum with full dentate nuclei		H&E, Beta-amyloid				Tau, Synuclein	
11 Midbrain at the level of the red nucleus		H&E, Synuclein, Beta-amyloid		Tau	X	Tau, Synuclein	CD68, GFAP, TDP43
12 Pons one section with basis pontis and 1 or 2 additional levels of locus ceruleus		H&E, Beta-amyloid		Tau	Synuclein	Tau, Synuclein	

13 Medulla at the level of inferior olivary nucleus		H&E, Beta-amyloid,		Tau	Synuclein	Tau, Synuclein	
14 Cervical Spinal cord		Luxol fast blue and H&E (one single stain)				Tau, Synuclein	
15 Motor Sensory Cortex		H&E, Biel, Beta-amyloid, Tau, GFAP					
16Cerebellar vermis		H&E					

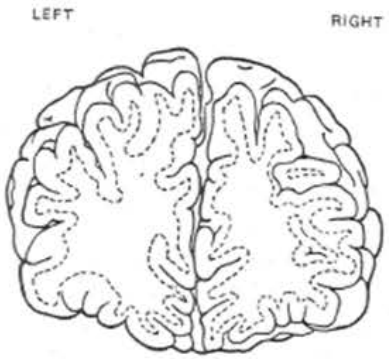
14-16 Optional

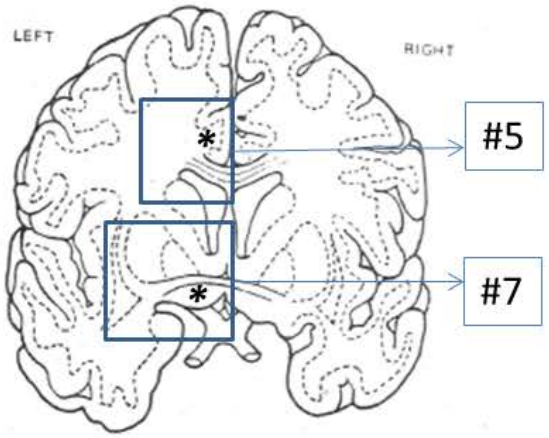
6.2. Blocking Diagrams for Neurodegenerative (ADRC) section 6.1

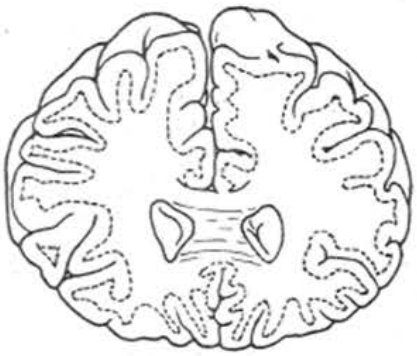
(See next page)

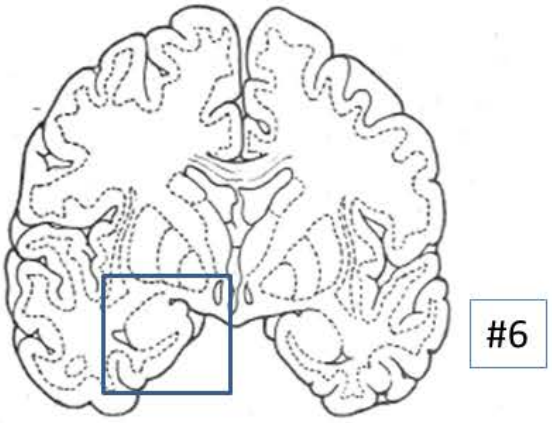
BLOCKING DIAGRAMS FOR NEURODEGENERATIVE DISEASES

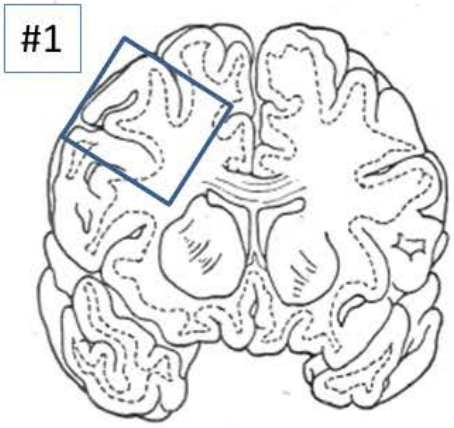
Coronal sections of Cerebrum

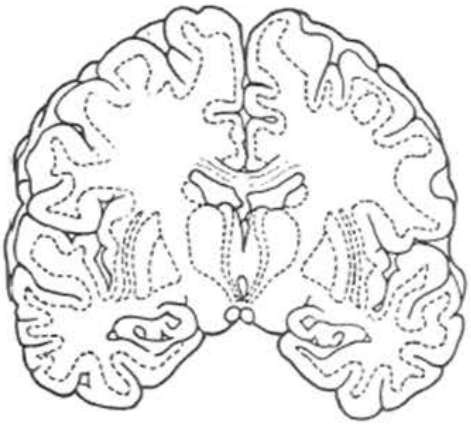




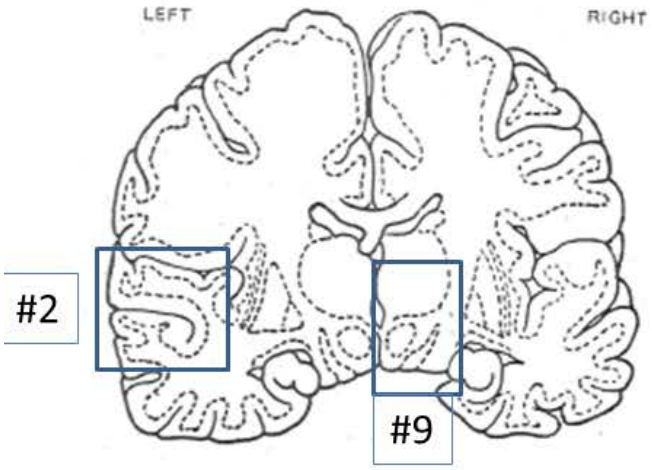


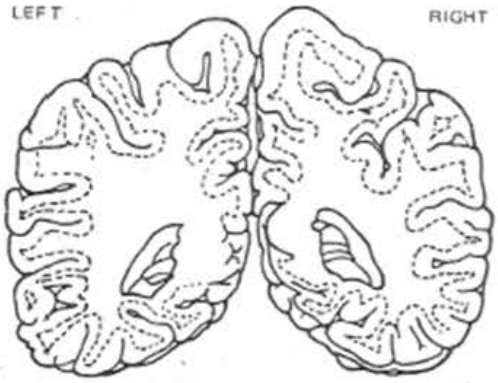


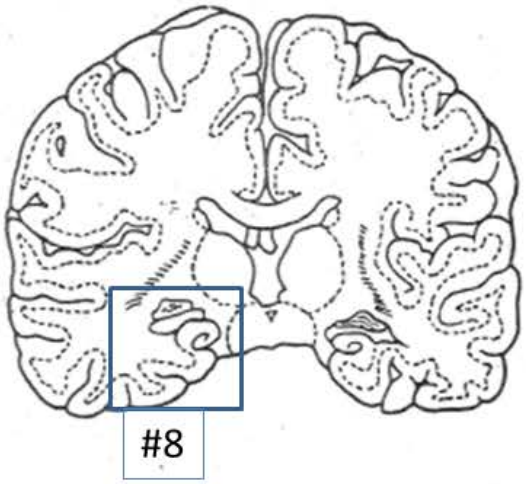


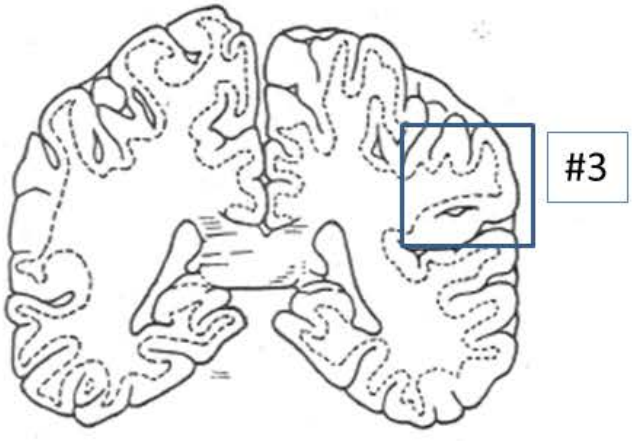


Coronal sections of Cerebrum

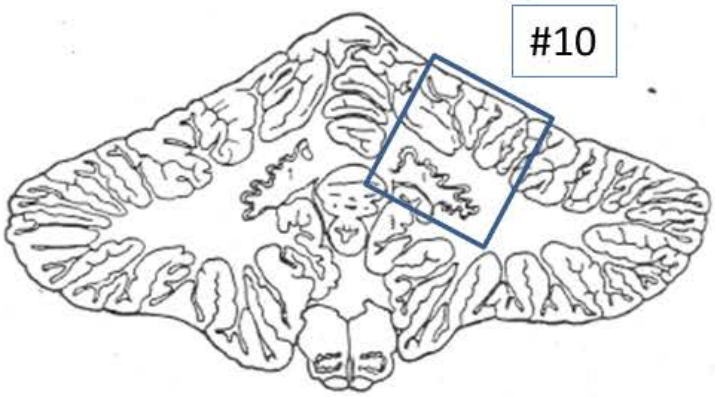








Cerebellum Transverse Sections

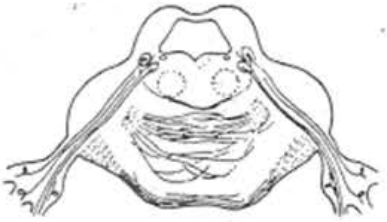


MIDBRAIN

#11

PONS

#12



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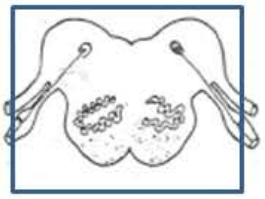
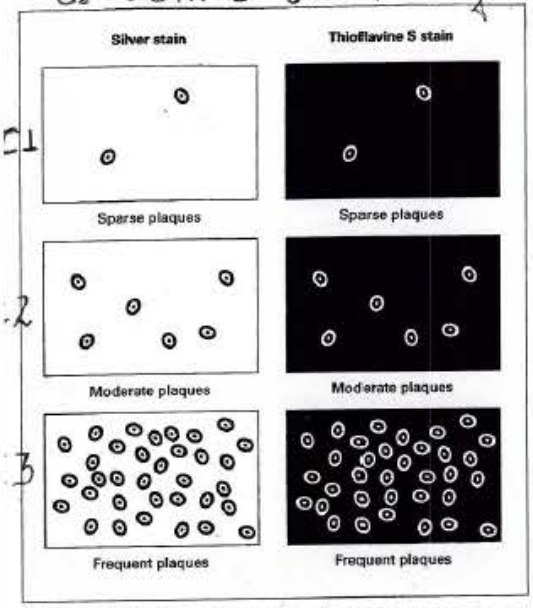


#13

6.3. Alzheimer's Disease ABC Staging (See also References)

C. CERAD (Neuritic Plaques) (NP)



31.27 CERAD plaque densities. When used in the NIA-AA diagnostic criteria for AD, the scores are: none = 0; sparse = 1; moderate = 2; frequent = 3.

Table 31.8 Age-related plaque score table

Age of patient at death (years)	Frequency of plaques: None	Sparse	Moderate	Frequent
<50	0	C	C	C
50–75	0	B	C	C
>75	0	A	B	C

The age-related plaque score corresponds to the following assessment: 0, No histologic evidence of Alzheimer's disease; A, Histologic findings are uncertain evidence of Alzheimer's disease; B, Histologic findings suggest the diagnosis of Alzheimer's disease; C, Histologic findings indicate the diagnosis of Alzheimer's disease.

Table 31.9 CERAD diagnostic groups

Normal (with respect to Alzheimer's disease or other dementing processes) if:
Either
No histologic evidence of Alzheimer's disease (0 score), and no clinical history of dementia, and absence of other neuropathologic lesions likely to cause dementia
Or
An A age-related plaque score and no clinical history of dementia
CERAD NP definite Alzheimer's disease
C age-related plaque score, and clinical history of dementia, and presence or absence of other neuropathologic lesions likely to cause dementia
CERAD NP probable Alzheimer's disease
B age-related plaque score, and clinical history of dementia, and presence or absence of other neuropathologic lesions likely to cause dementia
CERAD NP possible Alzheimer's disease if:
Either
A age-related plaque score, and clinical history of dementia, and presence or absence of other neuropathologic lesions likely to cause dementia
Or
B or C age-related plaque score and absence of clinical manifestations of dementia

ABC

Table 31.10 ABC scoring scheme for AD neuropathologic change

A	Thal plaque phase	B	Braak NFT stage	C	CERAD plaque score
0	0	0	None	0	None
1	1 or 2	1	I or II	1	Sparse
2	3	2	III or IV	2	Moderate
3	4 or 5	3	V or VI	3	Frequent

Modified from National Institute on Aging-Alzheimer's Association guidelines for the neuropathologic assessment of Alzheimer's disease, 2012.

A = Amyloid (Either NP or Diffuse plaque)

A1 = [Thal phase 1 & 2] → • Neocortical • Cingulate • Amygdala

A2 = Thal phase 3 → Thalamus, Striatum

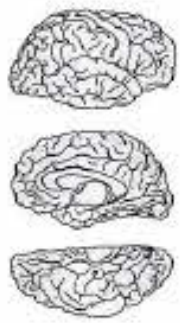
A3 = Thal phase 4 & 5 → • Subst Nigra • Red Nucleus • Central GM • Colliculi • Olivary N. • Cerebellum

Table 31.11 NIA-AA ABC scoring for Alzheimer neuropathologic change

AD neuropathologic change: A Score	C Score	B score: 0 or 1	2	3
0	0	Not	Not	Not
1	0 or 1	Low	Low	Low
	2 or 3	Low	Intermediate	Intermediate
2	Any C score	Low	Intermediate	Intermediate
3	0 or 1	Low	Intermediate	Intermediate
	2 or 3	Low	Intermediate	High

The probability that AD neuropathologic change accounted for the clinical dementia is assigned by applying an 'ABC' score. Aβ/amyloid plaques (A); NFT stage (B); and neuritic plaque score (C). 'Intermediate' or 'High' scores are considered to indicate that AD neuropathologic change was a sufficient explanation for dementia.
(Modified from National Institute on Aging-Alzheimer's Association guidelines for the neuropathologic assessment of Alzheimer's disease. Alzheimer's Dement 2012 8(1):1–13)

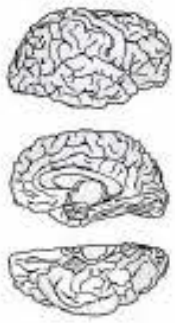
See B (Braak staging) Next page →



TRANSENTORHINAL
(Clinically asymptomatic)

Stage I: NFTs and NTs in small density, confined to transentorhinal cortex in pre-α cells

Stage II: Tangles present in moderate density in pre-α cells of entorhinal cortex. Small numbers develop in CA1 region of hippocampus

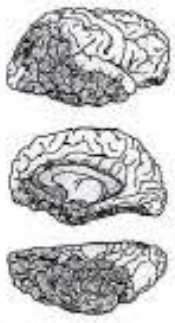


LIMBIC
(Incipient AD)

Stage III: There are modest numbers of NFTs and NTs throughout CA1 and in pyramidal cells in the subiculum. Small numbers appear in the fusiform gyrus lateral to the transentorhinal cortex as well as in the nucleus basalis of Meynert and amygdaloid complex

There is now severe involvement of pre-α cells with neuronal loss and gliosis

Stage IV: Severe involvement of areas affected in stage 3. Large numbers of ghost tangles in entorhinal and transentorhinal regions. Mild involvement of isocortex with sparing of primary sensory and motor cortices



ISOCORTICAL
(Symptomatic AD)

Stage V: Tangles in all sectors of hippocampus and subiculum. Widespread, moderate to severe isocortical involvement but still relative sparing of primary sensory and motor cortices. Tangles in claustrum, thalamus, hypothalamus. Ghost tangles with neuronal loss and astrocytic gliosis involving pre-α cells, CA1, antero-dorsal thalamic nucleus

Stage VI: Increased densities of tangles in regions affected in earlier stages. Tangles in dentate granule cell layer. Marked involvement of claustrum, thalamus, hypothalamus, substantia nigra

Mild

Moderate

Severe

Very severe

B. BRAAK STAGING

(Ellison & Love 3rd Edition)

6.4.Lewy Body Disease Staging

0 = none (not illustrated)
1 = mild (sparse LBs or LNs),
2 = moderate (more than 1 LB in a low-power field, and sparse LNs),
3 = severe (four or more LBs and scattered LNs in a low power field),
4 = very severe (numerous LBs and numerous LNs)

The Lewy body scores for individual areas are summated and the final score is used to subclassify Lewy body disease into brain stem, limbic, or neocortical types:

Assignment of Lewy body type based upon pattern of Lewy-related pathology in brain stem, limbic and neocortical regions

		Brainstem regions			Basal forebrain/limbic regions				Neocortical regions		
		IX-X	LC	SN	nbM	Amygdala	Trans-entorhinal	Cingulate	Temporal	Frontal	Parietal
Lewy body type	Brainstem predominant	1-3	1-3	1-3	0-2	0-2	0-1	0-1	0	0	0
	Limbic (transitional)	1-3	1-3	1-3	2-3	2-3	1-3	1-3	0-2	0-1	0
	Diffuse neocortical	1-3	1-3	1-3	2-3	3-4	2-4	2-4	2-3	1-3	0-2

IX = 9th cranial nerve nucleus, X = 10th cranial nerve nucleus
LC = locus ceruleus, SN = substantia nigra
nbM = nucleus basalis of Meynert

Neuropathologic diagnosis of DLB

Classification of Lewy Body Disease	
None	No Lewy bodies or related changes seen with α-synuclein staining
Brainstem predominant	Lewy bodies in midbrain, pons or medulla
Limbic (Transitional)	Lewy bodies in cingulated or entorhinal cortices, almost always associated with brain stem involvement
Neocortical (diffuse)	Lewy bodies in frontal, temporal or parietal cortices usually associated with brain stem and limbic involvement
Amygdala predominant	Lewy bodies in amygdale usually in the absence of involvement of the above regions

Modified from National Institute on Aging-Alzheimer's Association guidelines for the neuropathologic assessment of Alzheimer's disease. Alzheimers Dement. 2012 Jan;8(1):1-13

Reporting

A pathological diagnosis should be specified, irrespective of clinical history according to the classification above.
It is recommended that the presence of neocortical LBD can be regarded as a sufficient explanation for cognitive decline.
Amygdala-predominant LBD is usually seen in the context of advanced stage AD changes.

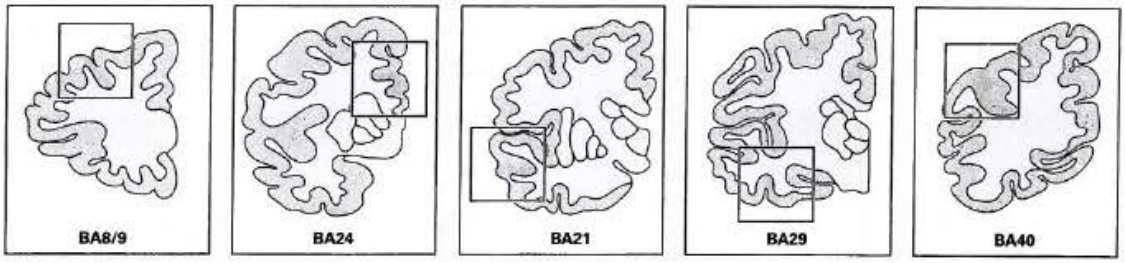
31.37 Diagnosis of Lewy body disease. A scheme for the pathologic categorization of Lewy Body Disease into the brain stem predominant, limbic, neocortical and amygdala predominant subtypes. Reporting: (1) A pathologic diagnosis should be specified, irrespective of clinical history according to the classification above. (2) It is recommended that the presence of neocortical LBD can be regarded as a sufficient explanation for cognitive decline. (3) Amygdala-predominant LBD is usually seen in the context of advanced stage AD changes. (Modified from National Institute on Aging-Alzheimer's Association guidelines for the neuropathologic assessment of Alzheimer's disease. Alzheimer's Dement 2012; 8(1):1–13)

Consensus criteria for pathologic assessment of Lewy Body Disease

Pathologic criteria for the evaluation of Lewy body disease have been proposed. Cases are divided into four main subtypes according to a distribution of Lewy bodies in brain stem, limbic, neocortical and amygdala regions.

Histologic sampling and staining

The following areas should be sampled:



Neocortical regions
(i) Frontal BA8/9
The middle frontal gyrus in the superior frontal sulcus in the coronal plane just anterior to the temporal tip.
(ii) Temporal BA21
The superior sulcal margin (superior temporal sulcus) of the middle temporal gyrus in the coronal plane of the mammillary body.
(iii) Parietal BA40
The superior sulcal margin (intraparietal sulcus) of the parietal lobule in the plane 1 cm posterior to the posterior pole of the splenium.

Limbic or paralimbic regions
(i) Anterior cingulate BA24
In the plane of the anterior commissure approximately 2 cm posterior to the anterior pole of the genu.
(ii) Transentorhinal BA29
The sulcal margin (collateral sulcus) of the parahippocampal gyrus in the plane of the red nucleus.

Amygdala and periamygdaloid region
Brain stem regions
Substantia nigra, locus ceruleus and dorsal nucleus of vagus.
Paraffin-embedded sections are cut at a thickness of 6–8 μm and stained with:
- hematoxylin and eosin
- anti-α-synuclein antibody (assess Lewy body pathology)
- anti-Aβ peptide antibody (assess AD plaque pathology)
- anti-phosphotau antibody (assess AD tau pathology).

Histologic assessment of Lewy body pathology

A formal assessment for AD should be performed, as described in the NIA-AA scheme (p.625). In each of the designated cortical areas, the density of Lewy bodies should be scored within the full thickness of the cerebral cortex according to comparison with standard images.
The areas are delimited as follows:
- Neocortical regions — from base to crest along the indicated sulcus of the selected gyrus
- Cingulate — along the full length of the gyrus in the indicated coronal plane of section
- Transentorhinal region — along the collateral sulcus from base to crest of the parahippocampal gyrus.

Scoring of density of cortical Lewy bodies

A semi-quantitative grading is made of severity of Lewy-related pathology into mild, moderate, severe and very severe (left to right below).

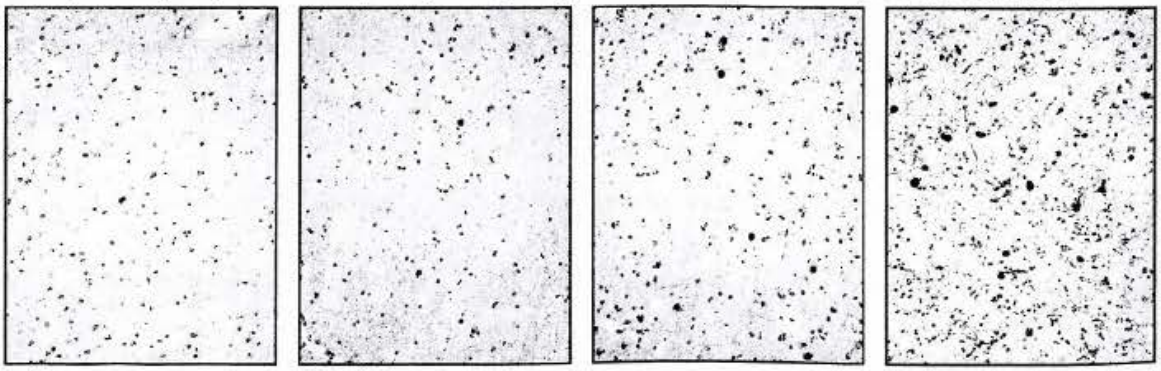
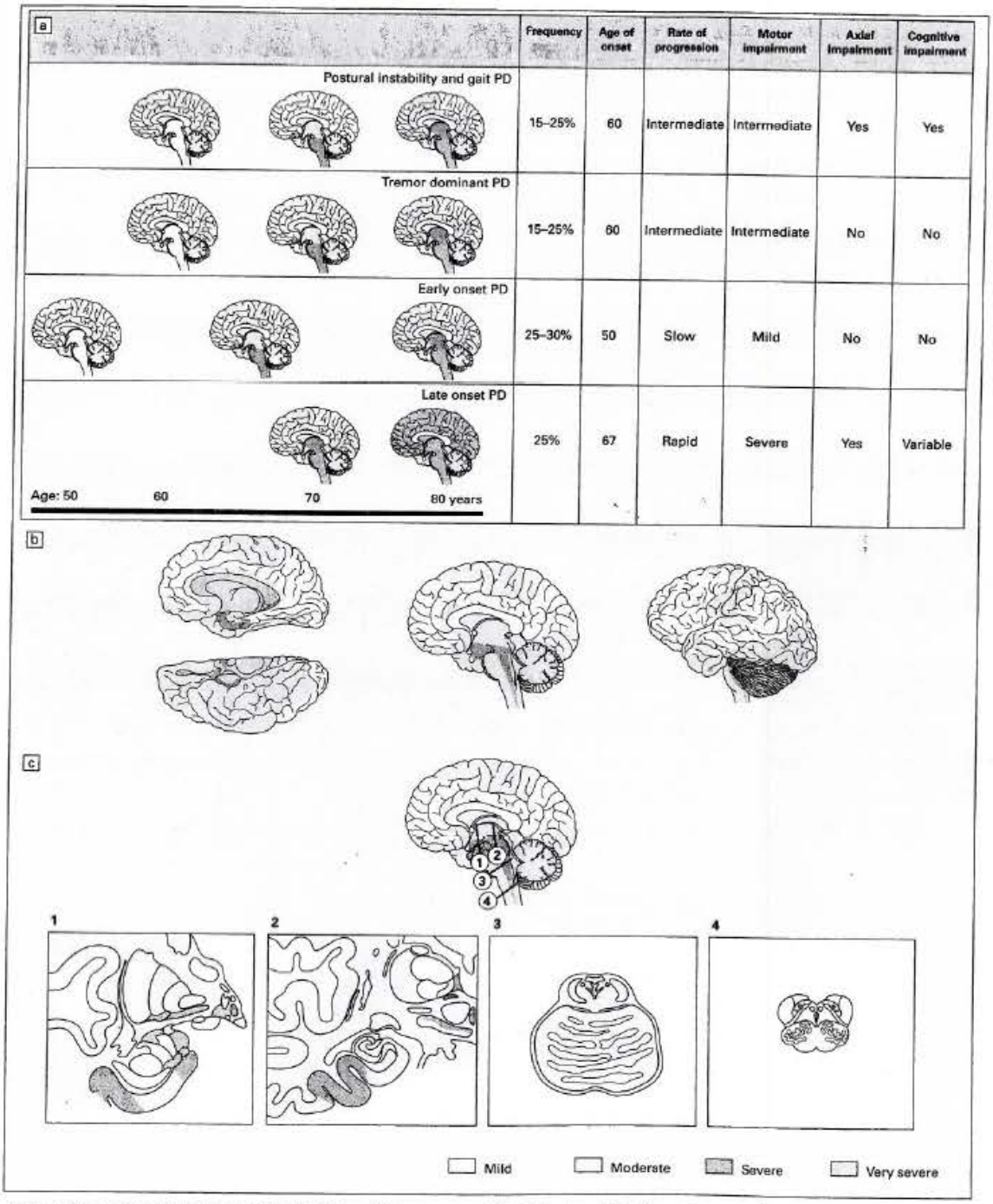


Fig 31.37



28.3 α-Synuclein pathology in Parkinson's disease. (a) Frequency and clinical features of the four major types phenotypes of PD. Brain schematics show increasing severity with age (blue bar). **(b,c)** Anatomic distribution of α-synuclein pathology. (Adapted from Halliday GM et al. 2011. Neuropathology underlying clinical variability in patients with synucleinopathies. Acta Neuropathol 122(2):187–204 and Braak H et al. 2003. Staging of brain pathology related to sporadic Parkinson's disease. Neurobiol Aging 24(2):197–211.)

7. References

7.1. NIAA guidelines for AD Staging 2012

National Institute on Aging-Alzheimer's Association guidelines for the neuropathologic assessment of Alzheimer's disease. **Hyman** BT, Phelps CH, **Beach** TG, et al . Alzheimers Dement. 2012 Jan;8(1):1-13