PRIMARY AUTO-IMMUNE CEREBELLAR ATAXIA(PACA)

By

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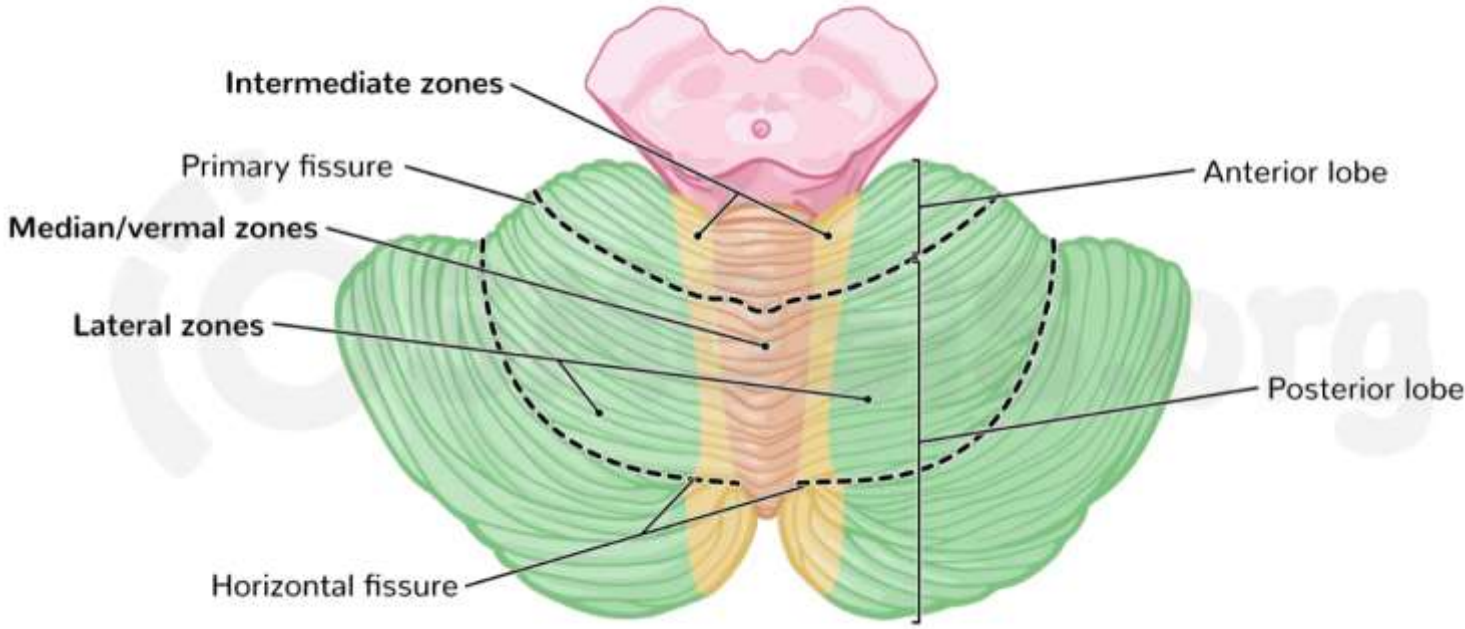
CEREBELLUM

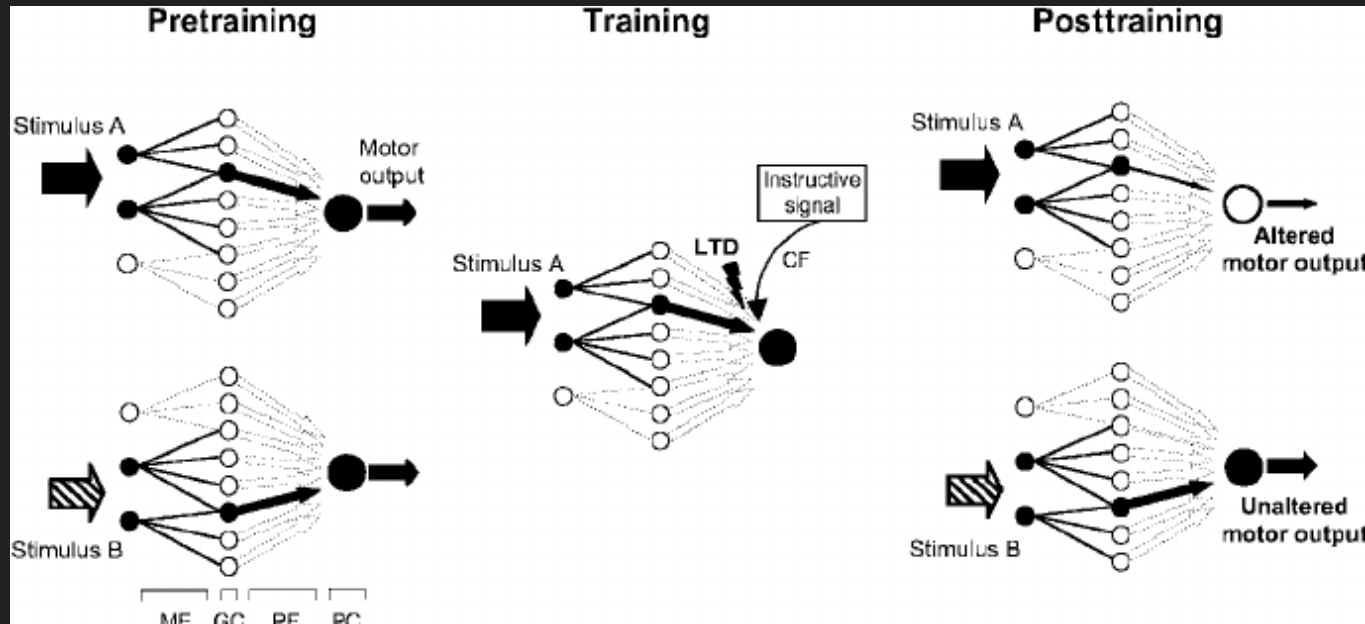


ANATOMIC AND FUNCTIONAL DIVISIONS OF THE CEREBELLUM

ANATOMIC REGIONS	OTHER DESIGNATIONS	FUNCTIONAL ZONES	FUNCTIONS	MAJOR INPUTS	DEEP NUCLEUS	MAJOR OUTPUTS
Vermis	Anterior lobe, Paleocerebellum	Spinocerebellum	Posture and axial coordination	Dorsal and ventral spinocerebellar tracts	Fastigial	Vestibulospinal tract, reticulospinal tract
Intermediate hemispheres	Anterior lobe, Paleocerebellum	Spinocerebellum	Appendicular (limb) coordination	Dorsal, ventral, and cuneospinocerebellar tracts	Interposed (globose and emboliform)	Contralateral red nucleus, rubrospinal tract
Lateral hemispheres	Posterior lobe, Neocerebellum	Cerebrocerebellum	Motor planning, procedural memory, fine motor movements	Corticopontine fibers	Dentate	Ventral lateral and ventral anterior nuclei of the contralateral thalamus, Contralateral red nucleus
Flocculonodular lobe	Archicerebellum	Vestibulocerebellum	Coordination of balance, eye movements, and head position	Vestibulocerebellar fibers	Lateral vestibular nucleus of Dieters	Vestibular nuclei

HOW DOES IT WORK

- The current understanding of how the cerebellum integrates Sensorimotor information is based on Marr – Albus - Ito theory.
- The cerebellum receives external input from sensory receptors such as tactile sensory system or vestibular system and provide proper movement in response.



ATAXIA

- Babinski - Asynergia or Dyssynergia—resulting in irregularity or fragmentation of the normal motor sequence.
- Holmes – Decomposition of a smooth movement into a series of irregular, jerky components .

Ataxia defined as incoordination of volitional movements.

PACA

- PACA is a type of Immune-Mediated Cerebellar Ataxia.
- Immune-Mediated Cerebellar Ataxia is a condition where the trigger is known such as Paraneoplastic Cerebellar Degeneration, Gluten Ataxia, Post-infectious Cerebellitis and Ataxia due to neuronal antibodies.
- Patients with PACA are suspected of Immune-mediated cerebellar ataxia in which neither a trigger nor Pathological neuronal antibodies are present.
- Patients with PACA sometimes show HLA-type DQ2.

IMCA Classification

- Cerebellar Auto-immunity secondary to a condition
  - Gluten ataxia
  - Postinfectious Cerebellitis
  - Opsoclonus myoclonus syndrome(not Anti-Ri)
  - Paraneoplastic cerebellar degeneration
- Cerebellar auto-immunity not due to secondary condition
  - Due to anti-neuronal Antibodies conditions.

CONDITIONS WITH NEURONAL AUTO-ANTIBODIES

- Anti-Sj / ITPR-1-Inositol 1,4,5-trisphosphate receptor type 1 autoantibody
- Anti-Ca/ARHGAP26 - Purkinje cell-specific autoantibody (anti-Ca) targeting rhoGTPase-activating-protein-26 (ARHGAP26).
- Anti-MAG - Anti-myelin-associated-glycoprotein (MAG) neuropathy.
- Anti-Septin-5 - Antibodies target septin-5, a guanosine triphosphate (GTP)-binding neural protein.
- Anti-Neurochondrin
- Anti-Nb/AP3B2 - Synaptic vesicle coat protein, the neuronal (B2) form of adaptor protein–3 (AP3).
- Anti-Homer-3
- Anti-GAD

DIAGNOSIS

- The following criteria need to be fulfilled to diagnose PACA:

✓ Presence of Ataxia

✓ MRI showing normal or cerebellar vermis atrophy with reduced MR spectroscopy (NAA/Cr ratio) of the vermis

✓ At least 2 of the following:

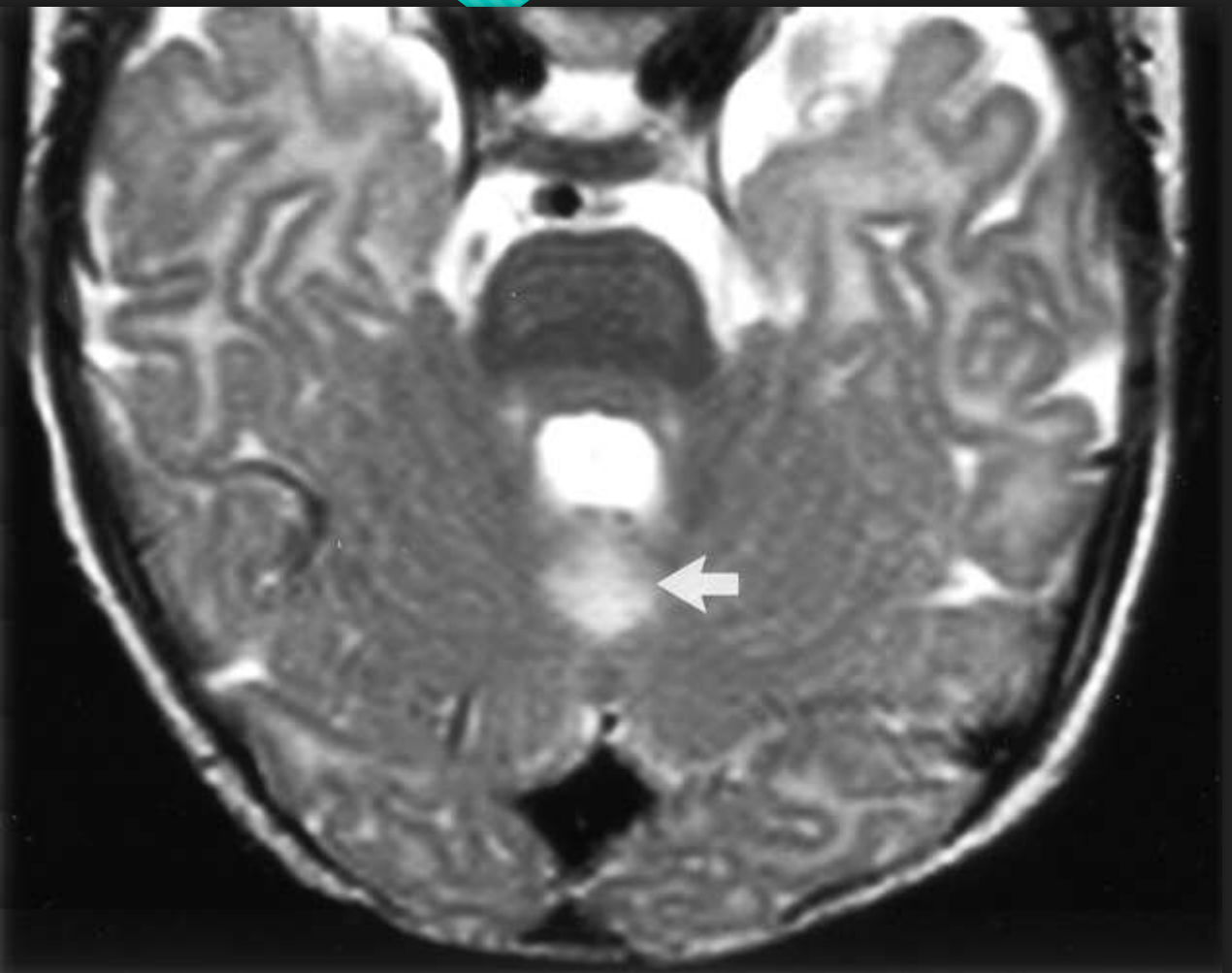
a. CSF pleocytosis / Positive CSF-restricted IgG oligoclonal bands

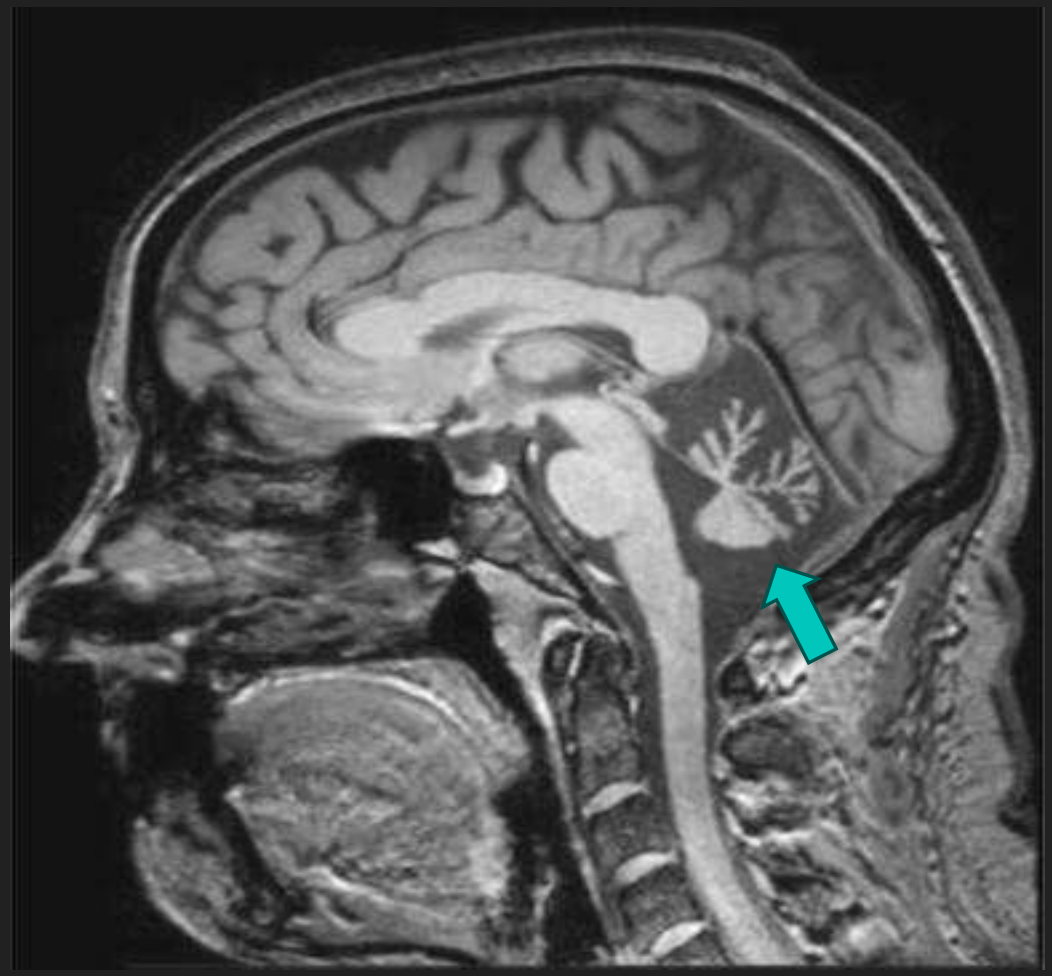
b. History of autoimmune disorders in first-degree relatives

c. Presence of antibodies that support autoimmunity but not yet shown to be involved in ataxia pathogenesis.

✓ Exclusion of alternative causes made by an experienced neurologist or ataxia specialist

MRI BRAIN

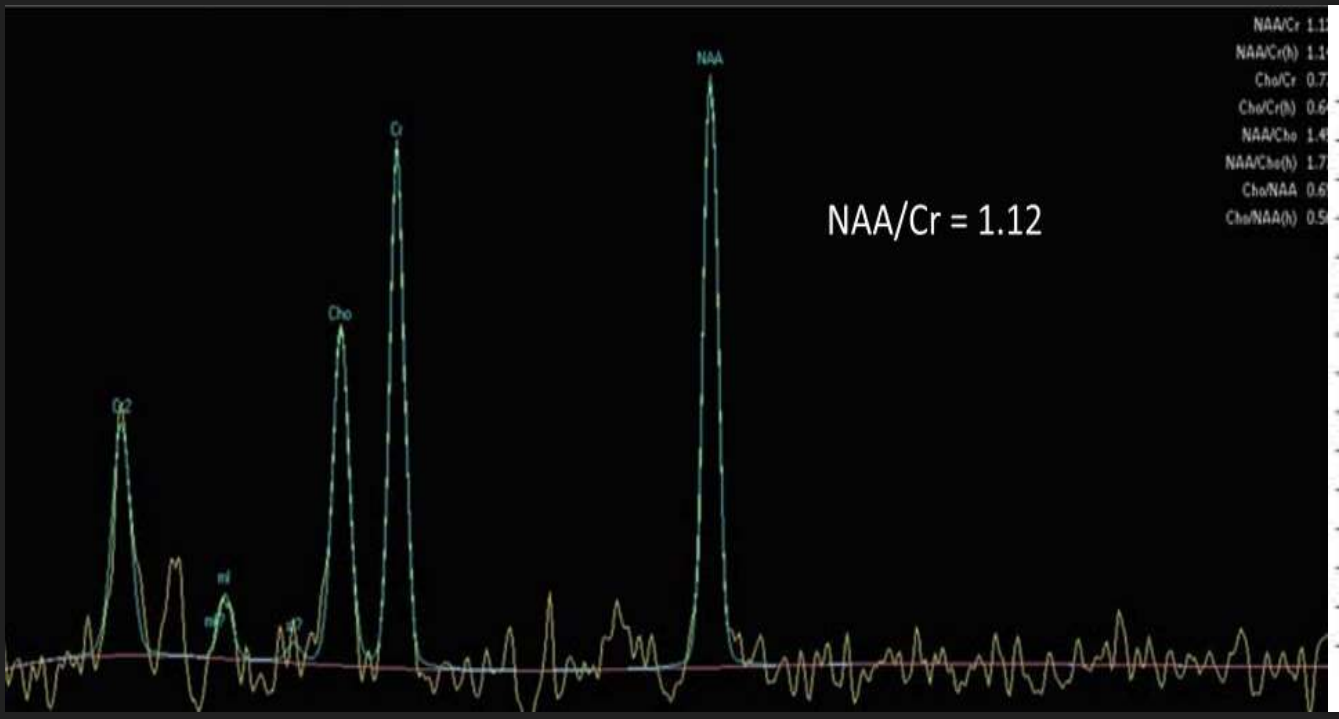


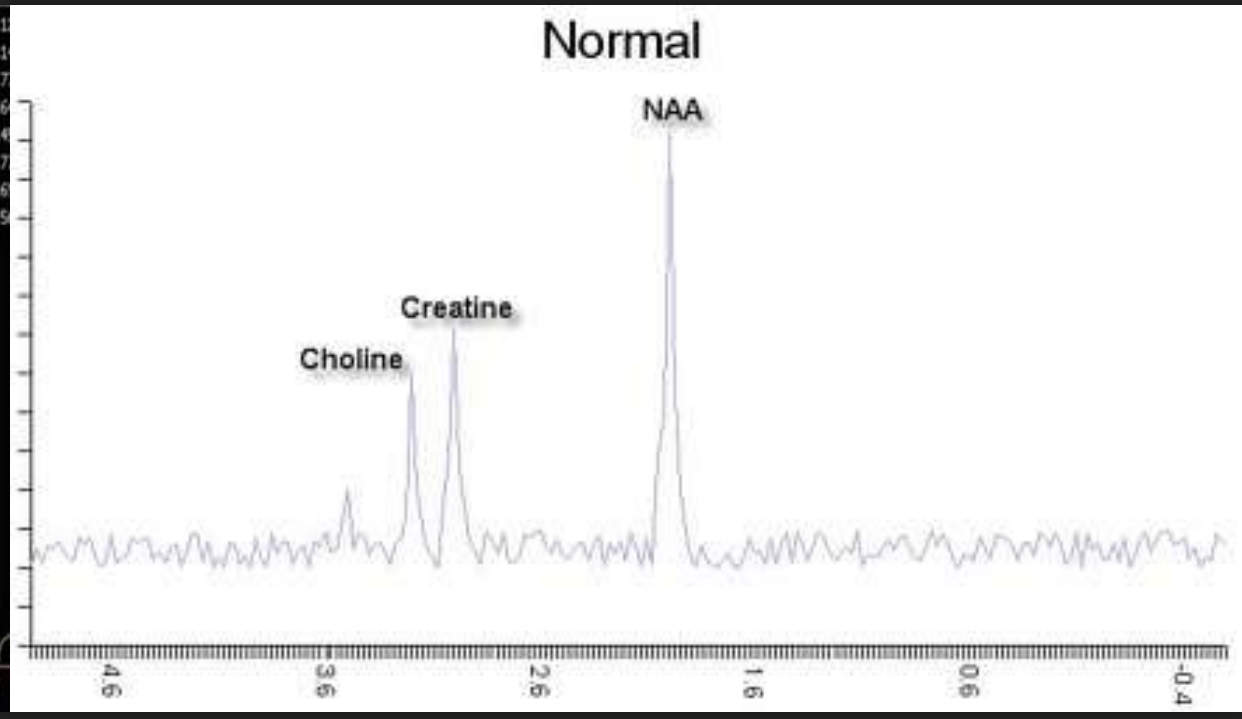


MRI SPECTROSCOPY

N-acetylaspartate (NAA): resonates at 2.0 ppm

Creatine: resonates at 3.0 ppm





OTHER INVESTIGATIONS

- There is some emerging evidence to suggest that immune-mediated ataxias are more likely to brain hyperexcitability indicated by cortical myoclonus in EEG and giant somatosensory evoked potentials in SSEP.Immunohistochemistry using SERA or CSF from patients with suspected PACA often shows reactivity with cerebellar tissue
- Tissue biopsy of peripheral nerve.

TREATMENT

- Immunotherapies are mainly used in the treatment of PACA.
- Effectiveness have been reported on IV-IG, Prednisolone, Plasmapheresis or Rituximab.
- Progression to wheel-chair dependence in patients with cerebellar ataxia due to neuronal antibodies conditions and PCD.
- MR Spectroscopy of the cerebellum is used in monitoring the response to immunotherapies.

REFERENCES

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- Diagnostic Criteria for Primary Autoimmune Cerebellar Ataxia—Guidelines from an International Task Force on Immune-Mediated Cerebellar Ataxias Marios Hadjivassiliou1 & Francesc Graus2 & Jerome Honnorat3 & Sven Jarius4 & Maarten Titulaer 5 & Mario Manto6 & Nigel Hoggard7 & Ptolemaios Sarrigiannis1 & Hiroshi Mitoma
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THANK YOU