GUTHY JACKSON Charitable Foundation

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IPND International Panel for Neuromyelitis Optica Diagnosis

Revised 2015 Diagnostic Criteria for NMO Spectrum Disorder (NMOSD)

Why are new diagnostic criteria necessary?

- Expanding disease spectrum (incomplete forms, brain lesions) not reflected in previous criteria
- Early diagnosis important and feasible, especially in AQP4-IgG seropositive individuals

How were the new criteria developed?

- International expert panel consensus after comprehensive review of available literature
- Review of vignettes of varying levels of clinical, MRI, serologic evidence

What are the key aspects of the new criteria?

- NMO spectrum disorder (NMOSD) is the umbrella term for NMO and the expanded spectrum of NMO presentations
- NMOSD patients are further stratified based on AQP4-IgG status
- Diagnosis can only be made in symptomatic individuals with compatible clinical presentations
- Clinical presentation is defined based on 6 neuroanatomically-based core clinical characteristics
- Only one core clinical characteristic is required in AQP4-IgG seropositive patients
- Criteria for AQP4-IgG seronegative NMOSD are similar to seropositive criteria but more stringent
- "Red flags" (clinical, neuroimaging, or laboratory findings) are identified that should raise concern about NMOSD diagnostic accuracy and identify conditions that could be mistaken for NMO
- The criteria address interpretation of AQP4-IgG results
- The criteria are applicable to children although caution is required regarding longitudinally extensive transverse myelitis lesions as this finding may also occur in children with MS

Comparison of old (2006) NMO and new (2015) NMOSD criteria

Characteristic	2006	2015
Symptoms compatible with NMO required	Yes	Yes
Signs compatible with NMO required	Yes	Not necessarily: vomiting, hiccups and anorexia are examples of symptoms that may occur without exam signs
Optic neuritis and myelitis	Both required	Neither required in AQP4-IgG seropositive cases
Incorporation of AQP4-IgG	Supportive	Stratifies NMOSD as AQP4-IgG seropositive or seronegative
Diagnosis possible with single clinical manifestation	No	Yes
Compatible brain syndromes and MRI lesion patterns specified	No	Yes
Coexisting autoimmune disorders	Not considered	Supportive of diagnosis

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Comparison of Requirements for Diagnosis of NMOSD with AQP4-IgG and NMOSD without AQP4-IgG

Requirements	NMOSD with AQP4-IgG	NMOSD without AQP4-IgG
Number of attacks	1+	1+
Number of different core clinical characteristics	1+	2+
Type of core clinical characteristics	Any 1 of 6	At least 1 of: • Optic neuritis with MRI criteria • Myelitis plus LETM criteria • Area postrema syndrome with MRI criteria
Additional supportive MRI criteria	No	Yes

What do the 2015 IPND criteria accomplish?

- Align with contemporary expert practice of patients with NMOSD
- Serve as a tool to educate clinicians and clinical trainees as to the current standards for diagnosis of NMOSD
- Facilitate treatment and clinical research by allowing for accurate diagnosis of patients with NMOSD at an early point in the disease
- Expand the pool of patients potentially suitable for clinical trials for NMOSD

What do the 2015 IPND criteria not accomplish?

- Provide a diagnosis for every potential presentation of NMOSD; detailed workup is essential for atypical cases and identification of alternative diagnoses necessary in appropriate patients
- Adequately characterize the heterogeneity of AQP4-IgG seronegative NMOSD

What are the next steps?

- Criteria validation based on retrospective and prospective follow-up data to identify pitfalls and misdiagnosis
- Continued assessment of the sensitivity and specificity of AQP4-IgG assays
- Better characterization of both AQP4-IgG seropositive and seronegative patient subsets to individualize prognosis and optimize treatment

References

Wingerchuk DM, Lennon VA, Pittock SJ, Lucchinetti CF, Weinshenker BG. Revised diagnostic criteria for neuromyelitis optica. Neurology 2006;66:1485-1489.

Wingerchuk DM et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology 2015;85:1-13.