European Reference Network | Neurological Diseases (ERN-RND)

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BRIEF + FOCUSED INFORMATION ON THE DIAGNOSIS OF ATYPICAL PARKINSONISM FOR GENERAL NEUROLOGISTS/GENERAL PRACTITIONERS

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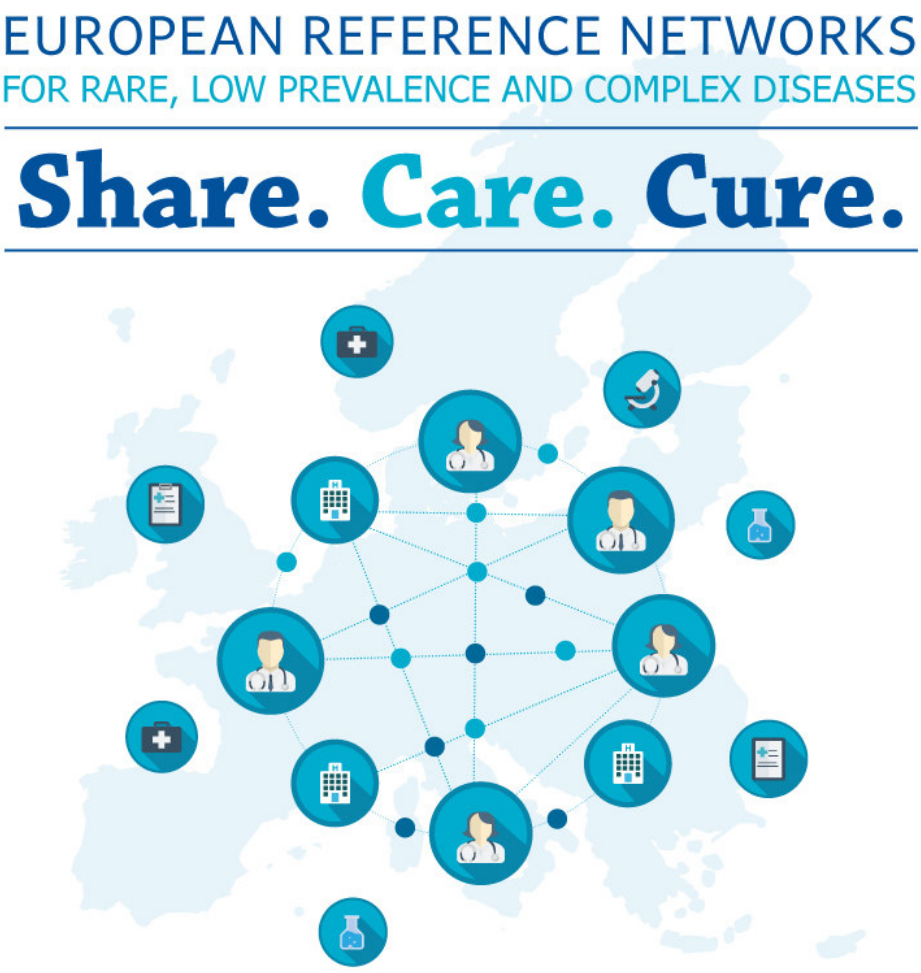

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1. INTRODUCTION TO THE EUROPEAN REFERENCE NETWORK FOR RARE NEUROLOGICAL DISEASES

ERN-RND is a European Reference Network established and approved by the European Union. ERN-RND is a healthcare infrastructure which focuses on rare neurological diseases (RND). The three main pillars of ERN-RND are (i) network of experts and expertise centres, (ii) generation, pooling and dissemination of RND knowledge, and (iii) implementation of e-health to allow the expertise to travel instead of patients and families.

ERN-RND unites 32 of Europe's leading expert centres in 13 Member States and includes highly active patient organizations. Centres are located in Belgium, Bulgaria, Czech Republic, France, Germany, Hungary, Italy, Lithuania, Netherlands, Poland, Slovenia, Spain and the UK.

The following disease groups are covered by ERN-RND:

- Ataxias and Hereditary Spastic Paraplegias
- Atypical Parkinsonism and genetic Parkinson's disease
- Dystonia, Paroxysmal Disorder and Neurodegeneration with Brain Ion Accumulation
- Frontotemporal Dementia
- Huntingtons' Disease and other Choreas
- Leukodystrophies

Specific information about the network, the expert centres and the diseases covered can be found at the networks web site www.ern-rnd.eu.

2. RECOMMENDATION FOR CLINICAL USE

The European Reference Network for Rare Neurological Diseases developed this *information on the diagnosis of atypical parkinsonism* to help guide the diagnosis. The Reference Network recommends the use of this information.

3. DISCLAIMER

Clinical practice guidelines, practice advisories, systematic reviews and other guidance published, endorsed or affirmed by ERN-RND are assessments of current scientific and clinical information provided as an educational service. The information (1) should not be considered inclusive of all proper treatments, methods of care, or as a statement of the standard of care; (2) is not continually updated and may not reflect the most recent evidence (new information may emerge between the time information is developed and when it is published or read); (3) addresses only the question(s) specifically identified; (4) does not mandate any particular course of medical care; and (5) is not intended to substitute for the independent professional judgement of the treating provider, as the information does not account for individual variation among patients. In all cases, the selected course of action should be considered by the treating provider in the context of treating the individual patient. Use of the information is voluntary. ERN-RND provided this information on an "as is" basis, and makes no warranty, expressed or implied, regarding the information. ERN-RND specifically disclaims any warranties of merchantability or fitness for a particular use or purpose. ERN-RND assumes no responsibility for any injury or damage to persons or property arising out of or related to any use of this information or for any errors or omissions.

4. METHODOLOGY

The development of this information was done by the Disease group for atypical parkinsonism of ERN-RND.

4.1. DISEASE GROUP ATYPICAL PARKINSONISM

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5. OVERVIEW ATYPICAL PARKINSONIAN SYNDROMES

Atypical parkinsonian syndromes (APS) comprise a group of disorders that can mimic Parkinson's disease (PD), especially in the early disease stages. The following disorders are typically summarized under the term APS:

- Multiple System Atrophy (MSA)
- Progressive Supranuclear Palsy (PSP)
- Corticobasal Syndrome (CBS) which may be a manifestation of PSP or Corticobasal degeneration (CBD)

Patients with these disorders usually show faster disease progression and no or poor response to continued levodopa therapy compared to patients with PD. The specific syndromes are clinically defined by a constellation of symptoms. A patient suspected to suffer from a parkinsonian disorder exhibiting the following symptoms early in the disease course after the onset of motor symptoms should prompt referral to a movement disorder specialist for further investigation whether an APS is present:

- No or poor response to levodopa
- Rapid disease progression
- Gait instability and early falls
- Development of dementia
- Vertical gaze palsy or slowing of vertical saccades
- Dysautonomia
- Early dysarthria, dysphagia, or stridor
- Prominent cerebellar signs
- Pyramidal tract signs
- Dystonia
- Apraxia
- Myoclonus

Apart from patient history and clinical examination additional diagnostic measures such as neuroimaging, cerebrospinal fluid examination, autonomic testing, and cognitive tests may all be helpful in supporting a clinical diagnosis. Currently there are no therapies to cure or stop/slow disease progression in APS. However, patient care to alleviate symptoms may be adapted when the correct diagnosis is established. A number of trials are currently under-way to better define the spectrum of symptoms and course of APS and to test the efficacy of different therapeutic approaches. Patients with a correct diagnosis of APS may benefit by enrolling in these studies (https://www.michaeljfox.org/trial-finder).

For more detailed information on APS see the consensus papers below.

5.1. CONSENSUS PAPERS

Consensus papers MSA:

- Pellecchia MT, Stankovic I, Fanciulli A, Krismer F, Meissner WG, Palma JA, Panicker J, Seppi K, Wenning GK on behalf of the MoDiMSA study group. Can autonomic testing and imaging contribute to the early diagnosis of MSA? A systematic review and recommendations by the MDS multiple system atrophy (MoDiMSA) study group. Mov Disord Clin Pract 2020, in revision.
- Stankovic I, Quinn N, Vignatelli L, Antonini A, Berg D, Coon E, Cortelli P, Fanciulli A, Ferreira JJ, Freeman R, Halliday G, Höglinger GU, Iodice V, Kaufmann H, Klockgether T, Kostic V, Krismer F, Lang A, Levin J, Low P, Mathias C, Meissner WG, Norcliffe Kaufmann L, Palma JA, Panicker JN, Pellecchia MT, Sakakibara R, Schmahmann J, Scholz SW, Singer W, Stamelou M, Tolosa E, Tsuji S, Seppi K, Poewe W, Wenning GK, on behalf of the Movement Disorder Society MSA Study Group. A critique of the second consensus criteria for multiple system atrophy. Mov Disord 2019;34:975-984.

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• Trojanowski JQ, Revesz T. Proposed neuropathological criteria for the post mortem diagnosis of multiple system. Neuropathology Working Group on MSA. Neuropathol Appl Neurobiol. 2007 Dec;33(6):615-20.

• Laurens B, Constanstinescu R, Freeman R, Gerhard A, Jellinger K, Jeromin A, Krismer F, Mollenhauer M, Schlossmacher M,G, Shaw LM, Verbeek MM, Wenning GK, Winge K, Zhang J, Meissner WG. Fluid biomarkers in multiple system atrophy: A review of the MSA Biomarker Initiative. Neurobiol Dis. 2015 Aug;80:29-41. doi: 10.1016/j.nbd.2015.05.004. Epub 2015 May 15.

Consensus papers PSP/CBD:

• Grimm MJ, Respondek G, Stamelou M, Arzberger T, Ferguson L, Gelpi E, Giese A, Grossman M, Irwin DJ, Pantelyat A, Rajput A, Roeber S, van Swieten JC, Troakes C, Antonini A, Bhatia KP, Colosimo C, van Eimeren T, Kassubek J, Levin J, Meissner WG, Nilsson C, Oertel WH, Piot I, Poewe W, Wenning GK, Boxer A, Golbe LI, Josephs KA Litvan I, Morris HR, Whitwell JL, Compta Y, Corvol JC, Lang AE, Rowe JB, Höglinger GU, for the Movement Disorder Society-endorsed PSP Study Group. How to Apply the Movement Disorder Society Criteria for Diagnosis of Progressive Supranuclear Palsy. Mov Disord 2019;34:1228-1232.

• Höglinger GU, Respondek G, Stamelou M, Kurz C, Josephs KA, Lang AE, Mollenhauer B, Müller U, Nilsson C, Whitwell JL, Arzberger T, Englund E, Gelpi E, Giese A, Irwin DJ, Meissner WG, Pan-telyat A, Rajput A, van Swieten JC, Troakes C, Antonini A, Bhatia KP, Bordelon Y, Compta Y, Corvol JC, Colosimo C, Dickson DW, Dodel R, Ferguson L, Grossman M, Kassubek J, Krismer F, Levin J, Lorenzl S, Morris HR, Nestor P, Oertel WH, Poewe W, Rabinovici G, Rowe JB, Schellen-berg GD, Seppi K, van Eimeren T, Wenning GK, Boxer AL, Golbe LI, Litvan I; Movement Disorder Society-endorsed PSP Study Group. Clinical diagnosis of progressive supranuclear palsy: The movement disorder society criteria. Mov Disord. 2017;32(6):853-864. doi: 10.1002/mds.26987.

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• Armstrong MJ, Litvan I, Lang AE, Bak TH, Bhatia KP, Borroni B, Boxer AL, Dickson DW, Grossman M, Hallett M, Josephs KA, Kertesz A, Lee SE, Miller BL, Reich SG, Riley DE, Tolosa E, Tröster AI, Vidailhet M, Weiner WJ. Criteria for the diagnosis of corticobasal degeneration. Neurology. 2013;80(5):496-503. doi: 10.1212/WNL.0b013e31827f0fd1.

Consensus papers DLB

McKeith et al. Neurology. 2017 Jul 4; 89(1): 88–100. doi: 10.1212/WNL.0000000000004058

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