Neuroimmunology is a rapidly developing field. With the description of new antibodies and new syndromes, both the clinical spectrum and our insights into disease pathophysiology and treatment expand. These developments also reflect on movement disorders associated with neuronal antibodies, a field that is continuously broadening. Although these conditions are rare overall, they are a not-to-miss diagnosis because of the treatment implications: the earlier immunotherapy is initiated, the better the outcome. The classic paraneoplastic (onconeuronal) antibodies are indicative of an underlying neoplasm; neuronal surface antibodies are less frequently associated with malignancy and have an overall better outcome (Figure). To facilitate prompt immunotherapy, new diagnostic criteria for autoimmune encephalitis highlight the importance of clinical recognition. Movement disorders may be the first or most prominent presentation of autoimmune encephalitis and can present with characteristic phenotypes, with associated red flags or other diagnostic clues (Box). Importantly, they may also be a differential diagnosis of degenerative disease, particularly when signs and symptoms develop slowly. This review provides an overview of the clinical spectrum of movement disorders with neuronal antibodies; supplementary Table e1 in the online version of the article provide a reference and glossary for the antibodies discussed.

**Chorea, Dyskineties, and Stereotypies**

Chorea may occur as a paraneoplastic syndrome, in particular with antibodies to Hu and collapsin response-mediator protein-5 (CRMP5) often combined with other signs. With antiCRMP5, additional signs include cognitive decline, neuropathy, optic neuritis, and myelitis; with anti-Hu, gastrointestinal pseudoobstruction, and sensorineuronal hearing loss are seen. Both often feature fluid attenuated inversion recovery sequence (FLAIR) MRI hyperintensities in white matter, basal ganglia, and the temporomesial lobe. Anti-Hu and antiCRMP5, as well as amphiphysin antibodies, can cause a dorsal root ganglionopathy with sensory ataxia and pseudoathetosis.

<table>
<thead>
<tr>
<th>Cell-surface antigens</th>
<th>Intracellular synaptic antigens</th>
<th>Intracellular cytoplasmic/nuclear antigens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathogenic antigens are accessible in vivo; typically play important roles in synaptic transmission, plasticity, or excitability</td>
<td>Controversial role in pathogenesis antigen may be transiently accessible during synaptic vesicle fusion and uptake</td>
<td>Markers of paraneoplastic syndrome; poor prognosis poor treatment response, autoimmunity mainly via cytotoxic T-cells; antigens inaccessible in vivo</td>
</tr>
<tr>
<td>CASPR2, DPPX, D2R, GABA_2R, GABA_3R, GlyR, LGI1, NMDAR</td>
<td>GAD, amphiphysin</td>
<td>Hu, Ri, CRMP5/CV2, Ma2</td>
</tr>
</tbody>
</table>

Figure. Categories of autoantibodies to neuronal antibodies, pathogenic roles, examples, treatment responses and tumor associations. Adapted with permission from Balint B, Vincent A, Meinck HM, Irani SR, Bhatia KP. Movement disorders with neuronal antibodies: syndromic approach, genetic parallels and pathophysiology. Reproduced with permission from *Brain*. 2018;141(1):13-36.

Antibodies to phosphodieserase 10A (antiPDE10A) have been recently described as a new marker of paraneoplastic chorea (and other movement disorders) with onset at median age 70 at equal rates in men and women. The full clinical and radiologic spectrum (basal ganglia FLAIR hyperintensities reported) remains to be determined. Similar to the classic paraneoplastic antibodies, the PDE10A is an intracellular antigen, with autoimmunity likely conveyed by cytotoxic T cells.
Chorea may also occur with antibodies to neuronal surface antigens (eg, leucine-rich glioma inactivated 1 [LGI1] or contactin-associated protein-like 2 [CASPR2]) with a lower likelihood of an underlying tumour. AntiLGI1 occurs more frequently in men age 60 to 70 (sex ratio 2:1) and antiCASPR2 more frequently in men age 50 to 60 (sex ratio 8:1). The clinical spectrum of antiCASPR2 includes also limbic encephalitis with cognitive decline, seizures, behavioral change, myoclonus (see below), ataxia, and pain, which can be an important diagnostic clue. AntiLGI1 cause faciobrachial dystonic seizures (FBDS) more often than chorea.

Antibodies to Immunoglobulin-like cell adhesion molecule 5 (IgLON5) also cause chorea equally in men and women in their 40s to 70s (peak in 60s). Diagnostic clues include sleep disorders (see below), prominent bulbar symptoms, or breathing difficulties. AntiIgLON5-associated disease may have a slowly progressive course and feature cognitive decline. In the context of chorea, it can resemble Huntington disease (see below for parkinsonian manifestations).

Chorea, focal or more complex dyskinesia, stereotypies, or combinations thereof may be caused by antibodies to the N-methyl-D-aspartate receptor (NMDAR), predominantly in girls and women (age 8 months to 85 years; sex ratio 4:1), normally with other features of encephalopathy. The younger the individual, the more likely is a movement disorder-predominant presentation. Antibodies to neurexin-3ct cause dyskinesia as part of an encephalopathy, but are quite rare.

Dystonia, Pseudodystonia, and Stiff Person Spectrum Disorders

Dystonia, typically with other signs or symptoms, can be a manifestation of neuronal antibody-related disease. Dystonia in autoimmune disease, however, features neither the pattern of isolated, idiopathic (hitherto called primary) dystonia nor a geste antagonsiste. The term pseudodystonia implies a different phenomenology and underlying mechanism from classical dystonia, which may be more appropriate for some of the descriptions of immune-mediated dystonia. Craniofacial dystonia including jaw closing or opening dystonia is seen with antiRi, a paraneoplastic antibody occurring predominantly in women age 47 to 87 (peak in 60s, sex ratio 4:1) and indicating breast cancer. The spectrum of antiRi syndrome is broad, with cerebellar ataxia (most frequent sign), other movement disorders, oculomotor disturbances, and encephalopathy. As a feature in a broader encephalopathic syndrome, dystonia has been described with a variety of antibodies, including antibodies to Ma2, CRMP5, PDE10A, GABAAR, and IgLON5, and is particularly frequent with antiNMDAR.

Classic pseudodystonia is seen in Miller-Fisher Syndrome or chronic inflammatory demyelinating polyradiculoneuropathy with ganglioside, neurofascin andCNTN1 antibodies because of proprioceptive sensory loss. Muscle stiffness, sometimes leading to abnormal postures and pseudodystonia-like lumbar hyperlordosis or foot plantar flexion is a core feature of stiff person spectrum disorders (SPSD; see Stiff-Person Syndrome in this issue), besides superimposed muscle spasms and excessive startle (hyperekplexia). Additional signs may occur (eg, cerebellar ataxia, focal epilepsy), particularly with antiGAD; other brainstem signs in progressive encephalomyelitis with rigidity and myoclonus (PERM), often with antiGlyR; long-lasting diarrhea with antiDPPX; sensory ataxia with antiamphiphysin). However, the clinical spectrum is broad, and the phenotype does not necessarily predict the underlying antibody, which is still important to identify because of possibly associated neoplasia and comorbidities (antiGlyR: thymoma; antiamphiphysin: breast or lung cancer; antiGAD: type 1 diabetes, thyroid disease, pernicious anaemia; antiDPPX: infrequently B-cell neoplasms). Very rarely, a SPSD phenotype has been reported with Ri or GABAAR antibodies.
Paroxysmal Dyskinesia

Classic, “primary” paroxysmal dyskinesias are a group of inherited disorders that manifest early in life and are characterised by brief self-limiting attacks of involuntary movement without impaired consciousness. The classic antibody-related paroxysmal movement disorder is FBDS with antiLG1. FBDS are very characteristic, brief (<3 seconds), frequent (hundreds/day) episodes of abnormal posturing, typically of the ipsilateral face and arm, although the affected side may alternate. Involvement of the legs gives rise to drop attacks, and various combinations of affected body parts including bilateral involvement can be seen. Although EEG findings are typically normal, some individuals may have automatisms, sensory aura, postictal fear or speech arrest. Brain MRI may show basal ganglia hyperintensities on T1- or T2-weighted sequences. Because FBDS, similar to episodic bradycardia and hyponatraemia, may precede the development of “full-blown” limbic encephalitis with cognitive impairment, early recognition and timely initiation of immunotherapy are of paramount importance. AntiLG1 occurs predominantly in men age 60 or more. In contrast, girls and women with a paroxysmal acquired movement disorder are more likely to have tonic spasms related to demyelinating disease. Painful tonic spasms occur more frequently in neuromyelitis optica spectrum disorders (NMOSD) than in multiple sclerosis, and seemingly more with antibodies to aquaporin-4 (AQP4) than to myelin oligodendrocyte glycoprotein (MOG). Rarely, brief dystonic posturing in young women is seen with antiNMDAR.

Myoclonus

Myoclonus may be a feature in various antibody-related movement disorders and can be a fairly indistinct feature (eg, encephalitis with antiNMDAR) or a more prominent sign (eg, antiGABAAR encephalitis, diagnostic clue: intractable seizures; or antidipeptidyl aminopeptidase-like protein 6 (DPPX) encephalitis, often combined with other neurologic or autonomic signs, particularly long-lasting diarrhea). Moreover, there are characteristic myoclonus syndromes, such as coarse myoclonus affecting the legs and hampering stance and gait with antiCASPR2. This phenomenology is distinctive and often accompanied by diagnostic clues like neuropathic pain or cognitive decline. Another characteristic myoclonus-syndrome is opsoclonus-myoclonus syndrome (OMS), a generalised myoclonus with chaotic-multidirectional saccades. OMS can be a paraneoplastic (in childhood with neuroblastoma, early adulthood with teratomas, and later adulthood mostly with lung and breast cancer) or postinfectious (eg, HIV seroconversion), with various but not disease-defining antibodies. Brainstem myoclonus with tactile or acoustic startle is part of SPSPD, particularly the PERM variant.

Parkinsonism

Autoimmune parkinsonism is a differential diagnosis of atypical parkinsonism that rarely occurs as an isolated syndrome and typically features other signs and symptoms not compatible with a diagnosis of simple Parkinson disease. Often, the tempo of the disease course cautions against a diagnosis of neurodegenerative disease.

Paraneoplastic encephalitis with antiMa2 may manifest as a syndrome resembling progressive supranuclear palsy (PSP)—predominantly rigid parkinsonism with gait instability, supranuclear vertical gaze palsy, and eye closure resembling lid opening apraxia. Further distinctive features such as weight gain and prominent sleep disorders including excessive daytime sleepiness, rapid eye movement (REM) behavior sleep disorder (RBD), and narcolepsy-cataplexy reflect the association of antiMa2 with hypothalamic-pituitary dysfunction. The possible features of antiMa2 encephalitis are broad and include limbic, diencephalic, and brainstem encephalitis, myelopathy, and radiculoplexopathy. Radiologically, antiMa2 encephalitis has a typical MRI pattern with thalamic and hypothalamic T2 hyperintensities. Basal ganglia involvement can be seen, but is more typical of paraneoplastic parkinsonism with antiCRMP5. Notably, there are rare reports of paraneoplastic parkinsonism without an identified antibody and with large T2 hyperintensities on MRI.

Parkinsonism has been reported with some neuronal surface antibodies without an underlying malignancy (antiLG1, antiCASPR2, antiDPPX, and in children, anti-NMDAR or, rarely antidopamine type 2 receptors [antiD2R]; See Autoimmune Movement Disorders in Children in this issue).

Parkinsonism with antiLG5 may pose a diagnostic challenge because symptoms may develop slowly over years as in classic neurodegenerative disease. The core features of antiLG5-related disease are sleep disturbances, bulbar symptoms (eg, dysphagia, dysarthria, or vocal cord paralysis), and breathing difficulties that can be severe enough to require tracheostomy. Gaze palsy, cognitive decline including executive dysfunction, apraxia or hallucinations, cerebellar ataxia, chorea, and fasciculations also occur with antiLG5 disease. Depending on the combination of signs and symptoms, antiLG5 disease may be in the differential for multisystem atrophy (MSA) if RBD, ataxia and dysautonomia are present, PSP if there is a vertical supranuclear gaze palsy and postural instability, or corticobasal syndrome (CBS) if asymmetric parkinsonism occurs with apraxia.

Movement Disorders in Sleep

Sleep disturbances including movement disorders during sleep are common in autoimmune encephalitis. AntiLG5 was identified by a characteristic nonREM (NREM) parasomnia with fine, purposeful movements (eg, manipulating an object or preparing food) that are different from the thrash-
ing. Violent movements seen in RBD.29 The spectrum of sleep disorders in antiIgLON5 disease is broad, however, encompassing RBD, periodic leg movements of sleep (PLMS), and sleep apnea. RBD or dream enactment can be a feature of antiMa2-, antiLG11, or antiNMDAR-encephalitis. PLMS was found in encephalitis with antiDPPX, antiMa2 or antiGI1.16,28 Symptoms of restless legs syndrome (RLS) were reported by patients with antiLG11 or antiNMDAR.25 The most classic sleep disorders in autoimmune disease are, however, status dissociatus (disintegration of wake/non-REM and REM sleep boundaries with motor hyperactivity) and agrypnia excitata (insomnia, motor and autonomic hyperactivity), which are hallmark features of Morvan syndrome with antiCASPR2.

Less commonly status dissociatus and agrypnia excitata have been observed in antiLG11-, antiNMDAR-, and antiGABAAR-associated encephalitis.2,28

Tremor, Myorhythmia, and More

Autoimmune tremor syndromes typically occur in the context of a cerebellar syndrome (See Immune-Mediated Cerebellar Ataxias in this issue),2 chronic inflammatory demyelinating neuropathy (CIDP), or as an indigestive feature in an encephalopathic syndrome, but not as isolated tremor.

Beside the classic antibodies to myelin associated glycoprotein (MAG), several newly described antibodies have been identified as the cause of CIDP; these target proteins close to the node of Ranvier (eg, contactin 1 [CNTN1], neurofascin 155 [NF155], neurofascin 140/186 [NF140/186], and contactin-associated protein-1 [CASPR1]).30 Antibodies that target glial filament acidic protein (GFAP) are typically associated with myelompolyneuropathies with a characteristic MRI findings of radial linear periventricular or cerebellar gadolinium enhancement and tremor and ataxia in up to 40% of cases.31 Headache caused by meningitis and blurred vision owing to optic disc edema may be diagnostic clues, although the phenotypic spectrum of antiGFAP-associated disease keeps expanding, possibly because of frequent co-occurrence of other antibodies in up to one-third of cases.31 GFAP is located intracellularly, but the tumor association (~20%) is less strong than with classic paraneoplastic antibodies to intracellular proteins.

Myorhythmia is typically associated with Whipple disease, particularly if occurring as oculomasticatory myorhythmia with vertical gaze palsy; however, myorhythmia can also be a feature of autoimmune disease, particularly with antiIgLON3,34 but also in antiNMDAR encephalitis.35

Movement disorders in autoimmune disease are often difficult to classify—because of the overlap with psychiatric symptoms and mixed presentations (eg, catatonia, clonic or tonic perseverations, or a combination with peripheral movement disorder mimics) or because of the unusual phenomenology of the movement disorders. Examples of this included abdominal dyskinesia caused by neuromyotonia seen in antiIgLON5 disease,46 trunk flexion or abdominal wall contractions superficially resembling psychogenic proprioceptive myoclonus with antiCASPR2,37 or movement disorders that defy classic movement disorder terminology in antiNMDAR- or antiGABAAR-associated encephalitis.9,38

Conclusions and Future Perspectives

Nearly all movement disorders categories and mimics with peripheral pathology may be seen with autoantibodies to neuronal antigens. A high index of suspicion and knowledge of clinical phenotypes are key to identifying who might benefit from immunotherapy. Some presentations are characteristic, if not pathognomonic for antibody-related disease, and sometimes there are distinct associated features pointing towards a specific antibody (Box). Sometimes, however, more general considerations (eg, unilateral symptoms without a corresponding lesion on imaging), typical MRI or cerebrospinal fluid (CSF) findings, or a propensity to autoimmunity, whether paraneoplastic, genetic, post infectious, or idiopathic, may point to the diagnosis (Box).

It is likely that we will see an increase in autoimmunity and antibody-related syndromes, including movement disorders, with the wider use of immune checkpoint inhibitors (ICIs) to treat cancer.39,40 ICIs are monoclonal antibodies that target and inhibit immune checkpoints, thereby unleashing an antitumor immune response. Although ICIs are efficacious in cancer treatment and have been a major step forward for treating many malignancies, they can also break immune tolerance to self-antigens. ICI-related autoimmunity can present with classic paraneoplastic antibodies, neuronal surface antibodies or as a seronegative syndrome.40-42 Moreover, those as yet seronegative syndromes will continue to be unriddled as illustrated with the recent discoveries of new antibodies in cerebellar ataxia and new antibody-identification techniques.43-46


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Disclosure
BB reports that she has no disclosures.
<table>
<thead>
<tr>
<th>Antibody target</th>
<th>Tumor association</th>
<th>Movement disorder signs</th>
<th>Other clinical features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aquaporin-4 (AQP4)</td>
<td>(+/-) (rarely; lung or breast cancer, teratoma)</td>
<td>Painful tonic spasms</td>
<td>Neuromyelitis optica spectrum disorders, typically with optic neuritis, pyramidal weakness, sensory symptoms, bladder disturbance</td>
</tr>
<tr>
<td>Contactin-associated protein 1 (CASPR1)</td>
<td>-</td>
<td>Tremor</td>
<td>Chronic inflammatory demyelinating polyneuropathy, sensory ataxia</td>
</tr>
<tr>
<td>Contactin-associated protein 2 (CASPR2)</td>
<td>+/- (in ~20%; thymoma &gt;&gt; lung, prostate, sigmoid or thyroid cancer, myeloma)</td>
<td>Cerebellar ataxia, chorea, neuropathy, myokymia</td>
<td>Morvan syndrome, limbic encephalitis, neuropathy (rarely Guillain-Barré-like syndrome), neuropathic pain</td>
</tr>
<tr>
<td>Contactin-1 (CNTN1)</td>
<td>-</td>
<td>Tremor</td>
<td>Chronic inflammatory demyelinating polyneuropathy, sensory ataxia</td>
</tr>
<tr>
<td>Dipeptidyl peptidase-like protein 6 (DPPX)</td>
<td>+/- (in ~7%; B-cell neoplasms)</td>
<td>Stiff person spectrum disorder, myoclonus, startle, ataxia, tremor, parkinsonism, opsoclonus myoclonus</td>
<td>Multifocal encephalitis or brainstem encephalitis with prominent gastrointestinal symptoms (prolonged diarrhea, constipation), other dysautonomic signs (urinary or erectile dysfunction, cardiac arrhythmia, thermoregulation, Raynaud phenomenon), sensory disturbance (allodynia, paraesthesia)</td>
</tr>
<tr>
<td>Dopamine 2 receptor (D2R)</td>
<td></td>
<td>Basal ganglia encephalitis in children with dystonia, chorea or parkinsonism; Sydenham’s chorea</td>
<td>Psychiatric and sleep disturbance</td>
</tr>
<tr>
<td>γ-aminobutyric acid A receptor (GABA_A)</td>
<td>+/- (in ~40%; thymoma, lung carcinoma, rectal cancer, myeloma)</td>
<td>Chorea, dystonia or ataxia (as part of a more widespread encephalopathy), opsoclonus myoclonus syndrome; possible association with stiff person spectrum disorder</td>
<td>Encephalopathy with epilepsy, behavioral or cognitive problems or reduced consciousness; frequent multifocal T2-hyperintensities; tendency to autoimmune predisposition (coexisting antibodies [e.g., antiGAD- or antiNMDAR], thyroid autoimmunity, idiopathic thrombocytopenic purpura, gluten sensitivity or myasthenia</td>
</tr>
<tr>
<td>γ-aminobutyric acid B receptor (GABA_B)</td>
<td>+/- (in ~60%; small cell lung cancer &gt;&gt; breast cancer multiple myeloma, rectal carcinoma, esophageal carcinoma)</td>
<td>Opsoclonus myoclonus ataxia syndrome, cerebellar ataxia, status dissociatus/agrypnia excitata</td>
<td>Limbic encephalitis with prominent seizures</td>
</tr>
<tr>
<td>Glycine receptor (GlyR)</td>
<td>+/- (in ~9%; thymoma &gt; small cell lung cancer, breast cancer, Hodgkin lymphoma, chronic lymphocytic leukemia)</td>
<td>Stiff person spectrum disorder, myoclonus, hyperekplexia, ataxia</td>
<td>Brainstem encephalitis, reported in optic neuritis, limbic / epileptic encephalopathy, epilepsy, steroid-responsive deafness (clinical relevance less clear)</td>
</tr>
<tr>
<td>IgLON family member 5 (IgLONS)</td>
<td>-</td>
<td>Gait instability, parkinsonism, chorea, cerebellar ataxia, myorhythmia, sleep movement disorders</td>
<td>Sleep apnea, stridor, dysphagia, oculomotor disturbance, cognitive decline, dysautonomia, neuromyotonia, fasciculations</td>
</tr>
<tr>
<td>Leucine-rich glioma inactivated protein 1 (LGI1)</td>
<td>(+/-) (in ~7% liver carcinoid, neuroendocrine pancreas tumour, mesothelioma, rectal carcinoma)</td>
<td>Faciobrachial dystonic seizures, chorea</td>
<td>Limbic encephalitis, hyponatremia, bradycardia</td>
</tr>
<tr>
<td>Myelin-associated glycoprotein (MAG)</td>
<td>++</td>
<td>Tremor</td>
<td>Chronic inflammatory demyelinating polyneuropathy</td>
</tr>
</tbody>
</table>

Table continues on p e2
<table>
<thead>
<tr>
<th>Antibody target</th>
<th>Tumor association</th>
<th>Movement disorder signs</th>
<th>Other clinical features</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antibodies targeting cell-surface synaptic antigens (continued)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neurofascin (NF140/186 and NF155)</td>
<td>-</td>
<td>Tremor</td>
<td>Chronic inflammatory demyelinating polyneuropathy, sensory ataxia</td>
</tr>
<tr>
<td>N-methyl-d-aspartate receptor (NMDAR)</td>
<td>+/- (in ~40% ovarian teratoma, extraovarian teratomas, ovarian carcinomas, lung, breast, testicular and pancreatic tumors)</td>
<td>Orofacial and limb dyskinesia, chorea, dystonia, myoclonus, ataxia, parkinsonism, paroxysmal dyskinesia</td>
<td>Prodromal infectious-like symptoms, neuropsychiatric disturbance, encephalopathy with epilepsy, cognitive deficits, reduced consciousness, dysautonomia, central hypoventilation</td>
</tr>
<tr>
<td>Neurexin-3α</td>
<td>-</td>
<td>Mild orofacial dyskinesia</td>
<td>Encephalopathy with epilepsy, reduced consciousness, memory deficits, psychomotor agitation</td>
</tr>
<tr>
<td><strong>Antibodies targeting intracellular antigens</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amphiphysin</td>
<td>+++(breast cancer, small cell lung cancer)</td>
<td>Stiff person spectrum disorder</td>
<td>Sensory ganglionopathy, myelopathy</td>
</tr>
<tr>
<td>Glutamic acid decarboxylase (GAD)</td>
<td>+/- (rarely, various tumours)</td>
<td>Stiff person spectrum disorder, cerebellar ataxia</td>
<td>Limbic encephalitis, focal epilepsy; often concomitant autoimmunity (eg, diabetes type 1, thyroid disease, vitiligo, pernicious anaemia)</td>
</tr>
<tr>
<td><strong>Antibodies targeting cytoplasmic and nuclear antigens</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRMP5/CV2, Collapsin response mediator protein S</td>
<td>+++(small cell lung cancer, thymoma)</td>
<td>Chorea, parkinsonism</td>
<td>Optic neuritis, myelitis (can mimic neuromyelitis optica), cognitive decline, neuropathy</td>
</tr>
<tr>
<td>Glial fibrillary acidic protein (GFAP)</td>
<td>+/- (in ~25% teratoma, prostate and gastroesophageal, adenocarcinomas, myeloma, melanoma, colonic carcinoma, parotid pleomorphic adenoma, other)</td>
<td>Cerebellar ataxia, tremor, chorea, parkinsonism</td>
<td>Meningoencephalomyelitis or limited forms, with headache, cognitive problems, optic, papillitis, sensory disturbance, gastrointestinal and urogenital dysautonomia, neuropathy; often concomitant autoimmunity (eg, diabetes type 1, thyroid disease, myasthenia, rheumatoid arthritis, alopecia)</td>
</tr>
<tr>
<td>Hu/ANNA-1, Hu proteins (HuD, HuC)</td>
<td>+++ (small cell lung cancer &gt;&gt; neuroblastoma or intestinal, prostate, breast, bladder, and ovary carcinoma)</td>
<td>Chorea, cerebellar ataxia, opsoclonus myoclonus ataxia syndrome</td>
<td>Encephalomyelitis, limbic encephalitis, brainstem encephalitis, sensory neuropathy, gastrointestinal pseudoobstruction</td>
</tr>
<tr>
<td>Ma2/Ta, PNMA2</td>
<td>+++ (testis &gt;&gt; lung cancer), rarely no neoplasia</td>
<td>Parkinsonism</td>
<td>Limbic, diencephalic or brainstem encephalitis, myelopathy or radiculoplexopathy, with encephalopathy, hypothalamic-pituitary endocrine dysfunction, weight gain, prominent sleep disorders, eye movement abnormalities (opsoclonus, supranuclear gaze palsies), dysphagia, muscular atrophy, fasciculations</td>
</tr>
<tr>
<td>Phosphodiesterase 10A (PDE10A)</td>
<td>++ (lung &gt;&gt; renal and pancreatic cancer)</td>
<td>Chorea &gt;&gt; parkinsonism, ataxia</td>
<td>Encephalopathy (confusion), hearing loss</td>
</tr>
<tr>
<td>Ri / ANNA-2, Nova-1, Nova-2</td>
<td>+++ (gynecological tumours, mainly breast cancer, and lung cancer)</td>
<td>Dystonia (jaw closing dystonia, laryngospasms), opsoclonus myoclonus ataxia syndrome, oculopalatal myoclonus, cerebellar ataxia, stiff person spectrum disorder,</td>
<td>Brainstem encephalitis with cranial nerve palsies, nystagmus, dysarthria, ataxia, rigidity, trismus, pyramidal signs</td>
</tr>
</tbody>
</table>

TABLE e1. NEURONAL AND GLIAL ANTIBODIES AND ASSOCIATED CLINICAL AND ONCOLOGIC SPECTRUM (continued)