Neurochemistry of REM behavior disorder in multiple system atrophy

Gilman et al. demonstrated that a greater severity of REM sleep behavior disorder (RBD) correlated with a decreased density of striatal monoaminergic terminals in 13 patients with multiple system atrophy. The results suggest that decreased nigrostriatal dopaminergic projections contribute to RBD in MS.

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Neurochemistry of obstructive sleep apnea in MSA

Gilman et al. found that a greater severity of obstructive sleep apnea (OSA) correlated with a decreased density of thalamic cholinergic terminals in 13 patients with multiple system atrophy. Decreased cholinergic projections from brainstem to thalamus may contribute to their OSA.

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Synucleinopathy pathology and RBD plus dementia or parkinsonism

Boeve et al. analyzed the clinical and neuropathologic findings in all 15 autopsied cases evaluated over a 12-year period who were diagnosed with REM sleep behavior disorder (RBD) and a neurodegenerative disorder. Although the clinical diagnoses varied widely, the neuropathologic diagnoses were only Lewy body disease in 12 and multiple system atrophy in 3. The findings suggest that in the setting of degenerative dementia or parkinsonism, RBD often reflects an underlying synucleinopathy.

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Sleep revisited

Commentary by Clifford Saper and Michael Ronthal

Current theory on the ascending arousal system holds that the wakefulness of the forebrain is largely due to two chemically defined systems: the cholinergic input to the thalamus from the pedunculopontine and laterodorsal tegmental nuclei, and the monoaminergic input to the cortex from the locus coeruleus (noradrenergic), midbrain raphe (serotoninergic and dopaminergic), and tuberomammillary hypothalamic (histaminergic) cell groups. Differential regulation of firing in these two systems is believed to be responsible for regulation of behavioral state, from wakefulness (both systems active), to slow-wave sleep (both systems inactive), to REM (rapid eye movement) sleep (cholinergic system active, monoaminergic system switched off). Both of these chemical systems also have descending projections that are believed to control brainstem aspects of sleep phenomena (e.g., motor tone and breathing). The role of these two systems in various sleep-wake disorders has been suspected, but difficult to prove. The pair of new articles from Gilman et al. critically tests these ideas by using differential methods for labeling cholinergic vs monoaminergic systems with SPECT and PET imaging. They find that REM behavior disorder in patients with multiple systems atrophy (MSA) is associated with loss of monoaminergic axons in the striatum, whereas obstructive sleep apnea in patients with MSA correlates with loss of cholinergic innervation of the thalamus. Although the measurements are made on the ascending components of these systems, and these symptoms may arise from damage to the descending components of the pathways, the former are large and measurable on PET images (whereas the descending pathways are not), and they give a measure of the degeneration in the cholinergic and monoaminergic systems more generally. Thus, these new studies support the view that REM behavior disorder is due to degeneration in the monoaminergic (particularly dopaminergic) system and that obstructive sleep apnea may be due to an abnormality in descending cholinergic control of muscle tone in the upper airway. Synucleinopathy is seen in the dopaminergic system.

Obstructive sleep apnea is thought to be predisposed by the presence of an anatomically narrow airway. Guilleminault et al. report on the development of obstructive sleep apnea after high anterior cervical fusion, which produced narrowing of the airway and tests the hypothesis. Surgeons should be aware of this potential complication, which might occur early in the perioperative phase due to local swelling and edema and later on due to the "hardware" itself or perhaps local scarring. There could also be intraoperative injury to the nerves that dilate the airway.

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Anterior cervical spine fusion and obstructive sleep apnea

Guilleminault et al. report 12 patients in whom anterior upper cervical spine fusion led to obstructive sleep apnea: placement of the anterior cervical plate resulted in anterior displacement of the posterior pharyngeal wall, narrowing the upper airway lumen.

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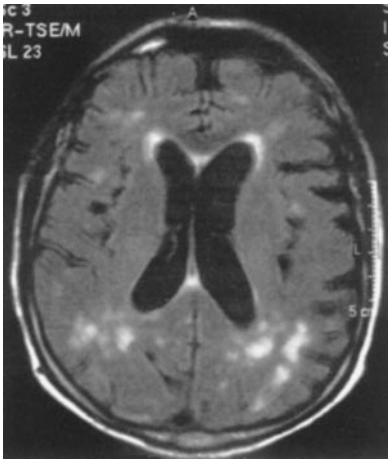
Meningoencephalitis after Aβ42 immunization in AD



Numerous high signal intensities in the deep white matter.

Dosing was suspended early in an international phase II study of anti-amyloid Aβ42 active immunization in AD after subacute meningoencephalitis was reported in 18/298 patients exposed (6%). Orgogozo et al. describe the case histories of patients with this complication, which was self-limiting in most patients.

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The accompanying editorial by Mathews and Nixon reviews the rationale for this treatment strategy for AD. They note that the meningoencephalitis likely relates to compromise of the blood–brain barrier and that a different immunization strategy will be needed for new clinical trials to be justified. However, the report of postmortem studies reported on another patient with AD in the trial suggested an encouraging, marked reduction in ß-amyloid burden.

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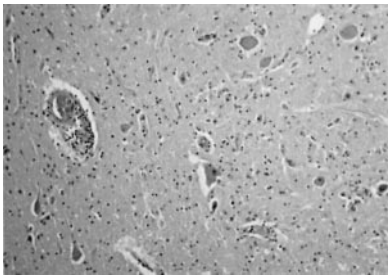
West Nile virus infection



Perivascular chronic inflammation and loss of anterior horn cells.

Jeha et al. report 23 cases of West Nile virus causing meningitis, encephalitis, and myelitis. Fever, confusion, and headache were the most common presenting complaints. Half the patients developed a rapidly progressive flaccid weakness resembling poliomyelitis. A CSF pleocytosis was noted and there was MRI evidence of inflammation in brain, spinal cord, and cauda equina. At autopsy, brain and spinal cord showed inflammation and there was a loss of anterior horn cells.

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Accuracy of family history data in PD

Elbaz et al. report that patients with PD (or their proxies) are more aware of PD among their first-degree relatives than controls (or their proxies); however, they over-report PD in relatives who are not affected. This causes a substantial family information bias.

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Marder et al. assessed the reliability (2225 relatives) and validity (141 relatives) of structured family history interviews for PD using different levels of diagnostic certainty. The conservative diagnosis of PD showed the best combination of sensitivity and specificity and also showed good to excellent reliability, making this the most useful diagnostic categorization for family studies.

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"Whenever possible, diagnosis should be verified by examination or if not possible by record review. . .studies using only family history methods may overestimate risks."

The accompanying editorial by Tanner considers the paradox that whereas case-control studies report a markedly increased risk of PD if first-degree relatives have the disease, twin studies do not support cause of PD. These two articles on the validity of a family history of PD found that PD in parents, siblings, and children is not always identified correctly by history. Patients with PD over-reported cases with PD to a greater extent than controls; both patients with PD and controls under-reported cases found to have PD by examination or neurologist record review.

see page 5

Neuropsychiatric systemic lupus erythematosus Association with antiphospholipid antibodies

Afeltra et al. documented that neuropsychiatric manifestations occurred in 72% of 61 patients with systemic lupus erythematosus. Patients with neuropsychiatric manifestations had higher levels of anticardiolipin.

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Corticosteroid psychosis

The prospective study by Chau and Mok noted a 4.8% incidence of psychosis in patients with systemic lupus erythematosus receiving corticosteroid therapy. Psychosis was not predicted by the corticosteroid regimen, but was independently associated with hypoalbuminemia.

see page 104

The accompanying editorial by Brey and Petri notes the continuing difficulty in adequately characterizing and explaining CNS systemic lupus erythematosus. They point out that it will only be possible to understand disease mechanisms in neuropsychiatric systemic lupus erythematosus if enough patients with the same clinical manifestations are studied.

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