Release of serotonin into ventricular CSF: Endocrine regulation of sleep?

Zeitzer et al. studied CSF serotonin in the lateral ventricle using a probe that extended from an in-depth electrode in the left anterior hippocampus (monitoring intractable seizures in a 24-year-old man). Combining polysomnography with measurements of CSF serotonin, they found that serotonin levels are five-fold greater in CSF than have been observed in the brain.

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Microdialysis probes: Opening a window on the sleeping but still behaving brain

Commentary by David B. Rye, MD, PhD

The neural basis of normal and pathologic behaviors has traditionally depended on study of animals and animal models of disease, or awaited an undesirable endpoint—the neuropathologist's knife. The limited behavioral repertoire and lack of direct homology between brains of most laboratory vertebrates and humans make it difficult to extrapolate many experimental findings to the human condition. This hurdle has been partially overcome by neuroimaging, which permits serial examination of neural, metabolic, and neurotransmitter/receptor specific systems.[1,2] However, neuroimaging has limitations, particularly in spatial and temporal resolution.[2] Monitoring of regional changes in human brain neurochemistry with 200 μm diameter microdialysis probes in an 'online' manner surmounts these limitations, as demonstrated by the work of Zeitzer et al. This group previously showed increases in extracellular dopamine in the human amygdala during cognitive tasks.[3] Here, they demonstrate that CSF serotonin varies with behavioral state, being highest during wakefulness and lowest during REM sleep, thus confirming working models of sleep/wake control established in laboratory animals. Their work raises important issues: (1) What are the sites of production (supraependymal plexus?) and action (choroid plexus, leptomeninges, cerebral vasculature?) of CSF serotonin? (2) What is the biologic significance of this system? (3) Are sleep stage–specific fluctuations in CSF serotonin cause or effect? Despite unanswered questions, microdialysis can provide insights when applied to interesting questions, such as the nature of complex information processing and behaviors. In providing a physiological window to view the brain's interstitial and CSF milieu it breaches the blood–brain barrier and promises to shed light on both normal and pathologic processes: sleep, cognition, affective disorders, anxiety, migraine, stroke, epilepsy, and head trauma.[4]

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Antioxidant vitamins and Parkinson's disease risk

Zhang et al. found that use of vitamins E, C, or multivitamin *supplements* was not associated with a change in PD risk in two large cohorts of men and women. However, higher *dietary* vitamin E intake appeared to reduce PD risk.

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CSF drainage as a treatment for AD

Silverberg et al. analyzed effects of chronic CSF drainage via a low-flow shunt in a randomized controlled phase I/II study. At 12 months, dementia rating scores for the shunted group remained at baseline levels compared with a marked decline among controls. The procedure and device were reasonably well tolerated.

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"Whether this procedure is ultimately added to the armamentarium of treatment options remains to be determined."

The accompanying editorial by Bennett and McDermott notes that current treatment strategies for AD, focused on acetylcholinesterase inhibition, do nothing to alter brain deposits of amyloid-ß peptide and abnormal tau protein. Since these accumulate in AD CSF and brain and correlate with clinical progression, a strategy to retard that deposition or enhance clearance is sensible. They note that the Silverberg et al. study had limitations: small numbers, exclusion of selected shunt-treated patients from efficacy analysis, as well as major adverse events.

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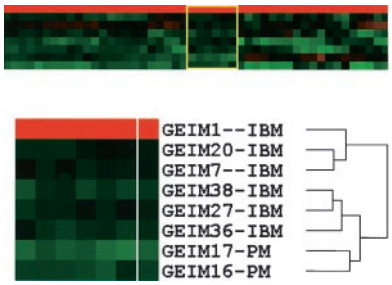
Micoarray gene expression study of inflammatory myopathies



Greenberg et al. studied the simultaneous expression of 10,000 genes in muscle tissues from patients with inflammatory and other myopathies. Using computational methods, distinct molecular signatures of inflammatory myopathies could be demonstrated and large numbers of differentially expressed genes identified.

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The accompanying editorial by Thornton and Welle reviews use of microarrays for diagnosis—now entering practice in leukemia and lymphomas—and on the horizon for developing targets for treatment. They also consider limitations and challenges of this new technique, among them the remarkable diurnal variation in gene expression. Moreover, methods of data analysis and reliability of clinical measures all require standardization.

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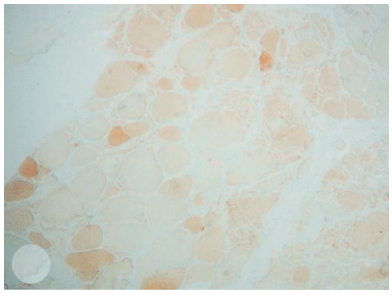
Mitochondrial DNA depletion and myopathy or spinal muscular atrophy



Mancuso et al. screened 16 children with neuromuscular presentation of the mtDNA depletion syndrome for mutations in the thymidine kinase 2 gene. They found pathogenic mutations in two sets of siblings. Three patients had fatal infantile myopathy, but one had both clinical and pathologic features of spinal muscular atrophy.

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Cost-effectiveness of spinal cord stimulation for RSD

Kemler and Furnée performed an economic analysis accompanying a randomized controlled trial on the effectiveness of spinal cord stimulation (SCS) for chronic reflex sympathetic dystrophy. In the first year, SCS proved more expensive than usual care as a result of the high initial expense. However, in the long run (i.e., from 3 years on) SCS appeared both more effective and less costly that the conventional treatment protocol.

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Guillain-Barré syndrome with malaria

Sokrab et al. describe 10 Sudanese patients with Guillain-Barré syndrome following acute falciparum malaria. GBS in these patients was characterized by severe bulbar paralysis and high mortality.

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