

# PEDIATRIC NEUROLOGY BRIEFS

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### MOVEMENT DISORDERS

#### DOPAMINE-SEROTONIN TRANSPORTER DISEASE

Investigators at the Hospital for Sick Children, University of Toronto, Canada report 8 children of a consanguineous Saudi Arabian family who had a similar movement disorder, with autosomal recessive inheritance and a mutation in the SLC18A2 gene that encodes vesicular monoamine transporter 2 [VMAT2]. VMAT2 translocates dopamine and serotonin into synaptic vesicles and is essential for motor control, stable mood, and autonomic function. The index patient had presented with hypotonia at 4 months of age, loss of acquired head control, episodes of oculogyric crisis, and slow development. She sat at 30 months and walked at 13 years. At 16 years of age, she had excessive diaphoresis, profuse nasal secretions, hypernasal speech, cold hands and feet, sleep disorder, and ataxia. Neurologic examination revealed ptosis, facial dyskinesia, impaired vertical gaze, and hand tremor. Gait was parkinsonian and dystonic. CSF showed normal levels of neurotransmitter metabolites, whereas urinary neurotransmitter tests revealed elevated levels of monoamine metabolites (5-hydroxyindoleacetic acid, homovanillic acid) and decreased levels of norepinephrine and dopamine. Treatment of the proband and 3 younger affected siblings with levodopa-carbidopa resulted in major immediate deterioration, with chorea and worsened dystonia. Rapid return to baseline function followed withdrawal of the medication. Immediate ambulation, near-complete resolution of the movement disorder, and improvement in development followed treatment with a direct dopamine-receptor agonist (pramipexole). The younger the affected child, the more substantial the recovery, and side effects after 32 months are minimal (overactivity and weight loss). (Rilstone JJ, Alkhatir RA, Minassian BA. Brain dopamine-serotonin vesicular transporter disease and its treatment. *N Engl J Med* 2013 Feb 7;368(6):543-50). (Reprint requests: Dr Minassian. E-mail: [berge.minassian@sickkids.ca](mailto:berge.minassian@sickkids.ca)).

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COMMENT. The monoamine neurotransmitter disorders are an expanding group of neurologic syndromes, usually diagnosed by measurement of neurotransmitter metabolites in the CSF. (Kurian MA, et al. **Lancet Neurol** 2011 Aug;10(8):721-33). Deficiency in dopamine is associated with movement disorder, deficient norepinephrine or epinephrine causes autonomic dysfunction, and serotonin deficiency results in sleep and psychiatric disorders. The members of the family described have symptoms of all neurotransmitter deficiencies but have no measurable deficiencies on CSF analyses. Symptoms result from impairment of synaptic transmission involving dopamine-serotonin vesicular transport and caused by a gene mutation. Whereas L-dopa treatment exacerbated symptoms, a direct dopamine agonist caused a reversal of symptoms.

Dopamine agonists (pramipexole, ropinirole) have a direct dopaminergic effect on striatal neurons and, in the treatment of Parkinson disease, they may have a modulating effect on L-dopa and are associated with fewer dyskinetic motor complications. As a substitute for L-dopa, dopamine agonists require further study. Dosage appears all important, even small doses when first introduced may cause orthostatic hypotension and unpredictable sleepiness in adults. (**Adams and Victor's Principles of Neurology**, 9<sup>th</sup> edition. Eds. Ropper AH, Samuels MA. New York, McGraw Hill Medical, 2009; 1041-42). Dopamine agonists have been used in the treatment of restless leg syndrome and are of benefit in the restoration of functional arousal, awareness, and communication in children following traumatic brain injury (Patrick PD et al. **J Child Neurol** 2006 Oct;21(10):879-85).

## CHOREA ASSOCIATED WITH HHV-6 ENCEPHALITIS

Investigators at Brown University, Providence, RI and other centers in the US and Canada report a 14-month old child with multiple episodes of febrile status epilepticus, followed by chorea and developmental regression, caused by human herpes virus-6 encephalitis. Chorea and seizures resolved following treatment with levetiracetam, IV immunoglobulin, and foscarnet, but developmental regression with loss of language skills persisted at 6 months follow-up. This is considered a novel manifestation of HHV-6 encephalitis. (Pulickal AS, Ramachandran S, Rizek P, Narula P, Scubert R. Chorea and developmental regression associated with human herpes virus-6 encephalitis. **Pediatr Neurol** 2013 Mar;48(3):249-51). (Response: Dr Pulickal, Division of Neonatology, Alpert Medical School of Brown University, Women & Infants' Hospital, 101 Dudley Street, Providence, RI 02889. E-mail: apulickal@wihri.org).

COMMENT. HHV-6B is the cause of one third of all febrile convulsions in children under age 2 years in the United States (Hall CB, et al. **N Engl J Med** 1994 Aug 18;331(7):432-8), and a cause of mesial temporal lobe epilepsy after febrile status epilepticus (Theodore WH, Epstein L, Gaillard WD, et al. HHV-6B: a possible role in epilepsy? **Epilepsia** 2008 Nov;49(11):1828-37). Other disorders attributed to HHV-6 infection include meningoencephalitis, encephalopathy, demyelinating diseases, ataxia, opsoclonus-myoclonus, and cranial neuropathies. In addition to symptoms of involvement of the cerebral cortex, brain stem, cerebellum, spinal cord, hippocampus, and mesial temporal lobe, HHV-6 infection may also present with symptoms of basal ganglia virus involvement, either direct or autoimmune.