PEDIATRIC NEUROLOGY BRIEFS
A MONTHLY JOURNAL REVIEW

J. GORDON MILLICHAP, M.D., F.R.C.P., EDITOR

Vol. 17, No. 11 November 2003

NEUROANATOMY OF LAUGHTER

NEURAL CORRELATES OF PATHOLOGICAL LAUGHTER

Laughter is a social expression of happiness in humans and in monkeys. Neural correlates of laughter and humor, with results of clinical, pathological, and imaging studies reported in the literature since 1985, are reviewed from the Universities of Tubingen, Germany, and Zurich, Switzerland. Responsive smiling develops in infants by 5 weeks of age and laughter, by the fourth month. Smiling and laughing occur spontaneously or may be elicited on command, each determined by separate neural pathways. Pathological laughter may be symptomatic of mania, schizophrenia, mood disorders, Alzheimer's disease, or Angelman syndrome. Pathological laughter arises; 1) in response to non-specific stimuli; 2) without change in affect; 3) without voluntary control of duration; and 4) without change in mood. Poeck's classification (1969, 1985) of symptomatic laughter differentiates: 1) that originating from motor neuron disease, vascular pseudobulbar paralysis, and extrapyramidal disorders; 2) *fou rire prodromique* heralding stroke; and 3) epileptic "gelastic" seizures, usually associated with hypothalamic hamartomas, tuberous sclerosis, or pathology in the frontal or temporal poles. Other neurologic disorders associated with pathological laughter include multiple sclerosis, and Foix-Chavany-Marie syndrome (progressive supranuclear motor system degeneration). Frontal and temporal lobes are involved in the perception of humor, and especially the non-dominant hemisphere. Patients with right frontal lesions show the greatest deficits in the appreciation of humor, and patients with temporal lobe epilepsy have impaired ability to perceive humor. In Parkinson's syndrome and basal ganglia lesions, spontaneous emotional expression is impaired but the perception of humor may be preserved.

Facial reactions and laughter invoked by humor are mediated by dorsal brainstem regions and inhibited by circuits in the ventral brainstem, via frontal motor/premotor networks. Pathological laughter is the result of damage to the inhibitory system located in

PEDIATRIC NEUROLOGY BRIEFS (ISSN 1043-3155) © 2003 covers selected articles from the world literature and is published monthly. Send subscription requests ($68 US; $72 Canada; $75 airmail outside N America) to **Pediatric Neurology Briefs - J. Gordon Millichap, M.D., F.R.C.P.-Editor,** P.O. Box 11391, Chicago, Illinois, 60611, USA.

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premotor/motor cortex and connections. A pontine 'coordination center' for laughter is postulated. Fibers from the periaqueductal grey, transmitting the signal to laugh, are located dorsally/tegmentally, whereas fibers inhibiting facial emotional expressions run ventrally from frontal motor areas, and may also involve the cerebellum. Two partially independent neuronal pathways are involved in the expression of laughter: 1) an 'involuntary' or 'emotionally driven' system, involving amygdala, thalamus, hypothalamus, subthalamus, and dorsal/tegmental brainstem; and 2) a 'voluntary' system originating in the premotor/frontal opercular areas, and passing via the motor cortex and pyramidal tract to the ventral brainstem. (Wild B, Rodden FA, Grodd W, Ruch W. Neural correlates of laughter and humour. Brain October 2003;126:2121-2138). (Respond: Dr Barbara Wild, Psychiatrische Universitatsklinik, Osianderstrasse 24, 72076 Tubingen, Germany).

COMMENT. In pediatric neurology practice, pathological laughter occurs in patients with Angelman syndrome, pseudobulbar palsy as in cerebral palsy and infantile hydrocephalus, hypothalamic hamartoma and gelastic epilepsy, infantile spasms (Lacy JR, Penry JK, 1976), and complex partial seizures. Gelastic seizures were controlled by removal of a cavernous hemangioma in the anterior cingulate gyrus in one child treated at Johns Hopkins Hospital, Baltimore, MD (Arroyo S et al. Brain 1993;116:757-780). Mirth and laughter were invoked by cortical stimulation of the parahippocampal and fusiform gyri in 2 additional children treated for complex partial seizures. (see Progress in Pediatric Neurology II, PNB Publ, 1994;pp41-42).

EVOLUTION OF GELASTIC EPILEPSY WITH HYPOTHALAMIC HAMARTOMA

The patterns of clinical presentation, evolution of the epilepsy, and electoclinical diagnostic features of hypothalamic hamartoma (HH) in 19 patients (8 children and 11 adults), seen between 1991 and 2001, were evaluated at Kings College Hospital and the Institute of Epileptology, London, UK. Of 16 with early-onset epilepsy, 15 had gelastic seizures, and epilepsy began between 0 and 5 years (mean, 2.1 years) in 14, one having infantile spasms in infancy. Precocious puberty (PP) developed in 6, and learning disability in 12. MRI was diagnostic in all. In 8 older patients in the early-onset group, HH was diagnosed between 19 and 54 years (mean, 33 years). Gelastic seizures disappeared in 2, or were reduced to "an urge to laugh" in adolescence and young adulthood. They were replaced by multiple seizure types and evolved into mainly complex partial epilepsy (5 of 8 adults), tonic seizures, or symptomatic generalized epilepsy with atypical absences, drop attacks, and secondarily generalized seizures with cognitive impairment (3 of 8 adults). Of 3 adult-onset patients, only one had gelastic seizures manifested by inappropriate smiling but no laughing, epilepsy was mild, and cognition normal. Of 14 patients with intrahypothalamic hamartomas, all had moderate to severe gelastic epilepsy, 5 had PP, and 13 had early onset epilepsy, whereas of 5 with parahypothalamic hamartomas, only 2 had gelastic seizures, and 3 had late-onset epilepsy. The larger the HH, the greater the number of seizure types associated. Minimally invasive stereotactic thermocoagulation appeared to be superior to open surgical resection of the HH in less severe cases. (Mullatti N, Selway