

PEDIATRIC NEUROLOGY BRIEFS

A MONTHLY JOURNAL REVIEW

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

Vol. 27, No. 10

October 2013

AUTISM SPECTRUM DISORDER

MRI BIOMARKER FOR EARLY DIAGNOSIS OF AUTISM

In order to identify early risk markers for autism spectrum disorder (ASD), investigators at University of California Davis School of Medicine and Davis Children's Hospital conducted a longitudinal brain MRI study of infant siblings in conjunction with behavioral assessments leading to an outcome classification at 24 months or later (mean age 32.5 months). Fifty-five infants (33 'high-risk' infants having an older sibling with ASD and 22 'low-risk' infants having no relatives with ASD) were imaged at three time points: 6-9 months, 12-15 months, and 18-24 months of age. Compared to infants classified as developmental delay or typical development, 10 infants who developed ASD had significantly greater extra-axial fluid at 6-9 months, which remained elevated at 12-15 and 18-24 months. The amount of extra-axial fluid detected at 6 months was predictive of more severe ASD symptoms at time of outcome. Infants who developed ASD also had significantly larger total cerebral volumes at both 12-15 and 18-24 months of age. These novel findings raise the potential for use of structural MRI to aid in early detection (6-9 months of age) of children at risk for ASD. (Shen MD, Nordahl CW, Young GS, et al. Early brain enlargement and elevated extra-axial fluid in infants who develop autism spectrum disorder. *Brain* 2013 Sep;136(Pt 9):2825-35). (Respond: David G Amaral, The MIND Institute, University of California, Davis School of Medicine, Sacramento, CA 95817. E-mail: dgamaral@ucdavis.edu).

COMMENT. The clinical diagnosis of ASD is usually delayed until at least 18 months of age. This study provides a potential brain MRI biomarker for the earlier diagnosis and treatment of ASD in at risk infants.

Extra-axial fluid accumulation (communicating hydrocephalus) with rapid head growth in the first year of life typically resolves without intervention, but it may be associated with seizures and motor delays (Hellbusch LC. *J Neurosurg* 2007;107:119-

PEDIATRIC NEUROLOGY BRIEFS © 1987-2013, ISSN 1043-3155 (print) 2166-6482 (online), is published monthly and covers selected articles from the world literature. The editor is Pediatric Neurologist at the Ann & Robert H. Lurie Children's Hospital of Chicago; Professor Emeritus, Northwestern University Feinberg School of Medicine. PNB is a continuing education service designed to expedite and facilitate the review of current scientific information for physicians and other health professionals. Apply to PediatricNeurologyBriefs.com for Subscriptions (12 issues, January-December). Digital Edition PDF: \$72 (Residents/Fellows \$36); Print + Digital: \$96 within US/UK, \$128 outside US/UK. Institutions: Digital \$188, Print + Digital \$228. Mail: Pediatric Neurology Briefs Publishers, PO Box 11391, Chicago, IL 60611

125) and now is associated with development of ASD. Extra-axial fluid and rapid head growth in infancy is not always a benign reversible disorder.

Neurobiological abnormalities in infants who later develop ASD.

Studies since 2009 showing abnormalities in head circumference, electrophysiological markers and interhemispheric synchronization and differences in various brain regions (amygdala, cerebellum, frontal and temporal cortex) are reviewed by investigators at the University of Glasgow, Scotland. Cross-disciplinary approaches are essential to elucidate sequence of developmental abnormalities during early infancy leading to ASD (Allely CS, Gillberg C, Wilson P. **Behav Neurol** 2013 Aug 20. [Epub ahead of print]).

Eyeblink conditioning (EBC) is proposed as a non-invasive biomarker for ASD that can be employed shortly after birth (Reeb-Sutherland BC, Fox NA. **J Autism Dev Disord** 2013 Aug 14. [Epub ahead of print]). The neural circuitry for EBC involves sensory information from the cornea to the trigeminal nucleus, the interpositus nucleus and cerebellar cortex.

DEMYELINATING DISORDERS

CHANGES IN T-CELL HOMEOSTASIS IN MULTIPLE SCLEROSIS

Investigators at University Hospital, Heidelberg, and other centers in Germany, studied the composition of the peripheral T-cell compartment and regulatory T cell (Treg) function in 30 pediatric MS patients by multicolor flow cytometry and proliferation assays. Data from pediatric patients were compared to those obtained from 26 adult patients and 67 age-matched control donors. The proportions of both naïve and Treg cells are highest in the youngest children and decrease steadily with age. Pediatric MS patients had lower numbers of naive T cells, including recent thymic emigrants, whereas percentages of memory T cells were increased. Homeostatic changes in circulating T cells paralleled the pattern in adult MS. Treatment with immunomodulatory drugs attenuated the changes. Signs of early thymic involution are found in pediatric MS, suggesting that an intrinsic compromise in thymic-dependent T-cell neogenesis might contribute to MS pathogenesis. (Balint B, Haas J, Schwarz A, et al. T-cell homeostasis in pediatric multiple sclerosis. **Neurology** 2013 Aug 27;81(9):784-792). (Response: Prof Dr Wildemann. E-mail: Brigitte.wildemann@med.uni.heidelberg.de).

COMMENT. The authors conclude that the similarities in the T-cell compartment between adult and pediatric MS patients support a shared disease pathogenesis, immunologic disease mechanism, and response to therapy. Immunomodulatory drugs used in adult-onset MS might have the same effects in pediatric MS. Further studies are warranted to address whether premature senescence of the thymus and T-cell pool occurs at the earliest detectable stages of disease in children (Bar-Or A, Muraro PA. Premature immune senescence in children with MS: Too young to go steady. **Neurology** 2013 Aug 27;81(9):778-9).