Biomedical Update:

Gene therapy: seizure cure of the future?

A pioneering study suggests that focal (partial) temporal lobe seizures could some day be treated by transporting a gene into specific cells in the brain.

Thomas McCown et al. used a virus to deliver a coded sequence for the production of galanin, a peptide that suppresses seizure activity, to the brains of rats with experimentally induced seizures. The "package" also included coded instructions for a sequence that caused the galanin to be secreted from the cells. In treated rats, sensitivity to focal seizures declined markedly. In another experiment, the researchers successfully delivered the genetic instructions to only one side of the brain, a crucial step in learning how to treat seizures that affect only one region.

"The treated side looked normal," McCown said. "This suggests that we can secrete an active peptide in a brain structure that's closely tied to temporal lobe seizures."

The researchers also were able to "turn off" the genetic instructions (by using the antibiotic doxycycline), which McCown notes is "an absolutely crucial component to human gene therapy."

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"Study points to new gene therapy tool in preventing epileptic seizures," news release, University of North Carolina at Chapel Hill School of Medicine, July 24, 2003.

Creatine transporter gene defect could be fairly common

The team of researchers who first discovered a gene defect that creates a deficiency of the amino acid creatine now believe that this defect could account for a significant number of cases of mental retardation and autistic-like behavior.

The defect, identified in 2001 by Kim Cecil, Ton DeGrauw and colleagues, involves the creatine transporter gene on the X chromosome. The researchers have now identified 13 male patients and 13 female carriers of the gene defect in seven unrelated families, four of which are from the same metropolitan area. This, the researchers say, "suggests that [the] deficiency may have a fairly high incidence."

Symptoms of the creatine transporter gene defect include expressive speech and language delay, seizures, autistic behavior, and developmental delay. While the disorder affects males more severely than females (because females have an additional X chromosome that can help counter its effects), the researchers note that half of the female carriers identified to date exhibit learning disabilities.

Creatine supplementation, while it is helpful in several conditions involving defects of creatine synthesis, does not appear to cause improvement of symptoms caused by the creatine transporter defect. However, the researchers are currently experimenting with a highly refined form of creatine to determine if it can be useful.

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"X-linked creatine transporter defect: an overview," G. S. Salomons, S. J. van Dooren, N. M. Verhoeven, D. Marsden, C. Schwartz, K. M. Cecil, T. J. DeGrauw, and C. Jakobs, *Journal of Inherited Metabolic Disorders*, Vol. 26, No. 2-3, 2003, 309-18. Address: G. Salomons, Department of Clinical Chemistry, VU University Medical Center, Amsterdam, The Netherlands, g.salomons@vumc.nl.

More on creatine: can it improve brain function?

While creatine supplementation may not substantially benefit children with the newly reported creatine transporter gene defect (see article above), a recent study indicates that the amino acid can powerfully enhance mental performance in many individuals.

In a double-blind crossover study, Caroline Rae and colleagues gave daily 5-mg creatine supplements or a placebo to 45 university students. The researchers selected vegetarian subjects because they obtain little creatine from their diets. (The creatine dose used was approximately equivalent to that in 2 kilograms—4-1/2 pounds—of meat.) The researchers administered cognitive tests before and after treatment, and found that participants taking creatine, but not those taking the placebo, improved their scores on memory and analytical tests. Rae notes, "The results were clear... creatine supplementation gave a significant measurable boost to brain power."

Creatine aids cells in storing energy in readily accessible form. Says Rae, "We know that creatine plays a pivotal role in maintaining energy levels in the brain. So it was a reasonable hypothesis that supplementing a diet with creatine could assist brain function." Earlier studies (see ARRI 13/2) have indicated that the amino acid can also be useful in treating neuromuscular diseases.

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"Brawny brains," B. Harder, *Science News*, Vol. 164, August 16, 2003. Original paper by Caroline Rae et al. will appear in the October 22 *Proceedings of the Royal Society of London B.*

—and—

"Boost your brain power," news release, Royal Society Proccedings B, August 13, 2003.

Rate of hearing loss high in PDD children

Many children with pervasive developmental disorder (PDD) may suffer from low-frequency hearing loss, according to a new report by researchers in Greece.

George Psillas and J. Daniilidis measured middle latency responses (MLR) in order to assess the low-frequency hearing of 35 young children with PDD. They also used auditory brainstem responses to evaluate the entire range of hearing. The children with PDD were compared to 15 non-disabled controls matched for sex and age.

Psillas and Daniilidis report that all 15 control subjects exhibited normal hearing. In contrast, they say, "Low-frequency hearing loss of sensory origin was noted in nine out of the 35 children with PDD (25 percent)." Seven of the nine affected children had one-sided hearing loss, while two had impaired hearing in both ears, and in seven children the hearing loss was either moderate or severe. High-frequency hearing was normal in the PDD subjects.

"It was interesting to note," the researchers say, "that in 44 percent of these children affected by low-frequency hearing loss, parents had not suspected hearing loss at all." The children's regular physicians had not ordered hearing tests that would have uncovered the problem.

Psillas and Daniilidis conclude, "Children diagnosed with PDD must be referred to thorough audiometric evaluation including low frequencies, even if their reaction to sound is normal." Early detection of hearing problems, they note, could help improve these children's responses to speech and language, and their interaction with their environment. In addition, they suggest that researchers study the possible genetic basis of hearing loss in PDD.

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"Low-frequency hearing assessment by middle latency responses in children with pervasive developmental disorder," G. Psillas and J. Daniilidis, *International Journal of Pediatric Otorhinolaryngology*, Vol. 67, No. 6, June 2003, 613-19. Address: George Psillas, ORL Clinic, Aristotelian University of Thessaloniki, AHEPA Hospital, 1, Stilponos Kyriakidi St., GR 540 06, Thessaloniki, Greece, psillasgeo@the.forthnet.gr.

SCHOOLS AND SERVICES

The Autism Research Institute maintains a list of schools and services for autistic individuals. If your facility should be included on our list, and you believe it may not be, please send a self-addressed, stamped envelope to receive our referral list questionnaire.