Stem Cells

To THE EDITOR: I was very interested in the recent article by González-Martínez et al. (González-Martínez JA, Bingaman WE, Toms SA, et al: Neurogenesis in the postnatal human epileptic brain. J Neurosurg 107:628–635, September, 2007) on stem cells located in the subventricular zone (SVZ) of the lateral ventricles and their migration as new neurons through the intermediate zones up to the epileptic neocortical zones (epileptogenic zones) of the temporal, frontal, parietal, and occipital lobes. These authors performed immunohistochemical studies in 47 patients with epilepsy, of whom ~70% were younger than 30 years of age. In the control group, however, stem cells were restricted to the SVZ.

Abstract

Object. The normal adult human telencephalon does not reveal evidence of spontaneous neuronal migration and differentiation despite the robust germinal capacity of the subventricular zone (SVZ) astrocyte ribbon that contains neural stem cells. This might be because it is averse to accepting new neurons into an established neuronal network, probably representing an evolutionary acquisition to prevent the formation of anomalous neuronal circuits. Some forms of epilepsy, such as malformations of cortical development, are thought to be due to abnormal corticogenesis during the embryonic and early postnatal periods. The role of postnatal architectural reorganization and possibly postnatal neurogenesis in some forms of epilepsy in humans remains unknown. In this study the authors used resected specimens of epileptic brain to determine whether neurogenesis could occur in the diseased tissue.

Methods. The authors studied freshly resected brain tissue obtained in 47 patients who underwent neurosurgical procedures and four autopsies. Forty-four samples were harvested in patients who underwent resection for the treatment of pharmacoresistant epilepsy.

Results. Using organotypic brain slice preparations cultured with 5-bromodeoxyuridine (a marker for cell proliferation), immunohistochemistry, and cell trackers, the authors demonstrate the presence of spontaneous cell proliferation, migration, and neuronal differentiation in the adult human telencephalon that starts in the SVZ and progresses to the adjacent white matter and neocortex in human neocortical pathological structures associated with epilepsy. No cell migration or neuronal differentiation was found in the control group.

Conclusions. The presence of spontaneous neurogenesis associated with some forms of human neocortical epilepsy may represent an erroneous and maladaptive mechanism for neuronal circuitry related with some forms of human neocortical epilepsy. For these reasons, in April 2002 we transplanted omentum on the carotid crotch, anterior perforated space, and left temporal lobe in a 10-year-old girl with a history of fetal suffering at birth, sleep disorders, cerebral palsy, attention deficit, stuttering, memory impairment, unsteady gait, and epilepsy (drop attacks and complex partial and/or generalized tonic–clonic seizures). Extracranial interictal electroencephalography showed generalized atypical spikes or hypsarhythm patterns. A preoperative computed tomography scan revealed slight atrophy in the anteromedial portions in both temporal lobes. During surgery, we found the following: 1) slight and moderate atrophy in the anteromedial portion of the left temporal lobe; and 2) the supracaloid carotid artery and its branches, without atherosclerosis (unpublished observations).

Subjective and objective clinical improvement occurred on the 2nd day after surgery, especially her look and facial expression; stuttering improved 50%. Eight days after surgery she had improvement in her gait and in the frequency and severity of attacks, and her stuttering had disappeared. Neurological improvement was better during the first weeks after surgery than in the following months. At present, 5 years after the operation, she has only episodes of irritability, and she receives 1 mg of clonazepam at night. Her recent memory is normal, and the epileptic seizures have stopped. The last electroencephalography studies have shown an improvement of ~85%. The clinical pre- and postoperative pictures are recorded on videotape.

Our experience with the neurosurgical modality of omental transplantation, which we have used in 4 patients, suggests that this reconstructive technique can reduce or stop the epileptic seizures by revascularization of the epileptogenic zone and neighboring areas. Thus, the residual nervous tissue in the epileptic foci receives an increase in blood flow, oxygen, neurotransmitters, cytokines, and neurotrophic factors. Although neurological improvement showed in our 10-year-old female patient, I believe it was also due to neuronal proliferation in the intraparenchymal territory of the left supracaloid carotid artery and its branches (anterior cerebral, middle cerebral, anterior choroidal, posterior communicating, and anterior perforating arteries). New neurons (microneurons) have 2 origins: 1) spontaneous neurogenesis starting from the stem cells lo-
cated in the SVZ;\textsuperscript{1,4,8} and 2) neurogenesis provoked by omental stem cells (adipose-derived stem cells).\textsuperscript{5}

In summary, I think that the neurogenesis in the postnatal human brain showed by González-Martínez and colleagues is hugely important to cerebral reconstruction. Note, however, that to prolong the survival of the new neurons (neurons of short axons) in the nervous tissue in ischemia and ischemic penumbra, the cerebral zones must be revascularized with omental tissue.

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**References**


**Response:** We thank Dr. Rafael for his interest in our paper regarding neurogenesis in the postnatal human epileptic brain. In his letter, Rafael discusses neural grafting using omental transplants to treat clinically refractory epilepsy. Since 1995, he and his group have observed seizure frequency reduction by placing omental tissue directly on the epileptogenic zone in 4 patients with medically intractable epilepsy. He believes that their excellent results were due to neuronal proliferation promoted by an improvement in the parenchymal perfusion and by the contribution of omental stem cells.

As concluded in our study, the pathogenic mechanisms responsible for the development of cerebral malformations in humans, its epileptogenicity and its relation to postnatal neurogenesis, are largely unknown. Morphogenesis of the mature cortical mantle is the result of an orchestrated sequence of temporally and spatially organized events that are regulated by genetic and environmental factors. The persistence of neurogenesis in the postnatal period may generate aberrant circuits in an already established neuronal network, which may exacerbate the epileptic condition; alternatively, postnatal neurogenesis could generate inhibitory interneurons, which would migrate and integrate into the abnormal epileptic circuits to suppress their excitatory activity.

Dr. Rafael’s concepts are controversial. There is a difference regarding ongoing cortical ischemic events and the pathological substrate leading to medically refractory epilepsy, which often have decreased (mesial temporal sclerosis) or increased (malformations of cortical development) neuronal density but normal or increased blood supply. Unfortunately, Rafael’s letter supporting the benefits of omental grafts to treat a variety of different neurological diseases fails to demonstrate a mechanistic explanation. Omental graft integration and its potential role in promoting neurogenesis and, ultimately, seizure control are possible, but the current literature has not yet provided “proof of principle” to justify any surgical treatment using this method. Proof of principle will require, at the least, a demonstration of clinical efficacy in animal models and elucidation of the potential biological mechanisms involved. Clinical efficacy will ultimately depend on behavioral and physiological studies. (DOI: 10.3171/JNS/2008/108/4/0841)

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**Cerebral Decompression**

To the Editor: We have read with interest the article in the September 2007 issue of the Journal of Neurosurgery in which Schmidt et al. discuss hinge craniotomy (Schmidt JH III, Reyes BJ, Fischer R, Flaherty SK: Use of hinge craniotomy for cerebral decompression. J Neurosurg 107:678–682, September, 2007).

**Abstract**

Decompresive craniectomy to relieve cerebral edema and intracranial hypertension due to traumatic brain injury is a generally accepted practice; however, the procedure remains controversial because of its uncertain effects on outcome, specific complications such as the syndrome of the sinking skin flap, and the need for subsequent cranioplasty. The authors developed a novel craniotomy technique using titanium bone plates in a hinged fashion, which maintains cerebral protection while reducing postoperative complications and eliminating subsequent cranioplasty procedures.

The authors conducted a retrospective review of data obtained in all consecutive patients who had undergone posttraumatic cerebral decompression craniotomy using the hinged technique at a Level I trauma facility between 1990 and 2004.

Twenty-five patients, most of whom were male (88%) and Caucasian (88%) with a mean age of 38.2 ± 16.1 years, underwent the hinge craniotomy. The in-hospital mortality rate was 48%, and good cerebral decompression was achieved. None of the patients required a repeat procedure, and the majority of patients achieved a GOS of 5.