Acute Ischemic Stroke: Adopting a New Vision

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The stroke neurologist today faces an impossible dilemma. On one hand, the natural course of events around ischemic stroke leaves the treating physician a very short window of opportunity, about 3–6 hours, to intervene and reverse the brain tissue damage using intraarterial thrombolysis. On the other hand, current practice wastes this precious time on unsupervised transportation to the hospital and admission, if lucky, to a stroke unit but in most cases to an internal medicine ward for supportive care only since there is no single treatment modality that can reverse damaged brain tissue [1,2].

The chances of reversing the brain damage after more than 3 hours from the time of arterial occlusion are very poor. Combining this short time frame with the fact that invasive neuroradiology is a complex and extremely demanding specialty, it is not surprising that intraarterial thrombolysis with recombinant tissue plasminogen activator has failed to gain worldwide acceptance.

An innovative technique for early recanalization of large intracranial arterial occlusion is described by Cohen et al. in this issue of IMAJ [3]. The use of a mechanical thrombectomy device ensures early restoration of cerebral perfusion and thus shortens the cerebral ischemic time and increases the chance of functional recovery. This recanalization technique is taken a step further in a case report by the same authors in this issue [4], where they describe their treatment of a patient with synchronous internal carotid artery occlusion and intracranial artery embolism. In a case like this, in order to enhance the potency of the thrombolytic therapy for distal carotid occlusion the mechanical thrombectomy device is used, enabling thrombolytic therapy [4].

This new technique raises a few technical issues. First, how do we prevent the thrombus from being dislodged distally during the endovascular manipulations? The current approach to treating carotid lesions by stenting is to use a protection device [5]. What is the place of such a device in a thrombosed artery? Second, resheathing the stent will surely cause endothelial injury of some kind, not yet defined. What are the long-term effects of such a maneuver on the atherosclerotic process in those arteries? Only time will tell.

However, the main question raised by Cohen and his team [3] is the change of attitude that must take place in the medical community. And it is not only the modern-day stroke neurologist who will need a conceptual change. Just as neurology will have to become an interventional field, as cardiology has, the current approach of the emergency services in Israel (Magen David Adom) to the stroke victim will also have to change. They will have to adopt the same treatment approach currently being applied to patients with acute coronary events, i.e., begin the appropriate treatment on the way to the hospital and admit the patient directly to the intensive care unit; here the diagnostic workup is completed ASAP and the patient is then transferred to the catheterization suite for revascularization. This means that the MDA would have to work with the neurologists in the same manner as they currently do with the cardiologist, and emergency room personnel will need to be reeducated with regard to the approach to stroke patients.

The technique described by Cohen and co-authors is a challenging one, and it is of paramount importance that more trained neurologists acquire such capabilities. Nevertheless, this technique should be limited to a few specialized centers with radiological neurointerventional ability.

It appears we are entering a new era of stroke treatment, which looks promising and could lead to better results and a better future for these patients.

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References

MDA = Magen David Adom
Inactivation of the p53 tumor suppressor pathway allows cell survival in times of stress and occurs in many human cancers; however, normal embryonic stem cells and some cancers such as neuroblastoma maintain wild-type human TP53 and mouse Tp53 (referred to collectively as p53 herein). Swarbrick and collaborators describe a miRNA, miR-380-5p, that represses p53 expression via a conserved sequence in the p53 3’ untranslated region (UTR). miR-380-5p is highly expressed in mouse embryonic stem cells and neuroblastomas, and high expression correlates with poor outcome in neuroblastomas with neuroblastoma-derived v-myc myelocytomatosis viral related oncogene (MYCN) amplification. miR-380 overexpression cooperates with activated HRAS oncoprotein to transform primary cells, block oncogene-induced senescence and form tumors in mice. Conversely, inhibition of endogenous miR-380-5p in embryonic stem or neuroblastoma cells results in induction of p53, and extensive apoptotic cell death. In vivo delivery of a miR-380-5p antagonist decreased tumor size in an orthotopic mouse model of neuroblastoma. Thus the authors demonstrate a new mechanism of p53 regulation in cancer and stem cells and uncover a potential therapeutic target for neuroblastoma.

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**Capsule**

**miR-380-5p represses p53 to control cellular survival and is associated with poor outcome in MYCN-amplified neuroblastoma**

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**Capsule**

**The motor skills of musical minds**

Movements are encoded in the brain by modular building blocks that can adapt to specialized skills such as playing a musical instrument. Classen at the University of Leipzig in Germany and his colleagues used a sensor glove to measure joint movements in the left hands of 15 skilled musicians while they played the piano or violin. The researchers then evoked random finger movements in musicians and non-musicians at rest using transcranial magnetic stimulation to excite neurons in the motor cortex. They broke these movements down into basic units and used these to reconstruct voluntary instrument-playing postures. The authors’ statistical analysis revealed that reconstructions of random movements made by musicians more closely matched the instrument-playing movements than did the reconstructions of non-musician controls.

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**Capsule**

**Weight gain is associated with reduced striatal response to palatable food**

Obese people are known to have a less sensitive reward center in the brain, which drives them to overeat. This may, in turn, further dampen their reward circuitry for food. Eric Stice at the University of Texas at Austin used functional magnetic resonance imaging to scan the brains of 20 overweight female volunteers of similar body mass index (BMI) as they sipped either a chocolate milkshake or a tasteless solution. The researchers repeated the tests 6 months later. They found that women who had a greater than 2.5% increase in their BMI over the interim period showed a reduced response in the brain’s striatum to the milkshake relative to their baseline response, as well as to women whose weight had remained steady over the 6 month period.

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“In a free country there is much clamor, with little suffering: in a despotic state there is little complaint but much suffering”

Lazare Hippolyte Carnot (1801-1888), French statesman

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