



7th World Stroke Organization International Meeting
Tbilisi 2018: Stroke prevention, Diagnosis and
Treatment

ABSTRACT BOOK



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Rehabilitation of stroke patients

Francesca R. Pezzella

Emergency Department, San Camillo Hospital Rome, Italy

The evidence base on specific stroke rehabilitation interventions has expanded considerably in recent years, although many gaps remain. Stroke rehabilitation requires a sustained and coordinated effort from a large team, including the patient and his or her goals, family and friends, other caregivers (eg, personal care attendants), physicians, nurses, physical and occupational therapists, speech-language pathologists, recreation therapists, psychologists, nutritionists, social workers, and others. Communication and coordination among these team members are paramount in maximizing the effectiveness and efficiency of rehabilitation and underlie this entire guideline. Without communication and coordination, isolated efforts to rehabilitate the stroke survivor are unlikely to achieve their full potential.

ESO-EAST Stroke Unit Nurse Education Project: past, present and future

Yuriy Flomin

Stroke and Neurorehabilitation Unit, Universal Clinic 'Oberig', Kyiv, Ukraine

First on-site training on a certified stroke unit under the ESO-EAST program was arranged by the ESO and Johannes Wesling Klinikum Minden, Germany in collaboration with the Ukrainian Anti-Stroke Association from October 3rd through November 9th, 2016.

There were 7e small groups with 2.5-day stay (weekdays). The stroke unit was certified by the German Stroke Society in 2016 (led by Dr. Joerg Glahn). All the participants of the workshop had an exposure to high-quality state-of-the-science stroke care (structure, processes & outcomes). The same type workshop has been organized in Kyiv several times and is being planned in Tbilisi and other participant cities of the ESO-EAST.

Ischemic stroke in the young

Turgut Tatlisumak

Department of Clinical Neuroscience, Salgrenska Academy Hospital,
University of Gothenburg, Gothenburg, Sweden

5% of all strokes occur in individuals under 45 years, 10% in those are under 50, and ¼ of cases occur in working-age individuals. Etiology of stroke is extremely diverse in the young as common causes in the elderly, such as large-artery atherosclerosis or atrial fibrillation, are rare. Similarly, risk factors differ considerably in young adults compared to those seen in older individuals. Genetic causes may be underlying indicating a need for genetic counseling. Predictors of mortality, recurrence, and poor functional outcome include expected general risk factors and comorbidities. Acute and preventive treatments are highly effective and safe. Efficient acute treatment and prevention of stroke in a young adult increases number of quality-weighted life years. Adequate treatments may improve long-term outcomes. The outcomes are not benign with frequent long-term disability

Organizing regional stroke pathways

Turgut Tatlisumak

Department of Clinical Neuroscience, Salgrenska Academy Hospital,
University of Gothenburg, Gothenburg, Sweden

Well-organized stroke service including prevention, acute care, and rehabilitation

is the only ethically acceptable option and it is widely available now in developed countries. It reduces the death rate, improves functional outcome, and saves resources, therefore it is highly efficient for the patient and for the society. All patients benefit from stroke unit care, therefore, all patients must be transferred to hospitals with 24/7 functioning stroke units. Approximately ¼ of those are eligible for intravenous thrombolysis; they should be transferred to hospitals with 24/7 imaging and intravenous thrombolysis treatment. Approximately 1/10 are eligible to endovascular treatment; they must reach a comprehensive stroke center offering 24/7 this therapy. Organizing patient flows

differs with geographics, population, health care systems (e.g. public vs private), mode of transportation, human resources, imaging capabilities and performance.

Genomics of stroke and cerebrovascular disease

Stéphanie Debette

Department of Neurology, Bordeaux University Hospital, Bordeaux, France

Conventional risk factors (hypertension, diabetes, smoking, hypercholesterolemia) explain only a fraction of stroke risk. There is compelling evidence from family studies and more recently from large GWAS that stroke is heritable. Genetic risk factors contribute to stroke mostly as part of multifactorial predisposition. Recently, the number of loci associated with stroke risk could be tripled, despite the phenotype heterogeneity. Variants predisposing to stroke may act at various levels. Genetics of MRI-defined endophenotypes of stroke helpful to unravel genomic determinants of cerebral small vessel disease.

Stroke burden and increasing risk factors

Şerefnur Oztürk

Department of Neurology and Neurointensive Care Unit, Selcuk University Faculty of Medicine, Konya, Turkey

Stroke is the second leading cause of death and a major cause of disability worldwide. Its incidence is increasing because the population ages. In addition, more young people are affected by stroke in low- and middle-income countries. Ischemic stroke is more frequent but hemorrhagic stroke is responsible for more deaths and disability-adjusted life-years lost. Incidence and mortality of stroke differ between countries, geographical regions, and ethnic groups. In high-income countries mainly, improvements in prevention, acute treatment, and neurorehabilitation have led to a substantial decrease in the burden of stroke over the past 30 years. It is of paramount importance for every country to have national plans for stroke encompassing the entire chain of care from primary prevention to life after stroke.

Stroke prevention – focus on lifestyle modification

Vida Demarin

International Institute for Brain Health, University of Zagreb, Zagreb, Croatia

A big component of our lifelong brain health and development depends on what we do with our brains. Environment plays 80% of a role while genes are only 20% responsible. Individuals who lead mentally stimulating lives, through education, occupation and leisure activities, have reduced risk of developing Alzheimer's disease and stroke. They have 35-40% less risk of manifesting the disease. Pillars of brain health consist of control of conventional cerebrovascular disease risk factors, physical exercise, healthy nutrition, stress relaxation and mental stimulation.

TIA and the risk of subsequent stroke

Daniel Berezcki

Department of Neurology, Semmelweis University, Budapest, Hungary

The American Heart Association and the American Stroke Association (AHA/ASA) define TIA as a brief episode of neurological dysfunction with a vascular cause, with clinical symptoms typically lasting less than one hour, and without evidence of infarction on imaging.

This definition of TIA is based on tissue injury rather than duration of clinical signs. Stroke follows TIA more frequently than previously thought and its risk after TIA can be stratified by traditional stroke risk factors and clinical features. The importance of early intervention cannot be underestimated. Rapid treatment following a stroke or TIA can minimize cerebrovascular damage and prevent recurrence; addressing modifiable risk factors can reduce the risk of subsequent cardiovascular and cerebrovascular events. Facilitating the initiation of effective secondary preventive therapy must become a priority in managed care.

Stroke prevention in carotid atherosclerosis

Zurab Nadareishvili

Stroke Center, Virginia Hospital Center, Arlington, USA

Atherosclerosis is a diffuse, degenerative disease of the arteries that results in the formation of plaques composed of necrotic cells, lipids, and cholesterol crystals. These plaques can cause stenosis (see the image below), embolization, and thrombosis. Atherosclerosis has a predilection for certain arteries, including the extracranial carotid artery. Carotid endarterectomy is the preferred treatment for most patients with symptomatic carotid stenosis > 50%, except women with 50-69% stenosis. The benefit of revascularization in asymptomatic carotid stenosis (ACS) is questionable because of low risk of stroke on medical therapy. In ACS noninvasive diagnostics may identify population at higher risk of stroke who might benefit from carotid revascularization.

Secondary stroke prevention - antiplatelet update

Natan Bornstein

Brain Division, Department of Neurology, Shaare Zedek Medical Center, Jerusalem, Israel

Antiplatelets are the major therapy for the secondary stroke prevention. The most commonly used antiplatelets agents are aspirin, clopidogrel, and extended-release dipyridamole. A lot of progress had been made in last years regarding aspirin resistance and genotyping of clopidogrel metabolism. According to the results of the accomplished studies it is difficult to broadly recommend one antithrombotic agent in favor of the other. Instead, a review of the currently published data suggests the importance of focusing on the individualizing approach in antiplatelet therapy. Aspirin plus ER-DP or clopidogrel alone may be of more benefit in recurrent stroke prevention than aspirin alone. Clopidogrel is an alternative for those with allergy to aspirin or gastrointestinal side effects. For patients who do not tolerate dipyridamole because of headache, either aspirin or clopidogrel is appropriate.

Patent foramen ovale: management to prevent recurrent stroke

Heinrich Mattle

University Department of Neurology, Inselspital, University of Bern, Bern, Switzerland

Patent foramen ovale is found in 24% of healthy adults and 38% of patients with cryptogenic stroke. This ratio and case reports indicate that patent foramen ovale and stroke are associated, probably because of paradoxical embolism. In healthy people with patent foramen ovale, embolic events are not more frequent than in controls, and therefore no primary prevention is needed. However, once ischaemic events occur, the risk of recurrence is substantial and prevention becomes an issue. Acetylsalicylic acid and warfarin reduce this risk to the same level as in patients without patent foramen ovale. Patent foramen ovale with a coinciding atrial septal aneurysm, spontaneous or large right-to-left shunt, or multiple ischaemic events potentiates the risk of recurrence. Based on the recent randomized trials transcatheter device closure has become the first line treatment for stroke prevention in the latter clinical conditions.

Cardioembolic stroke due to NVAF - Which NOAC to whom?

Natan Bornstein

Brain Division, Department of Neurology, Shaare Zedek Medical Center, Jerusalem, Israel

The majority of cardioembolic strokes can be prevented by treatment with oral anticoagulation therapy. The advent of non-vitamin K antagonist oral anticoagulants (NOACs) has resulted in a choice of therapeutic agents available to physicians for anticoagulation for stroke prevention in patients with AF beyond the long-established vitamin K antagonists (VKAs). Pivotal trials have demonstrated non-inferiority of NOACs compared with VKAs, and in some cases superiority, for the prevention of stroke and systemic embolism in non-valvular atrial fibrillation. There are no direct head-to-head comparator trials for the efficacy of NOACs, however, assessment of the clinical outcomes of the pivotal phase III NOAC clinical trials, in conjunction with consideration of individual patient-specific factors can help to guide the choice of NOACs in patients with non-valvular AF.

Brain imaging strategies in stroke

Andrew Farrall

School of Clinical Sciences, University of Edinburgh, Edinburgh, Scotland, UK

Advanced neuroimaging of acute ischemic stroke is essential for correct patient treatment triage. The ischemic penumbra is characterized on imaging as regions of reduced blood flow and increased transit time on computed tomography (CT) perfusion, magnetic resonance (MR) perfusion, or arterial spin labeling (ASL). Pial collaterals may be imaged noninvasively with CT angiography, MR angiography, perfusion imaging, or ASL techniques. Robust pial collaterals may play a significant protective role in brain preservation in acute ischemic stroke. They may contribute to superior outcomes after the endovascular treatment of acute ischemic stroke.

Clot morphology in acute occlusive stroke

Bartłomiej Piechowsky-Jozwiak

Department of Neurology, Cleveland Clinic Abu Dhabi, Abu Dhabi, UAE

Endovascular mechanical thrombectomy devices have provided the opportunity to directly investigate freshly retrieved thrombi which until recently were inaccessible. The recent clot composition studies make available vital insights concerning the histopathology, MR and CT imaging aspects, and detailed structural analysis of thromboemboli, which commonly cause acute ischemic strokes. The histopathologic assessment of fresh thrombi with light microscopy permits new understanding of the pathogenesis of and treatment for large-vessel ischemic stroke. There is a relationship between HMCAS on CT or BA on GRE and thrombi composed mostly of RBCs while lack of these imaging findings might mean a fibrin-dominant thrombus that is likely to be more refractory to thrombolytic drugs. Presence of chronic histopathologic features in clots such as endothelization and calcification might render tPA less effective due to decreased penetration.

Neurosonology role for patients with CVD and acute stroke

Alexander Razumovsky

Sentient NeuroCare Services, Inc., Hunt Valley, MD, USA

Transcranial Dopplerography (TCD) is the only non-invasive examination that provides a reliable evaluation of intracranial blood flow patterns in real-time, adding physiological information to the anatomical information obtained from other neuroimaging modalities. TCD is relatively cheap, can be performed bedside, and allows monitoring both in acute emergency settings as well as for prolonged periods with a high temporal resolution making it ideal for studying dynamic cerebrovascular responses. Extended applications of TCD in enhancing i/v thrombolysis in acute stroke, emboli monitoring, right-to-left shunt detection and vasomotor reactivity provide important information about the pathophysiology of cerebrovascular ischemia. Advanced applications of TCD make it an important and valuable tool for evaluating stroke mechanisms, plan and monitor treatment and determine prognosis

Stroke in the context of systemic and hematological diseases

José Ferro

Department of Neurology, University of Lisbon, Lisbon, Portugal

Systemic vasculitis can have a variety of manifestations in the central nervous system including stroke (either haemorrhage or infarct), seizures, anterior ischaemic optic neuropathy, and meningoencephalitis. This can be due to an arterial occlusion secondary to inflammation of the blood vessel wall or due to a thrombotic angiopathy of the small blood vessels. Hematologic abnormalities lead to thrombosis in the cerebral vasculature, causing ischemic cerebrovascular events. However, the majority of patients with ischemic cerebrovascular events do not have a well-defined hematologic abnormality. Coagulation disorders that predispose to strokes remain poorly defined but have been implicated in venous strokes (cerebral venous thrombosis) rather than arterial strokes. Platelet function abnormality, inherited hemostatic abnormality, and vascular injury promote thrombosis.

Neuropsychiatric consequences of stroke

José Ferro

Department of Neurology, University of Lisbon, Lisbon, Portugal

Stroke survivors are often affected by psychological distress and neuropsychiatric disturbances. About one-third of stroke survivors experience depression, anxiety or apathy, which are the most common neuropsychiatric consequences of stroke. Neuropsychiatric sequelae are disabling, and can have a negative influence on recovery, reduce quality of life and lead to exhaustion of the caregiver. Despite the availability of screening instruments and effective treatments, neuropsychiatric disturbances attributed to stroke are currently underdiagnosed and undertreated. Stroke severity, stroke-related disabilities, cerebral small vessel disease, previous psychiatric disease, poor coping strategies and unfavourable psychosocial environment influence the presence and severity of the psychiatric consequences of stroke. Investigation into the management of these conditions must be continued, and should include pilot studies to assess the benefits of innovative behavioural interventions and large-scale cooperative randomized controlled pharmacological trials of drugs that are safe to use in patients with stroke.

Embolic stroke of undetermined source

George Ntaios

Department of Internal Medicine, University of Thessaly, Larissa, Greece

Embolic stroke of undetermined source (ESUS) designates patients with nonlacunar cryptogenic ischemic strokes in whom embolism is the likely stroke mechanism. ESUS comprises about 1 ischemic stroke in 6. Patients with ischemic stroke meeting criteria for ESUS are relatively young compared with other ischemic stroke subtypes and had, on average, minor strokes, consistent with small emboli. Retrospective methods of available studies limit confidence in stroke recurrence rates but support a substantial (>4% per year) rate of stroke recurrence during (mostly) antiplatelet therapy. There is an important need to define better antithrombotic prophylaxis for this frequently occurring subtype of ischemic stroke.

Space-occupying brain infarction

Bart H van der Worp

Department of Neurology, University Medical Center Utrecht, Utrecht, Netherlands

Space-occupying middle cerebral artery infarction can be predicted by neuroradiological and clinical examination. Decompressive hemicraniectomy is effective for malignant middle cerebral artery infarction, with dramatic reduction in mortality and improved functional outcome, although many patients remain with permanent disability (eg, shift from modified Rankin scale 5 to modified Rankin scale 3–4) and require costly support.

Current data indicate that also patients aged >60 years may benefit; however, each case should be considered individually because the patients are invariably left with moderate to severe disability. Timely surgery is recommended to minimize further injury because of cerebral edema and herniation.

Basilar artery occlusion: diagnosis and treatment

Heinrich Mattle

University Department of Neurology, Inselspital, University of Bern, Bern, Switzerland

The clinical presentation of basilar artery occlusion (BAO) ranges from mild transient symptoms to devastating strokes with high fatality and morbidity. Often, non-specific prodromal symptoms such as vertigo or headaches are indicative of BAO, and are followed by the hallmarks of BAO, including decreased consciousness, quadriparesis, pupillary and oculomotor abnormalities, dysarthria, and dysphagia. When clinical findings suggest an acute brainstem disorder, BAO has to be confirmed or ruled out as a matter of urgency. If BAO is recognised early and confirmed with multimodal CT or MRI, intravenous thrombolysis or endovascular treatment can be undertaken. The goal of thrombolysis is to restore blood flow in the occluded artery and salvage brain tissue; however, the best treatment approach to improve clinical outcome still needs to be ascertained.

Hemorrhagic stroke: what is new?

Daniel F Hanley

Division of Brain Injury Outcomes, Johns Hopkins Medical Institutions, Baltimore, USA

Craniotomy, according to the results from trials, does not improve functional outcome after intracerebral haemorrhage. Whether minimally invasive catheter evacuation followed by thrombolysis for clot removal is safe and can achieve a good functional outcome is not known. We investigated the safety and efficacy of alteplase, a recombinant tissue plasminogen activator, in combination with minimally invasive surgery (MIS) in patients with intracerebral haemorrhage.

MIS plus alteplase seems to be safe in patients with intracerebral haemorrhage, but increased asymptomatic bleeding is a major cautionary finding. These results, if replicable, could lead to the addition of surgical management as a therapeutic strategy for intracerebral haemorrhage.

Intracerebral hemorrhage in patients on oral anticoagulation therapy

Alexander Tsiskaridze

Department of Neurology, Ivane Javakhishvili Tbilisi State University, Tbilisi, Georgia

The benefit of anticoagulation for thromboembolism prophylaxis in patients with atrial fibrillation is well established. Although highly effective, anticoagulant treatment comprises significant bleeding risks. The oral anticoagulation-related intracerebral hemorrhage (OAT-ICH) is a major bleeding, resulting in a life-threatening condition. Established risk factors for OAT-ICH are advanced age, race, intensity of anticoagulation, hypertension and history of cerebrovascular disease.

Mortality rates in patients with OAT-ICH range from 52% to 67%, and are higher than those observed in patients with spontaneous ICH with higher rate of disability. Therapeutic strategy in OAT-ICH consists of similar measures used for spontaneous ICH including general supportive care, prevention and treatment of complications, and neuro-

surgical intervention when indicated. Specific for OAT-ICH treatment implies prevention of hematoma expansion by immediate reversal of anticoagulation. Resumption of anticoagulation after OAT-ICH is a matter of debate. Although there are no formal guidelines on this issue, limited data suggest that anticoagulation could be safely restarted within 4 weeks of ICH in selected group of AF patients with high risk of thromboembolism.

Best practice stroke care: a success story

Robert Mikulik

Cerebrovascular Center, St. Anne's University Hospital, University of Brno, Brno, Czech Republic

In the Czech Republic, the change in stroke management was driven mostly by introducing reperfusion therapies into clinical practice. So the very first changes were already happening 20 years ago when we started to build our experience with intravenous thrombolysis. Since 2003, when Actilyse was approved, every neurology department had to become familiar with thrombolytic treatment. Moreover, since 2006, many university and some other hospitals started to offer interventional treatment. In 2010, stroke units were required to be certified by the Ministry of Health to be included in the official network of stroke units. In 2012, triage of patients was regulated by the Ministry of Health so essentially since then, any acute stroke that happens in the Czech Republic must be transferred to a certified stroke unit where further therapy is provided according to state of the art evidence. In the last few years, primarily the Czech Stroke Society has been organising many quality improvement programs. Due to a focused effort to improve quality of stroke services and involvement of key stakeholders such as hospitals, the Czech Stroke Society and the Ministry of Health, the Czech Republic had over a 20% thrombolytic rate in 2017 at population level (around 30% at hospital level) and a door-to-needle time of around 25 minutes. For the further target we are proposing an action 20-20-20, and we believe that in 2020, our national thrombolytic rate will be not only over 20%, but our door-to-needle time will also be below 20 minutes.

Intravenous thrombolysis decision-making: who should and should not be treated?

Andrew Demchuk

Department of Clinical Neurosciences, Calgary Stroke Program, Calgary University, Calgary, Canada

Constant efforts are being made in the stroke community to aim for maximum benefit from thrombolytic therapy since the approval of intravenous recombinant tissue plasminogen activator (rt-PA; alteplase) for the management of acute ischaemic stroke. However, fear of symptomatic haemorrhage secondary to thrombolytic therapy has been a major concern for treating physicians. Certain imaging and clinical variables may help guide the clinician towards better treatment decision making. Aggressive management of some predictive variables that have been shown to be surrogate outcome measures has been related to better clinical outcomes. Achieving faster, safer and complete recanalization with evolving endovascular techniques is routinely practiced to achieve better clinical outcomes. Selection of an 'ideal candidate' for thrombolysis can maximize functional outcomes in these patients. Although speed and safety are the key factors in acute management of stroke patients, there must also be a systematic and organized pattern to assist the stroke physician in making decisions to select the 'ideal candidate' for treatment to maximize results.

Endovascular treatment update 2018: what have we learned and where do we need more data?

Andrew Demchuk

Department of Clinical Neurosciences, Calgary Stroke Program, Calgary University, Calgary, Canada

Rapid and effective revascularization is the mainstay of acute ischemic stroke treatment. Until recently, intravenous recombinant tissue-type plasminogen activator (r-tPA) was the only established therapeutic option. Five recently published trials have now proven the benefit of endovascular treatment, changing dramatically the evaluation and treatment of acute ischemic stroke. Thrombectomy with stent retrievers is now recommended as the standard of care for acute ischemic

strokes with a proximal large vessel occlusion in the anterior circulation. There are 3 major challenges that need to be addressed. First, effective implementation of trial results across large populations; second, monitoring, encouraging, and approving only the new innovative therapies that result in further improvement in patient outcomes; and third, creating a framework to allow extrapolation of trial results to patient populations that were not tested in the trials. Finally, we wish to stimulate future discussions on increasing accessibility to endovascular therapy in developing nations.

Pre-hospital stroke management in the era of thrombectomy

Heinrich J Audebert

Department of Neurology with Experimental Neurology, Charité University Hospital, Berlin, Germany

Brain cells die rapidly after stroke and any effective treatment must start as early as possible. In clinical routine, the tight time-outcome relationship continues to be the major limitation of therapeutic approaches: thrombolysis rates remain low across many countries, with most patients being treated at the late end of the therapeutic window. In addition, there is no neuroprotective therapy available, but some maintain that this concept may be valid if administered very early after stroke. Recent innovations have opened new perspectives for stroke diagnosis and treatment before the patient arrives at the hospital. These include stroke recognition by dispatchers and paramedics, mobile telemedicine for remote clinical examination and imaging, and integration of CT scanners and point-of-care laboratories in ambulances. Several clinical trials are now being performed in the prehospital setting testing prehospital delivery of neuroprotective, antihypertensive, and thrombolytic therapy as well as delivery the patients suitable for thrombectomy to comprehensive stroke centers. These new approaches in prehospital stroke care will not only shorten time to treatment and improve outcome but will also facilitate hyperacute stroke research by increasing the number of study participants within an ultra-early time window.

Early neurorepair approaches in acute stroke: what direction should we move to?

Jerzy Krupinski

Cerebrovascular Diseases Unit, University Hospital Mútua Terrassa, Barcelona, Spain

Stroke is the second to third leading cause of death and the main cause of severe, long-term disability in adults. However, treatment is almost reduced to fibrinolysis, a therapy useful in a low percentage of patients. Given that the immediate treatment for stroke is often unfeasible in the clinical setting, the need for new therapy strategies is imperative. After stroke, the remaining impairment in functions essential for routine activities, such as movement programming and execution, sensorimotor integration, language and other cognitive functions have a deep and life-long impact on the quality of life. An interesting point is that a slow but consistent recovery can be observed in the clinical practice over a period of weeks and months. Whereas the recovery in the first few days likely results from edema resolution and/or from reperfusion of the ischemic penumbra, a large part of the recovery afterwards is due mainly to brain plasticity, by which some regions of the brain assume the functions previously performed by the damaged areas. Neurogenesis and angiogenesis are other possible mechanisms of recovery after stroke. An understanding of the mechanisms underlying functional recovery may shed light on strategies for neurorepair, an alternative with a wide therapeutic window when compared with neuroprotective strategies.

Promotion of post-stroke recovery based on reprogrammed and immune cells

Zaal Kokaia

Laboratory of Stem Cells & Restorative Neurology, Lund Stem Cell Center, Lund University Hospital, Lund, Sweden

Stem cell-based approaches hold much promise as potential novel treatments to restore function after stroke. Studies in animal models have shown that stem cell transplantation can improve function by replacing neurons or by trophic actions, modulation of inflammation,

promotion of angiogenesis, remyelination and axonal plasticity, and neuroprotection. Endogenous neural stem cells are also potential therapeutic targets because they produce new neurons after stroke. However, like with all other brain diseases, there is currently no proven stem cell therapy for stroke. Only with a long-term commitment to high-quality basic and clinical research, which addresses the crucial issues, will it be possible to offer stem cell-based treatments providing patients with stroke with substantial improvements of their quality of life.

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