NIH Public Access
Author Manuscript
Stroke. Author manuscript; available in PMC 2014 June 01.

Published in final edited form as:
Stroke. 2013 June ; 44(6 0 1): S111–S113. doi:10.1161/STROKEAHA.113.000970.

Stroke Progress Review Group: Summary of Successes and Lack of Progress

James Grotta, MD
Department of Neurology, University of Texas--Houston, Co-Chairman; Stroke PRG

Stroke PRG: History and Process

The Stroke PRG was formed in 2001 to produce research recommendation to NINDS for the next 10 years. The PRG produced a progress report in 2006, and a final report in 2012. The PRG process employed expert study groups covering 16 Areas of research. Each group was tasked to summarize progress in their field and then come up with research priorities. The proceedings were published in the journal Stroke(refs) and on-line[1,2].

http://www.ninds.nih.gov/find_people/groups/stroke_prg/index.htm

http://www.ninds.nih.gov/find_people/groups/stroke_prg/09_2006_stroke_prg_report.htm

http://www.ninds.nih.gov/find_people/groups/stroke_prg/2012-stroke-prg-full-report.htm

For planning the next decade, NINDS has reconfigured the PRG process with the intention of identifying a narrowed focus on the most critically important priorities, and obtaining more input from the wider community of health care workers involved with stroke, and from the public using a dedicated web page: http://www.ninds.nih.gov/strokerfi

Eventually, work-groups will be configured on Stroke Treatment, Stroke Prevention, and Stroke Recovery with the intention to narrow down priorities to 2-3 per area.

Progress to date

I will describe progress based on the current decision to of NINDS to divide the field into 3 broad topics, acute stroke treatment, stroke prevention, and stroke repair/recovery/rehab. Other aspects of stroke research that were considered priorities by the PRG between 2001 and 2012 will be covered in a 4th category (“Other”).

Acute Stroke Treatment

1. Improve reperfusion therapy: The first priority in the area of acute stroke treatment which was identified in the reports of 2001, '06, and '12 was to improve reperfusion therapy. The following is a list of research progress in this area:
    1. Enhanced thrombolysis- Randomized trials: TNK, Ancrod, DIAS, CLEAR-ER, Argatroban, Ultrasound

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain

NIH-PA Author Manuscript
NIH-PA Author Manuscript
NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

2. Device development and FDA approval: MERCI, Penumbra, Stent retrievers
3. Intervention-Randomized trials: MR Rescue, IMS
4. Collateral augmentation: Partial aortic occlusion

2. Effective neuroprotection: This priority was also identified in the reports of 2001, '06, and '12. The following is a list of research progress in this area:
    1. Completed randomized trials: NXY-059, Citicoline, Minocycline
    2. Ongoing randomized trials: Magnesium, Hypothermia, Albumin, Near-infrared laser, Caffeinol, Glyceryl trinitrate, Lovastatin
3. Increased clinical focus on blood vessel/clot pathology: This research priority was mentioned in the report of 2001. Little progress has been achieved in this area at least with regard to acute stroke treatment.
4. Improve stroke care delivery: This priority was mentioned in the report of 2006. The following is a list of research progress in this area:
    1. Development of Stroke centers, Get With The Guidelines QA measures and database, Improved reimbursement for thrombolytic and endovascular treatment
    2. Registry for Pediatric stroke and organization of thrombolytic trials, additional study of Gender and Diversity issues
    3. Telemedicine
5. Stroke Networks: This priority was mentioned in the most recent report in 2012. The following is a list of progress in this area.
    1. The following network of centers to carry out acute stroke trials were developed: IPSS, NETT, SPOTRIAS
6. Hemorrhage at the cellular level: A better understanding of the effect of brain bleeding was identified in the reports from 2001, '06, and '12. The following areas of research have emerged from NIH funded laboratory studies:
    1. Cortical spreading depression after ICH and SAH
    2. Iron toxicity, inflammation
    3. Early brain injury after SAH
7. Trials on blood pressure reduction, minimally invasive surgery, hematoma evacuation, and critical care management: The need for clinical trials in these areas was identified in the reports from 2006, and '12. The following trials have been completed or are underway.
    1. Hematoma growth: INTERACT, ATACH, FAST, STOP-IT, SPOTLIGHT
    2. Vasospasm: Clazosentin, magnesium, statins, albumin
    3. Surgery: STICH, STICH-2, MISTIE, ICES, CLEAR 1,2,3
    4. Inflammation: Deferoxamine, Pioglitizone
    5. AVMs: ARUBA
    6. Critical care: Better outcomes after ICH and SAH

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

Prevention

1. Aggressive implementation of prevention measures: This priority was mentioned in the reports of 2001 and '12. One study addressed this issue.
    1. SAMMPRIS
2. New prevention strategies: This priority was also mentioned in 2001 and '12. A number of important studies of stroke prevention have been carried out in the last decade, most of which have resulted in substantial changes in our clinical management.
    1. Risk factors: VISP, ALLHAT, Statins, aggressive blood glucose control, niacin plus statins
    2. Antiplatelets: WASID, aspirin + dipyridamole, cilostazol, aspirin + clopidogrel, SSPS
    3. Atrial Fib: aspirin + clopidogrel,_dabigatran, apixaban and rivaroxaban, prolonged monitoring
    4. Carotid stenosis: CREST
    5. Carotid occlusion: COSS
    6. PFO: CLOSURE, RESPECT, GORE
    7. Sickle cell: Blood transfusion, hydroxyurea
    8. Aneurysms: ISAT, ISUIA, FIA
3. Better risk assessment tools: This priority was mentioned in 2001 and '12 but little progress has been made in this area.
4. “Personalized” prevention – genetics: This priority was mentioned in 2006 but little progress has been made in this area.
5. Specific secondary prevention issues: This priority was mentioned in 2006.
    1. Stenting of intracranial stenosis
    2. Timing of blood pressure control and antithrombotic therapy
    3. Antiplatelet therapy in children
6. High risk population-based primary prevention: These populations have been identified as being particularly high risk.
    1. Metabolic syndrome
    2. Perinatal stroke
    3. Pro-inflammatory states

Repair, Recovery and Rehabilitation

1. Plasticity; molecular, cellular and network changes in the brain that lead to good recovery: This priority was identified in the reports of 2001, '06 and '12. It included a call to develop better preclinical animal models. Much progress has been made in the past decade.
    1. Role of astrocytes and microglia
    2. Responses to restorative therapy--neurite outgrowth, splenic cytokines, gene expression, etc

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

3. Sprouting transcriptome—molecular neural repair pathways
4. Inhibition/excitation balance and stunned circuits in peri-infarct cortex
5. Behavioral effects on recovery; learned non-use
6. Broad time window for intervention

2. Neuroimaging to detect recovery and predict outcome: This priority was identified in 2001 and '06. The following represents progress in this area.
    1. MRI: fMRI, microvessel density, BBB transfer, DTI, stem cell migration
    2. In vivo imaging of dendritic spines and synaptogenesis; Micro-PET of gene expression
3. New clinical interventions: This priority was identified in 2001 and '12. The following progress has occurred as a result.
    1. Activity based therapy, robotic therapy, cortical stimulation
    2. Cell based therapies
    3. Depression treatment

Other Successes/Priorities

1. Appreciation of Neurovascular Unit
2. Defining stroke at the molecular level using genomic, proteomic and metabolomic markers
3. Genetic consortia; identification of ischemic risk loci on gp21 and 16g22 and others, and APOE e2 with ICH
4. Imaging the penumbra
5. Vascular cognitive impairment -- neuroimaging correlates

Conclusion

In conclusion, while some areas identified have received little attention, there has been huge research progress in the stroke field with many examples reflected in the research presented at this Princeton Conference. There is much to be done to build on these successes, and it will be a challenge to narrow down future priorities to just a few in 3 broad topics.

Acknowledgments

Disclosures: Dr Grotta receives NINDS funding for Argatroban, CLOTBUST, Hypothermia, Caffeinol and Pioglitizone studies. He is a consultant for Lundbeck, and holds a patent on Caffeinol

References

1. Grotta, JC.; Moskowitz, MA.; Jacobs, TP.; Marler, J.; Woodbury-Harris, K.; Radziszewska, B.; Scott, PA., editors. National Institute of Neurological Disorders and Stroke. 2002. Report of the Stroke Progress Review Group.
2. Grotta JC, Jacobs TP, Koroshetz WJ, Moskowitz MA, Grotta JC. The NINDS Stroke Program Review Group Report. Stroke. 2008; 39:1364–1370. [PubMed: 18309142]