Stroke

Why aren't there more effective drug treatments for stroke?

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Despite high national standards for medical care, of all the Australians who have strokes each year, the chance of survival is only about 70%. Of those survivors, approximately half will recover fully, but the rest will face a permanent disability. If the stroke is severe, the probability for survival is substantially worse, dropping as low as 20%. One tool in the physicians' arsenal are clot-busting drugs such as tPA (tissue plasminogen activator), which if applied within a short window of opportunity immediately after an ischemic stroke can re-open blood vessels and restore circulation to the affected area of the brain. However, the subsequent phases of fluid accumulation and brain swelling after severe strokes or traumatic brain injuries are a major concern, strongly correlated with dysfunction and death.

Given the fact that brain oedema after stroke is such a serious problem with life-threatening consequences, why don't we have a better array of pharmaceutical agents in hand? Why hasn't ongoing research, aimed at finding therapies for stroke, been more successful in designing new drugs that can be used to prevent the onset and to speed repair and recovery of the major consequences of stroke events?

The answer is that this is a complex and challenging area of work, for several reasons.
One is that we are born with the maximum number of neurons that we will have for life; the brain and spinal cord do not regenerate more than a relative handful of neurons over time, so the neurons that are lost due to injury, over-excitation by released transmitters, lack of oxygen and lack of nutrients after stroke and injury, are just gone. However, with rehabilitation, some of the neurological damage can be compensated. Stem cells are an ongoing area of research interest for future approaches involving neuronal replacement, but at present is not sufficiently well defined to be considered for a standard medical approach.
A second reason is that the findings of work done in animal models, which have been aimed mainly at preventing the early stages of neuronal death from processes such as over-excitation, have not proven to be easily transferred to the human situation in clinical trials.
A third reason is that research has focused on treatments that could be useful mainly during the early phases post-stroke. There has been little information and thus little potential for drug-based intervention in the later stages of subsequent brain swelling during the hours and days after the stroke event.

A future with better treatments for serious brain oedema is not without hope. One area of research in multiple laboratories around the world (including Europe, Japan, the United States, and Australia) has been the investigation of a specialised class of membrane proteins that govern water movement across cell and tissue interfaces in the body. These protein pathways for water flow are known as "aquaporins" (water channels). The brain water channel, Aquaporin-4, provides a steady background regulation of brain water balance, but is thought to be a weak point for unwanted water entry into the brain and resultant swelling during periods immediately after stroke and traumatic injury. New work is identifying novel pharmacological agents that block and that potentiate the Aquaporin-4 activity, and offer promise for development of targeted approaches for the treatment of brain oedema in the foreseeable future.