Hypothermia protects the brain against damage during stroke

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Thromboembolic stroke, caused by a blood clot in the brain, results in damage to the parts of the brain starved of oxygen. Breaking up the clot with tissue plasminogen activator (tPA) reduces the amount of damage, however, there is a very short time window when the value of the treatment outweighs the side effects. New research published in BioMed Central's open access journal *Experimental & Translational Stroke Medicine* shows that, during the first 24 hours after a stroke, mild hypothermia (34C) can reduce the side effects of tPA and potentially increase the window of opportunity for tPA treatment.

When a blood clot blocks off blood flow in the brain (ischemic stroke) the part starved of oxygen quickly begins to die. In order to prevent significant damage tPA must be given to the patient as early as possible after the onset of symptoms - doctors recommend that it must be administered within the first four and a half hours. Delayed treatment also increases the patient's risk of intracerebral hemorrhage and brain swelling (edema).

Mild hyperthermia is known to be neuroprotective and to reduce damage caused by the return of blood flow to an area of the brain starved of oxygen by a clot. Researchers from the University of Erlangen, led by Dr Rainer Kollmar, tested whether mild hyperthermia could also prevent damage to the brain due to tPA treatment in rats. After 24 hours they found that, while hypothermia reduced the amount of swelling and damaged tissue in the brain after a stroke, tPA (administered 90 minutes after the onset of stroke) increased it. However, they also discovered that

hypothermia therapy was able to offset the damage due to tPA.

This seemed to be true for all the measurements they looked at. Dr Kollmar explained, "Patients often loose brain function such as control over parts of their body, speech or memory after stroke. We looked at 'neuroscore', to examine how much control of the body had been affected, and at markers for inflammation (TIMP-1 and sICAM) or evidence of damage to the blood brain barrier. In all cases hypothermia was able to offset the side effects of tPA."

While these results are still experimental, new techniques which prevent shivering mean that this technique is easier to administer in conscious patients. Preliminary clinical trials are also beginning to show that it is possible to treat patients, who have had a stroke, with tPA plus hypothermia. Our results suggest that hypothermia can offset the side effects of tPA and further studies will show if it is also able to increase the window of opportunity of tPA treatment in patients.

More information: Mild hypothermia of 34C reduces side effects of rt-PA treatment after thromboembolic stroke in rats, Bernd Kallmünzer, Stefan Schwab and Rainer Kollmar, *Experimental & Translational Stroke Medicine* (in press)

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