CLINICALLY APPROVED DRUGS WITH HYPOTHERMIC ADVERSE EVENTS MAY BE THE FUTURE FIRST CHOICE IN THERAPEUTIC HYPOTHERMIC STROKE TREATMENT

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Therapeutic hypothermia in stroke patients is solely based on forced mechanical cooling but drug-induced regulated hypothermia may have less adverse effects. Therefore, we have tested hypothermia induced by the Parkinson patient dopamine agonist, talipexole, and the serotonergic agonist human test drugs Ipsapirone and S 14671 (4-[(thenoyl-2) aminoethyl]-1- (7-ethoxynaphtyl-piperazine) in a rat stroke model.

All rats had middle cerebral artery occlusion (MCAO) for 60 minutes and were then sacrificed 7 days later. Body core temperature was monitored for 20 hours (h) by a peritoneal radio-pill-implant. 30 min after MCAO, one group of rats (n=10) had a bolus of 2 mg talipexole followed by 20 hours continuous talipexole infusion (0.08 mg h-1); a second group (n=10) had a bolus injection of S 14671 (0,25mg) and a continuous infusion of 0.021 mg h-1 S 14671 for 20 h; a third group of rats (n=10) had a bolus of Ipsapirone (0,25mg) and a continuous infusion of 0.25 mg h-1 Ipsapirone for 3 h. Controls (n=9, n=10; n=10) had similar amounts of vehicle as bolus and continuous infusion. Infarct volumes were stereotaxically quantified.

Temperature post-stroke was reduced 1.0-3.0 ºC as compared to controls for 20 h with talipexole and S14671; and for 6 h with Ipasapirone. Infarct volumes were significantly ($p < 0.05$) reduced by more than 50% in all hypothermic rats.

We have in an animal model exemplified that hypothermia, induced by drugs already used in patient treatment, might be useful in stroke treatment. Drug induced cooling can be initiated instantly and anywhere.