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The combination of pharmacological hypothermia - dihydrocapsaicin (DHC) and intra-arterial regional cooling infusions (RCI) was found to enhance the efficiency of hypothermia and efficacy of hypothermia-induced neuroprotection in acute ischemic stroke. The aim of this study of Wu et al., from Xuanwu Hospital was to explore whether the combination could induce a long-term neuroprotective effects, as well as the underlying mechanism.

Sprague-Dawley rats were subjected to middle cerebral artery occlusion (MCAO) for 2 h using intraluminal hollow filament. The ischemic rats were randomized to receive pharmacological hypothermia by intraperitoneal (i.p.) injection of DHC, physical hypothermia by RCI of 6 ml cold saline (4°C), the combination, and no treatment. Over a 21-day period, brain damage was determined by infarct volume with MRI, and neurological deficit with grid-walking and beam balance tests. Blood brain barrier (BBB) was assessed by Evans-Blue (EB) contents. Inflammatory cytokines were determined in peri-infarct area by antibody array and ELISA.

The combination of DHC and RCI reduced (p<0.05) infarct volume and neurologic deficit after stroke. BBB leakage and pro-inflammatory cytokines (IFN- $\gamma$ , IL-2, and TNF- $\alpha$ ) were significantly decreased (p<0.05) because of the combination, while protective cytokines (IL-4 and IL-10) were increased (p<0.05) in the peri-infarct area.

The combination approach enhanced the efficacy of hypothermia-induced neuroprotection following ischemic stroke. Our findings provide a hint to translate the combination method from bench to bedside <sup>1)</sup>.

1)

Wu D, Zhi X, Duan Y, Zhang M, An H, Wei W, Dong K, Zhang Y, Shi J, He X, Zhang J, Wu C, Meng R, Ding Y, Ji X. Inflammatory cytokines are involved in dihydrocapsaicin (DHC) and regional cooling infusion (RCI)-induced neuroprotection in ischemic rat. Brain Res. 2018 Dec 22. pii: S0006-8993(18)30659-0. doi: 10.1016/j.brainres.2018.12.033. [Epub ahead of print] PubMed PMID: 30584925.

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