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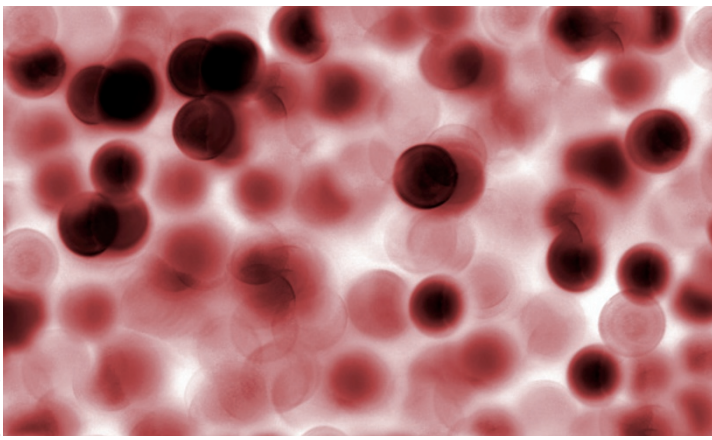
AGEING

Could young blood combat age-related cognitive decline?



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Blood-consuming vampires remain eternally youthful, and blood might also rejuvenate us mortals: two recent studies demonstrate that systemic administration of blood from young mice could counteract brain ageing in old mice. In both studies, the investigators connected the circulatory systems of old mice to the circulatory system of either another old mouse or a young mouse, and found that young blood could reverse existing age-related changes in cognitive function, neurovasculature and neurogenesis.

In an article published in *Nature Medicine*, Saul Villeda and colleagues described the beneficial effects of young blood on hippocampal spine density, plasticity and learning. The old mice that received blood from young mice showed higher dendritic spine density in the dentate gyrus than those receiving blood from other old mice. Furthermore, long-term synaptic potentiation—thought to indicate capability for learning and memory—was restored in the old mice receiving young blood.

To assess the effects of young blood on cognitive function, the researchers injected blood from young mice into the circulation of old mice. Plasma from young mice restored the age-related impairment in contextual fear conditioning and spatial navigation tasks—both thought to depend on the hippocampus, a brain area that undergoes atrophy in Alzheimer disease.

A second study by Lida Katsimpardi and colleagues, published in *Science,* focused on how circulating factors can enhance brain vasculature and neurogenesis in the ageing brain. "We found that factors in young blood can rejuvenate the aged neurogenic niche in the subventricular zone, promote neurogenesis and olfactory discrimination, and induce vascular remodelling in the subventricular zone, hippocampus and cortex," Katsimpardi summarizes.

The factors mediating the effects of young blood remain largely elusive. One candidate could be growth differentiation factor 11 (GDF11): Katsimpardi and colleagues discovered that GDF11 injections reproduced some of the effects of young blood on brain vasculature and neurogenesis. Another possibility is that conjoined circulation reduces levels of 'pro-ageing' factors circulating in the blood of the old animals—a hypothesis that is supported by both the findings by Katsimpardi *et al.* and previous work by Villeda and co-workers. In the present study by Villeda *et al.*, abrogation of Creb signalling mitigated the increase in dendritic spine density and hippocampus-dependent learning, suggesting that the effects of the 'pro-youth' factors could involve the Creb pathway.

Although caution is needed in translating the findings to humans, the discoveries open up the possibility of developing novel therapies for neurodegenerative and neurovascular disorders associated with ageing. "The two studies make a very strong case for the idea that age-related changes in blood can have a direct effect on brain functions," concludes Villeda. "I think it is warranted to now extend studies to ageing humans in a controlled and appropriate way."

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Original articles Villeda, S. A. *et al.* Young blood reverses age-related impairments in cognitive function and synaptic plasticity in mice. *Nat. Med.* doi:10.1038/nm.3569 | Katsimpardi, L. *et al.* Vascular and neurogenic rejuvenation of the aging mouse brain by young systemic factors. *Science* doi:10.1126/science.1251141