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**Young blood reverses age-related impairments in cognitive function and synaptic plasticity in mice.**

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**Public Summary:**

As human lifespan increases, a greater fraction of the population is suffering from age-related cognitive impairments, making it important to elucidate a means to combat the effects of aging. Here we report that exposure of an aged animal to young blood can counteract and reverse pre-existing effects of brain aging at the molecular, structural, functional and cognitive level. Genome-wide microarray analysis of heterochronic parabionts-in which circulatory systems of young and aged animals are connected-identified synaptic plasticity-related transcriptional changes in the hippocampus of aged mice. Dendritic spine density of mature neurons increased and synaptic plasticity improved in the hippocampus of aged heterochronic parabionts. At the cognitive level, systemic administration of young blood plasma into aged mice improved age-related cognitive impairments in both contextual fear conditioning and spatial learning and memory. Structural and cognitive enhancements elicited by exposure to young blood are mediated, in part, by activation of the cyclic AMP response element binding protein (Creb) in the aged hippocampus. Our data indicate that exposure of aged mice to young blood late in life is capable of rejuvenating synaptic plasticity and improving cognitive function.

**Scientific Abstract:**

As human lifespan increases, a greater fraction of the population is suffering from age-related cognitive impairments, making it important to elucidate a means to combat the effects of aging. Here we report that exposure of an aged animal to young blood can counteract and reverse pre-existing effects of brain aging at the molecular, structural, functional and cognitive level. Genome-wide microarray analysis of heterochronic parabionts-in which circulatory systems of young and aged animals are connected-identified synaptic plasticity-related transcriptional changes in the hippocampus of aged mice. Dendritic spine density of mature neurons increased and synaptic plasticity improved in the hippocampus of aged heterochronic parabionts. At the cognitive level, systemic administration of young blood plasma into aged mice improved age-related cognitive impairments in both contextual fear conditioning and spatial learning and memory. Structural and cognitive enhancements elicited by exposure to young blood are mediated, in part, by activation of the cyclic AMP response element binding protein (Creb) in the aged hippocampus. Our data indicate that exposure of aged mice to young blood late in life is capable of rejuvenating synaptic plasticity and improving cognitive function.

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