nature medicine

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

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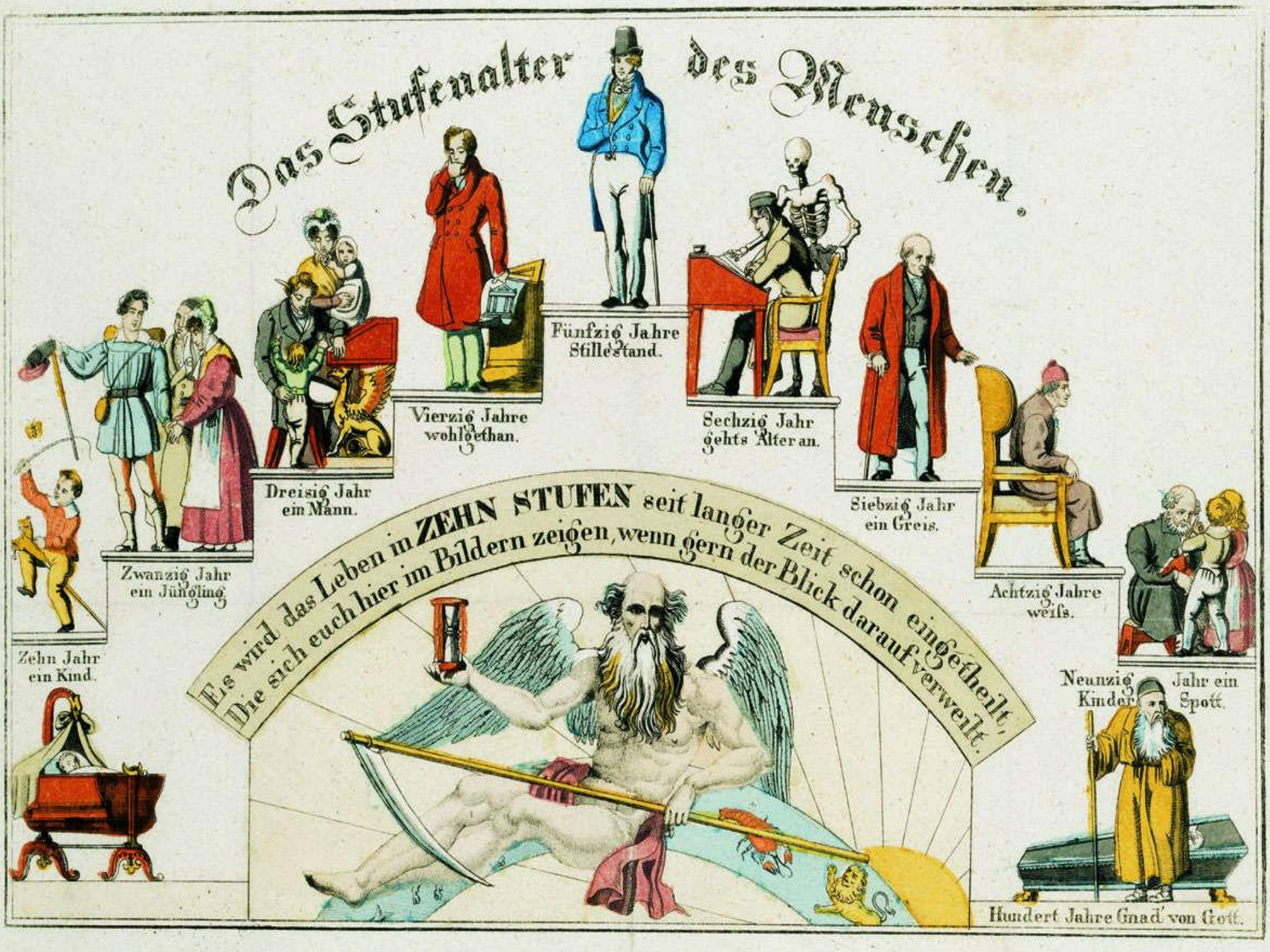
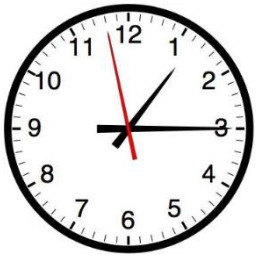
Das Stufenalter des Menschen.



Theories of Aging



Programmed theory

Programmed Longevity

Endocrine Theory

Immunological Theory

Telomere theory

Damage or Error theory

Wear and Tear theory

Rate of living theory

Cross- linking theory

Free radicals theory

Somatic DNA damage theory

Modern Biological Theories of Aging

Aging Dis. Oct 2010; 1(2): 72–74.

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Methods

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Animal model: male C57BL/6 mice
- young 3 months
- aged 18 months

Gene microarray analysis

Western blot analysis

Immunohistochemistry

Golgi staining

Extracellular electrophysiology

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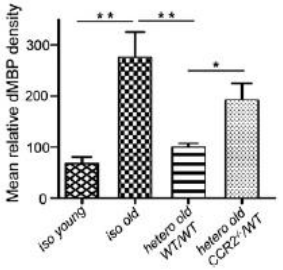
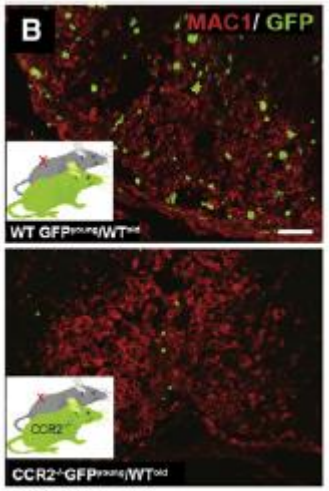
Previous work

Rejuvenation of regeneration in the aging central nervous system

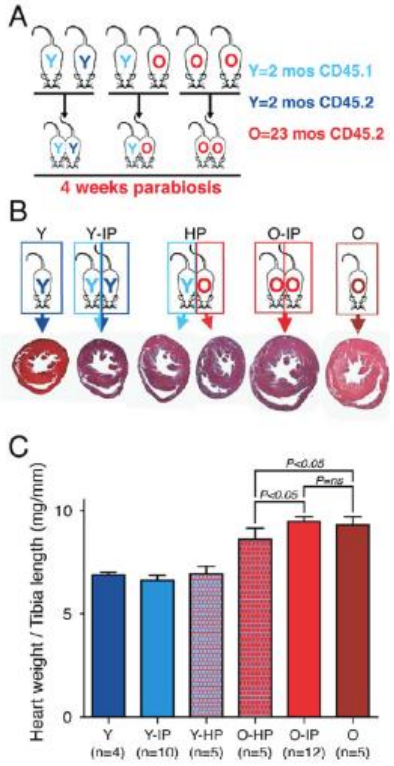
blood-derived monocytes





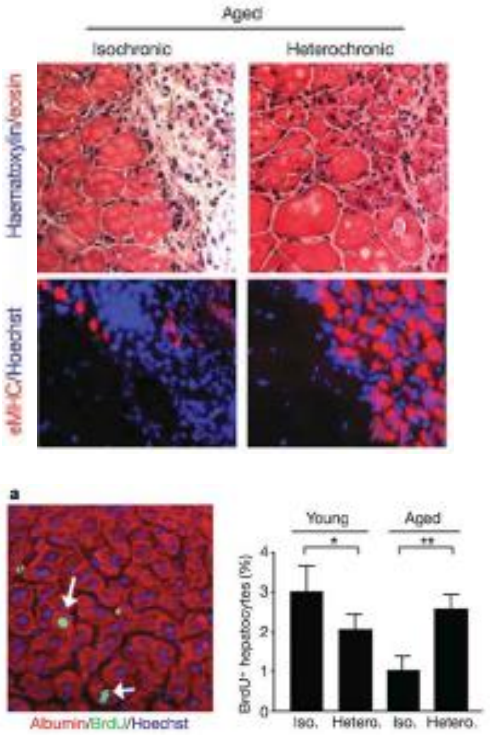
Cell Stem Cell **10**, 96–103 (2012)

Growth Differentiation Factor 11 is a Circulating Factor that Reverses Age Related Cardiac Hypertrophy



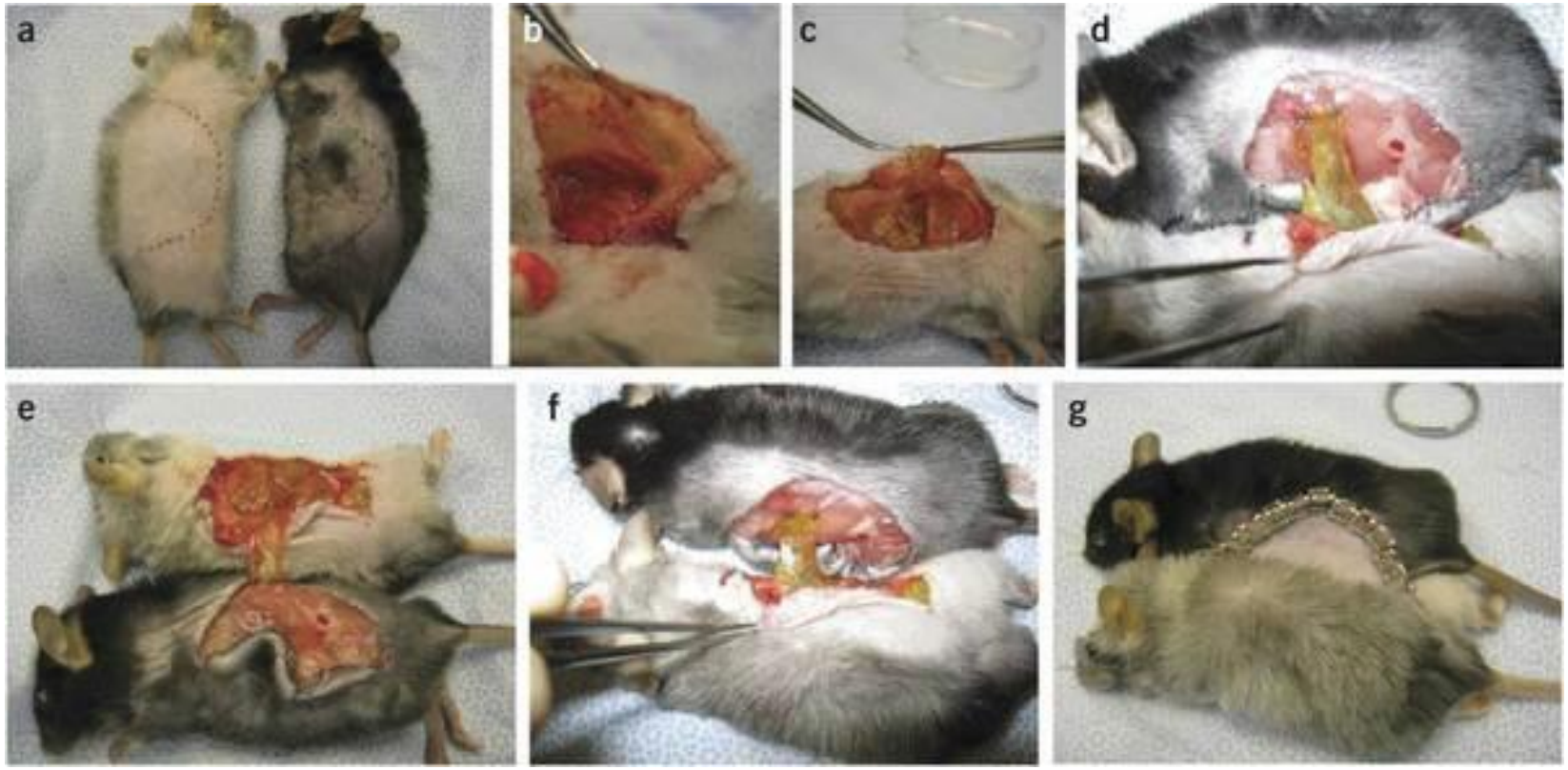
Cell **153**, 828–839 (2013)

Rejuvenation of aged progenitor cells by exposure to a young systemic environment

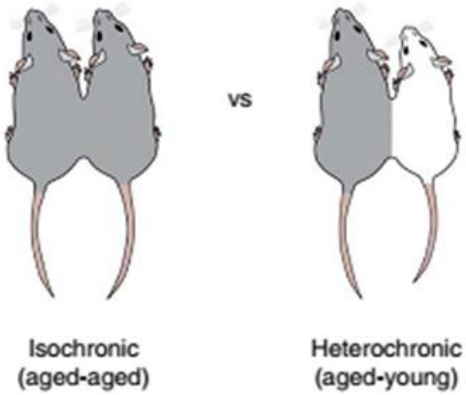


Nature **433**, 760–764 (2005)

Parabiontic Stage


a
b
c
d
e
f
g

Results



Genome-wide microarray analysis of hippocampi from aged (18 months) isochronic (aged-aged) and aged (18 months) heterochronic (aged-young)

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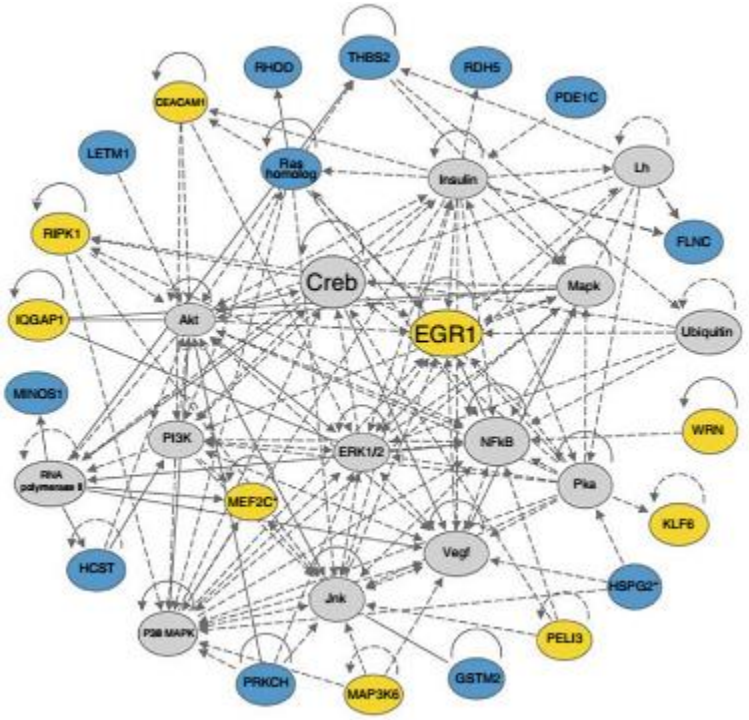
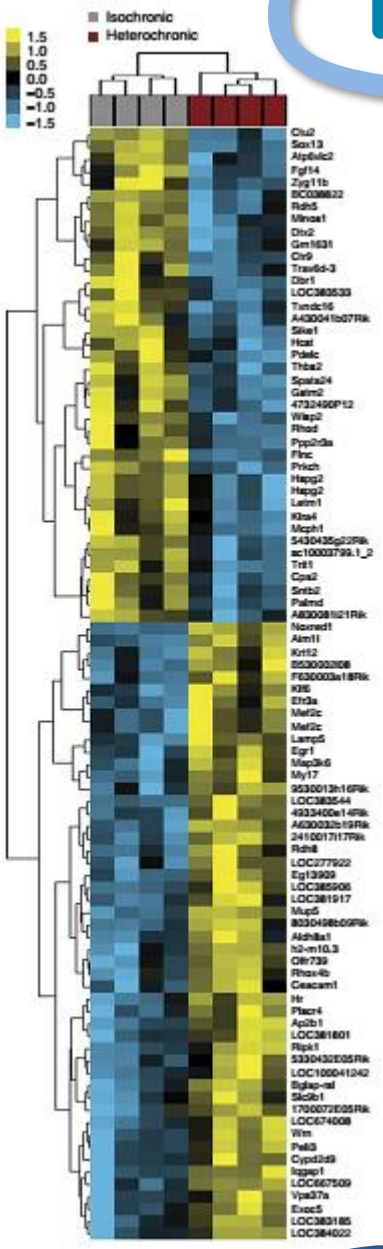




Wien 2014

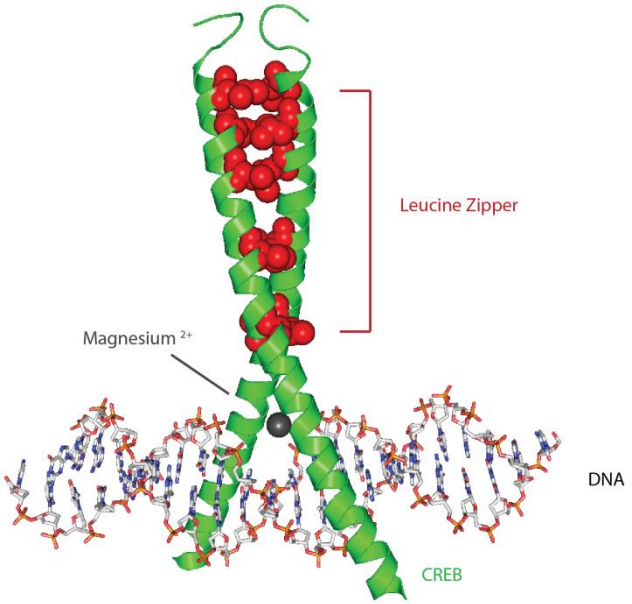
Creb

-

Cyclic AMP response element-binding protein

CREB has a well-documented role in neuronal plasticity and long-term memory formation in the brain. CREB has been shown to be integral in the formation of spatial memory.

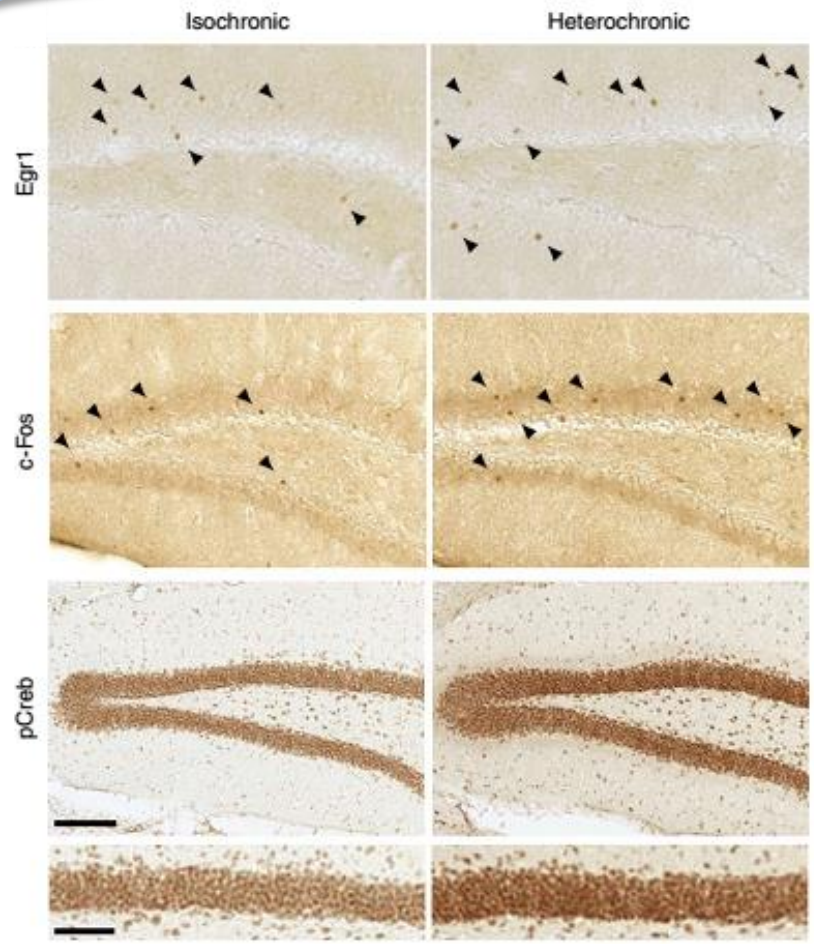
Chronic downregulation of CREB-mediated transcription results in decrease of CREB content in the hippocampal neurons of patients with Alzheimer's disease which may contribute to exacerbation of disease Progression.



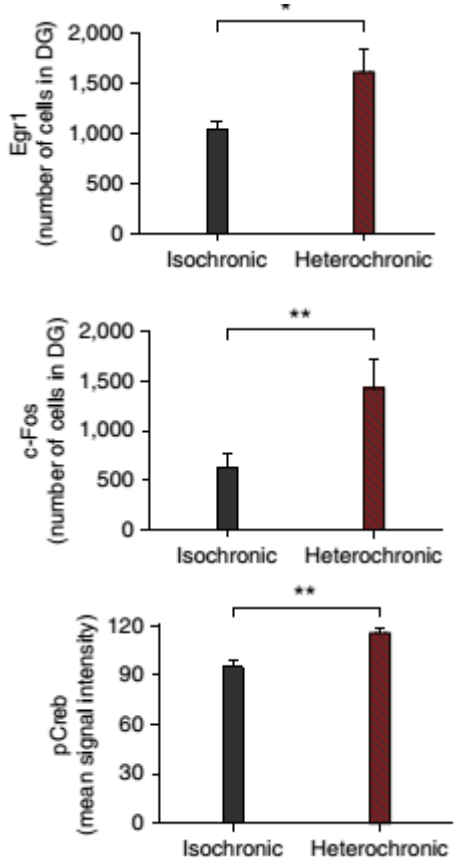
Downregulation of CREB expression in Alzheimer's brain and in Ab-treated rat hippocampal neurons
Pugazhenthi et al. Molecular Neurodegeneration 2011, 6:60

CREB and memory.
Silva et al. Annu Rev Neurosci. 1998;21:127-48.

Results



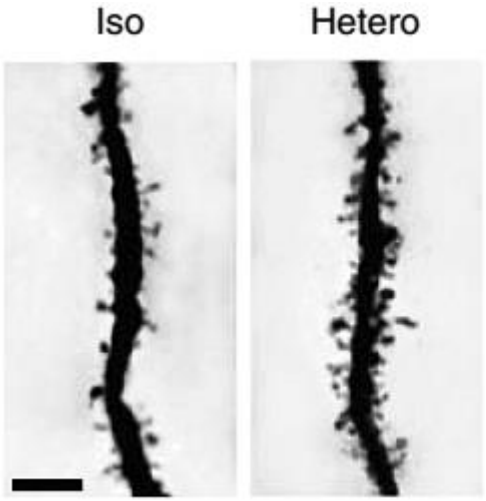
Immunohistochemical staining on the dentate gyrus of hippocampi

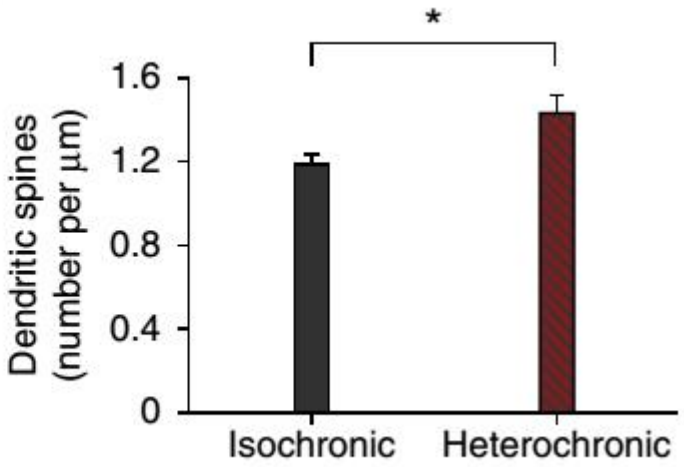


n=5

Results

Synaptic plasticity





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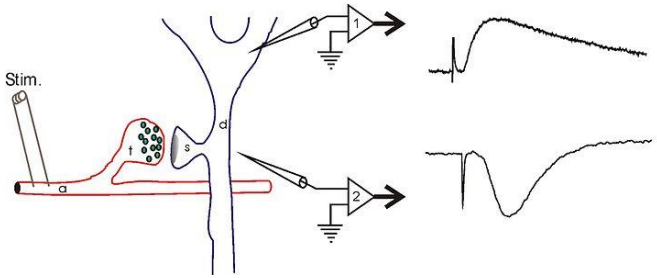
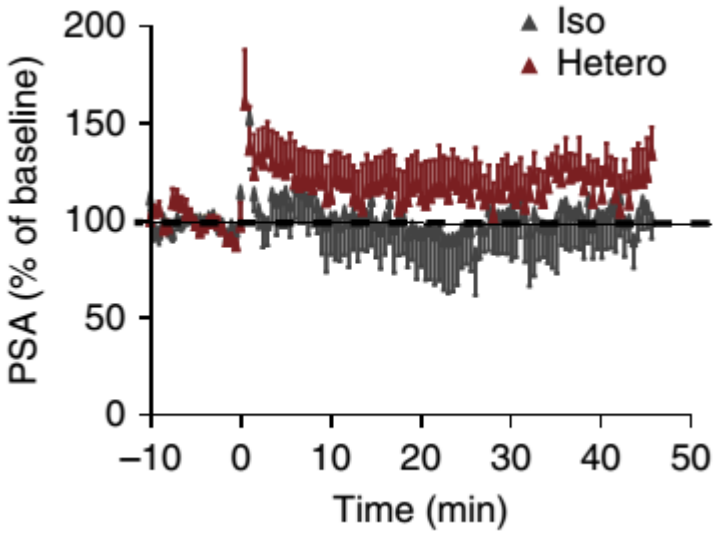
Results

Synaptic plasticity



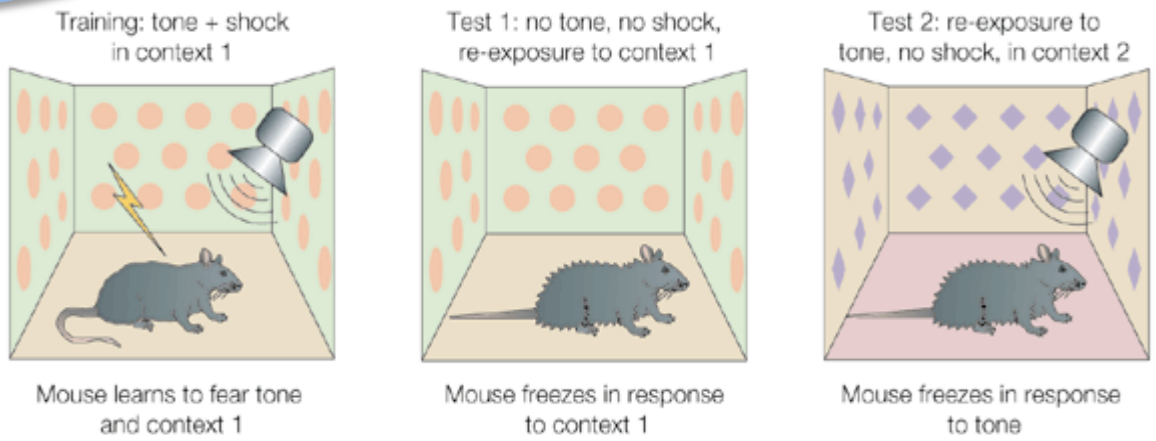
Long-term potentiation stayed above baseline
-> sign for enhanced synaptic plasticity



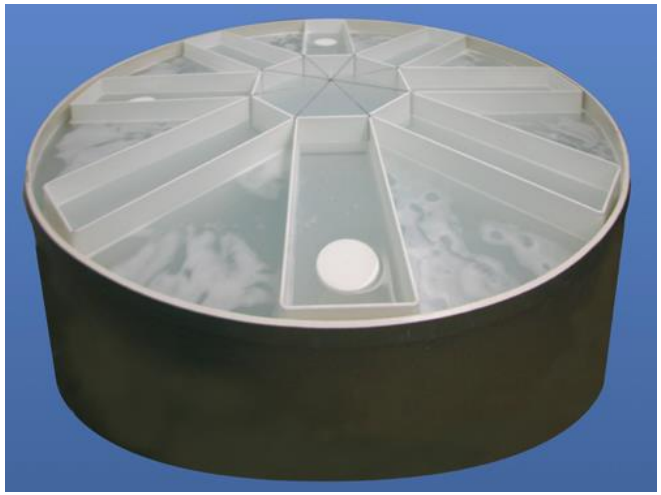
Extracellular electrophysiology

Blood Stage

Fear conditioning

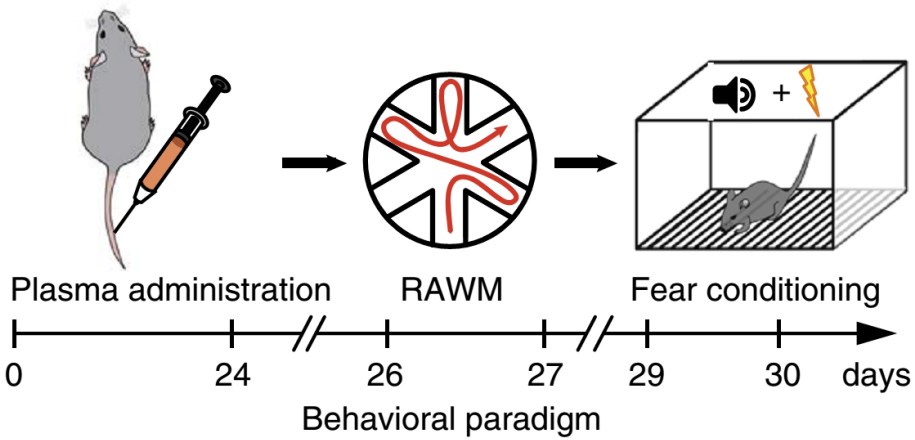


Radial arm water maze

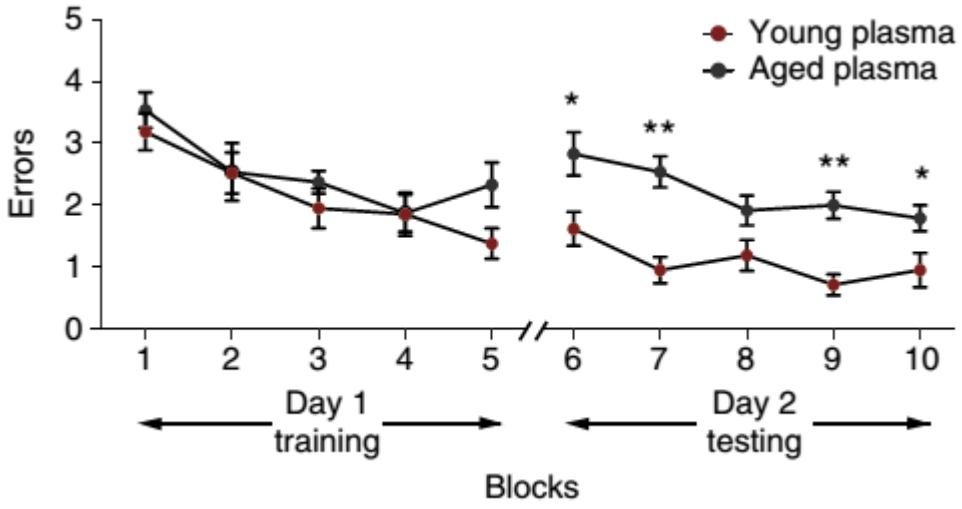


Setup

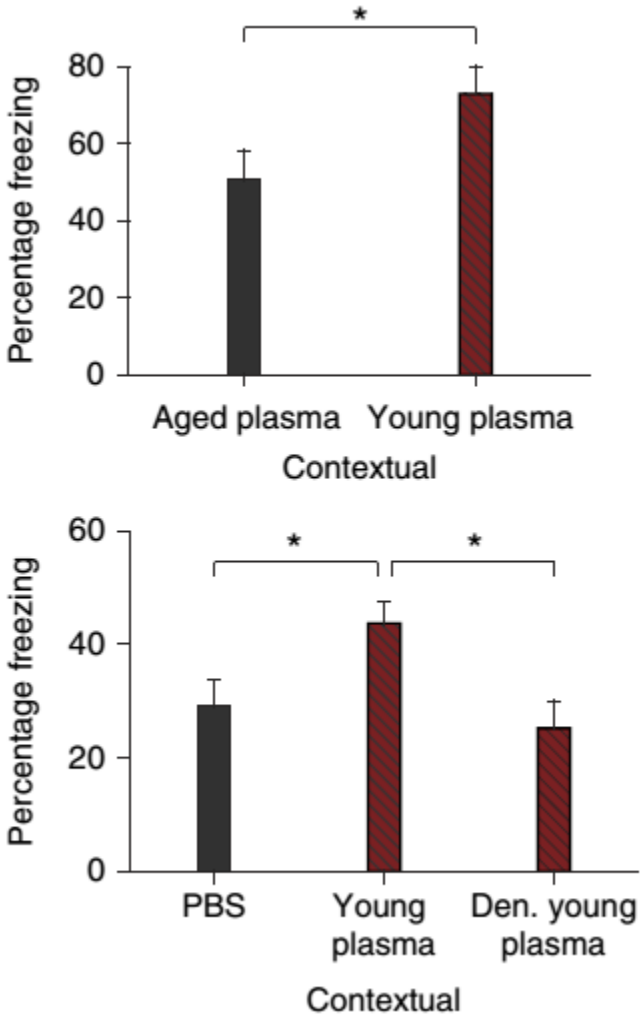
intravenously injected 100 µl of young (3 months) or aged (18 months) plasma eight times over 3 weeks



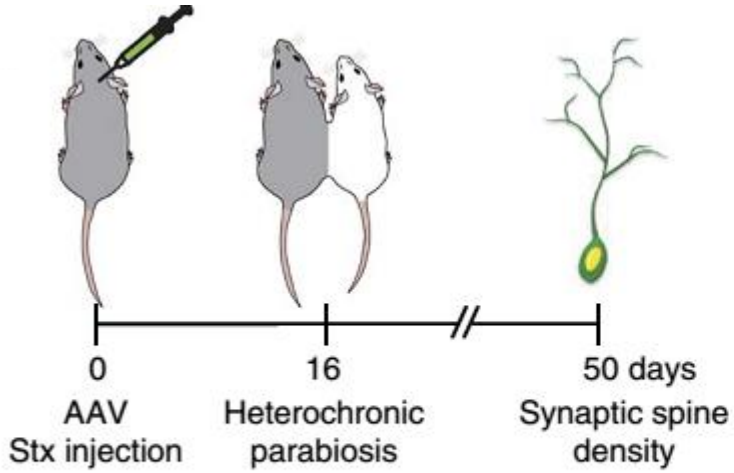
RAWM - Results

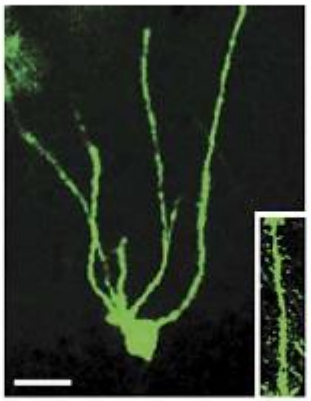


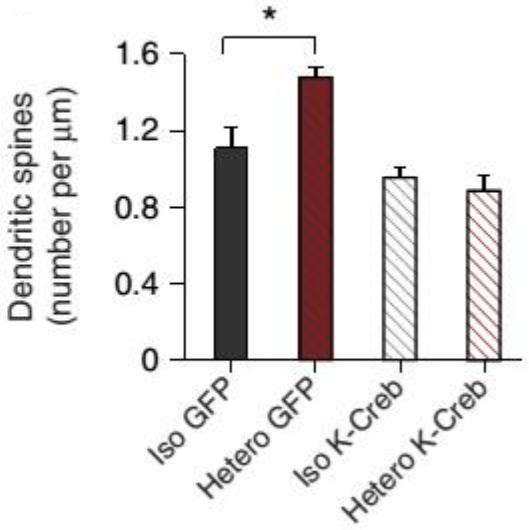
Fear conditioning - Results



Results







Dominant-negative DNA binding–
incompetent form of Creb (K-Creb)

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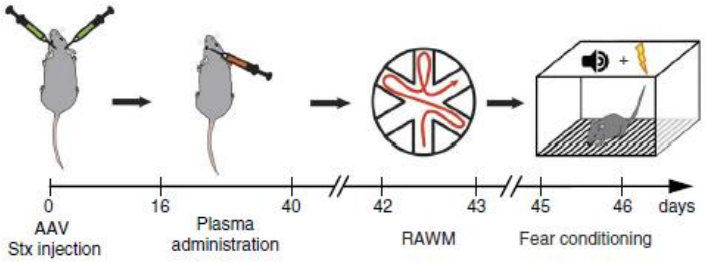
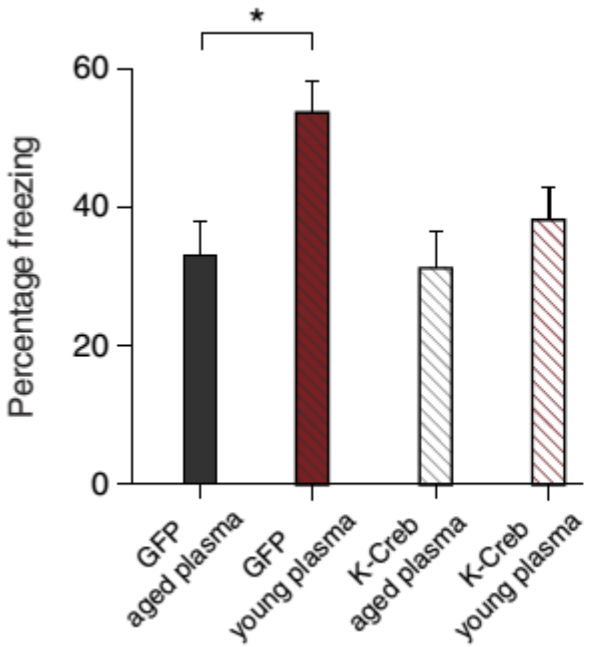
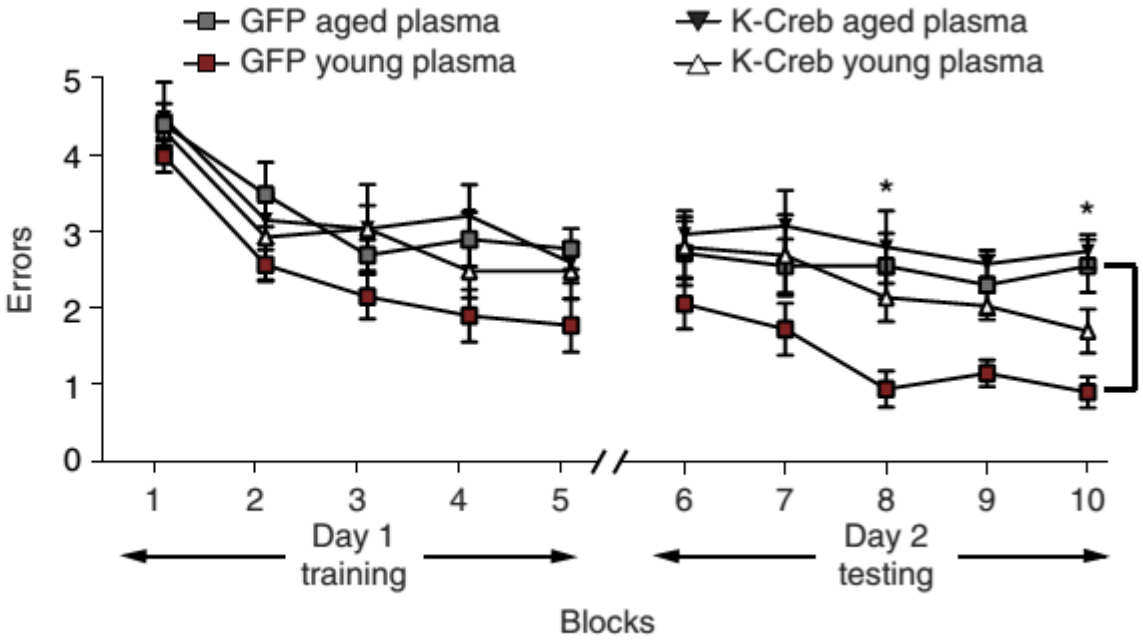
Results







Conclusion

Exposure to young blood counteracts aging at the molecular, structural, functional and cognitive levels in the aged hippocampus

Two possible strategies: pro-youthful factors from young blood to reverse age-related impairments in the brain

or

remove pro-aging factors from aged blood

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Thank you for your attention