Astrocytes, the new trending topic in aging and neurodegeneration

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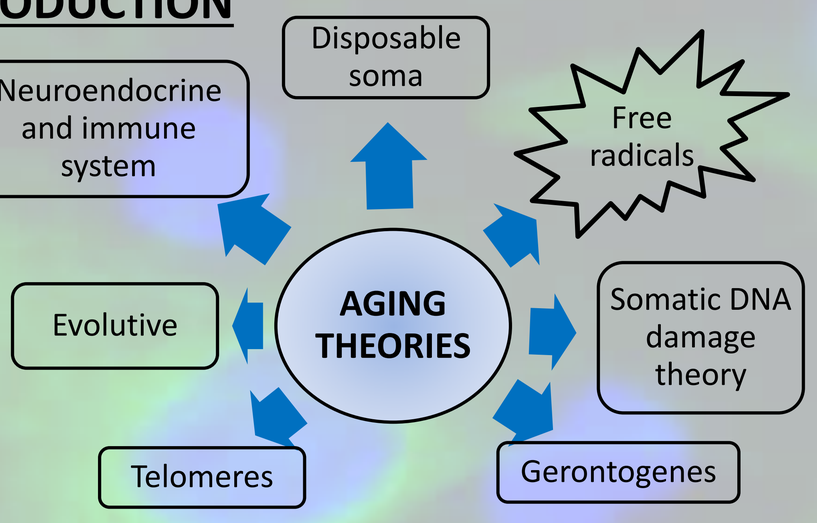
OBJECTIVES

Aging is the result of different morphological, psychological, functional and biochemical changes.
This review intends to sum up the different aging theories and the molecular changes in an aging brain. Also the aim of the project is to enhance astrocyte functions and there relation to neurodegeneratives processes.
Additionally some interesting results of the neuroprotective capacity and the changes in aging animal models are shown.

INTRODUCTION

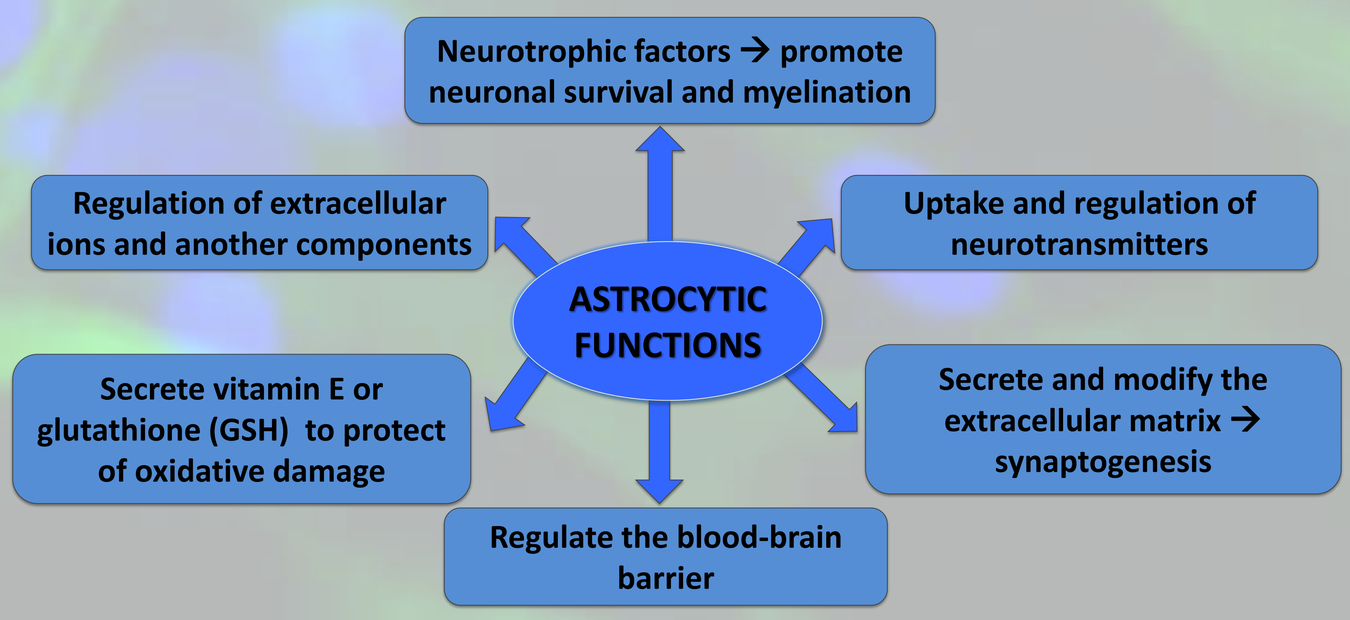


MOLECULAR CHANGES IN AGING

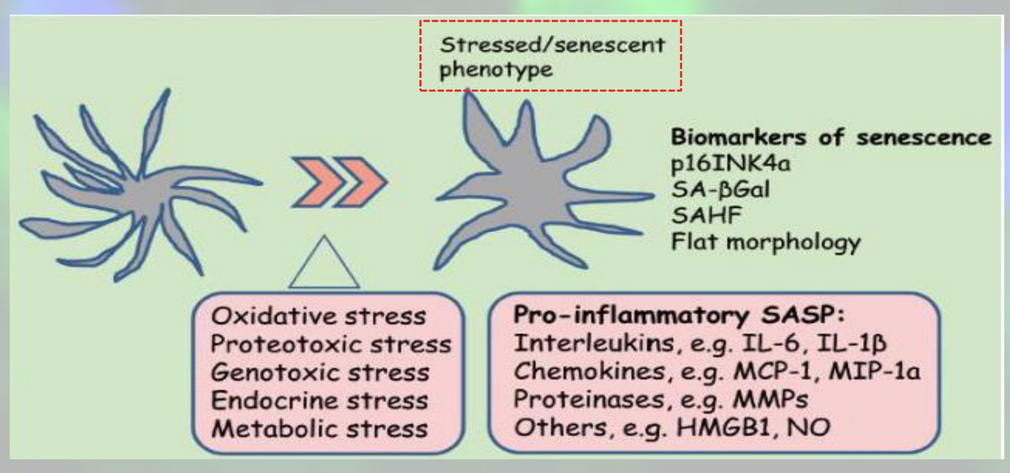
- Decrease levels of grow factors: nerve growth factor (NGF), brain-derived neurotrophic (BDNF), neurotrofin 3 (NT-3) and glial cell-derived neurotrophic factor (GDNF).
- Low energetic metabolism due to mitochondrial damage.
- Calcium homeostasis:
  - Stimulation of long term potentiation (LTD).
  - Altered proteins → increase of apoptotic rate.
- Excitotoxicity: increase d levels of neurotransmitters in the synaptic cleft due to the decreasing levels of EAAT (excitatori amino acid transporter).

ASTROCYTES FUNCTIONS

Astrocytes are the most numerous cell type in the brain and they have a significant role in brain injury, both in the prevention of damage and later in ensuring its repair.



SENESCENCE-ASSOCIATED SECRETORY PHENOTYPE (SASP)[1]



❖ SENESCENCE-ACCELERATED MICE PRONE (SAMP8)

Murin model that manifest irreversible advancing senescence with pathological, biochemical and behavioural alterations related to aging.

RESULTS OF THE STUDIES

1. Proteomic study of neuron and astrocyte cultures from senescence-accelerated mouse SAMP8 reveals degenerative changes.
2. Epigenetic alterations in hippocampus of SAMP8 senescent mice and modulation by voluntary physical exercise.
3. Neurons from senescence-accelerated SAMP8 mice are protected against frailty by the sirtuin 1 promoting agents melatonin and resveratrol.

1)

Protein type	Protein identified	Gene name	Change SAMP8 versus SAMR1	SAMR1 mean ± SD	SAMP8 mean ± SD	Ratio SAMR1/ SAMP8	*p*	Spot
Energy metabolism	Adenylate kinase isoenzyme 4	Ak3l1	Up	ND	0.069 ± 0.029	NA	NA	671
	Acyl-coenzyme A thioesterase 2	Acot2	Up	ND	0.149 ± 0.020	NA	NA	273
	Cytochrome *c* oxidase subunit 4 isoform 1	Cox4i1	Down	0.054 ± 0.018	0.018 ± 0.010	3.0	0.0353	970
Biosynthesis	Dihydropteridine reductase	Qdpr	Down	0.741 ± 0.187	0.340 ± 0.110	2.2	0.0330	634
	S-methyl-5′-thioadenosine phosphorylase	Mtap	Increased pI	0.119 ± 0.033	0.092 ± 0.025	NA	NA	604[a] 1088
Transduction and signaling	Protein-arginine deiminase type-2	Padi2	Up	ND	0.090 ± 0.003	NA	NA	412
	Poly(rC)-binding protein 1	Pcbp1	Up	0.108 ± 0.050	0.234 ± 0.047	0.5	0.0011	336
Stress response	Sodium/hydrogen exchanger 5	Slc9a5	Up	ND	0.075 ± 0.021	NA	NA	364
	Aldehyde dehydrogenase	Aldh2	Up	0.056 ± 0.016	0.106 ± 0.033	0.5	0.0333	597
Cytoskeletal	Stomatin-like protein 2	Stoml2	Up	0.075 ± 0.021	0.159 ± 0.065	0.5	0.0134	361
	Myosin light polypeptide 6	Myl6	Up	0.833 ± 0.305	1.527 ± 0.551	0.5	0.0224	903
	Macrophage-capping protein	Capg	Down	0.138 ± 0.017	0.061 ± 0.024	2.3	0.0002	1075
	Actin, cytoplasmic 2	Actg	Down	0.123 ± 0.071	0.039 ± 0.022	3.2	0.0402	969
Miscellaneous	Coatomer subunit epsilon	Cope	Down	0.529 ± 0.126	0.254 ± 0.027	2.1	0.0053	500

Note: The normalized mean volumes of SAMR1 and SAMP8 differential protein spots and its ratio are indicated along with the changes shown by SAMP8. Normalized volumes were compared using a Student's *t*-test. Protein parameters are described in Table S2. ND, not detectable; NA, not applicable; SAMP8, senescence-accelerated prone mouse strain 8; SAMR1, senescence-accelerated resistant mouse strain 1. [a]First spot number for SAMR1 and second for SAMP8.

Results of the different expressed proteins in astrocytes cultures of SAMR1 (senescence-accelerated resistant mouse strain 1, control model) and SAMP8.

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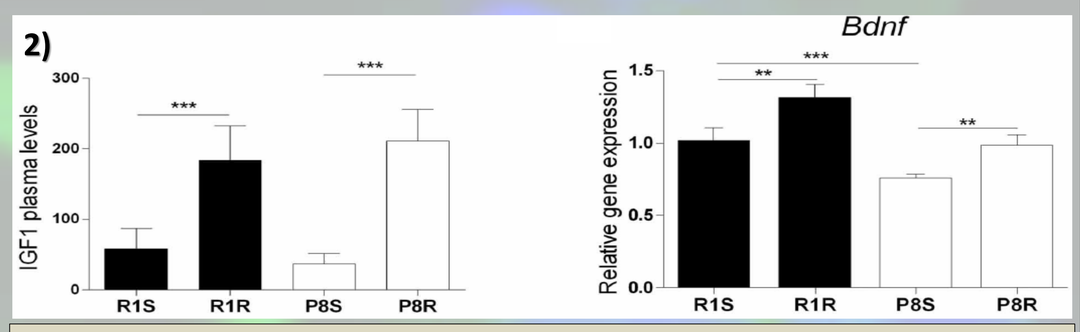
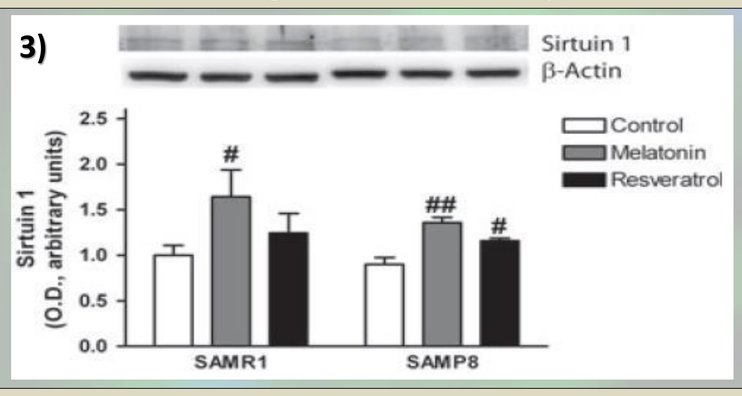


Beneficial effects of 8 weeks of exercise training in SAMP8 and SAMR1 model. Increasing levels of IGF-1 and BDNF (neurotrophics factors expressed in astrocytes) in both murine models due to the regular exercise. (R=running and S= sedentary).

3)



Increased levels of sirtuin 1, a longevity protein, with treatments of melatonin and resveratrol in both animals models, SAMP8 and SAMR1.

CONCLUSIONS

1. There is an extremely relation between astrocytes and aging processes, where these cells will experiment some molecular changes that could compromise their neuroprotective capacity or their biological functions.
2. SASP is the phenotype that astrocytes will adopt in aging and SAMP8 and SAMR1(used like a control) are animal models in relation of this phenotype.
3. There are some studies that confirm the proteomic differences between both models mentioned and also the beneficial effects of anti-oxidant components or regular exercise, which could improve the levels of neurotrophic factors or the expression of proteins that promote longevity.

References:
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2. Cristofol R, Porquet D, Corpas R, Coto-Montes A, Serret J, Camins A et al. Neurons from senescence-accelerated SAMP8 mice are protected against frailty by the sirtuin 1 promoting agents melatonin and resveratrol. J Pineal Res 2012; 52(3):271-281.
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