Come si difende il Sistema Nervoso Centrale dalle malattie neurodegenerative?

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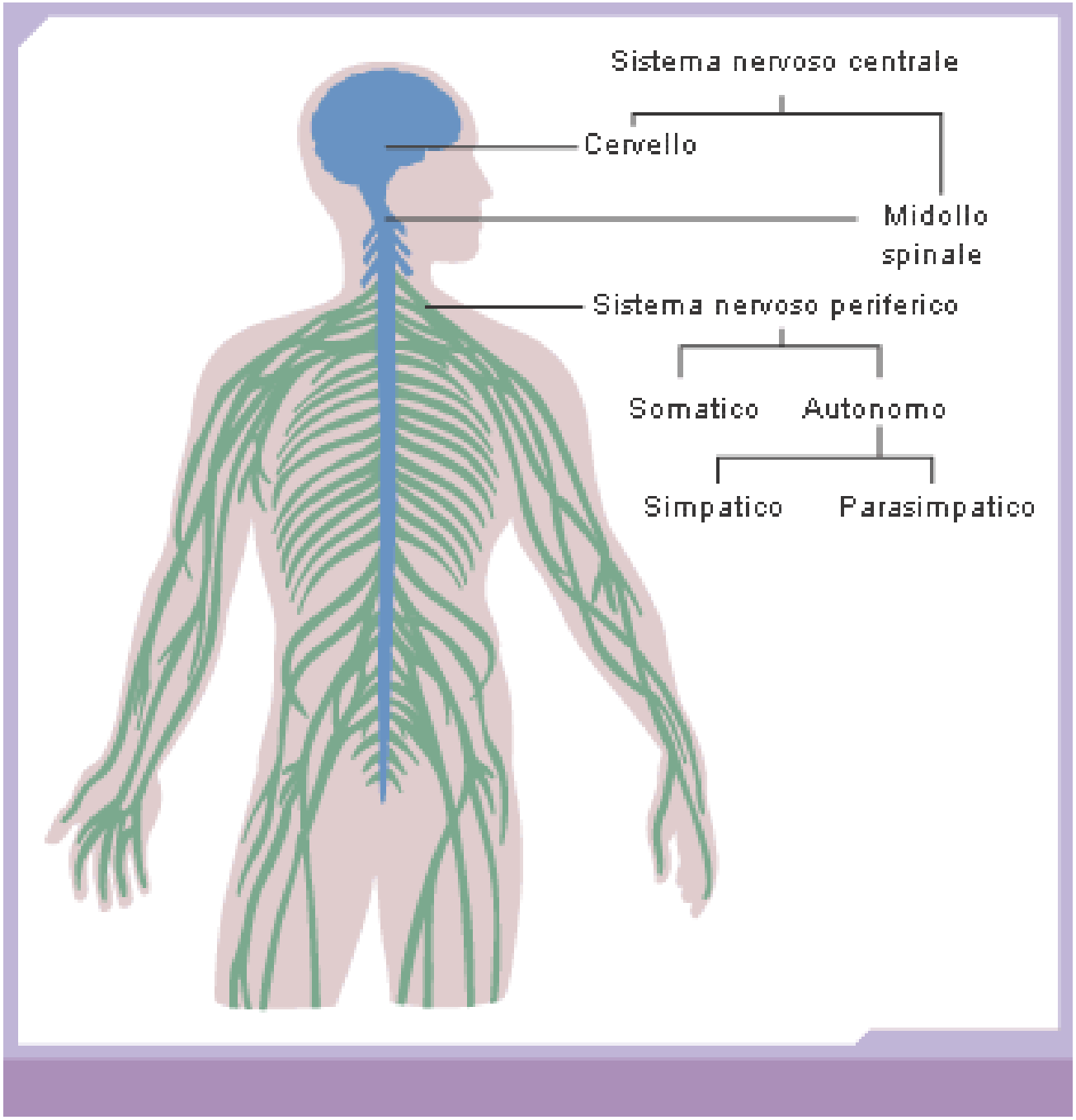
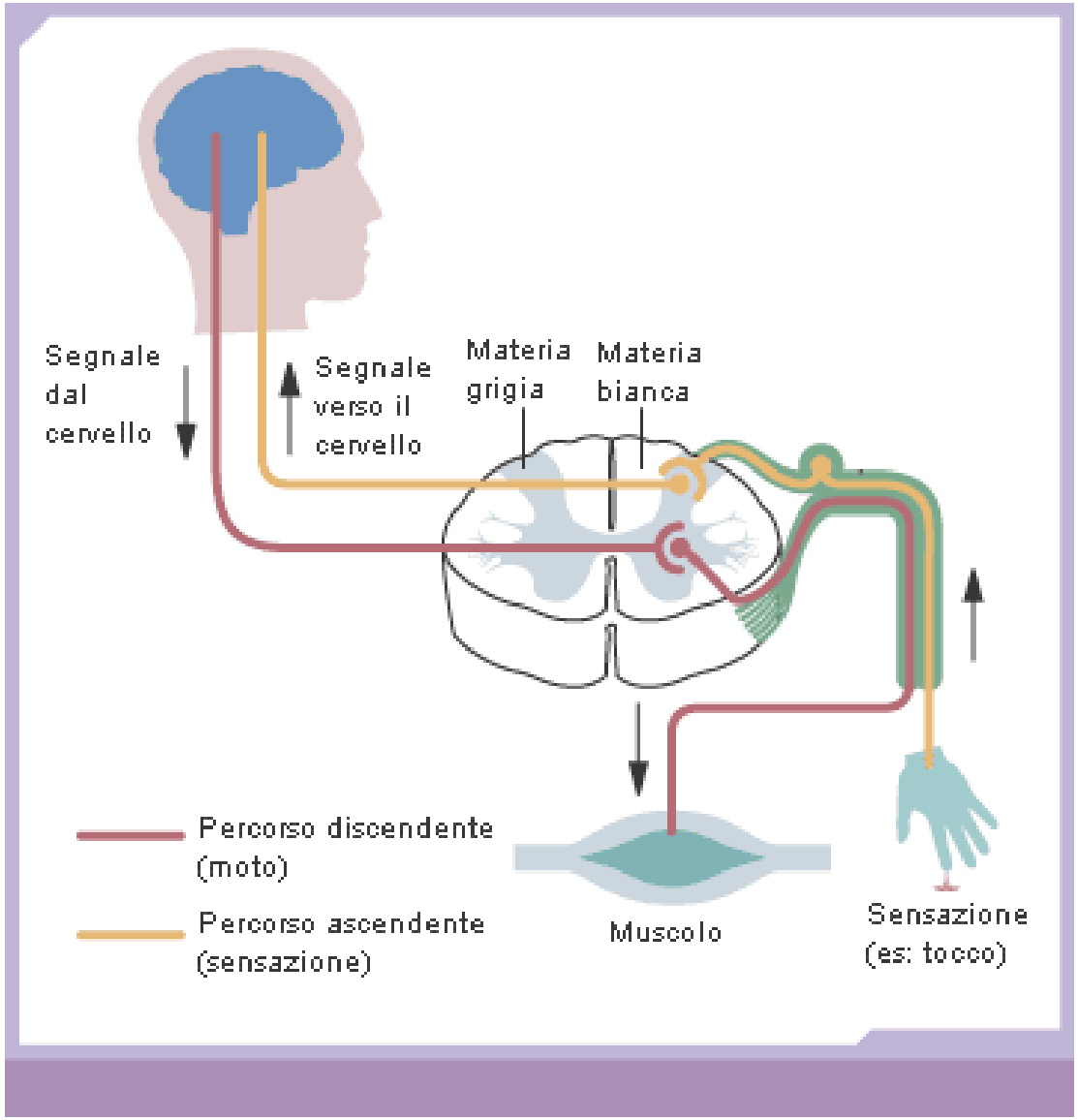

Sistema nervoso centrale
Cervello
Midollo spinale
Sistema nervoso periferico
Somatico
Autonomo
Simpatico
Parasimpatico

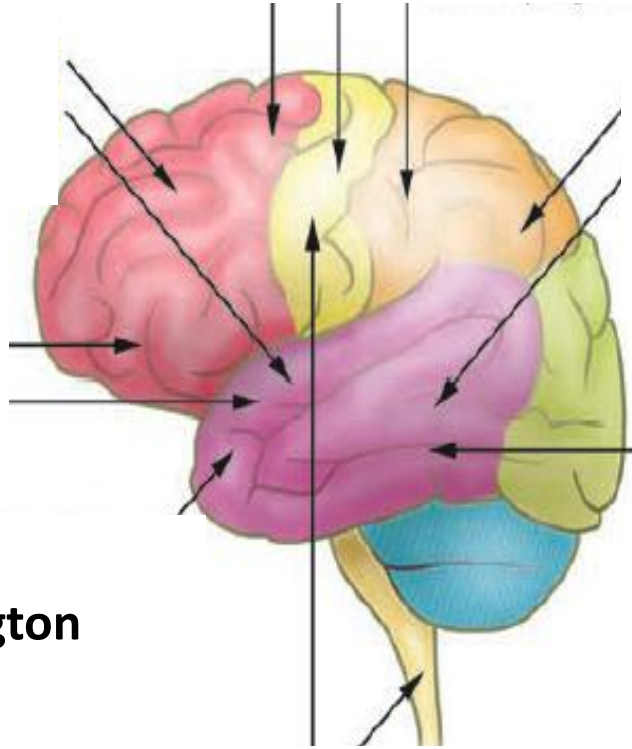
Il cervello reagisce e comanda il nostro corpo attraverso il midollo spinale



Le malattie neurodegenerative dell'adulto

Malattia da prioni o della mucca pazza

Demenza Fronto Temporale



Malattia di Alzheimer

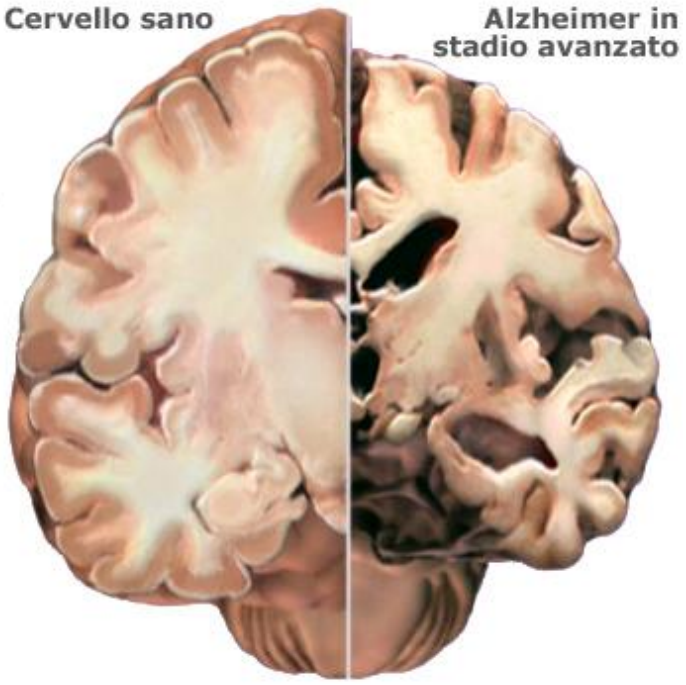
Demenza Lewy Body

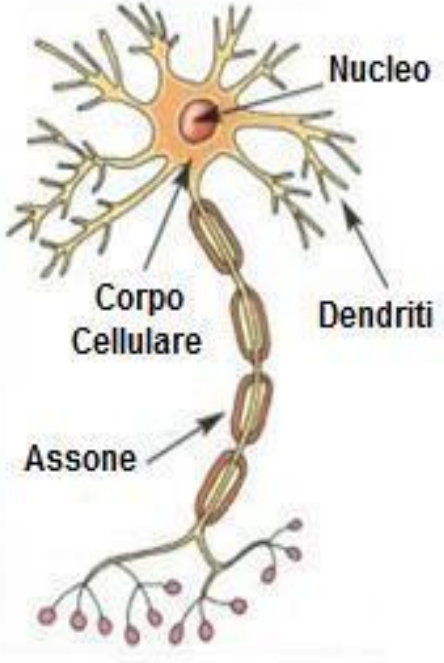
Morbo di Parkinson

Chorea di Hungtington

Sclerosi Laterale Amiotrofica

Le malattie neurodegenerative sono caratterizzate dalla progressiva perdita di neuroni (la materia grigia) in aree specifiche del sistema nervoso





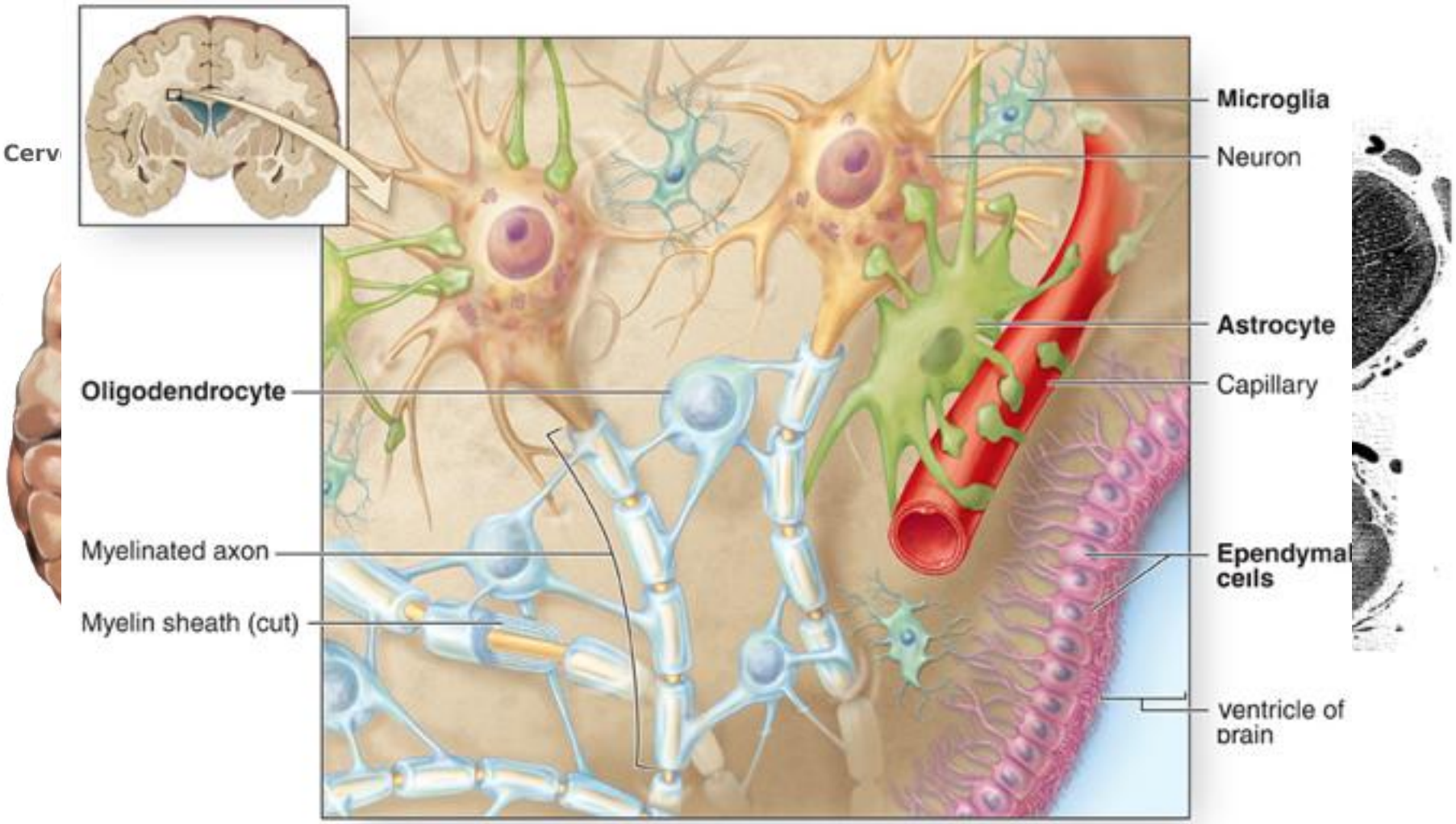
Neurone

Midollo spinale cervicale

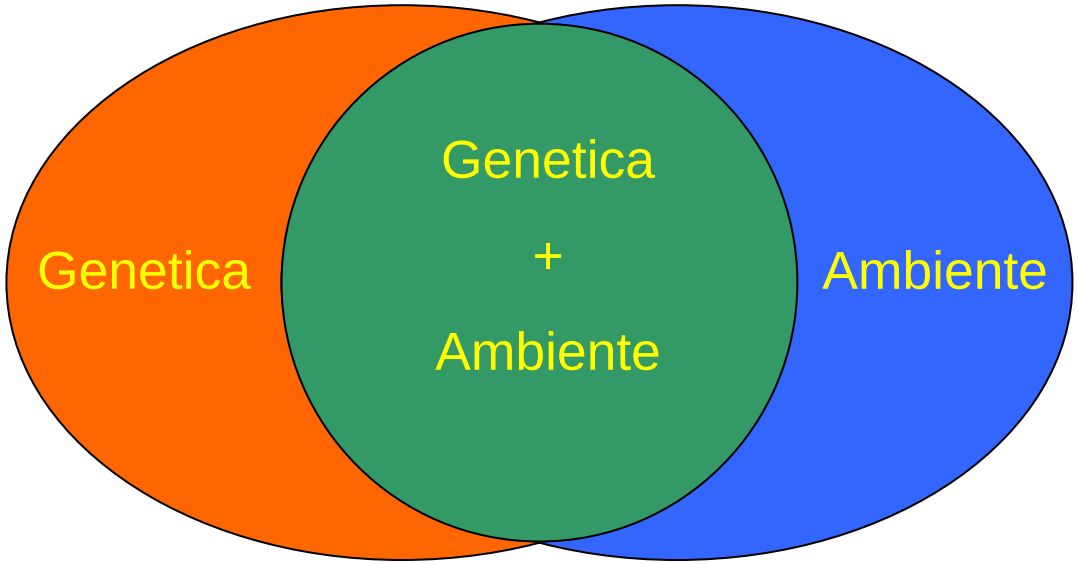
Controllo sano

Paziente SLA

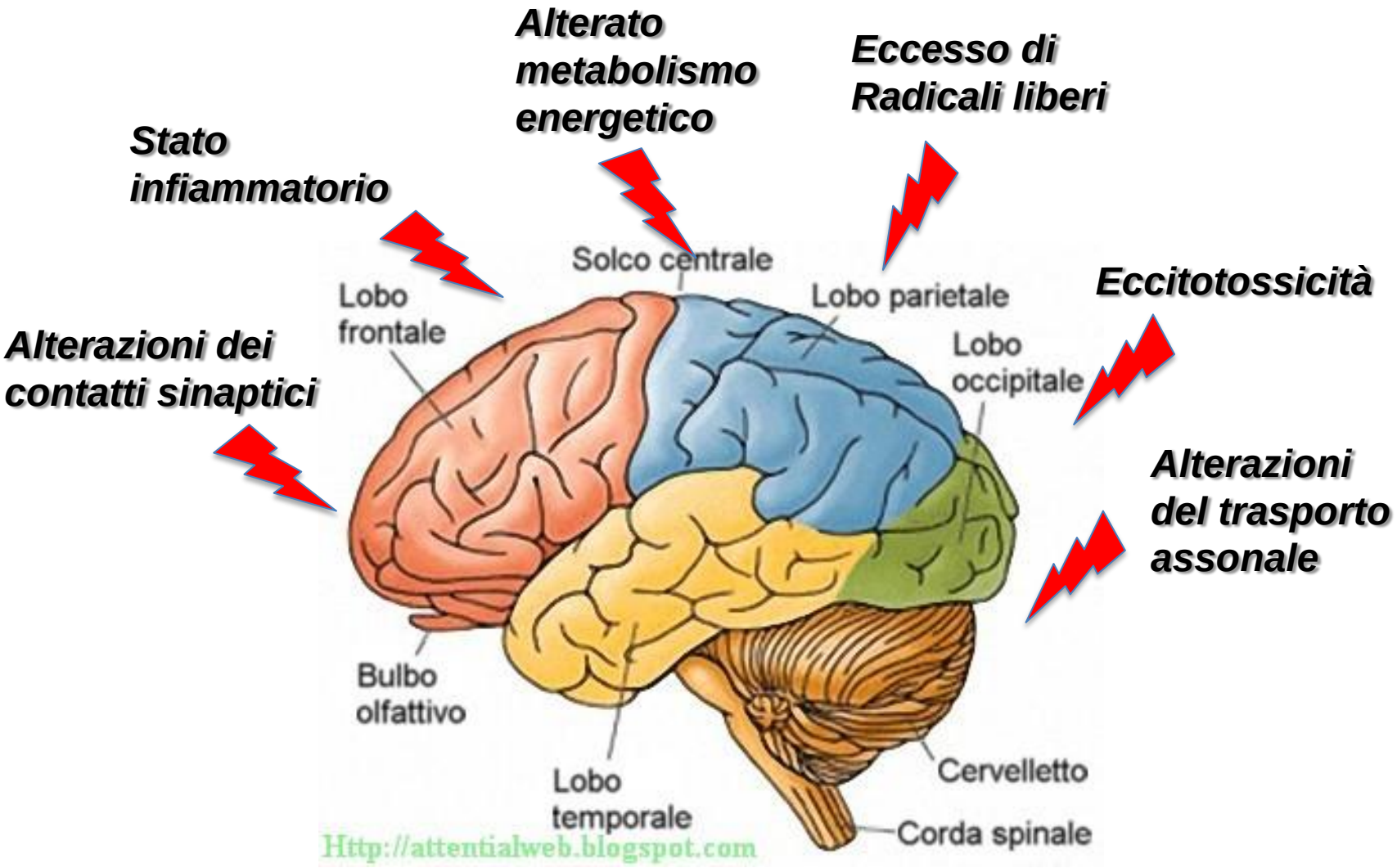
Le malattie neurodegenerative sono caratterizzate dalla progressiva perdita di neuroni (la materia grigia) in aree specifiche del sistema nervoso



Quali i fattori che scatenano le malattie neurodegenerative ?

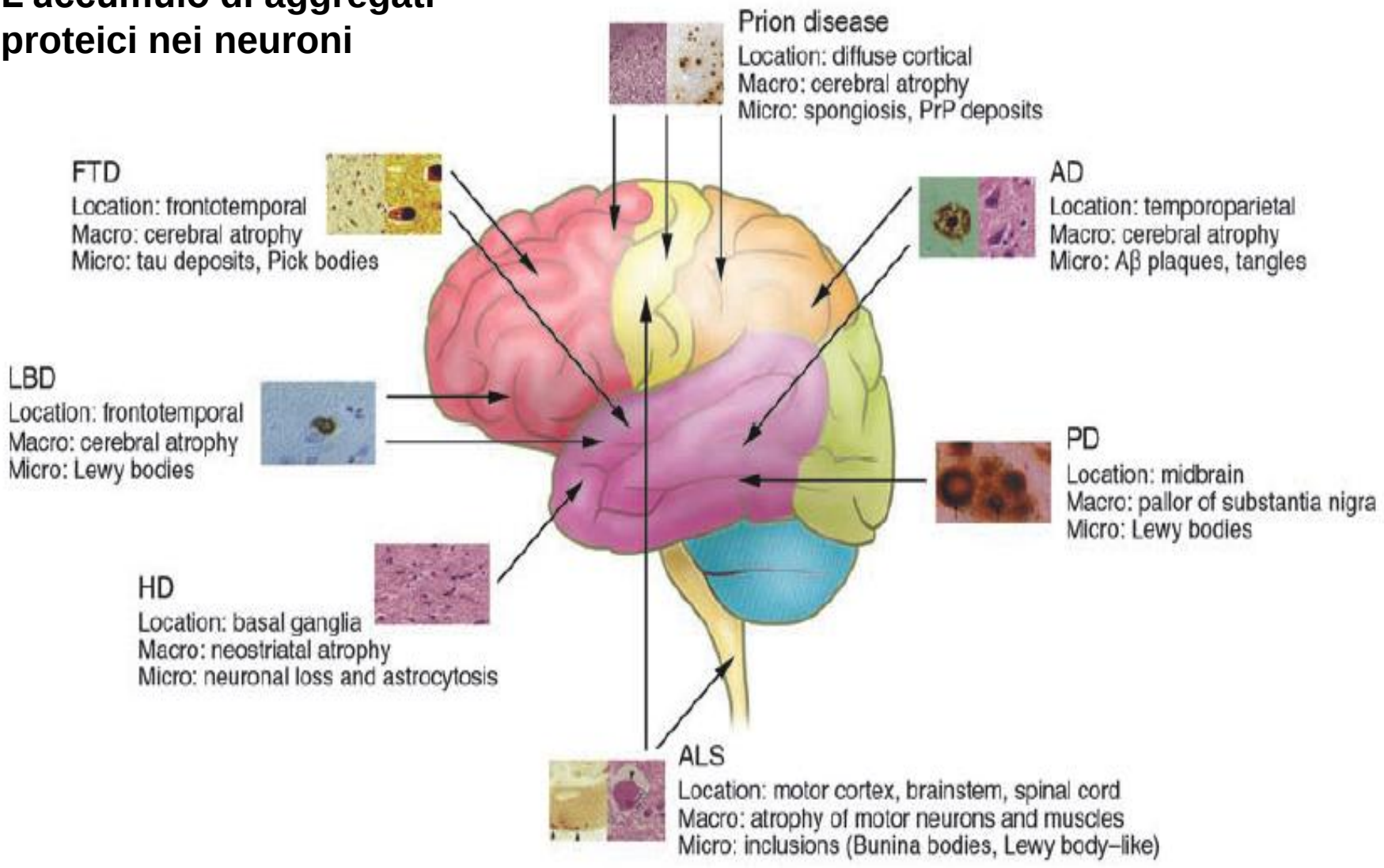


Quali i meccanismi che stanno alla base delle malattie neurodegenerative ?



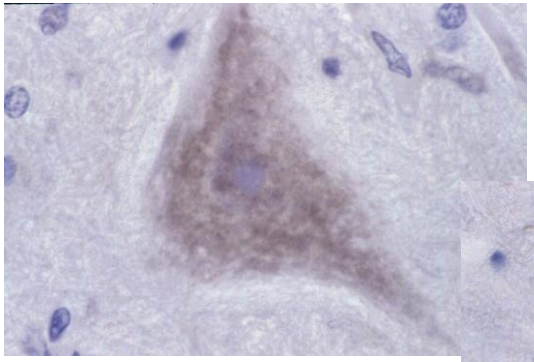
Quali i meccanismi che stanno alla base delle malattie neurodegenerative ?

L'accumulo di aggregati proteici nei neuroni

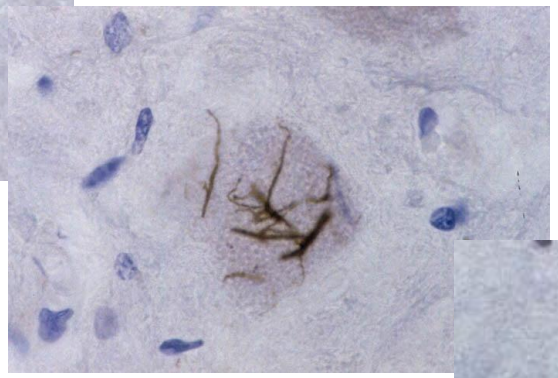


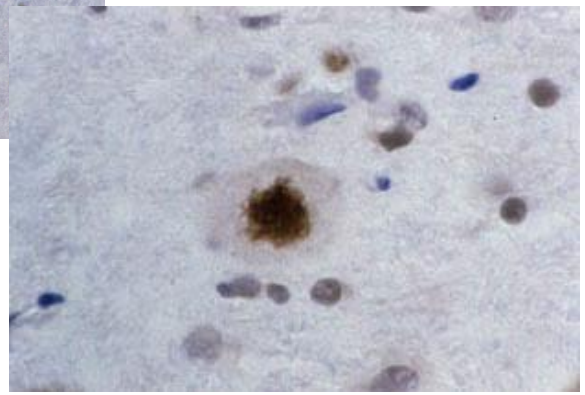
Le proteine si accumulano in modo anomalo nei neuroni e formano degli aggregati

Motoneurone controllo

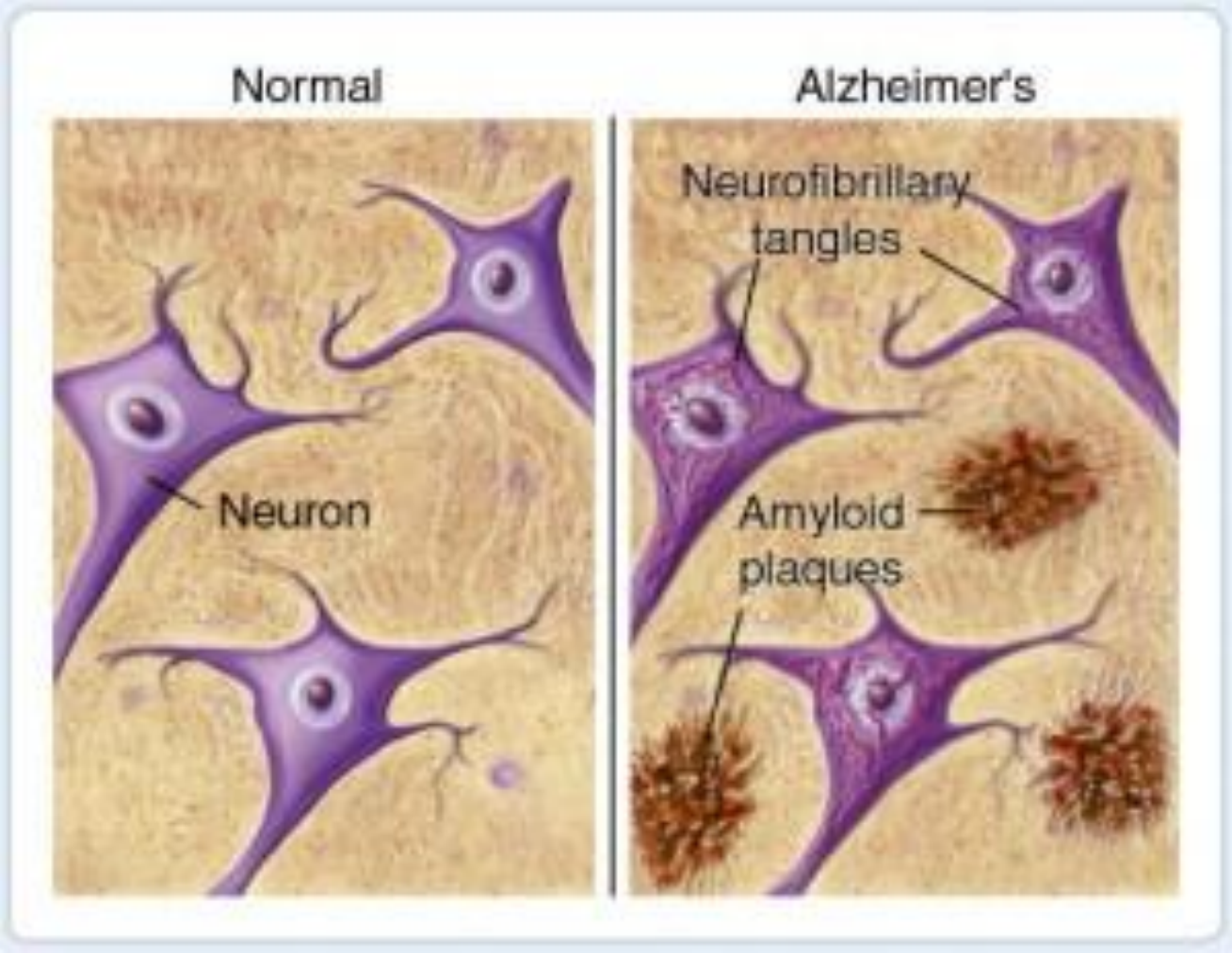


Motoneuroni di pazienti SLA





Le proteine si accumulano in modo anomalo anche esternamente ai neuroni e formano degli addensamenti proteici chiamati placche



Quali sono le risposte di difesa del cervello e del midollo spinale ai meccanismi che scatenano il danno neuronale?

- **gli spazzini delle cellule**
- **la plasticità neuronale e sinaptica**
- **il sistema immunitario**

Quali sono le risposte di difesa del cervello e del midollo spinale ai meccanismi che scatenano il danno neuronale?

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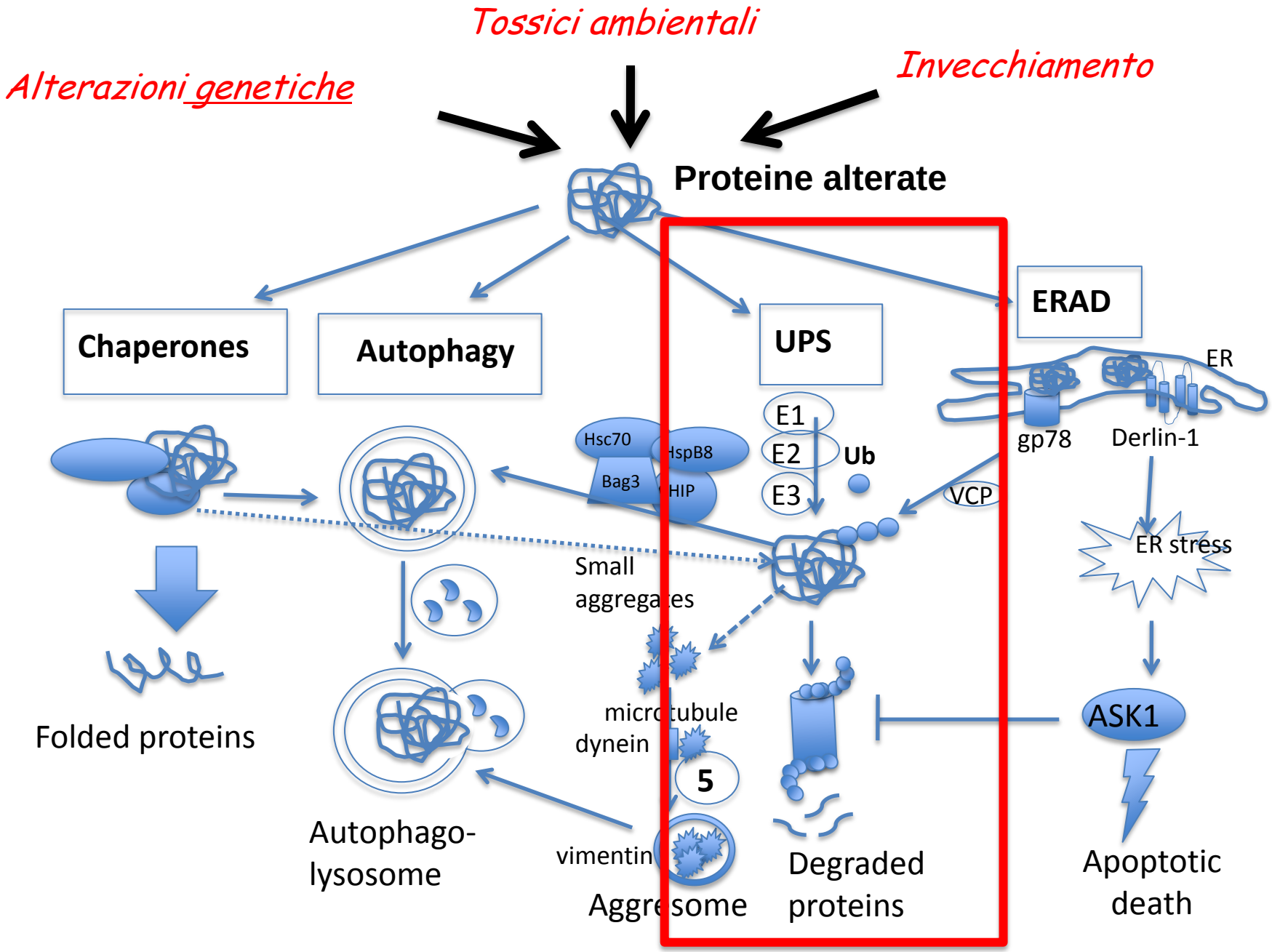
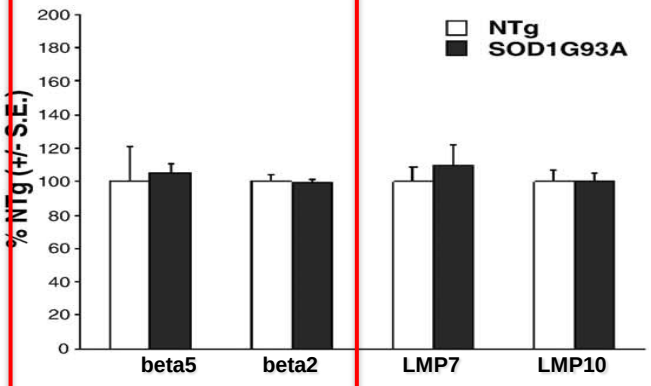
Gli “spazzini” dei neuroni

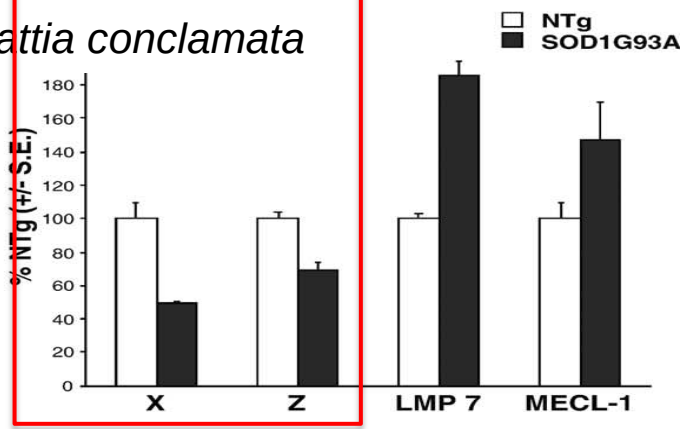


Diminuzione del proteasoma nei motoneuroni di topi con la SLA

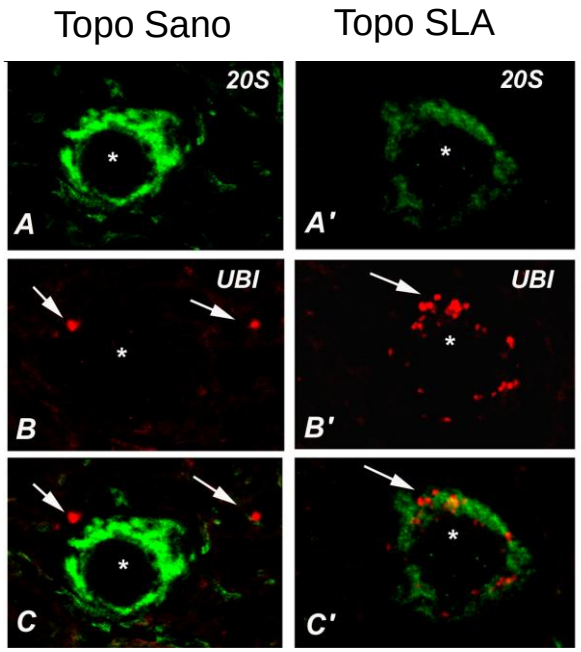
Prima della malattia



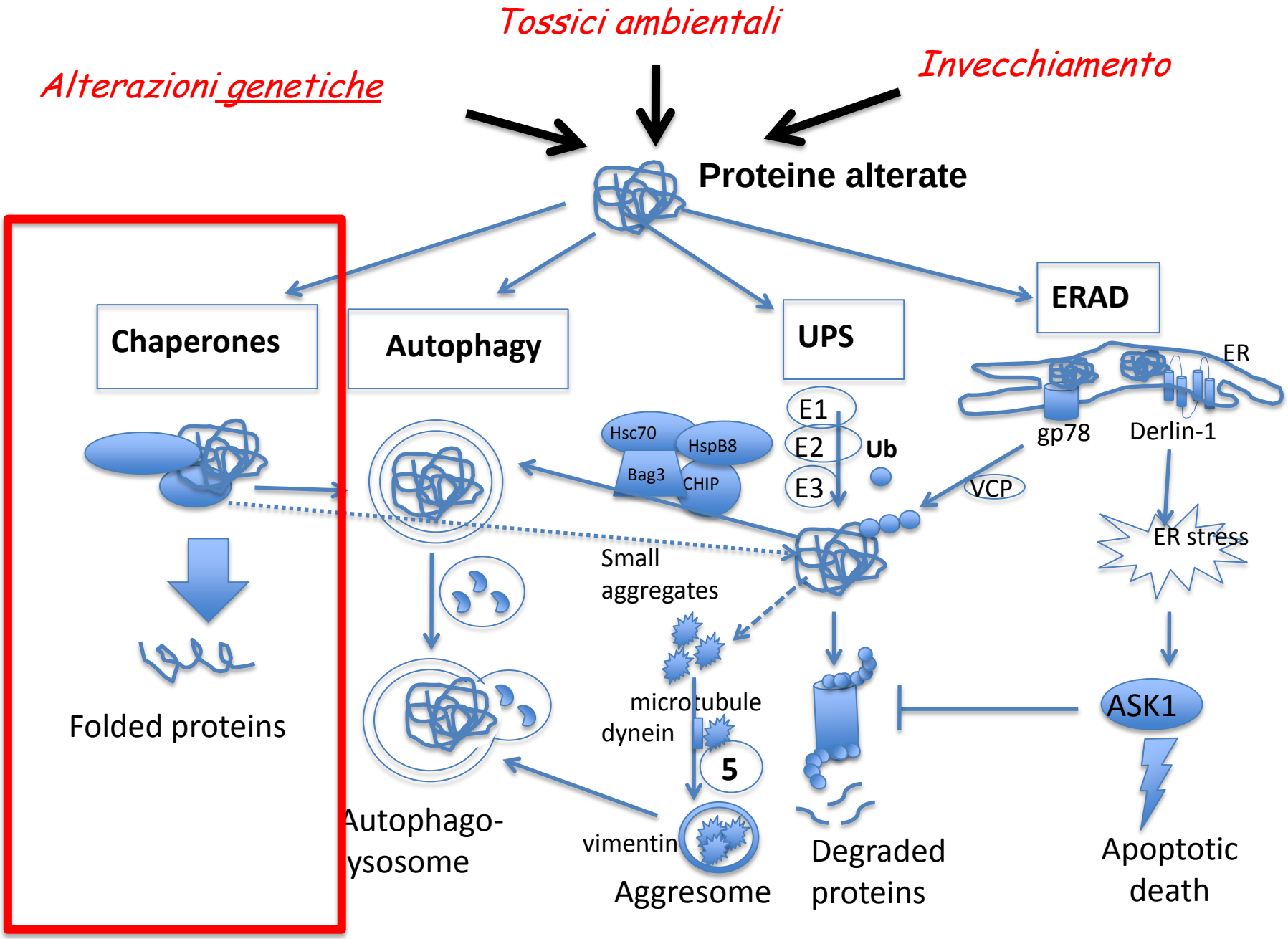
Malattia conclamata



Motoneuroni

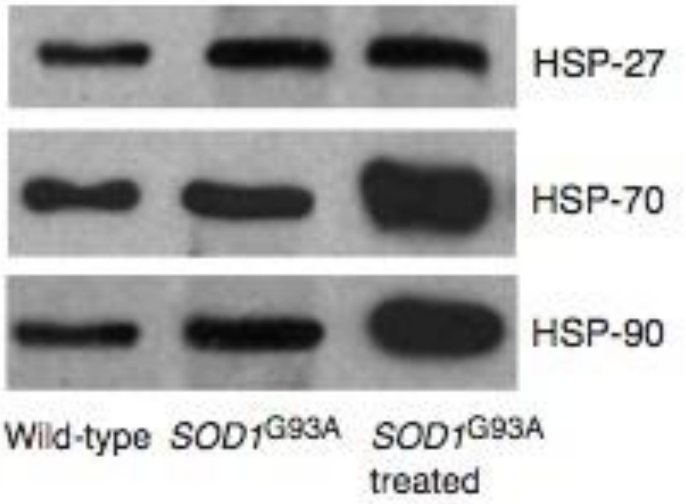


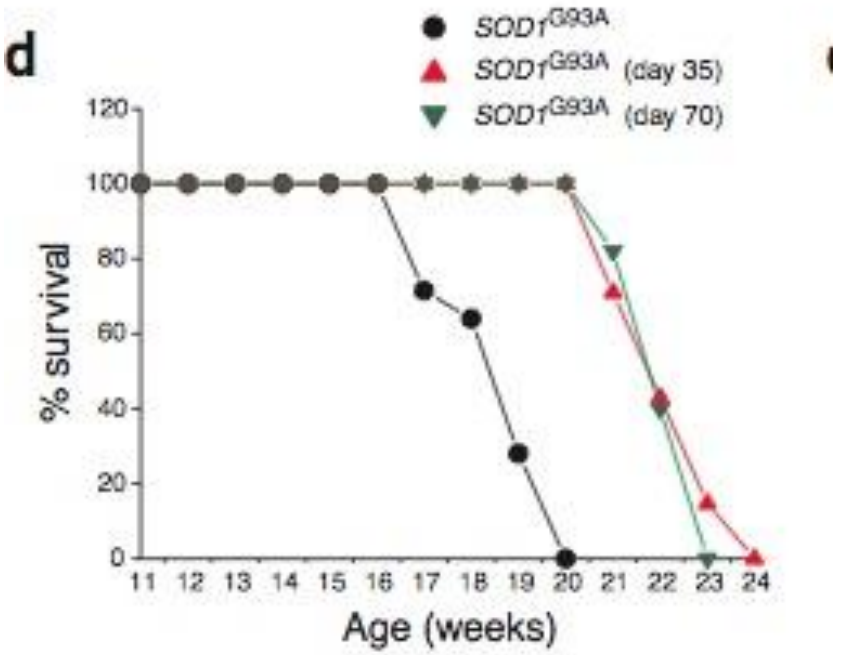
Gli “spazzini” dei neuroni



Quando gli “ spazzini” sono attivati i topi vivono di più

Livelli di Chaperones





Phase II/III Randomized, Placebo-controlled Trial of Arimoclomol in SOD1 Positive Familial Amyotrophic Lateral Sclerosis

Emory University, Atlanta, USA

Quali sono le risposte di difesa del cervello e del midollo spinale ai meccanismi che scatenano il danno neuronale?

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- **la plasticità neurale e sinaptica**
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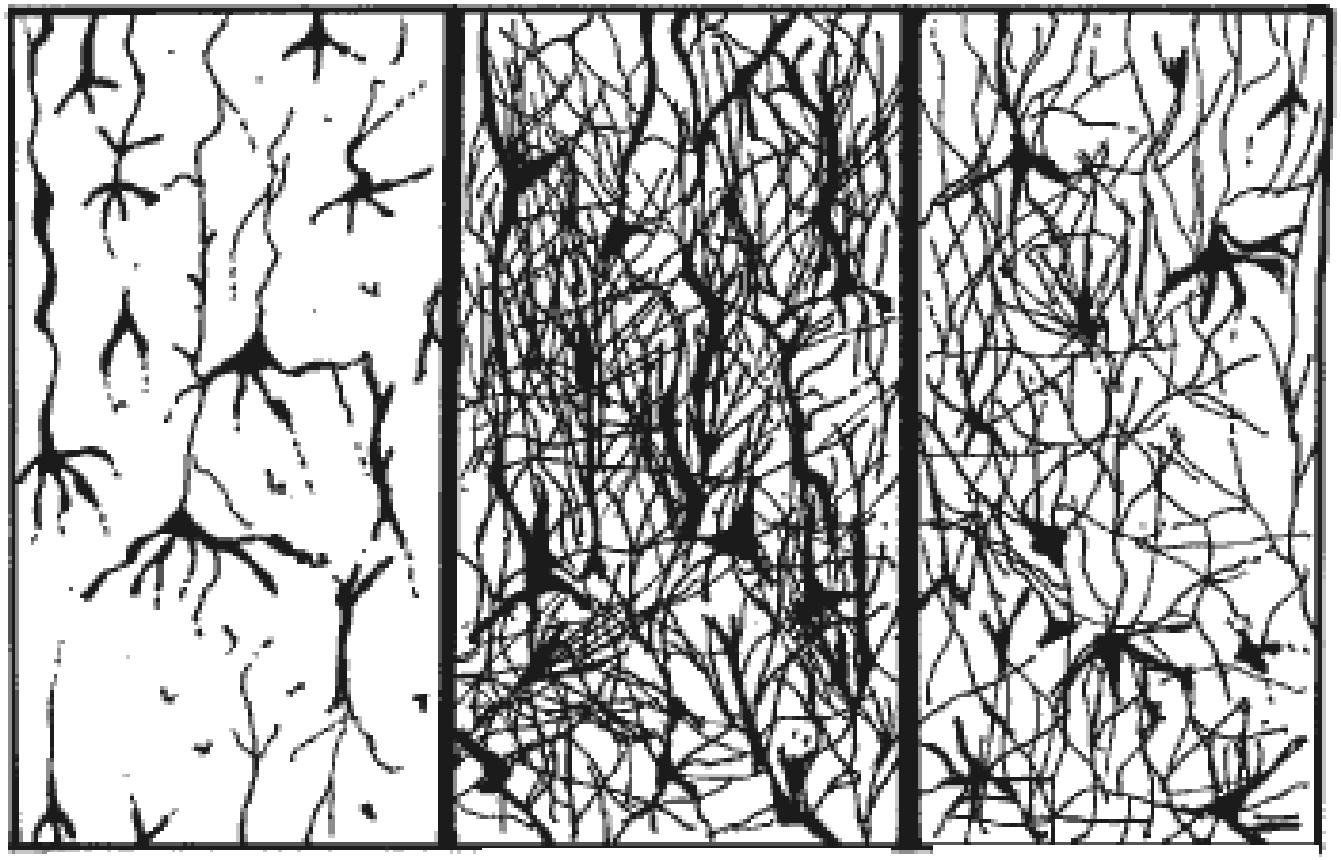
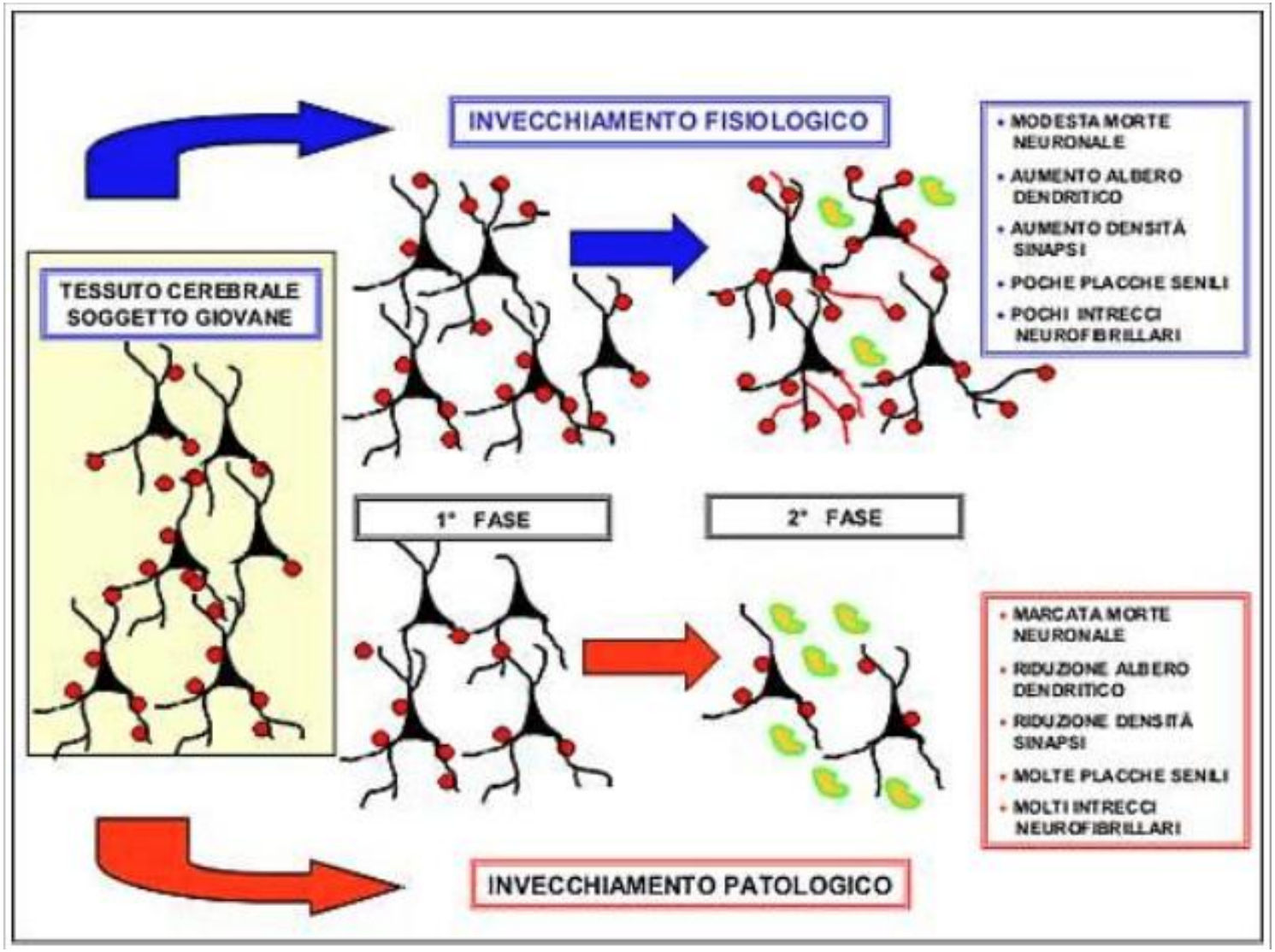
La plasticità neurale durante lo sviluppo

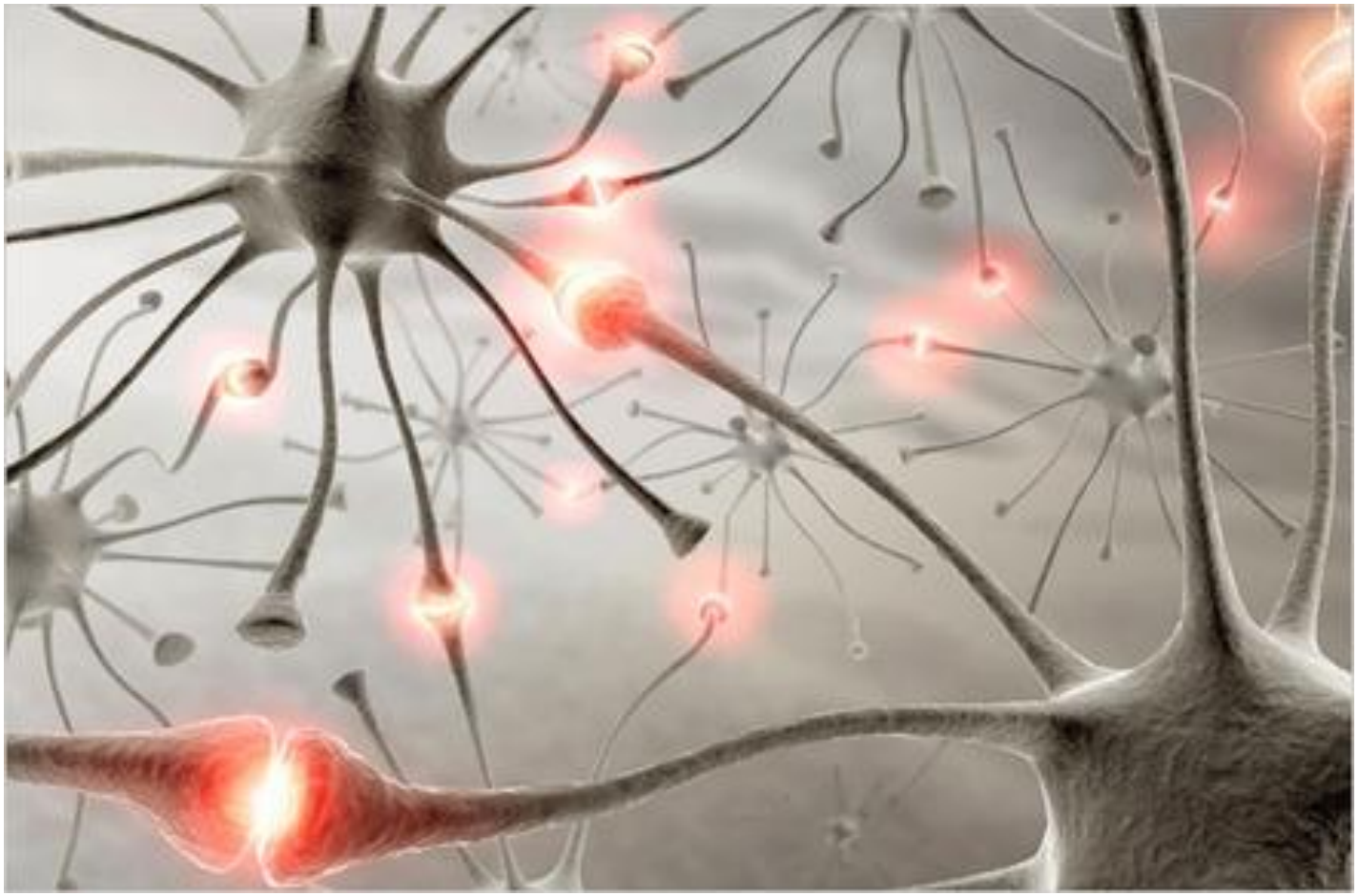


Alla nascita **Età 7 anni** **Età 15 anni**

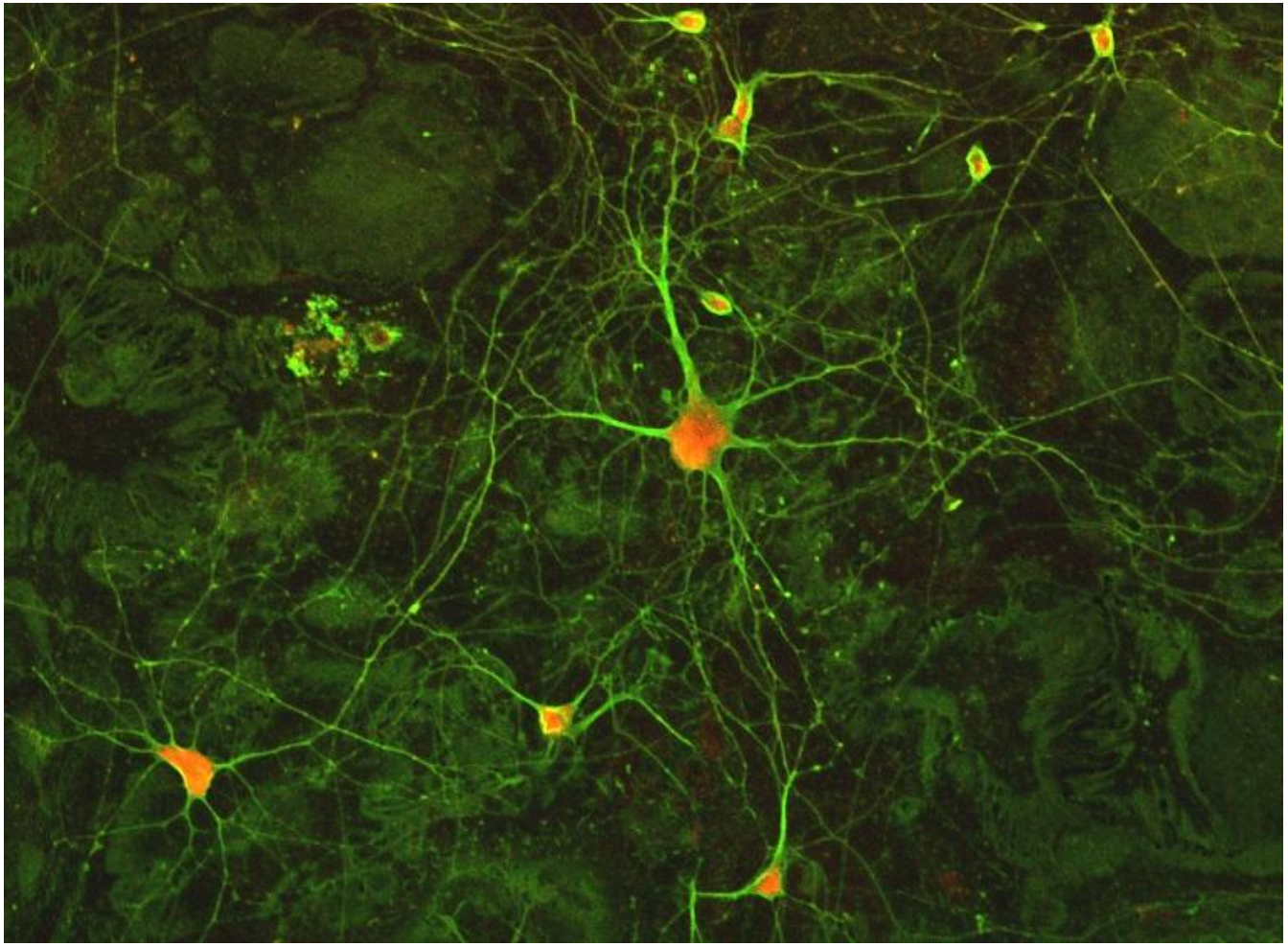
La plasticità neurale durante l'invecchiamento e nella malattia



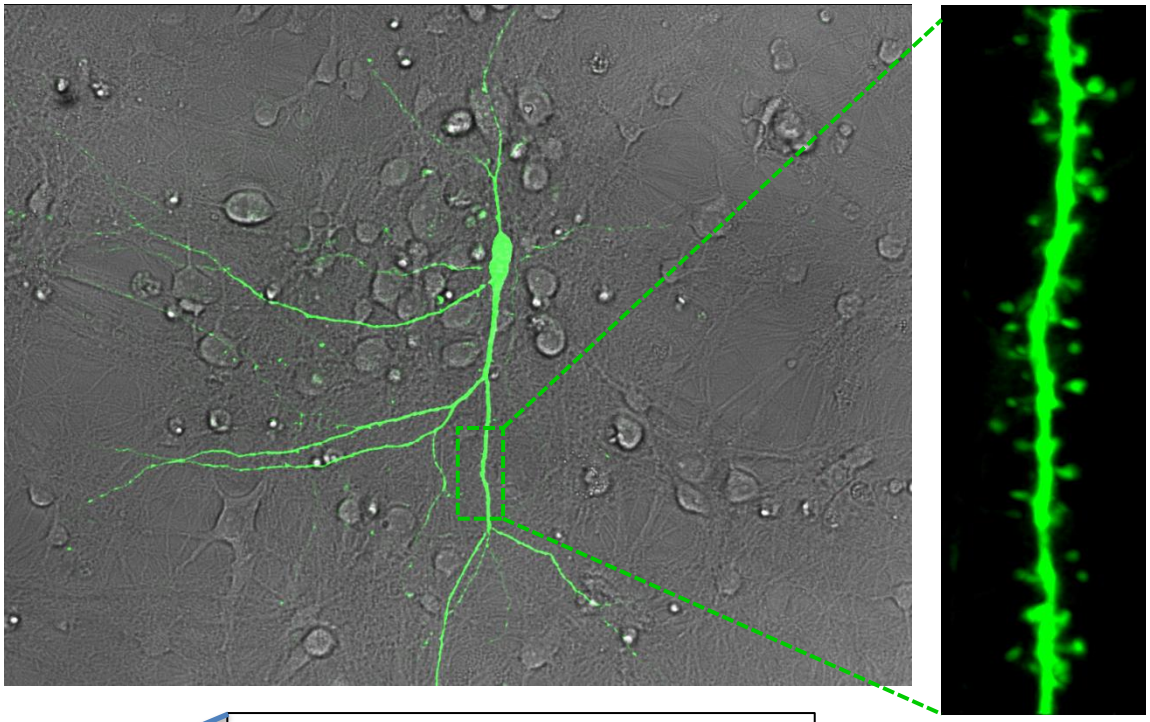
La sinapsi: la fantasia



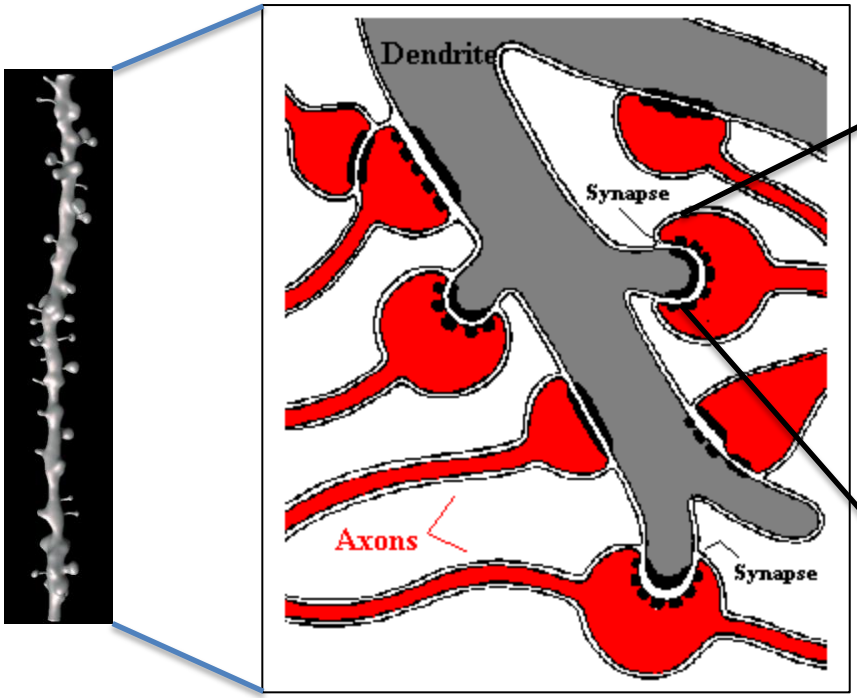
La sinapsi: la realtà

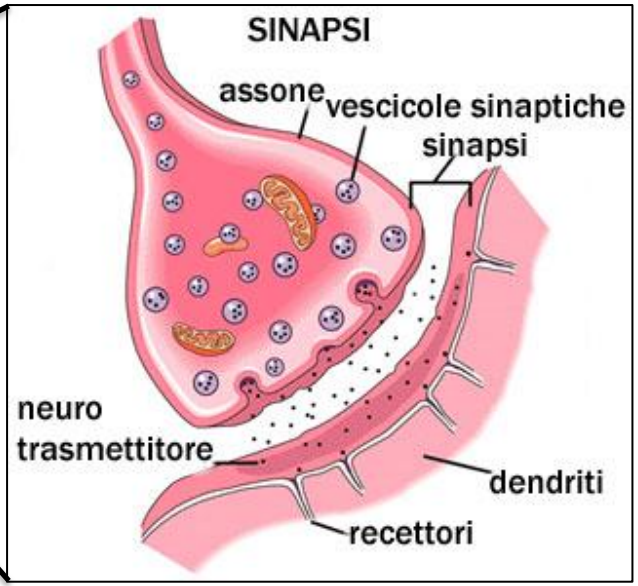


Motoneuroni di topo in coltura

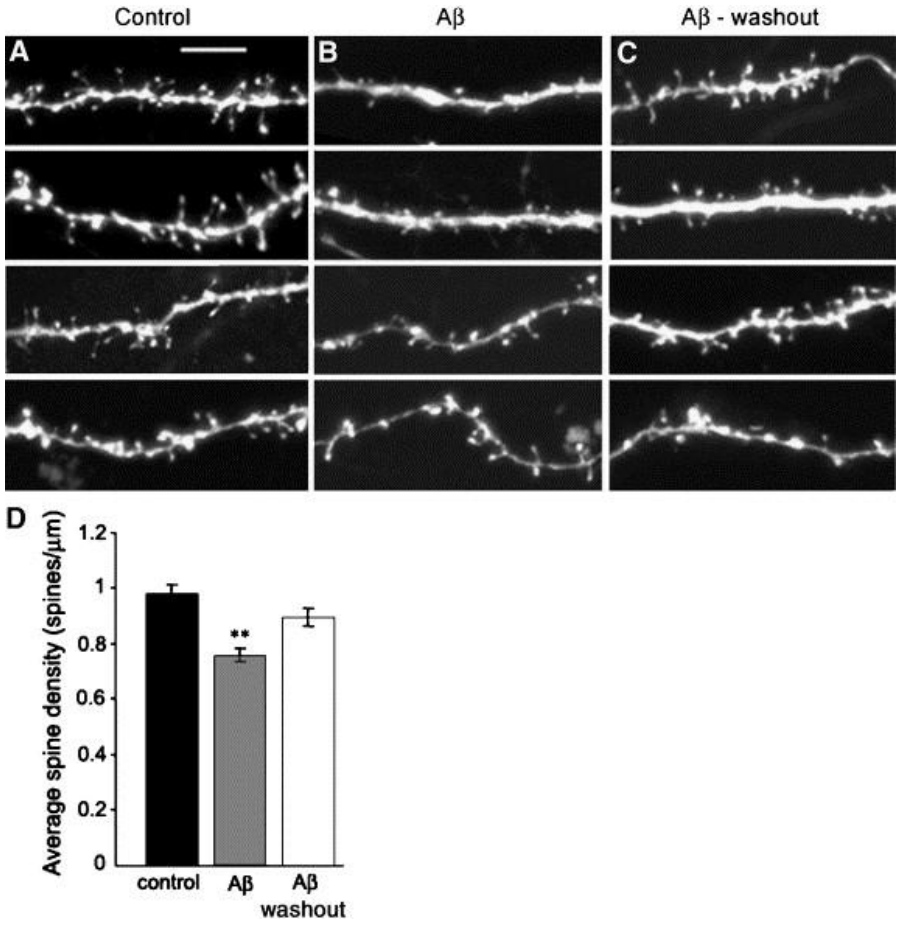


Spine dendritiche di un neurone di ippocampo in coltura

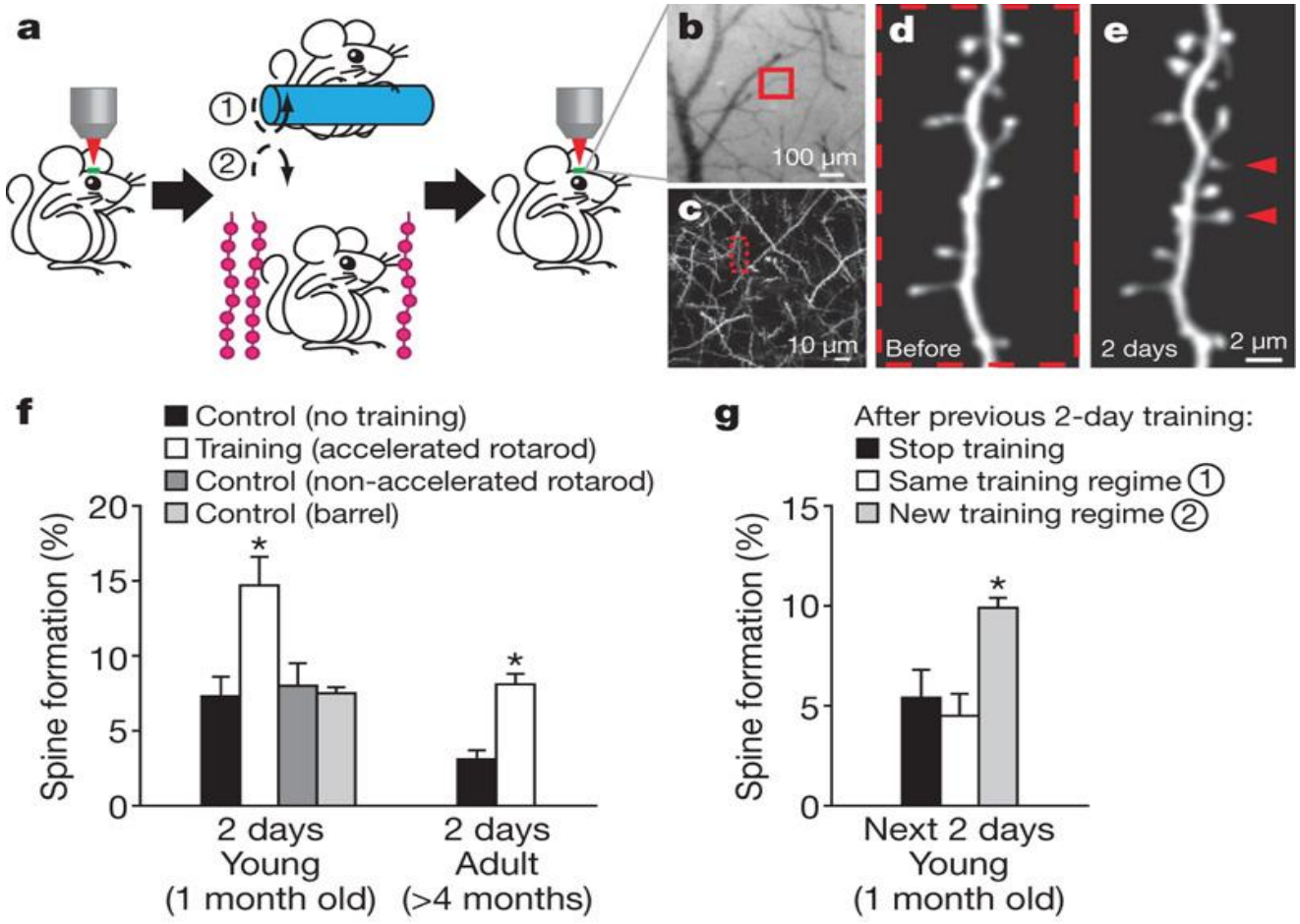




L’amiloide beta che forma le placche riduce il numero di spine dendritiche



L’apprendimento e l’esercizio fisico aumentano le spine dendritiche



L’attività fisica è associata con un ridotto rischio di Alzheimer

Total daily physical activity and the risk of AD and cognitive decline in older adults

A.S. Buchman, MD
P.A. Boyle, PhD
L. Yu, PhD
R.C. Shah, MD
R.S. Wilson, PhD
D.A. Bennett, MD

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ABSTRACT

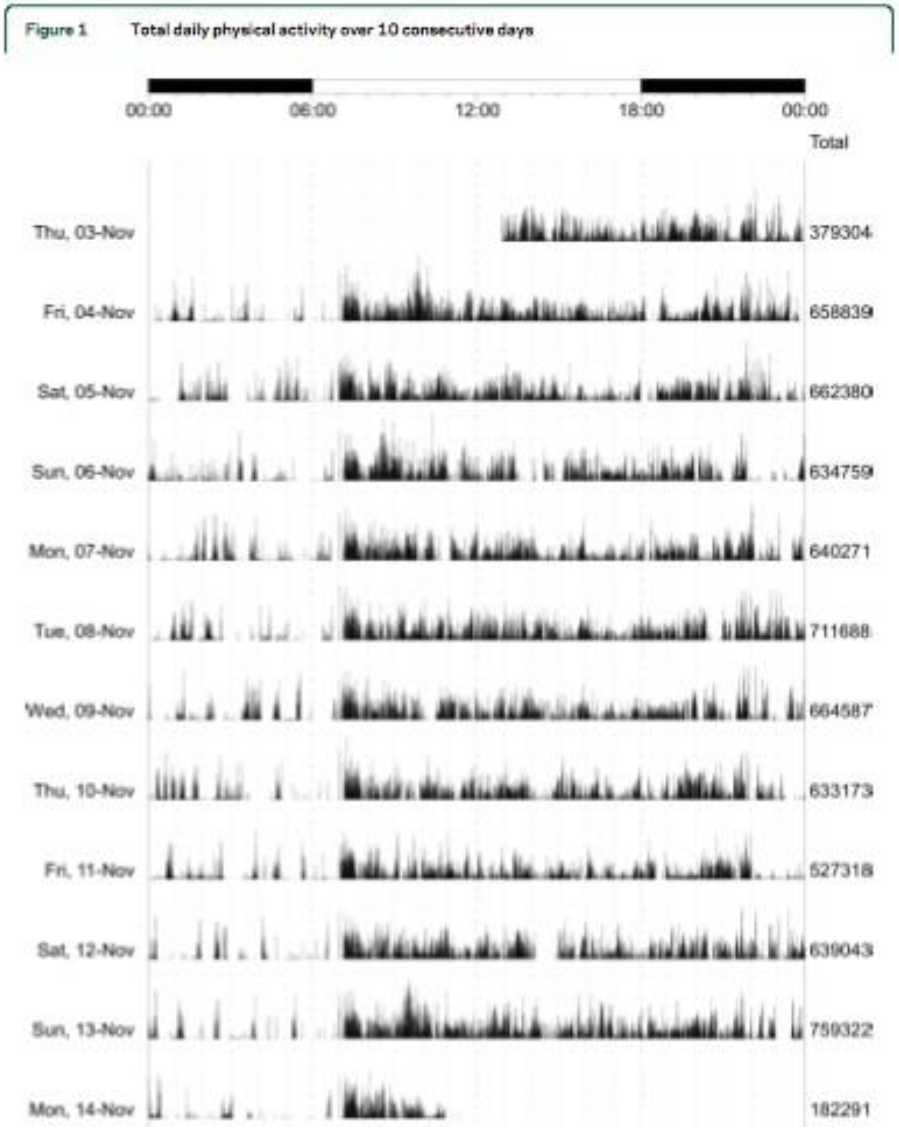
Objective: Studies examining the link between objective measures of total daily physical activity and incident Alzheimer disease (AD) are lacking. We tested the hypothesis that an objective measure of total daily physical activity predicts incident AD and cognitive decline.

Methods: Total daily exercise and nonexercise physical activity was measured continuously for up to 10 days with actigraphy (Actical®; Philips Healthcare, Bend, OR) from 716 older individuals without dementia participating in the Rush Memory and Aging Project, a prospective, observational cohort study. All participants underwent structured annual clinical examination including a battery of 19 cognitive tests.

Results: During an average follow-up of about 4 years, 71 subjects developed clinical AD. In a Cox proportional hazards model adjusting for age, sex, and education, total daily physical activity was associated with incident AD (hazard ratio = 0.477; 95% confidence interval 0.273–0.832). The association remained after adjusting for self-report physical, social, and cognitive activities, as well as current level of motor function, depressive symptoms, chronic health conditions, and *APOE* allele status. In a linear mixed-effect model, the level of total daily physical activity was associated with the rate of global cognitive decline (estimate 0.033, SE 0.012, $p = 0.007$).

Conclusions: A higher level of total daily physical activity is associated with a reduced risk of AD. ***Neurology*® 2012;78:1323–1329**

L’attività fisica è associata con un ridotto rischio di Alzheimer



Attività :
- Camminare
- Giardinaggio
- Bicicletta
- Nuoto
- Acqua gymn

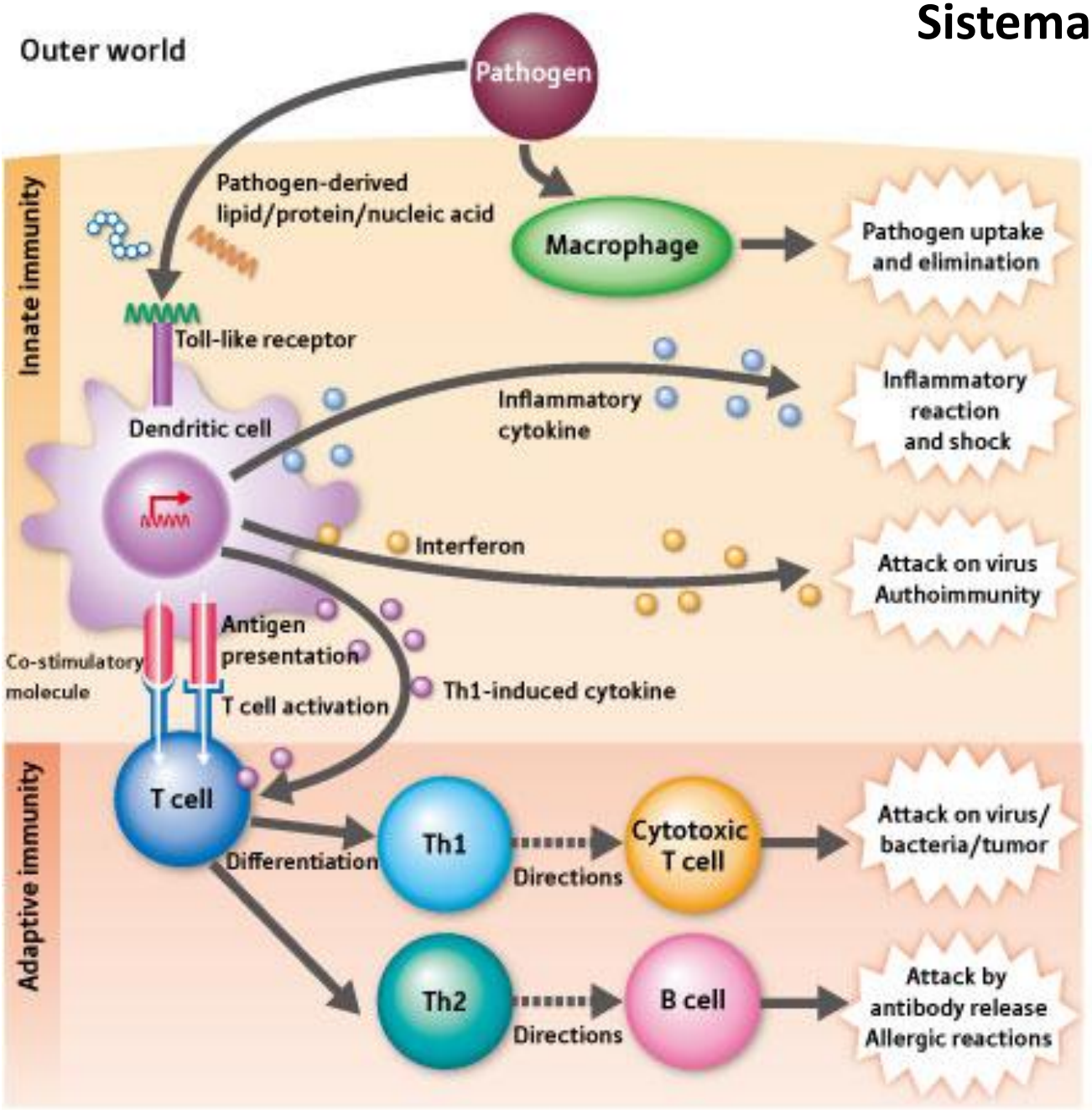
- Interazioni sociali

- Stimoli cognitivi

Quali sono le risposte di difesa del cervello e del midollo spinale ai meccanismi che scatenano il danno neuronale?

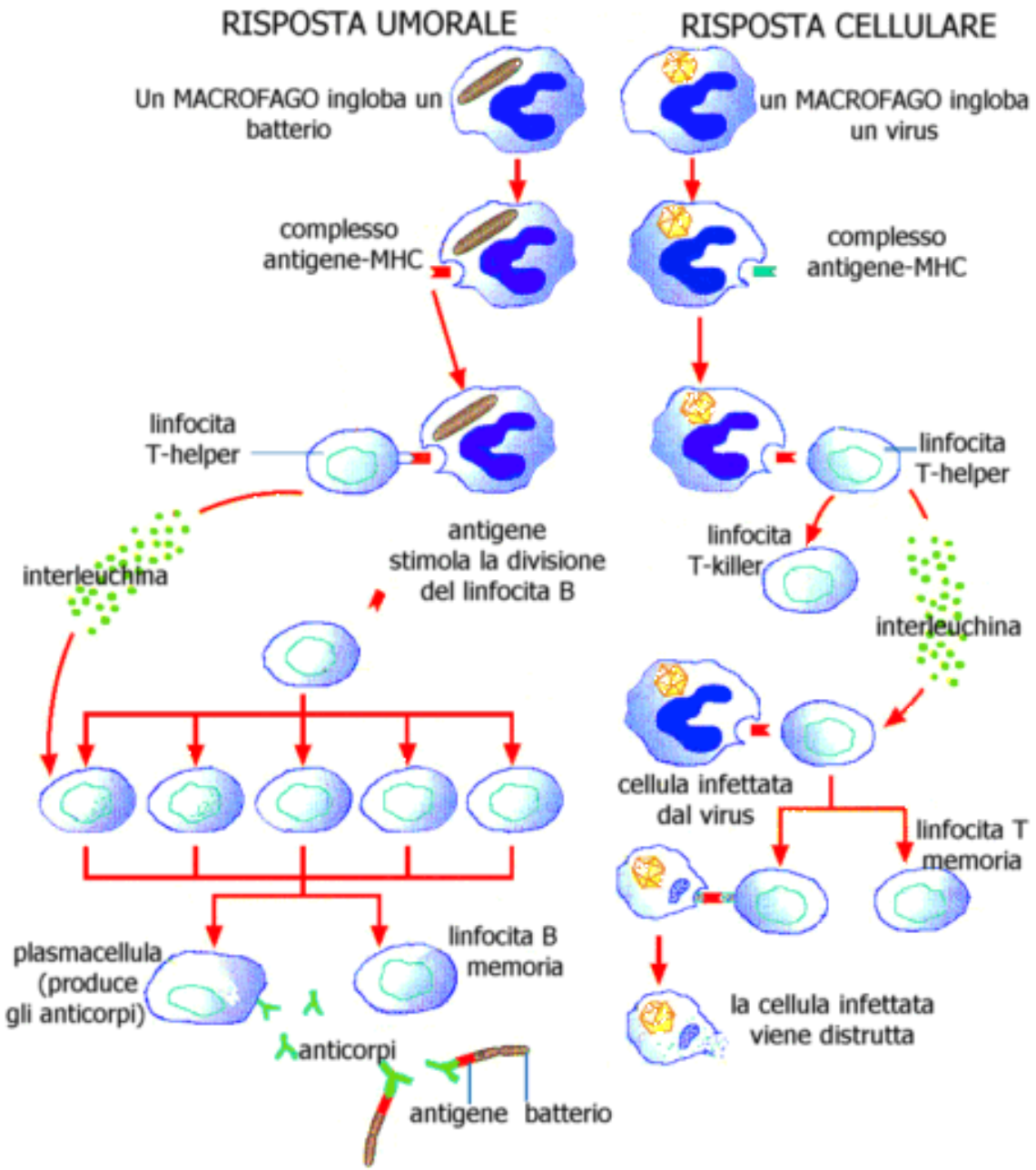
- gli spazzini delle cellule
- la plasticità neurale e sinaptica
- il sistema immunitario

Sistema Immunitario



Immunità innata (aspecifica)
prima linea di difesa, pone l'organismo in stato di allarme

Immunità adattativa (specifica)
risposta difensiva più potente e mirata in grado di riconoscere qualunque forma di antigene, ma più lenta

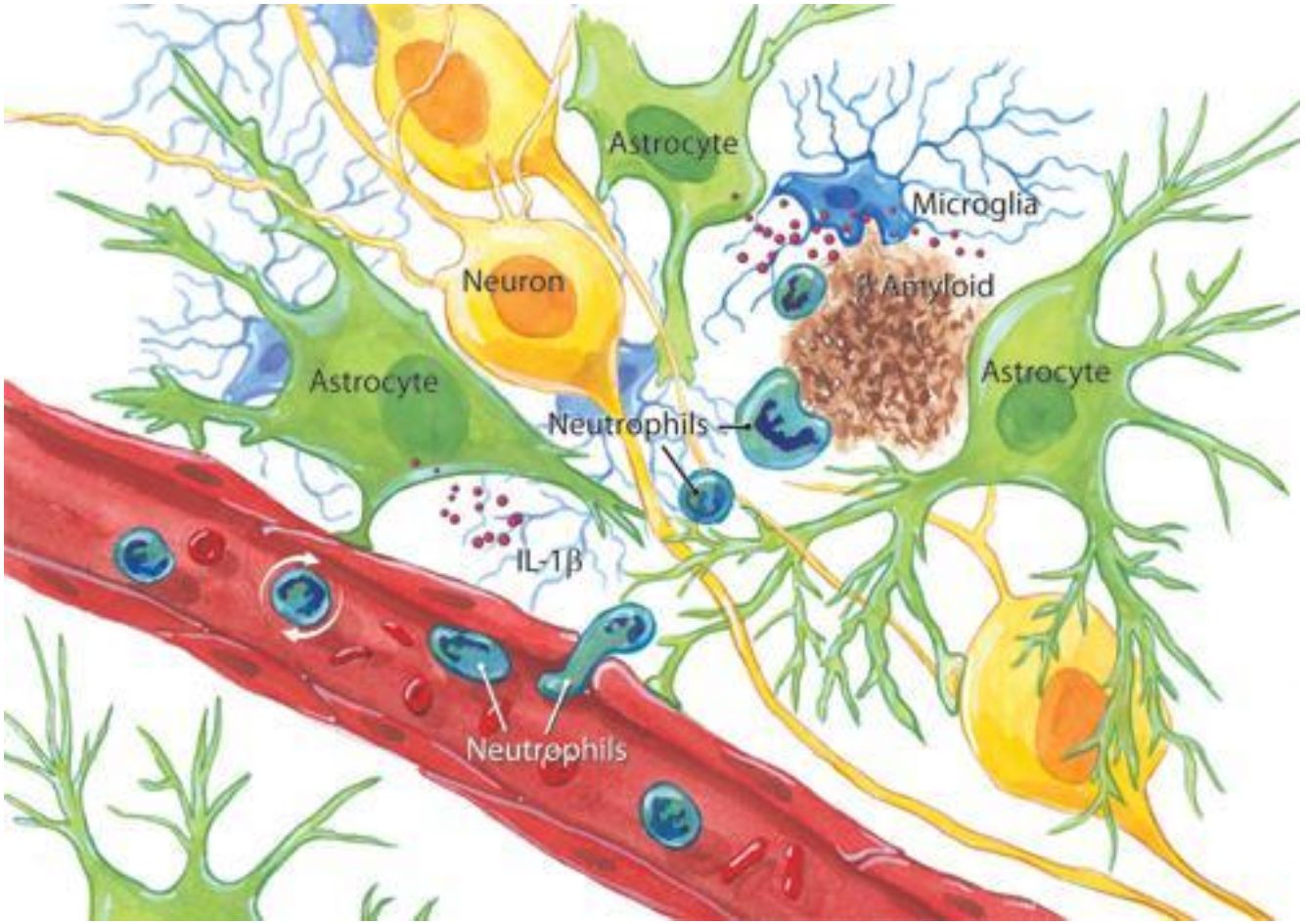


Risposta immunitaria specifica

Organi coinvolti:

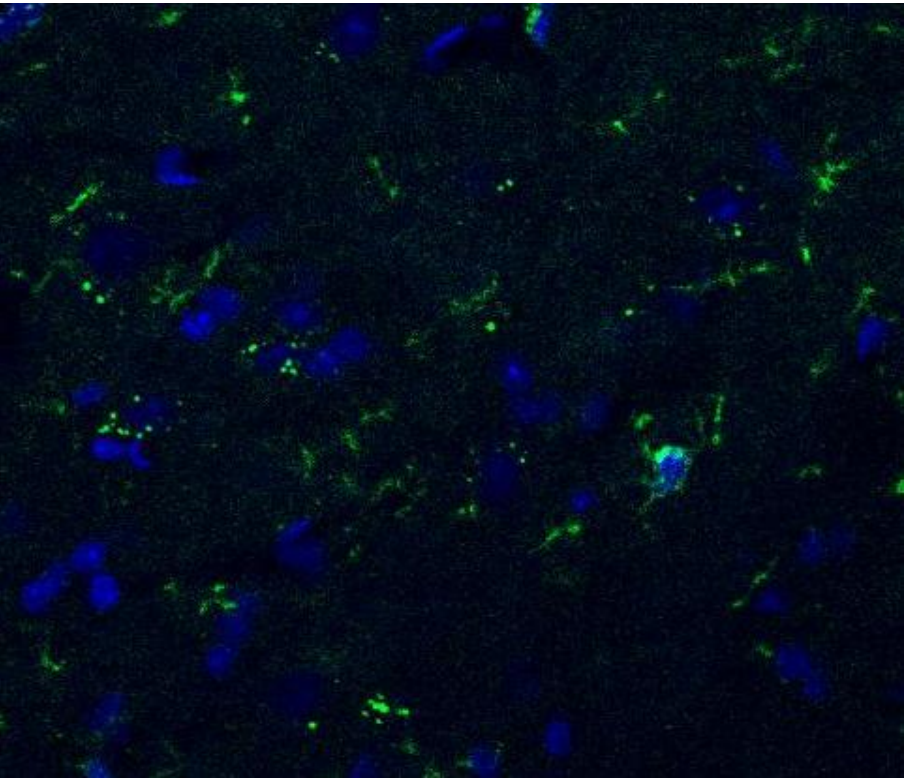
- Tonsille,
- Linfonodi,
- Timo,
- Milza,
- Midollo osseo

La microglia è la cellula immunitaria del SNC

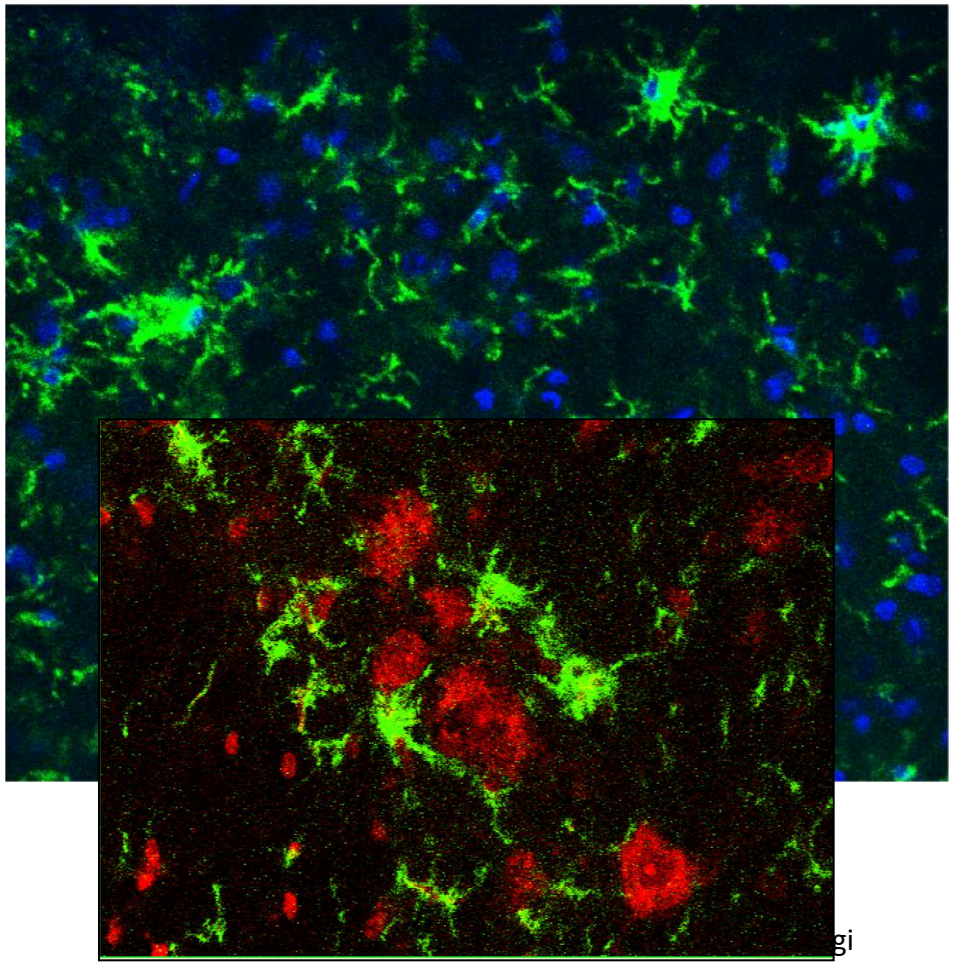


La microglia vista al microscopio

Non transgenico



Topo SLA

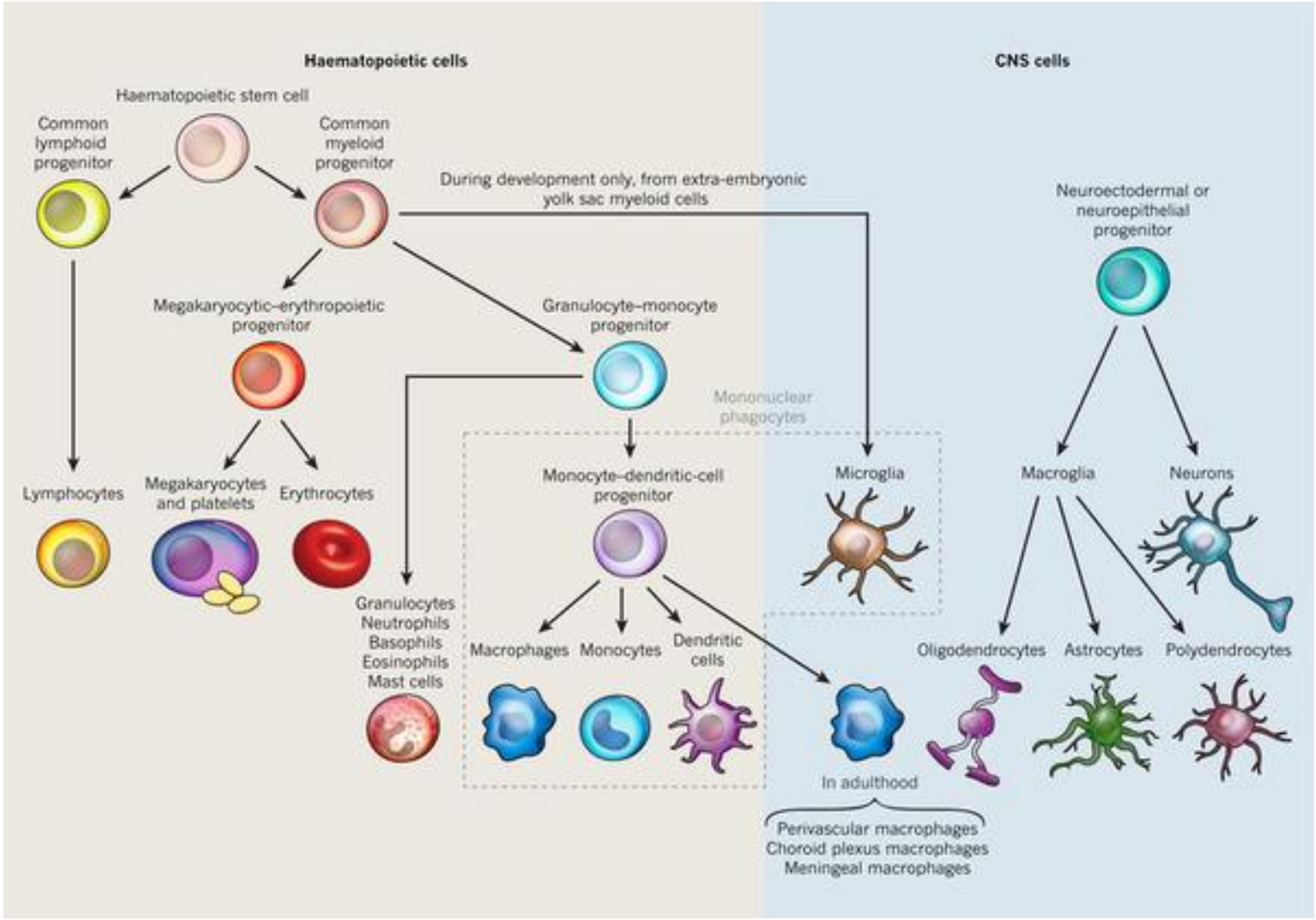


Midollo spinale Corna ventrali
40x

gi

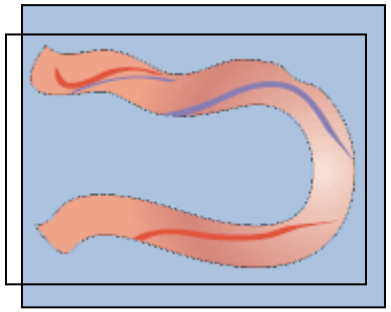
DAPI nucleo cellulare

La microglia deriva anche dalle cellule staminali del midollo osseo

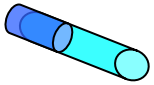


Ransohoff and Cardona, Nature 2010

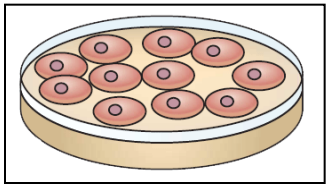
Cordone ombelicale umano



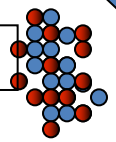
Marcatura delle cellule con sostanza flurescente blu

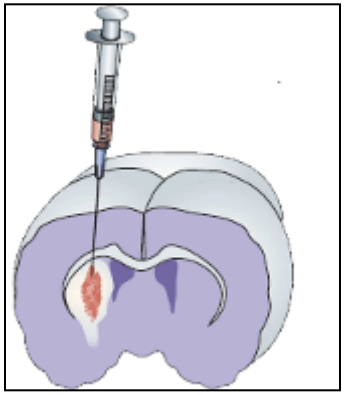


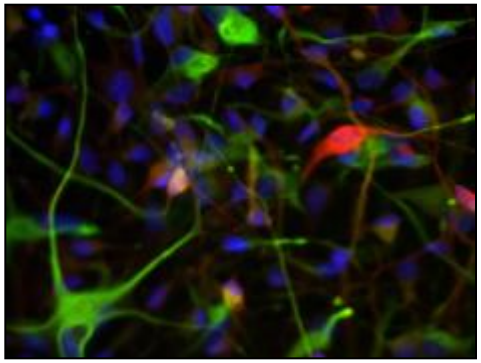
Cellule iniettate ICV in topi SOD1 e wobbler trattati con ciclosporina



Cellule staminali





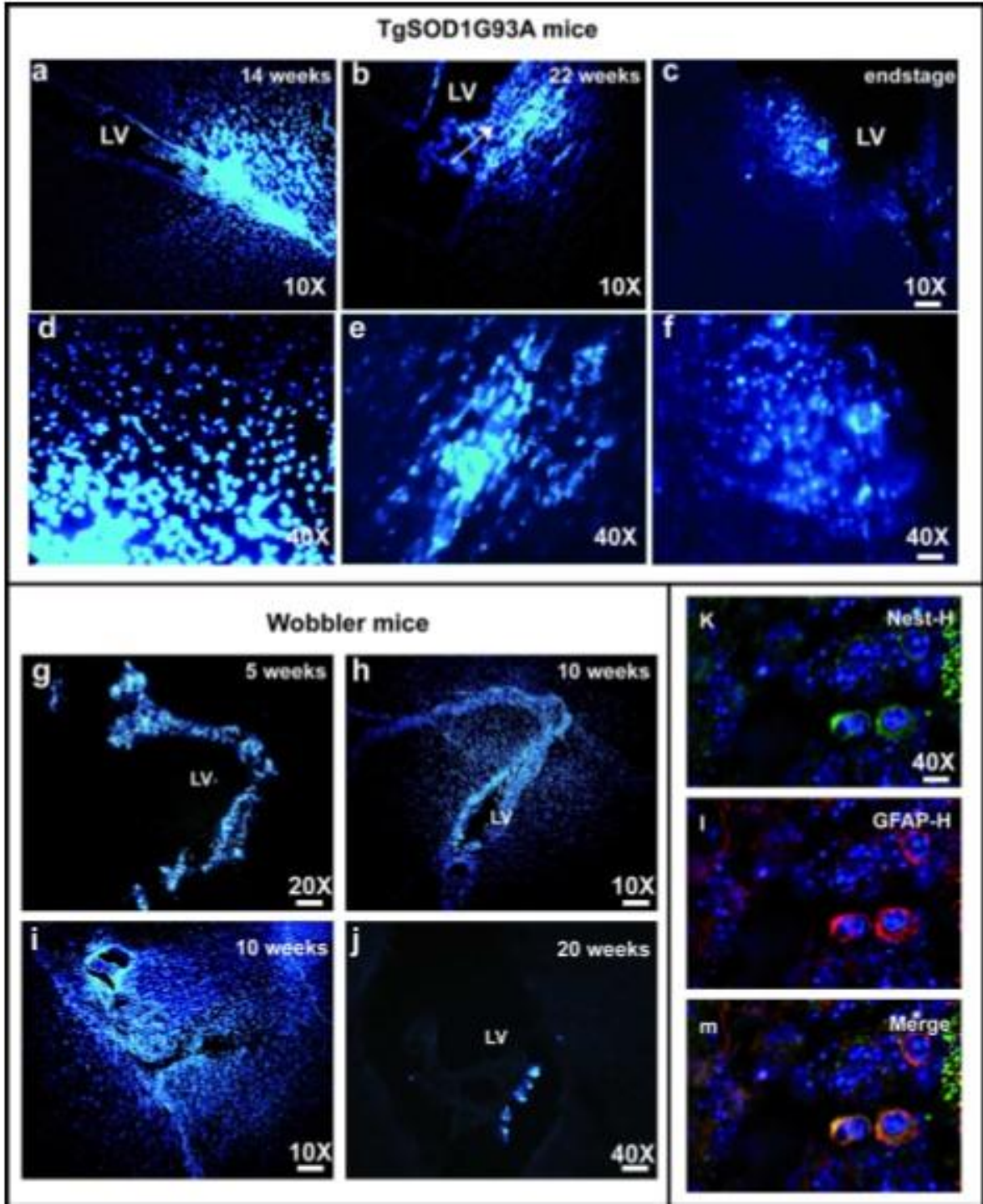


Espressione e rilasscio di citochine e fattori neurotrofici

•comportamento motorio
•Sopravvivenza
•istopatologia

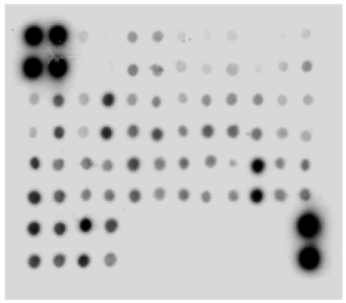
Differenziamento delle cellule

Le cellule staminali ombelicali rrimangono nel sito di iniezione e diminuiscono nel corso della patologia nei topi SOD e wobbler.
Inoltre non si trasformano in neuroni o astrociti

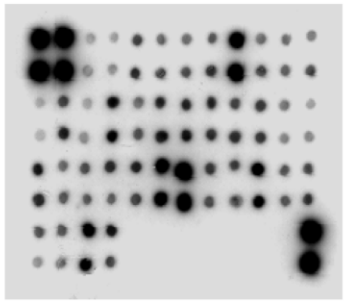


Le cellule staminali ombelicali rilasciano numerosi fattori neurotrofici

A



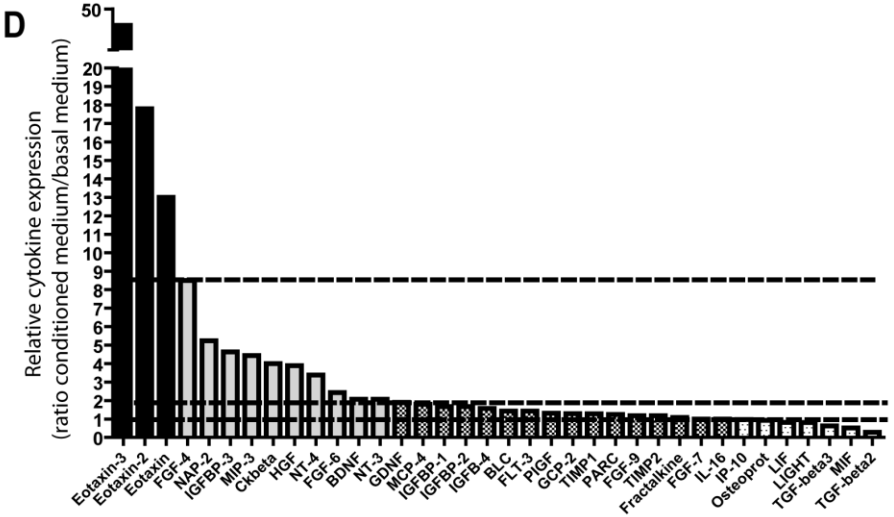
B



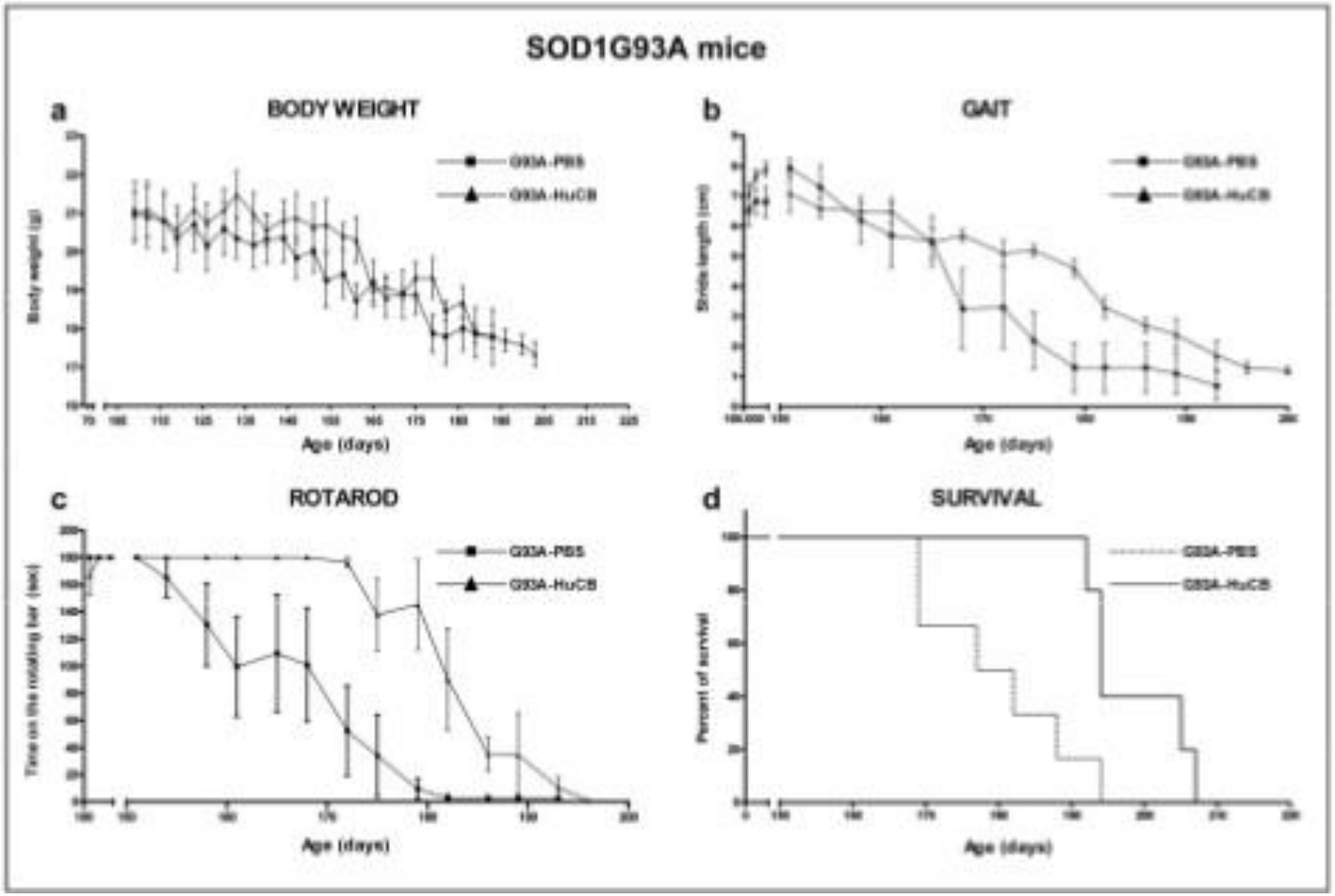
C

POS	POS	NEG	NEG	BDNF	BLC	Ckbeta 3-1	Eotaxin	Eotaxin-2	Eotaxin-3	FGF-4
POS	POS	NEG	NEG	BDNF	BLC	Ckbeta 3-1	Eotaxin	Eotaxin-2	Eotaxin-3	FGF-4
FGF-7	FGF-9	Flt-3 ligand	Fractalkine	GCP-2	GDNF	HGF	IGFBP-1	IGFBP-2	IGFBP-3	IGFBP-4
FGF-7	FGF-9	Flt-3 ligand	Fractalkine	GCP-2	GDNF	HGF	IGFBP-1	IGFBP-2	IGFBP-3	IGFBP-4
IP-10	LIF	LIGHT	MCP-4	MIF	MIP-3alpha	NAP-2	NT-3	NT-4	Oste protegenin	PARC
IP-10	LIF	LIGHT	MCP-4	MIF	MIP-3alpha	NAP-2	NT-3	NT-4	Oste protegenin	PARC
TGF-beta2	TGF-beta3	TIMP-1	TIMP-2	Blank	Blank	Blank	Blank	Blank	Blank	Blank
TGF-beta2	TGF-beta3	TIMP-1	TIMP-2	Blank	Blank	Blank	Blank	Blank	Blank	Blank

D



Le cellule staminali ombelicali migliorano il deficit motorio e aumentano la sopravvivenza dei topi SLA



Obiettivi futuri per migliorare la difesa del nostro Sistema Nervoso Centrale

- Attivare “i sistemi di pulizia” dei neuroni in modo più efficace e specifico

- Migliorare la plasticità sinaptica anche attraverso un buon esecizio fisico

- Migliorare le condizioni per una maggior efficacia delle cellule staminali ematopietiche