IMMUNOSENESCENCE AND STROKE

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Background

- 65+ - 30% of the total population by 2030. (Japan)
- 2050. most of the world – Africa and Middle East
- >20% 65+ = SUPERAGED SOCIETY
- 65+ - 27.4% of the total population by 2025. Croatia
- 2002 – life expectancy 78.6 y F, 71.0 M
- further increase in the expected life expectancy

http://croatia.eu

Aging and breakdown of BBB

Aging → BBB dysfunction – hypertension, seizure, stroke
- ↑ inflammatory cytokines and free radicals
- extravasation of plasma proteins into the brain → neuroinflammatory responses

Aging → BBB/blood-cerebrospinal fluid barrier degeneration → ↑ albumin, fibrinogen, IgG (Alzheimer’s disease)

12 h after ischemic stroke→ several weeks

“Stroke – induced immunodeficiency syndrome”
- ↓ T cells and other immune cells (spleen, thymus and lymph nodes)
- hyperactivity of the sympathetic nervous system (SNS) and hypothalamic-pituitary-adrenal axis (HPA)
- ↑ apoptosis of immune cells
- secondary lymphatic organs atrophy
- shift from the production of cytokine TH1 to Th2
- infectious complications after stroke → worse outcomes

“SNS-mediated stroke-induced immunodepression” → post-stroke infections

PANTHERIS (Preventive Antibacterial Treatment in Acute Stroke)
post hoc analysis – the impact of distinct lesion patterns on SNS activation, immunodepression and frequency of post-stroke infections

impaired immune function / higher susceptibility to post-stroke infections:
- large stroke volume – not independently associated
- regions of the MCA cortex – independent risk factor

SNS activation (↑ norepinefrin) – independent risk factor

circulating costimulatory cells
(splenic non-T cells - mice)

proinflammatory cytokine-mediated activation SNS + HPA

vagal cholinergic anti-inflammatory pathway
(acetylcholine + macrophages)

potential mediators and therapeutic targets of stroke-induced immunodepression

SNS-mediataed stroke-induced immunodepression

IMMUNOMODULATION THERAPY?

Results

Conclusions

age-standardized incidence, mortality, prevalence and DALYs/YLDs 1990 - 2015 ↓
- the absolute number of people affected by stroke ↑

POPULATION GROWTH AND AGING

THE GLOBAL STROKE BURDEN ↑
- geographical (country and regional) differences
- (low- and middle-income countries)
- the global burden of neurological disorders ↑
- policy makers and health-care providers