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Micronutrients & Co. for concussion

Scientific data, possibilities and limitations

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Pathophysiological cascades of TBI

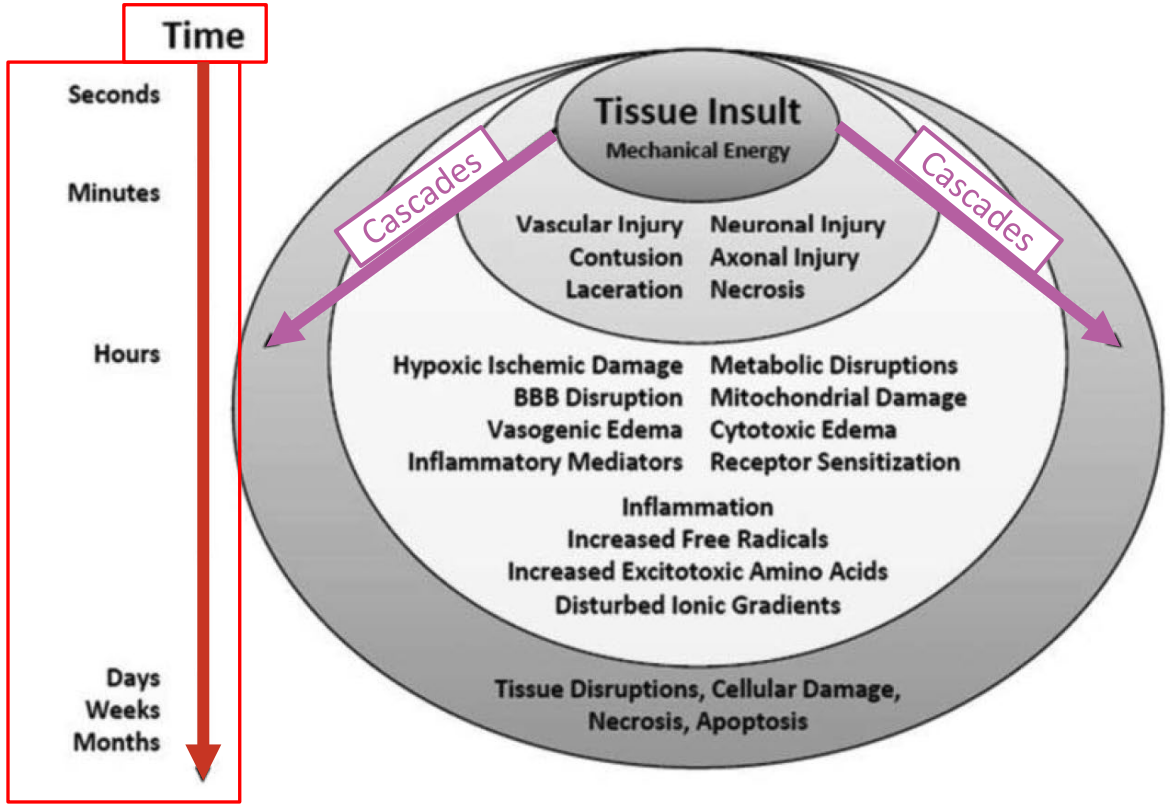


Fig. 1. The primary injury of TBI is caused by a transfer of mechanical injury to the brain tissue. This is followed by the secondary injury that occurs over minutes to hours to days and even weeks and months. It is characterized by numerous metabolic and biochemical cascades that may cause more damage than the initial tissue insult itself.

Adapted from Lewis MD et al.2019

Pathophysiology

↑Release of excitatory neurotransmitters

Disruption Blood-Brain Barrier

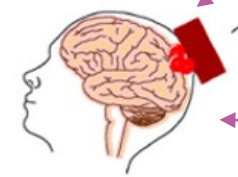
Cerebral electrolyte imbalance

Mitochondrial dysfunction

↓Cerebral blood flow

Damage / cell death neuronal cells

Insulin resistance



↑ Excitotoxicity
Apoptotic cell death

↑ Energy requirements
↓ Energy production
→ "Energy crisis in the brain"

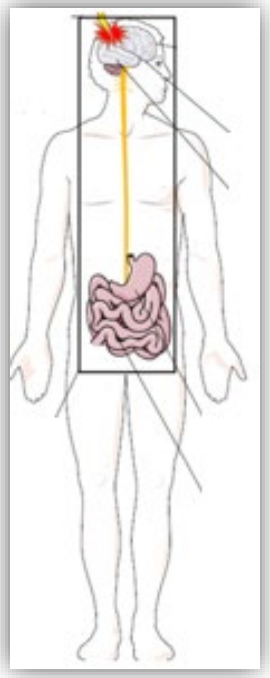
↑ Oxidative stress

↑ Neuroinflammation

Systemic response

physiological, psychological, neurological consequences, e.g.

- Disruption of the gut-brain axis
- ↑sytem. Inflammation (IL 6)



Conti F et al. 2024/ Howell DR et al. 2021/ Freire MA et al. 2023/ Giza CC et al.2014/ Jacquens A et al. 2022/ Lewis MD et al.2019/ Sulhan SJ et al. 2020/ Visser et al. 2022

Nutrition

Special interventions needed for mTBI / sports concussion?

Hypermetabolism / catabolism

- **In severe TBI:** up to > 70 % malnourished → increased morbidity/mortality
- **Reasons:**
  - ↑ energy requirements, ↑ catabolism (inflammation, immobility)
  - Delayed gastric emptying (45-50% of TBI patients)
  - Nausea / vomiting, less appetite / disturbances smell - taste... → «Eating as a burden»

  → Risk of negative energy balance, malnutrition

- **In mTBI :** not so pronounced; focus if noticeable impairment daily life after injury (symptoms above)

Curtis L et al.2014/ Erdman J et al.2011/Lee HY et al.2022/ Patel PR et al.2023/ Poblete RA et al.2023/ Scrimgeour AG et al.2014

Avoid malnutrition

Target nutrition:

- **Adequate supply of energy, protein / nutrients and micronutrients** (cachexia / sarcopenia)
- **Choose a well-tolerated form** (liquid, concentrated drinkable food)
- **Also: avoid** directly stimulating substances such as caffeine etc., alcohol and too much fructose in the acute phase

Poblete RA et al.2023/ Lee HY et al.2022/ Patel PR et al.2023/ Scrimgeour AG et al.2014/ Curtis L et al.2014/ Erdman J et al.2011

Therapy options medical supplements micronutrients & Co.

Scientific data on supplements for (m)TBI

Quite scientific literature available; often reviews, meta-analyses

- Numerous papers on nutrients in TBI are detailed **reviews, meta-analyses**, often **small studies** (case studies, hardly any classic RCTs)
- **TBI models** are used frequently

Reason: RCTs difficult to conduct

- Standardization patients / standards diagnosis / tools with high subjectivity etc.
- But: measurable parameters are increasingly being added (MRI scans, blood parameters) Progression measurement possible

Important: differentiate between mild TBI (concussion) and more severe brain injuries, where the overall situation is even more complex and mortality also increases

Barrett EC et al. 2014/ Conti F et al.2024/ Lucke-Wold B et al.2025/ Poblete RA et al.2023

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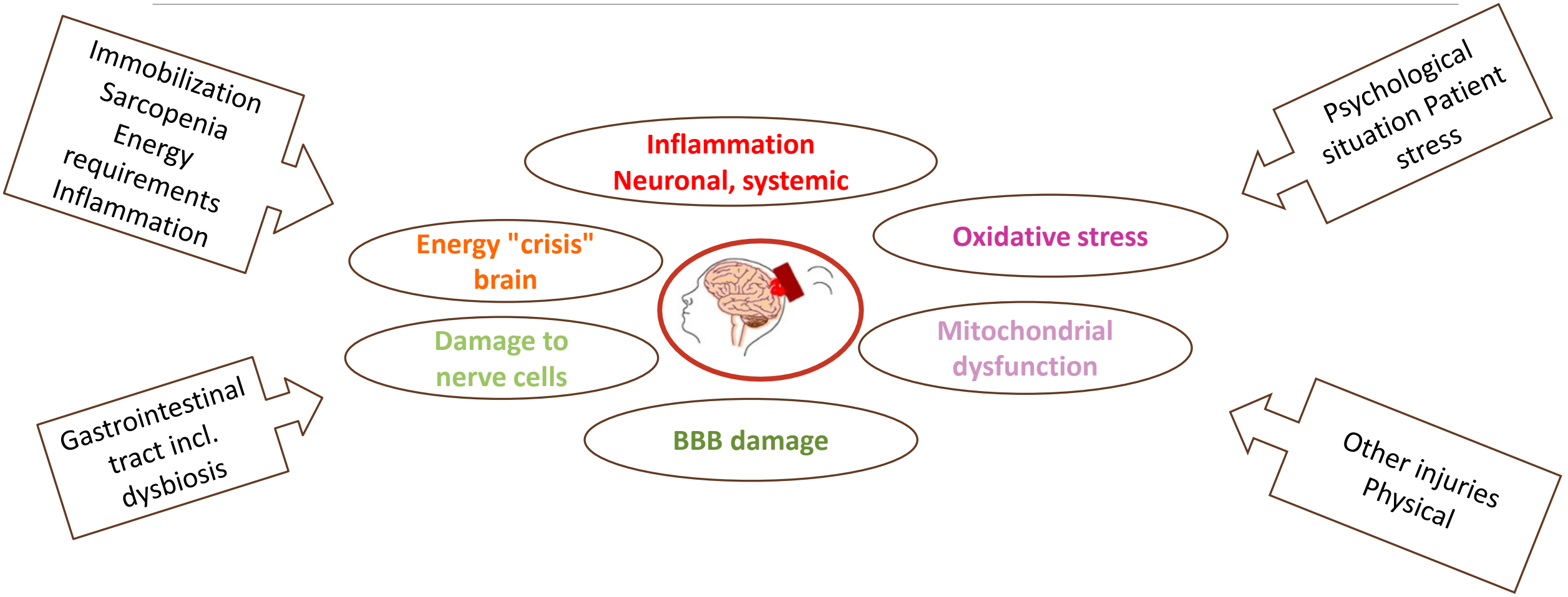
Challenges



Substances & targets

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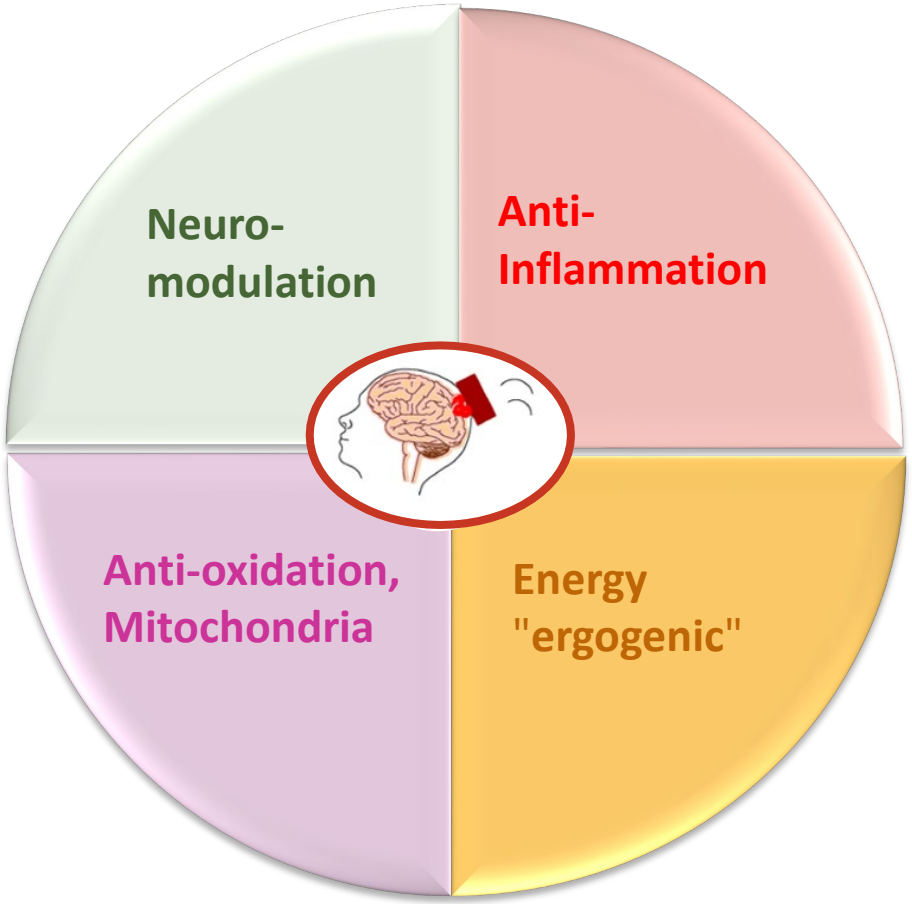
- **Omega 3 (DHA-focus)**
- **Magnesium**
- **B vitamins/ B2/ choline**
- **Phosphatidylserine**
- Zinc
- Vit D
- Lutein/ Zeaxanthin?

- **Omega 3 (DHA-focus)**
- **Quercetin / Resveratrol**
- **N-acetylcysteine**
- Alpha lipoic acid (ALA)
- Q10



- **Omega 3 (DHA-focus)**
- **Curcuma, Boswellia**
- **Resveratrol / Berry polyphenols**
- **Vitamin D**
- Selenium
- Zinc

- **Vitamin B2**
- **Creatine**
- BCAA / EAA
- Taurine
- L-glutamine

Ashbaugh A, McGrew C.2016/ Bailes JE et al.2020/ Cassol G et al.2019/ Conti F et al.2024/ Finnegan E et al.2022/ Jacquens A et al.2022/ Lai JQ et al.2023/ Lucke-Wold BP et al.2018, 2025/ Poblete RA et al.2023

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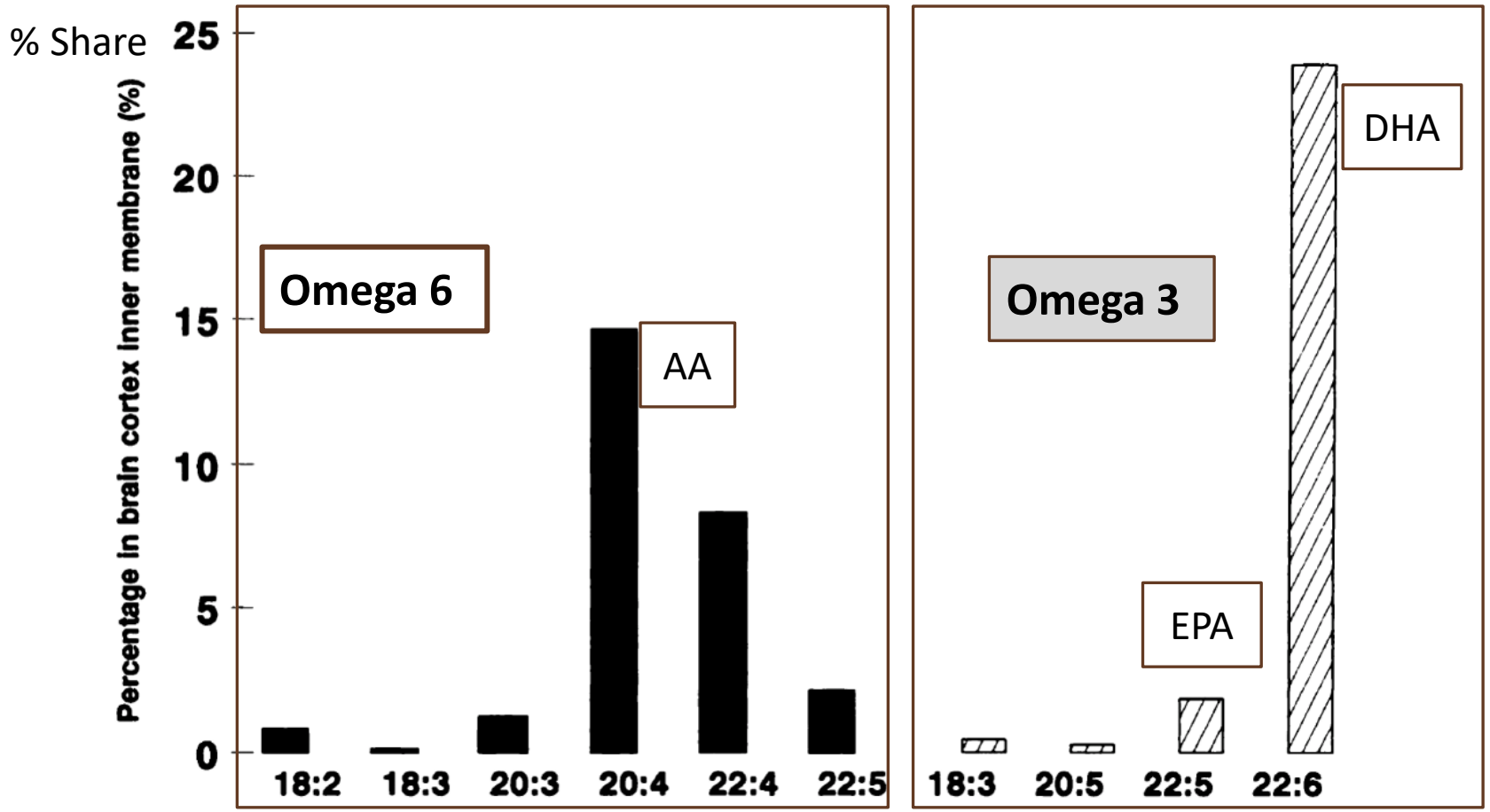
Fatty acids share human brain



Adapted from Crawford MA et al.1997

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Omega-3 and brain

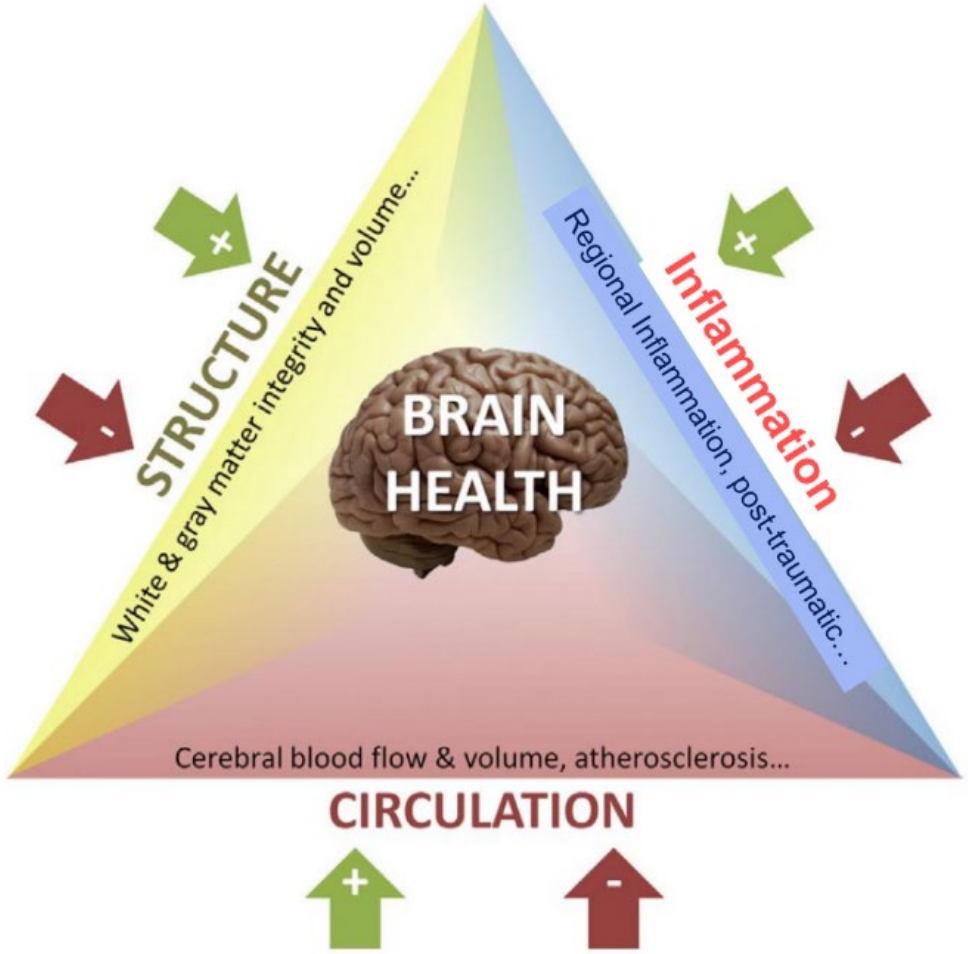

Image from: Haast RA et al.2015

Omega-3 and TBI

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TBI

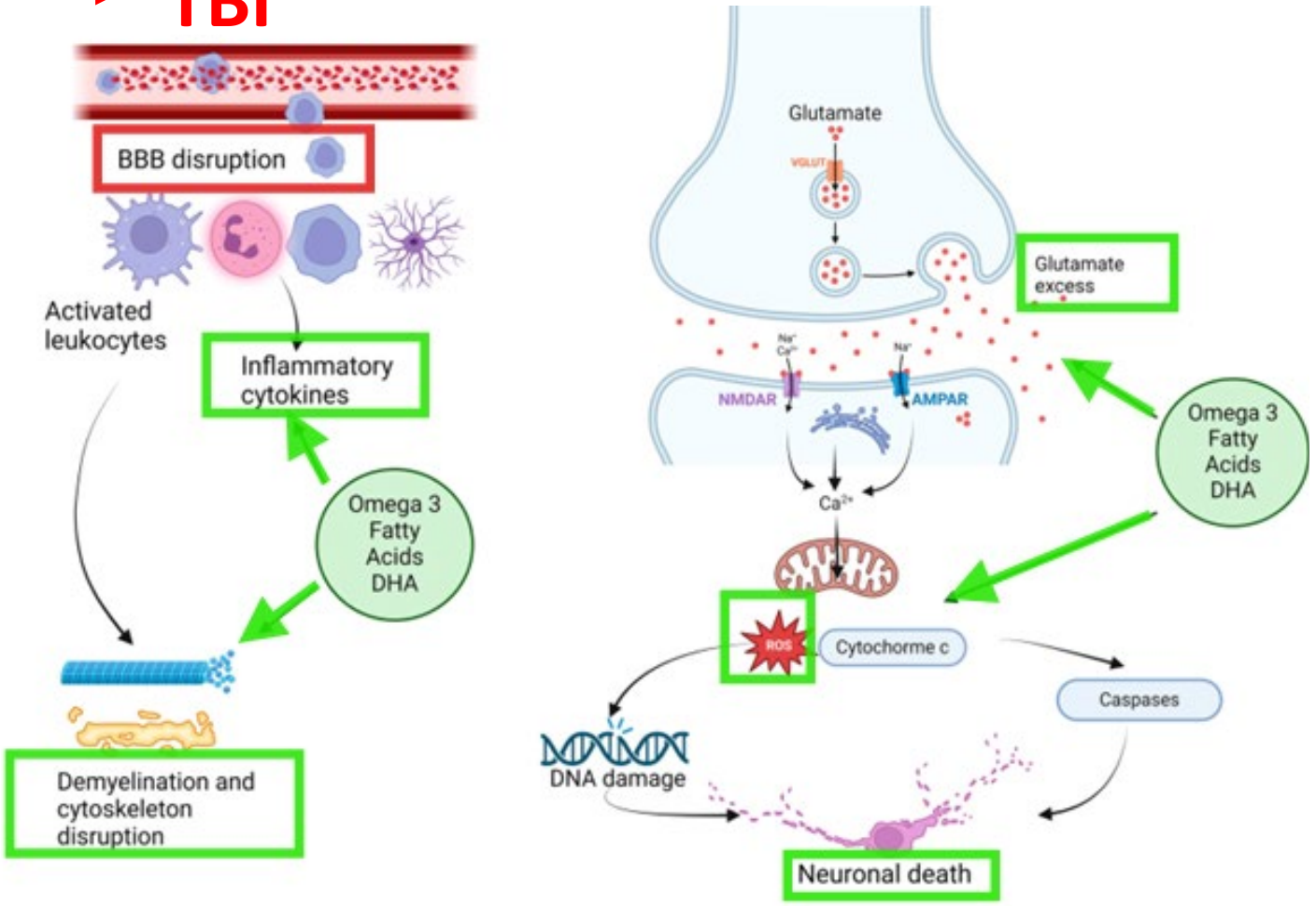

Figure 1. Target Pathways of Omega-3 Fatty acids. Created with biorender.com.

- Reduction of **neuro-inflammation**
- Reduction of **excitotoxicity**
- Reduction of **oxidative stress**
- Improve **synaptogenesis**
- Support **cognition**
- Support **faster recovery**

Graphic adapted from : Lucke-Wold BP et al. 2025

Barrett EC et al. 2014/ Lucke-Wold BP et al.2018, 2025/ Oliver JM et al. 2016/ Poblete RA et al. 2023/ Ryan T et al.2023/ Scrimgeour AG et al.2014

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Omega 3 dosages

- Omega - 3 dosages in the range 2000 - 3,600 mg (up to 6 g) EPA plus DHA
- Choose **products high in DHA** (DHA in the range 1,500 - > 2,000 mg per day)
- Caution:
  - Pay attention to the amount of especially DHA in the dosages (not the total amount of fish oil)!
  - Take preferably **once** daily and always **WITH a main meal containing fat**

→ Can be used **prophylactically** in cases of previous / increased risk of recurrent TBI
→ Reduction of axonal damage, apoptosis, neuroprotective

Bailes JE et al.2020/ Barrett EC et al. 2014/ Finnegan E at al.2022/ Lucke-Wold BP et al.2018, 2025/ Oliver JM et al. 2016/ Poblete RA et al. 2023/ Ryan T et al.2023/ Scrimgeour AG et al.2014

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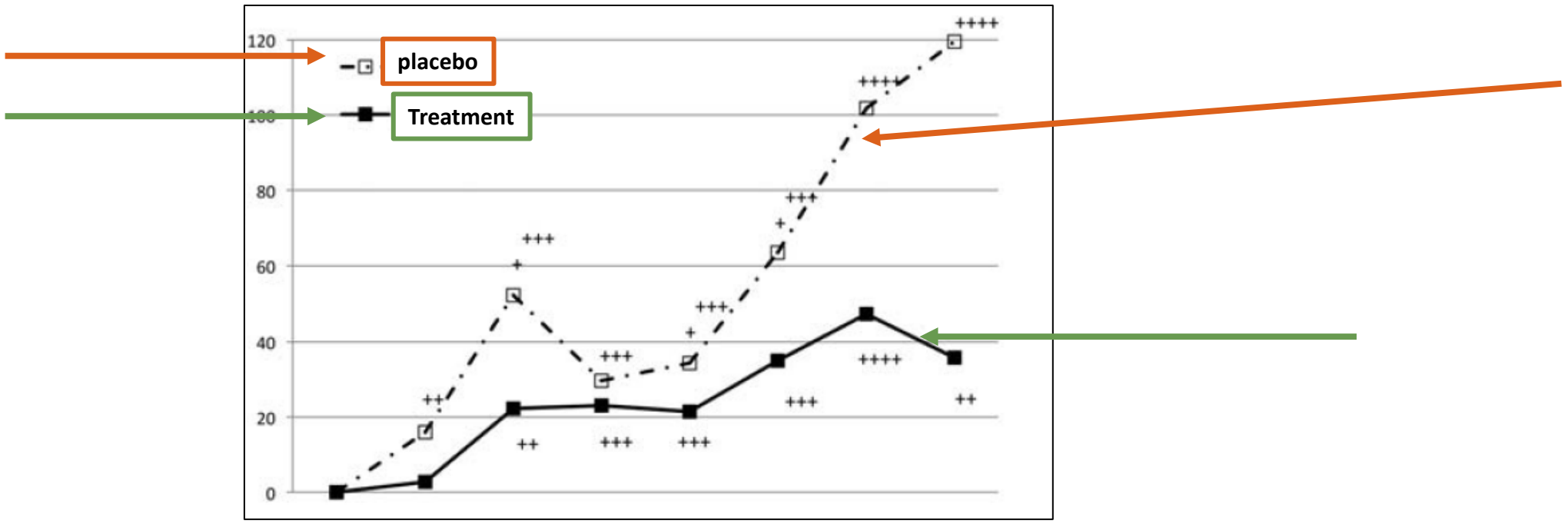
Omega 3: also preventive

Effect of supplementation on **NFL* levels** in starters (placebo, 2g, 4g, 6g)



Averaged over dosages

NFL: Neurofilament Light Chain: Biomarker for neurodegenerative processes or acute nerve damage

Oliver JM et al. 2016

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B vitamins / vitamin B2

Important functions overview
- Energy metabolism
- Nerve function
- Neurotransmitter synthesis
- Cell division
- DNA synthesis / methylation
- Amino acid metabolism
- Neuroprotective
- Antioxidant

B vitamins

TBI and B vitamins
- Repair / regeneration of nerve tissue, cells
- Synaptogenesis
- ↓Neurotoxicity, excitotoxicity

Dosages
- Use a balanced combination of all important B vitamins ("B complex")
- Also, higher doses in the medium term **(B2: 400 mg/day)**
- B6 not long-term > 12.5 mg (UL EFSA)

Jacquens A et al.2022/ Lucke-Wold BP et al.2018,2025

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Magnesium

Important functions Overview
- Neurotransmitter synthesis
- Stabilization of cell membrane
- Important for nerve cell excitability
- Neuroprotective
- Protein balance
- …

TBI and magnesium
- **↓ Mg level after TBI / Mg homeostasis disturbed**
- ↑ Risk of prolonged symptoms
- Protective role against overexcitation (excitotoxicity / apoptosis)
- After supplementation:
  - ↑ somatic scores (e.g. GCS*) in patients with TBI
  - Improvement of acute symptoms, faster recovery

Dosages
- In the range of 200 (-400) mg/day
- Replace losses / aim good supply

*GCS: Glasgow Coma Scale

Creatine

Important functions Overview

- Energy balance (ATP)
- Intracellular buffer
- Mitochondrial function, Antioxidant
- 95% found in skelet. muscles…
- Neuromodulation? (at synapses)
- Brain:
  - Own synthesis of Cr
  - Via BBB via transporter protein (small capacity with intact BBB)

Creatine

Creatine and TBI

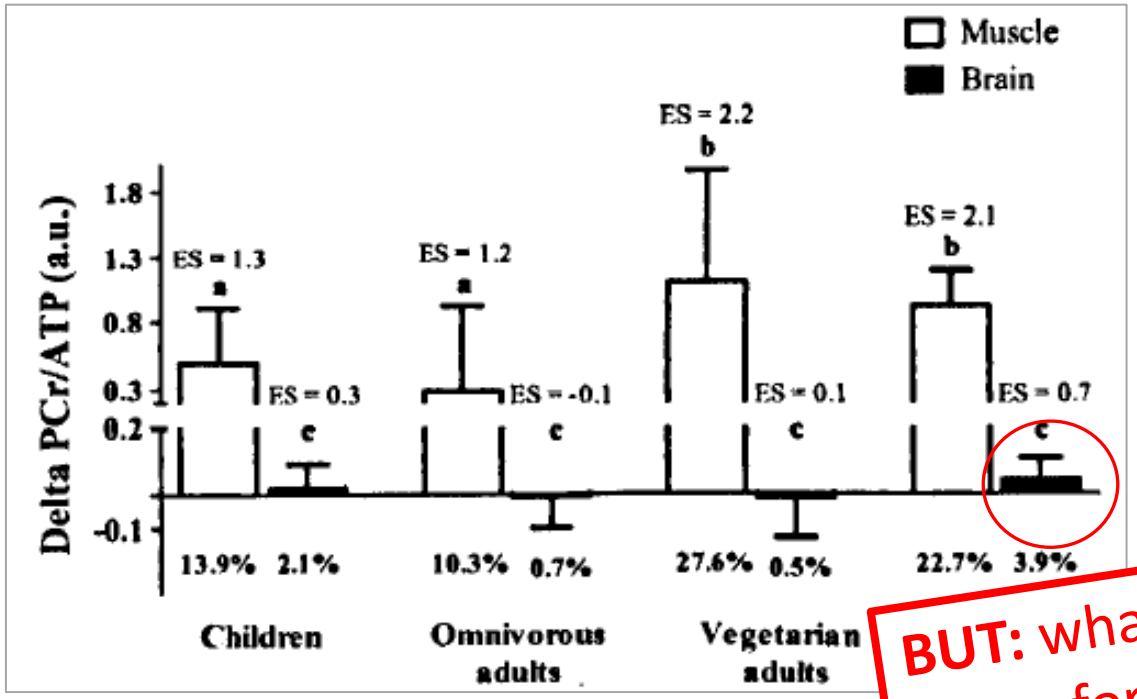
- Regulation / promotion of energy balance after mTBI (first phase)
  - Hyper-/ hypo-metabolism
- Support of mitochondrial function
- Neuroprotection (buffer, antiox)
- Too little creatine → massive disruption of neuronal function

Dosages

- In studies often very high doses (4 x 5 g) or with tube feeding (0.3 - 0.4 g/kg bw), longer term (6 mths)
- Many studies on TBI animal models / high doses
- Moderate doses useful in the longer term (3-5 g/d) –compliance…
- Prophylactic use is discussed (high risk athletes)

Cassol G et al.2019/ Forbes SC et al.2022/ Freire Royes LF et al.2016/ Newman JM et al.2023

Creatine uptake brain



7d / Children, adults, elderly people
Dosage: 0.3 g/kg and day **(70 kg = 21 g/d)**
→ different effects!
→ 7 d Supplementation: hardly any increase in creatine in the brain

BUT: what if BBB is impaired?
e.g. for concussion / TBI?

Difference muscle/brain

Solis MY et al.2017

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Vitamin D3

Important functions Overview

- Ca homeostasis
- Immunomodulatory
- Inflammation modulation
- Cell cycle control
- Neurological/muscular function
- Neuroprotective
- Brain
  - own VitD receptors
  - own Vit D metabolism (enzymes for activation)
  - Calcitriol levels do not correlate with plasma (25-OH does)

Vitamin D3

TBI and vitamin D3

- **Calcitriol: neuroprotective effects**
- ↑ Regenerative processes of the brain
- ↓Ca-influx / excitotoxicity
- Severity of TBI has a significant relationship with patients' levels of Vitamin D
- Severe TBI: suppl. of Vitamin D improved GSC

Dosages:

- Acute ≥ 50 mcg / 2000 IU/day
- Aim for good levels
- In some studies, single administration of very high doses (?)

*GCS: Glasgow Coma Scale

Finnegan E et al.2022/ Jacquens A et al.2022/ Lai JQ et al.2023/ Lucke-Wold B et al.2025/ Lawrence DW et al.2016/ Sharma S et al. 2020

Zinc

Important functions Overview

- Cofactor > 300 enzymes
- Central function in neurobiology
- Antioxidant
- Anti-inflammatory
- ↓ Apoptosis / cell death
- Protein balance
- ...

TBI and zinc

- **Zinc depletion (urinary excretion ↑)**
- Locally high concentrations can occur in more severe brain injuries (release from tissue)
- Zinc too low: ↑ risk of cell death
- Sufficient zinc: ↓ Risk of long-term psychological symptoms (depression - feared consequence of TBI, e.g.)
- Improvement in GCS*, protein balance

Dosages

- Not too high doses, only p.o.
- In the range of 20 mg/day
- Replace losses / aim for good supply → "neuronal recovery"

*GCS: Glasgow Coma Scale

Cope EC et al. 2012/ Li W et al.2015/ Poblete RA et al.2023/ Lucke-Wold BP et al.2018,2025/ Jacquens A et al.2022/ Scrimgeour AG et al.2014

Plant substances

Boswellia (frankincense)
Curcuma
Resveratrol
Berry extract
Quercetin
Saffron
Rhodiola

- Anti-inflammatory
- Antioxidant
- Neuroprotective
- Mitochondrial metabolism
- Angiogenesis
- Mood/sleep

→ Gastrointestinal tract

→ Systemic Musculature

→ Brain

Use of plant substances: Set priorities and prioritize 1 -2 of them, dose correspondingly
Attention: extracts should be standardized - choose dosages appropriately!

Ashbaugh A, McGrew C.2016/ Curtis L et al.2014/ Khan H et al.2020/ Lai JQ et al.2022/ Sulhan S et al.2020

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Other substances

- N-acetylcysteine
- Alpha-lipoic acid
- Vitamin E, vitamin C

antioxidant
anti-inflammatory
neuroprotective

- Amino acids, AS-like
  - taurine, L-glutamine, L-arginine, L-carnitine
  - BCAA, EAA

energy metabolism
Neurotransmitter metabolism

- Phosphatidylcholine
- Citicoline / Citicholine
  - Building component phosphatidycholine

regeneration of neurons
nootropic

- Probiotics

dysbiosis

- Melatonin

Neurotransmitters, sleep

- **Medication** (severe forms of TBI, e.g. corticoids, EPO, antidepressants)

Cassol G et al.2019/ Curtis L et al.2014/ Finnegan E ET AL.2022/ Jacquens A et al.2022/Lucke-Wold BP et al. 2018,2025/ Poblete RA et al.2023/ Ryan T et al.2023/ Soltani A et al.2023/ Sulhan S et al.2020/ Zafonte RD et al.2012/

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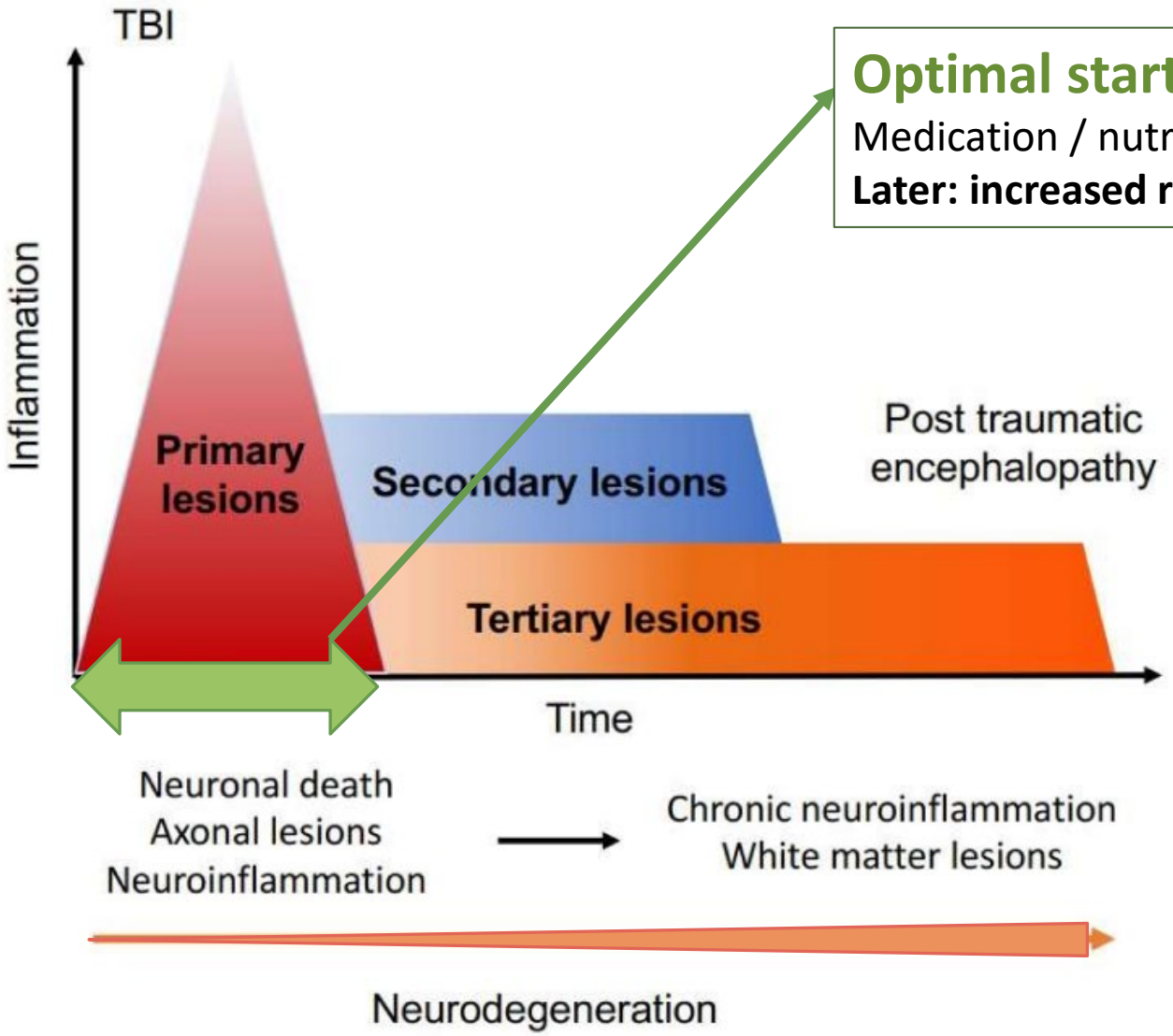
Optimal start interventions now:
Medication / nutritional interventions / supplements
Later: increased risk of injuries becoming "established"



Jacquens A et al.2022

Conclusion

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Brain is not an isolated organ!

Injuries result in cascades of processes - effects not only local, but systemic

Record the course / progression of symptoms (consider individuality)

Nutrition: Prevent malnutrition - in severe TBI *cave* sarcopenia, cachexia!

- Sufficient energy / 3 protein pulses with meals, possibly + 1 additional in phases with a lot of lying down
- Sufficient micronutrients

Medical supplements: according to the severity of the injury

- Omega 3/DHA -focused
- Suitable combination of vitamins, minerals, plant extracts
- ! Set priorities - especially with additional plant extracts
- Supplement long enough, make adjustments
- **Check individualized options for medical supplements (personalized mixtures / formulations)**

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Medical supplements in the recovery of (m)TBI …

… an interesting component mainly addressing the amelioration in the progression of neuroinflammatory and neurodegenerative processes…

…useful as a complement to other important measures, but not a substitute for them.

Literatur

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online

- https://www.mayoclinic.org/diseases-conditions/chronic-traumatic-encephalopathy/symptoms-causes/syc-20370921
- AIS: Concussion and Brain Health Position Statement 2024 (https://www.concussioninsport.gov.au/)

Paper

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