Soirée pour les membres

Journal Club 6

le mercredi 24 mai 2023

Programme de la soirée :

Présentation d'un article scientifique

par Adrien Kristiansen

étudiant en 4ème année de médecine

Discussion puis apéro !

Le rôle de la neuroinflammation dans les traumatismes crâniens

Basé sur l'article :

The far-reaching scope of neuroinflammation after traumatic brain injury, Simon & al., Nature reviews neuroscience, 2017

L’histoire de Gabriel(le),
stagiaire médecin aux HUG

Un beau jour de printemps, en rentrant de stage

Le drame

Traumatisme crânien (cranio-cérébral)

Traumatic brain injury (TBI), a form of acquired brain injury, occurs when a sudden trauma causes damage to the brain. TBI can result when the head suddenly and violently hits an object or when an object pierces the skull and enters brain tissue. NINDS
CBI

1ère cause de mortalité des jeunes de 15-25 ans

Classification :

Mineur (mild) : GCS 13-15

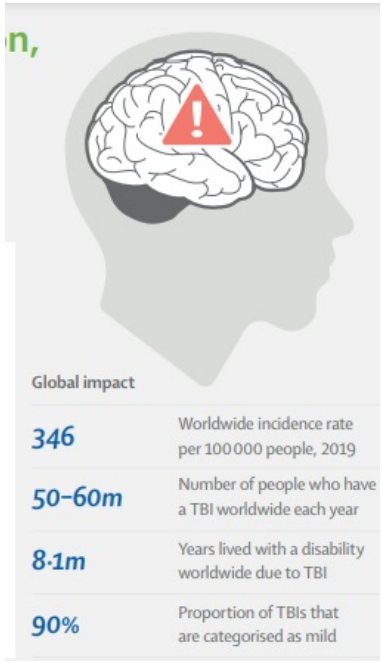
Moyen (moderate) : GCS 9-12

Sévère (severe) : GCS<9

Criteria	Mild	Moderate	Severe
ARLINGHAUS ET AL. (16)			
Glasgow coma scale	13–15	9–12	≤8
Loss of consciousness	30 min or less or none	30 min to 1 week	More than 1 week
Post-traumatic amnesia	Less than 24 h	More than 24 h less than 1 week	More than 1 week
VA/DoD			
Glasgow coma scale	13–15	9–12	≤8
Loss of consciousness	0–30 min	30 min to 24 h	More than 24 h
Post-traumatic amnesia	Less than 24 h or none	More than 24 h less than 1 week	More than 1 week
Alteration of consciousness/mental state	A moment up to 24 h	>24 h, severity based on other criteria	>24 h, severity based on other criteria

Epidémiologie

Incidence par rapport à d'autres maladies neurologiques fréquentes ?



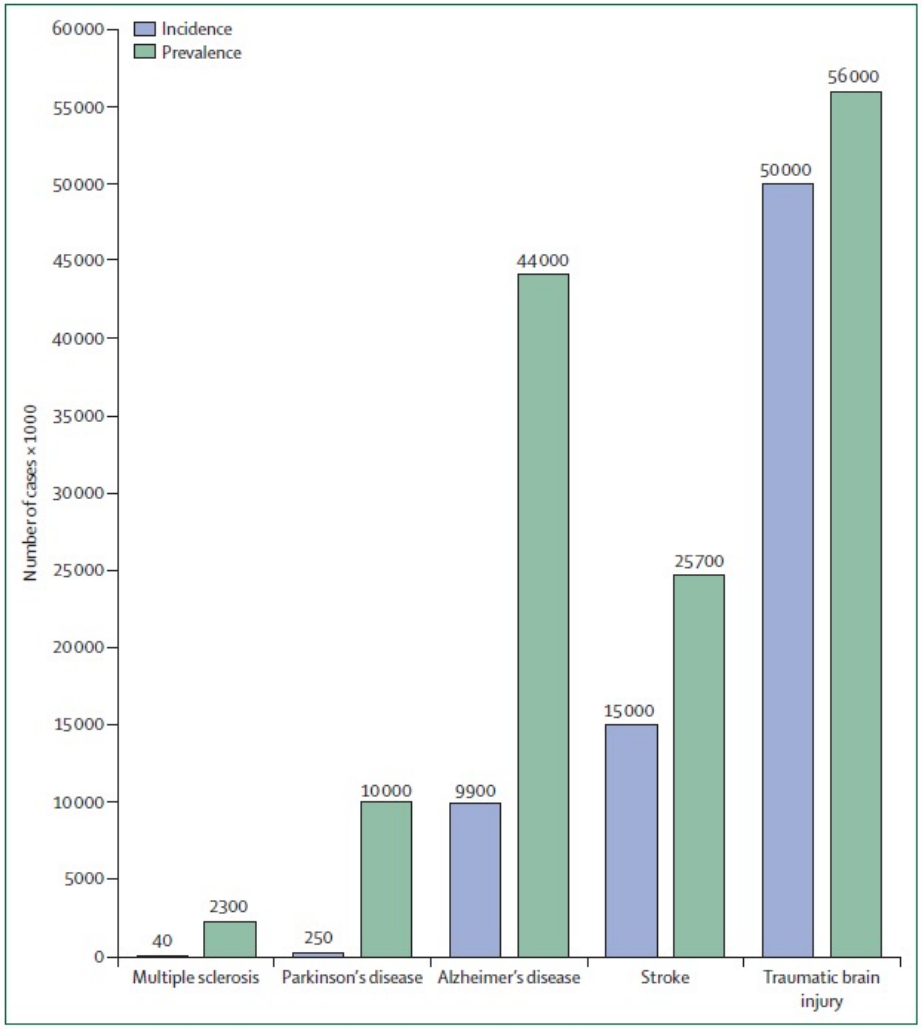
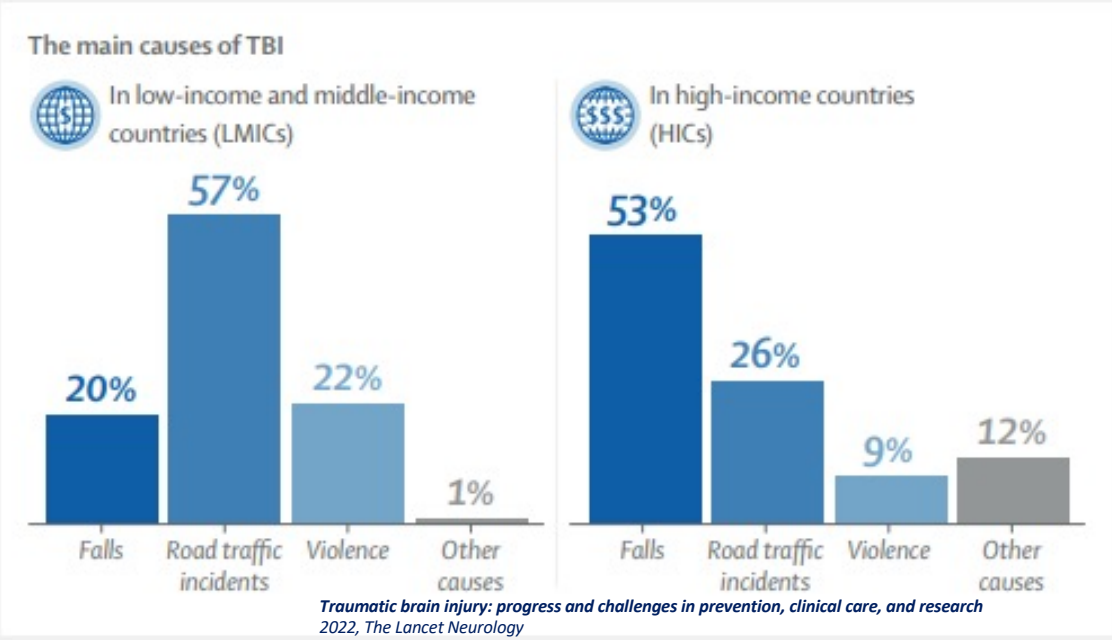


Figure 1: **Global incidence and prevalence of traumatic brain injury compared with other common neurological diseases**

Traumatic brain injury: progress and challenges in prevention, clinical care, and research
2022, The Lancet Neurology

Quelles sont les causes de TCC ?

- Chutes - #1
- Circulation
- Violence et
- Sport et ac
- Autres



Traumatic brain injury: progress and challenges in prevention, clinical care, and research
2022, The Lancet Neurology

Âge et incidence

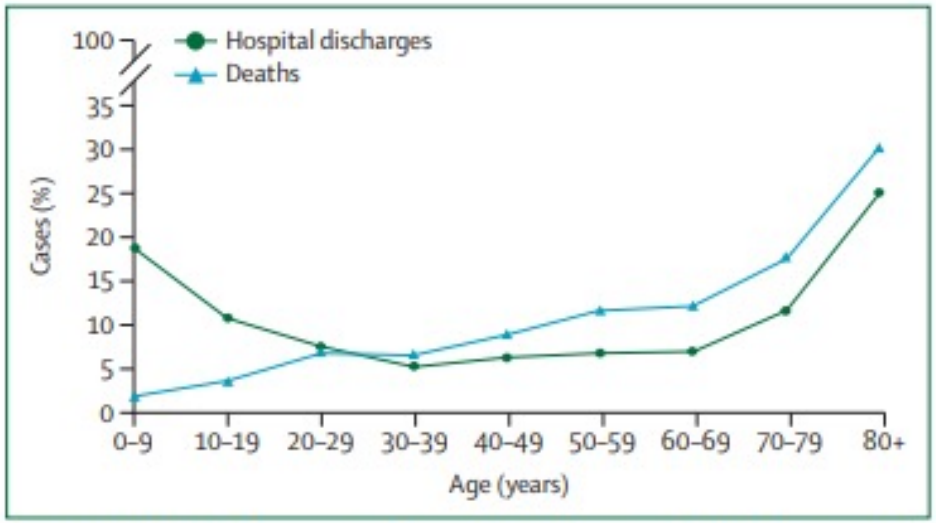


***Figure 3*: Estimated frequency of hospital discharges and deaths in cases of traumatic brain injury by age group in Europe**
Figure created using data from Majdan et al.[3]

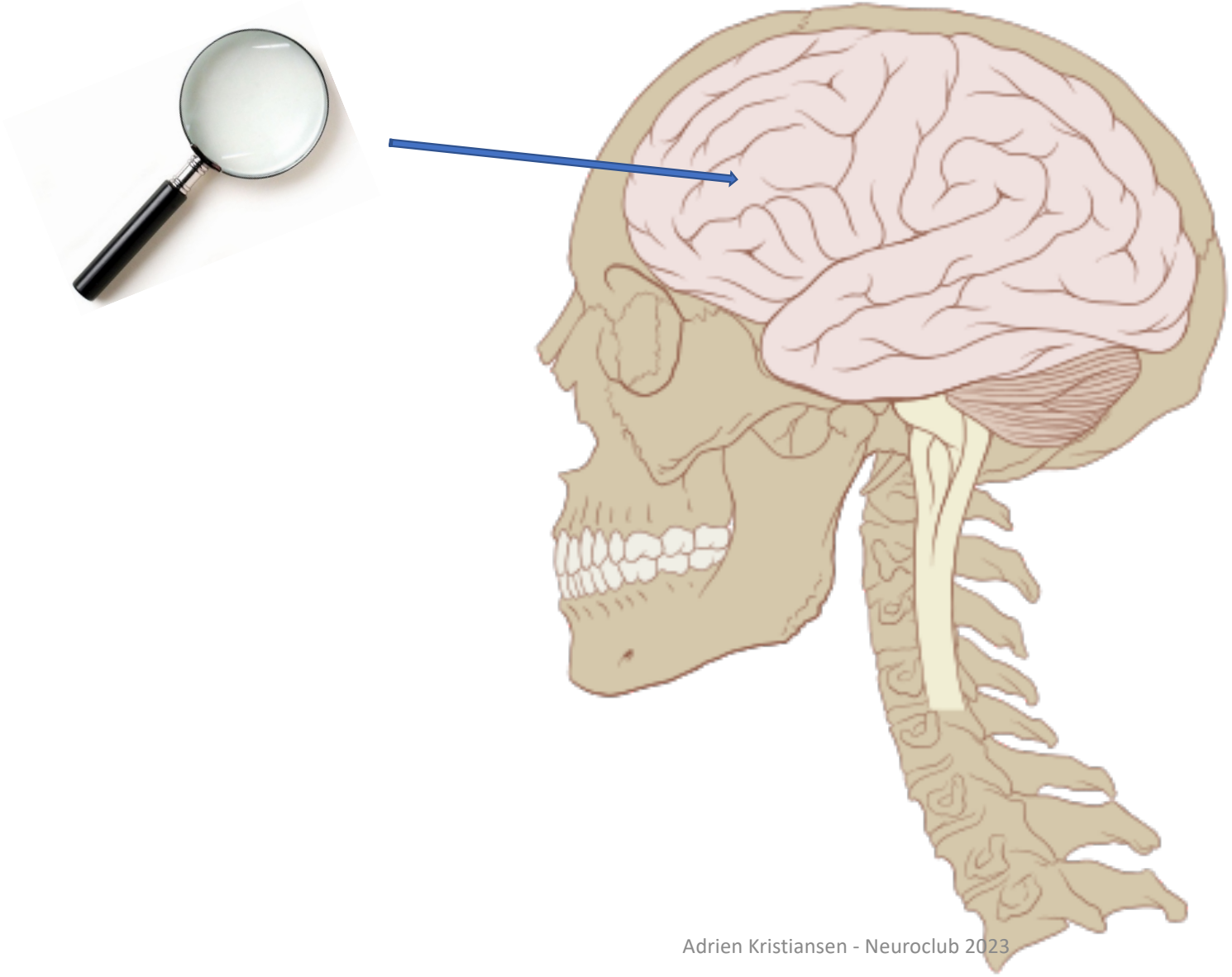
Traumatic brain injury: progress and challenges in prevention, clinical care, and research
2022, The Lancet Neurology

Quelle échelle est utilisée pour mesurer l'outcome d'un traumatisme crânien?

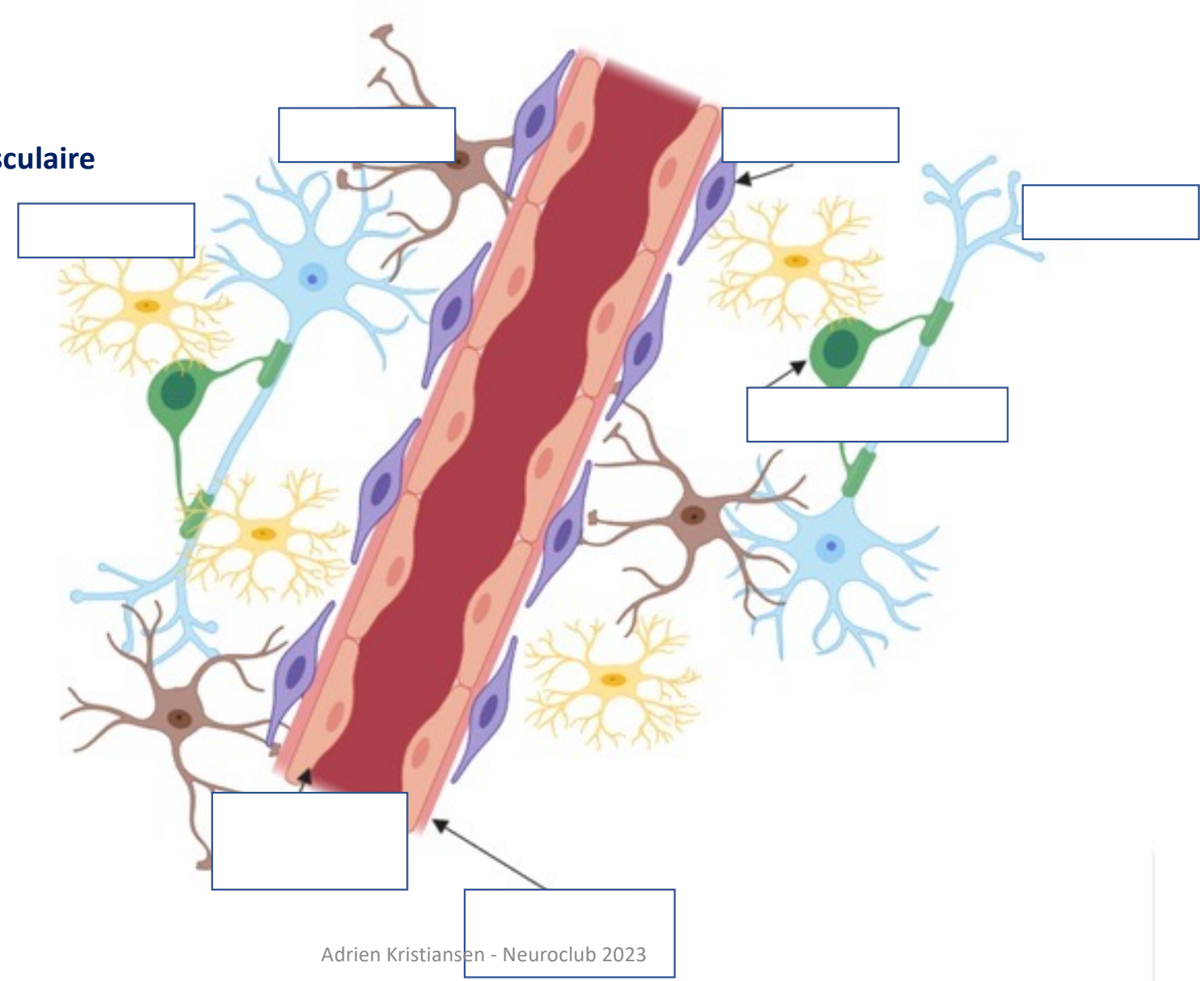
GOS	GOSE	Interpretation
1 = Dead	1 = Dead	Dead
2 = Vegetative state	2 = Vegetative state	Absence of awareness of self and environment
3 = Severe disability	3 = Lower severe disability	Needs full assistance in ADL
	4 = Upper severe disability	Needs partial assistance in ADL
4 = Moderate disability	5 = Lower moderate disability	Independent, but cannot resume work/school or all previous social activities
	6 = Upper moderate disability	Some disability exists, but can partly resume work or previous activities
5 = Good recovery	7 = Lower good recovery	Minor physical or mental deficits that affects daily life
	8 = Upper good recovery	Full recovery or minor symptoms that do not affect daily life

ADL = activities of daily living.

GOS=Glasgow outcome scale
GOSE = Glasgow outcome scale extended



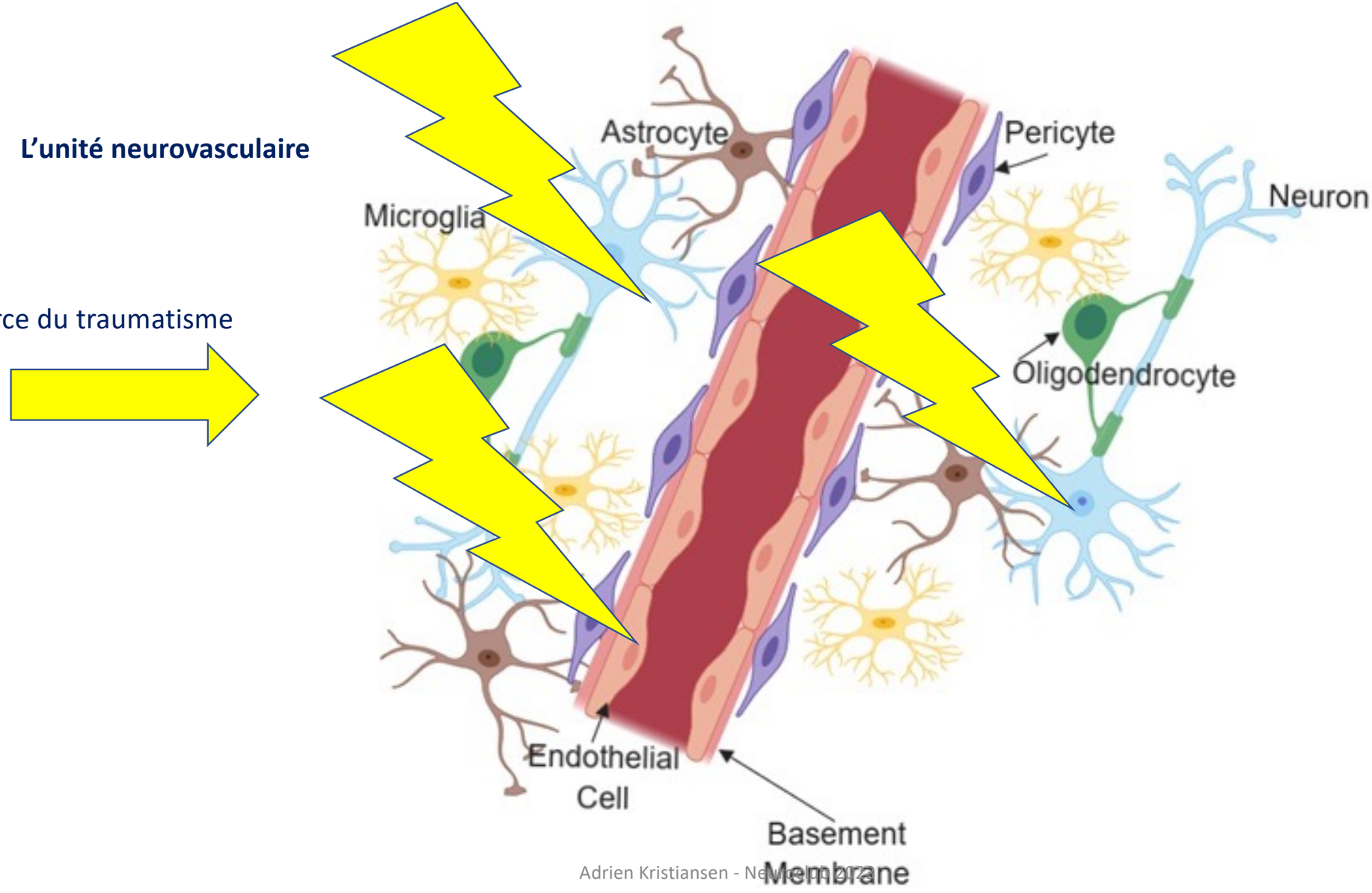
L’unité neuro-glio-vasculaire



Journal of Alzheimers & Neurodegenerative Diseases, 2019, Alzou & al

L’unité neurovasculaire

Force du traumatisme



Journal of Alzheimers & Neurodegenerative Diseases, 2019, Alzou & al

Une lame à double tranchant

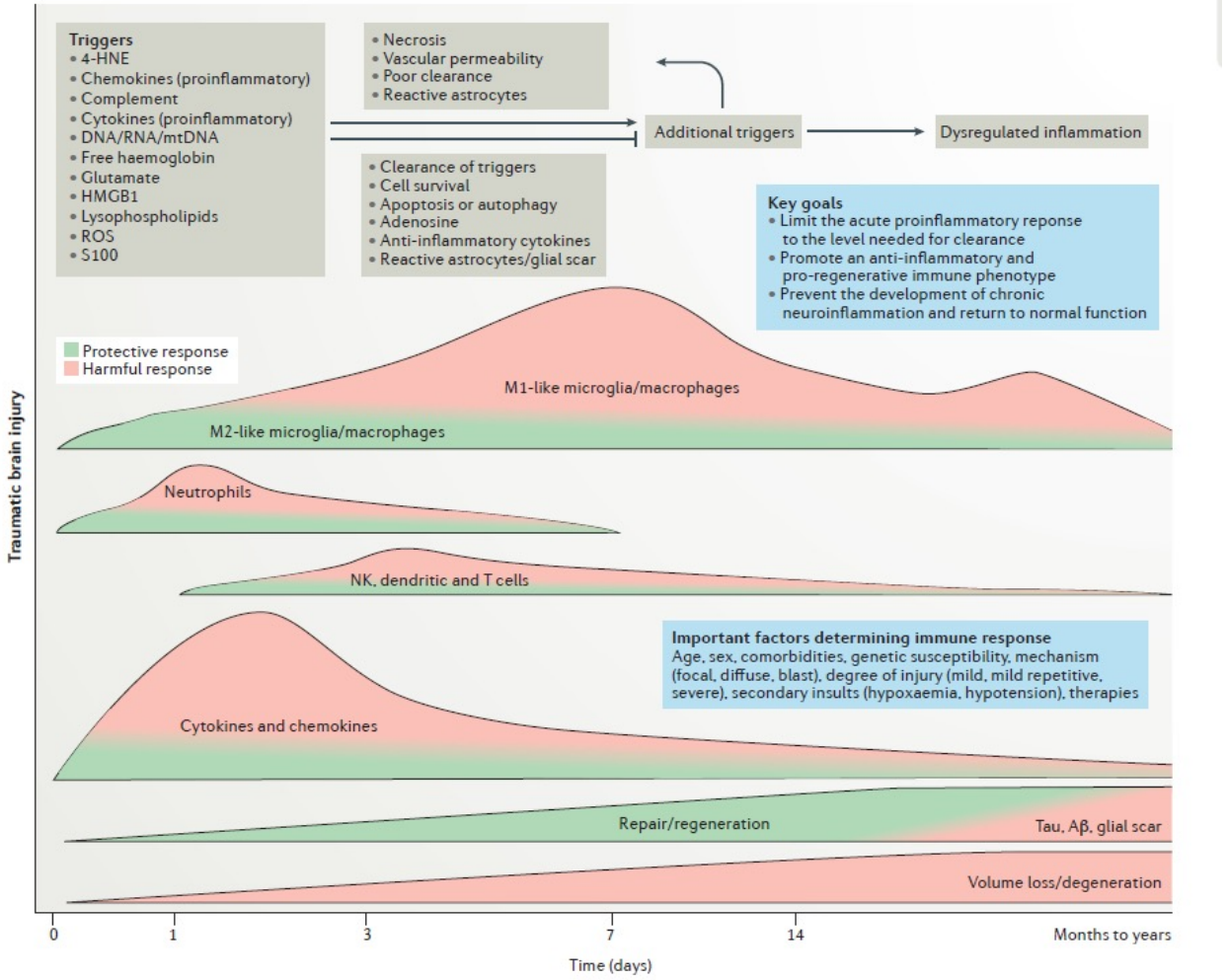
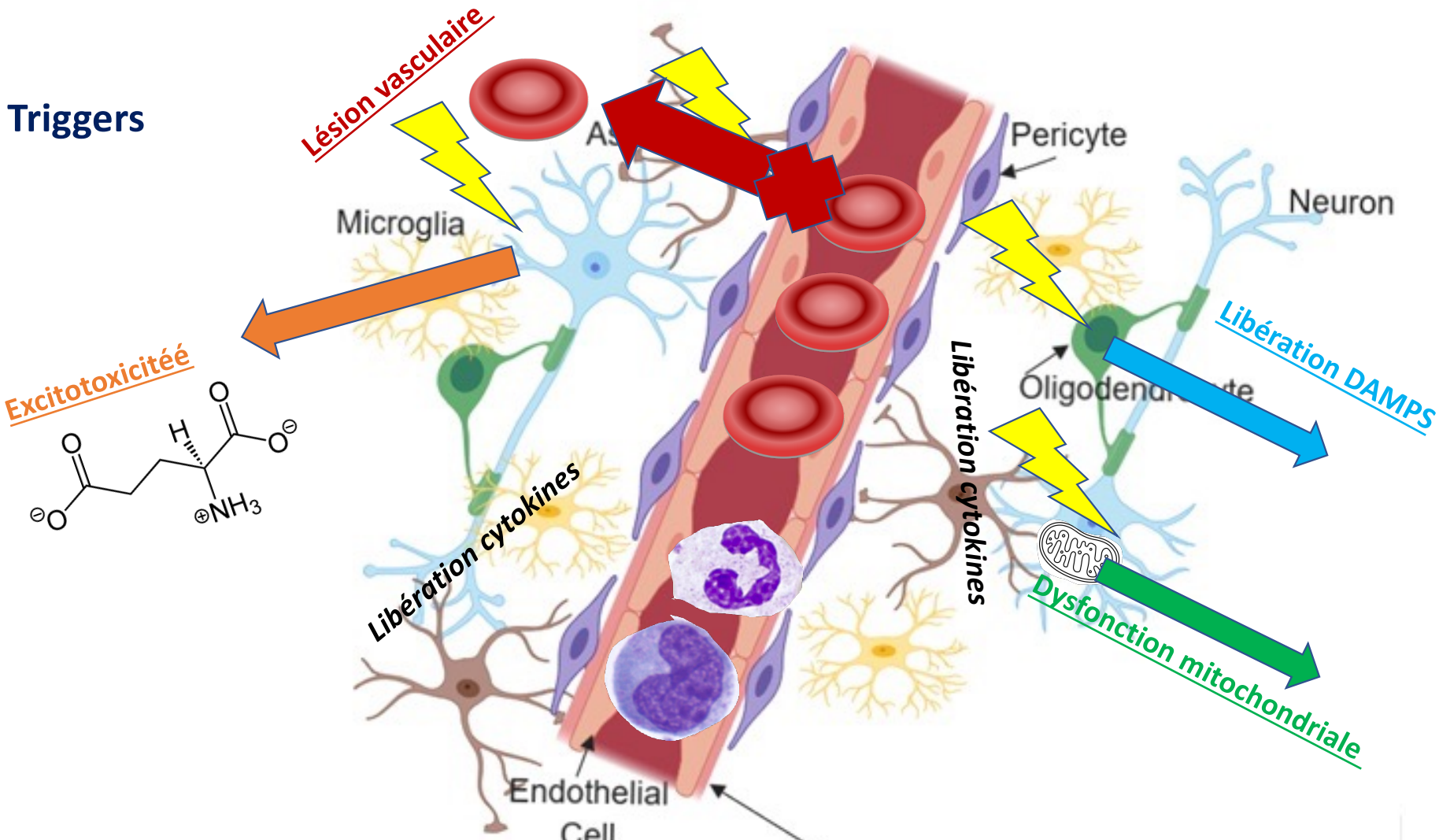


Figure 1 | **Neuroinflammation after traumatic brain injury.**

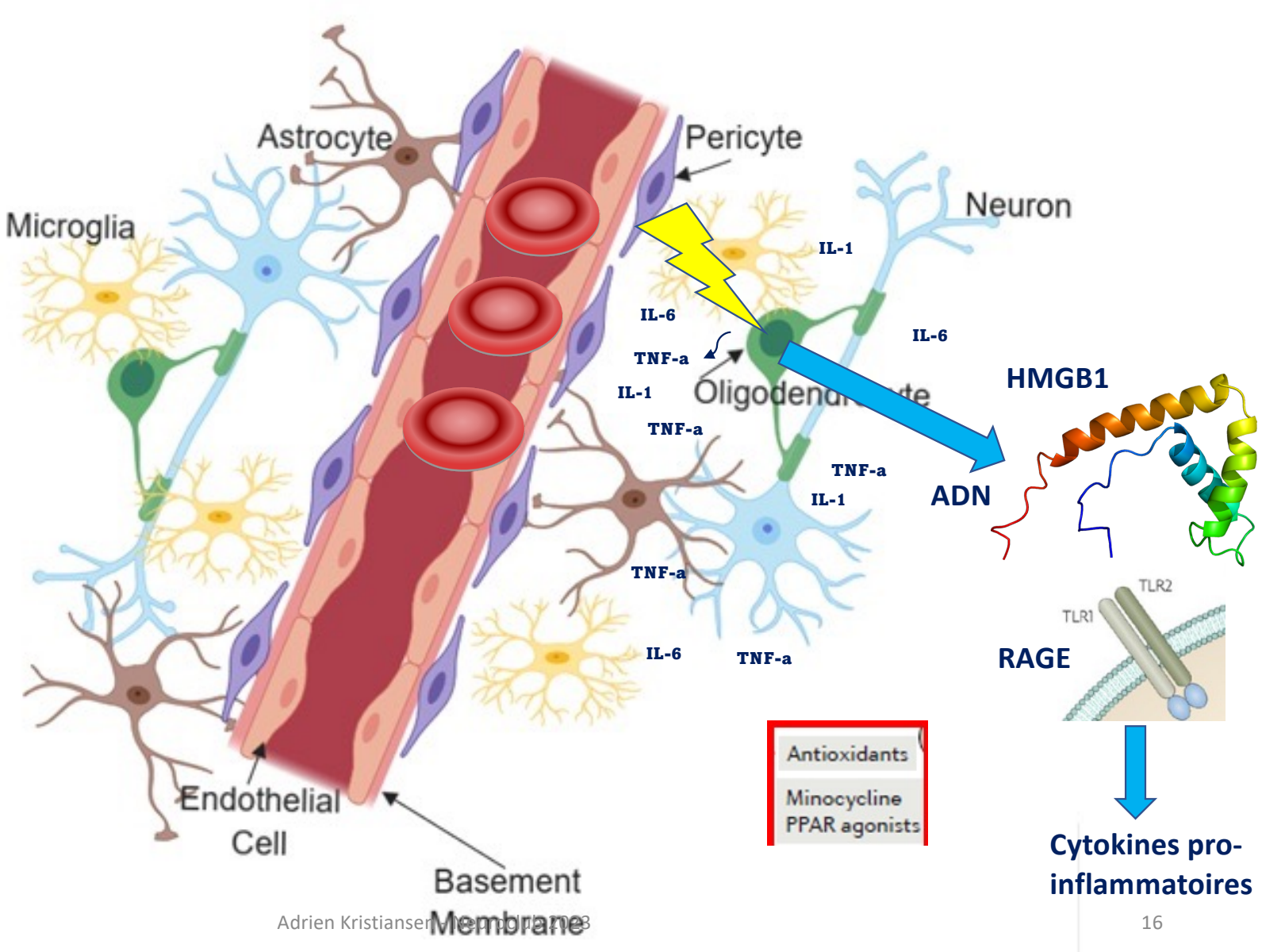
Triggers

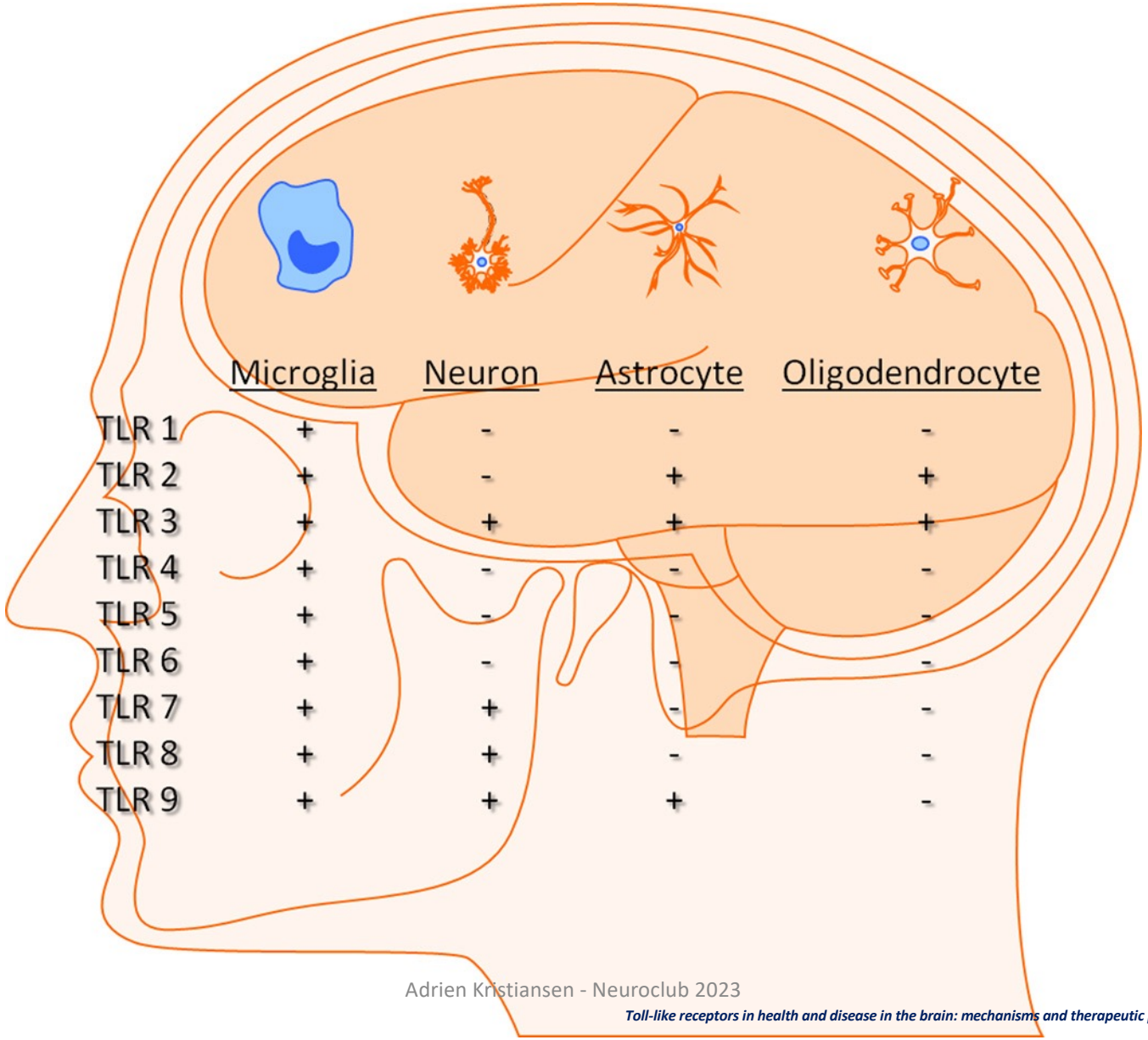

Lésion vasculaire
Microglia
Pericyte
Neuron
Excitotoxicitéé
Libération DAMPS
Libération cytokines
Libération cytokines
Dysfonction mitochondriale
Endothelial Cell
Basement Membrane

1. DAMPS

Dammage associated molecular pattern

- Libération cytokines

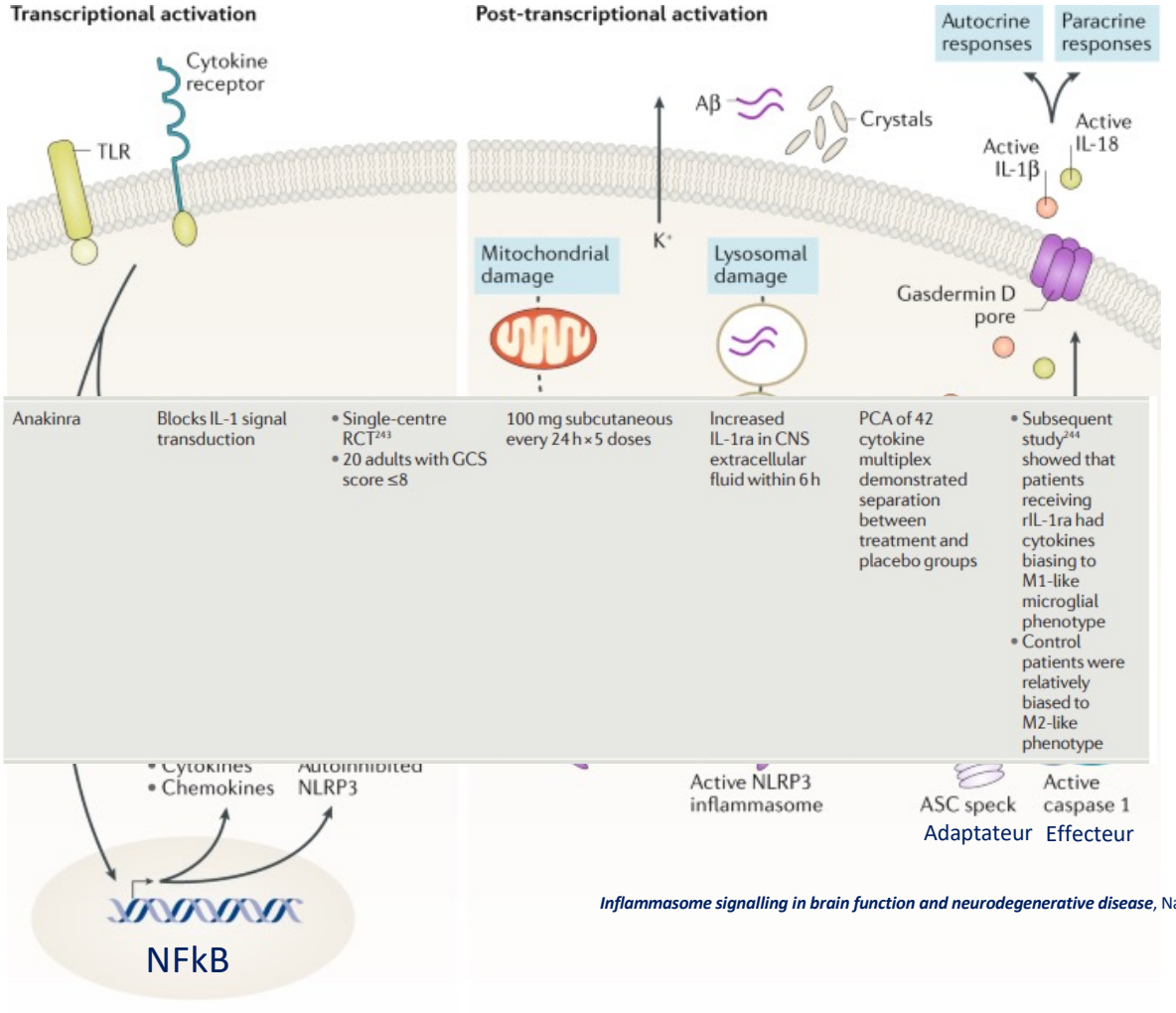




***Toll-like receptors in health and disease in the brain: mechanisms and therapeutic potential*,** 2011, clinical science

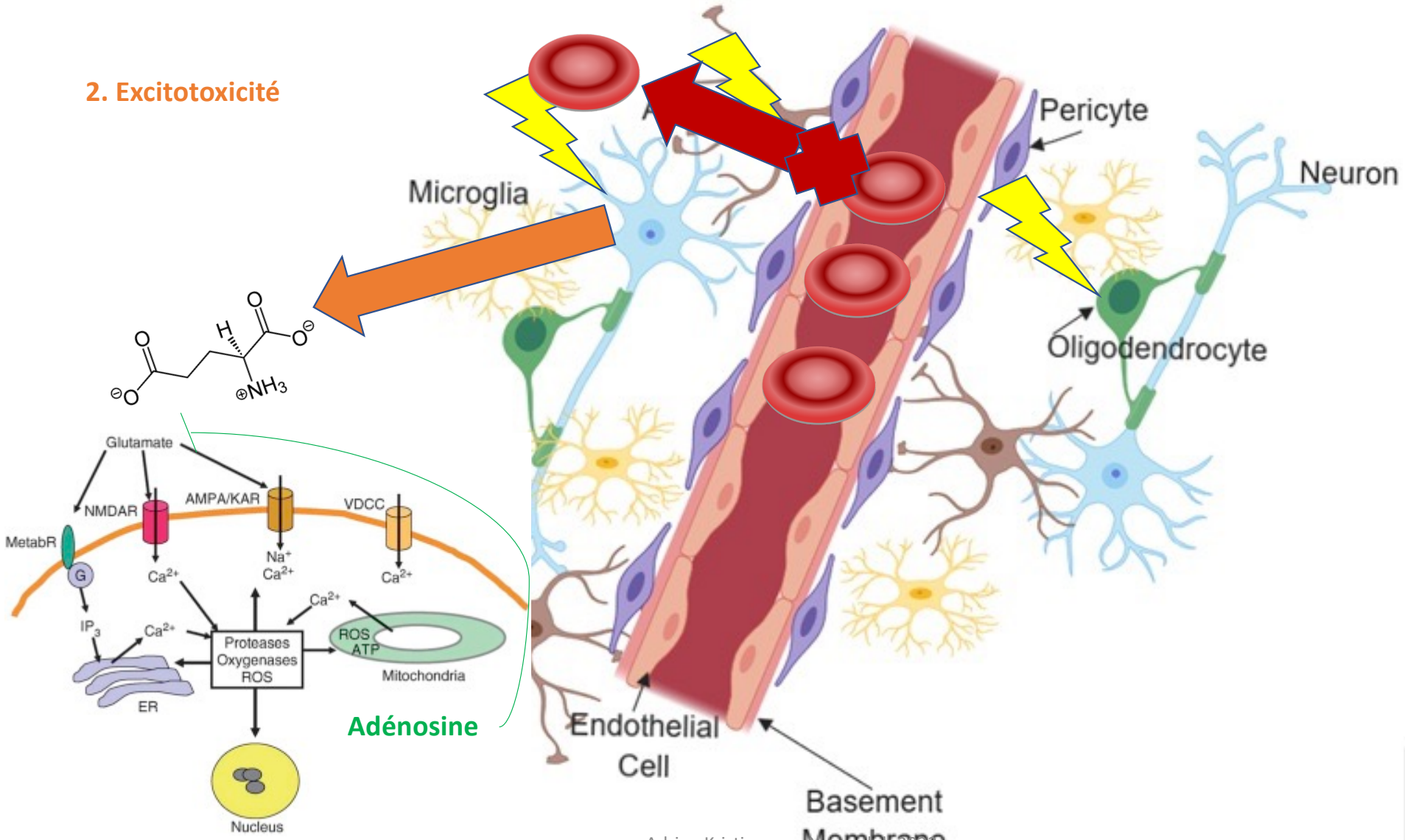
IL-1ra

Anakira



Inflammasome signalling in brain function and neurodegenerative disease, Nature reviews neuroscience, 2018

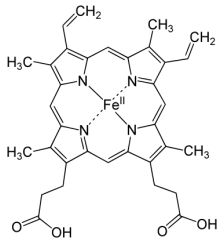
2. Excitotoxicité

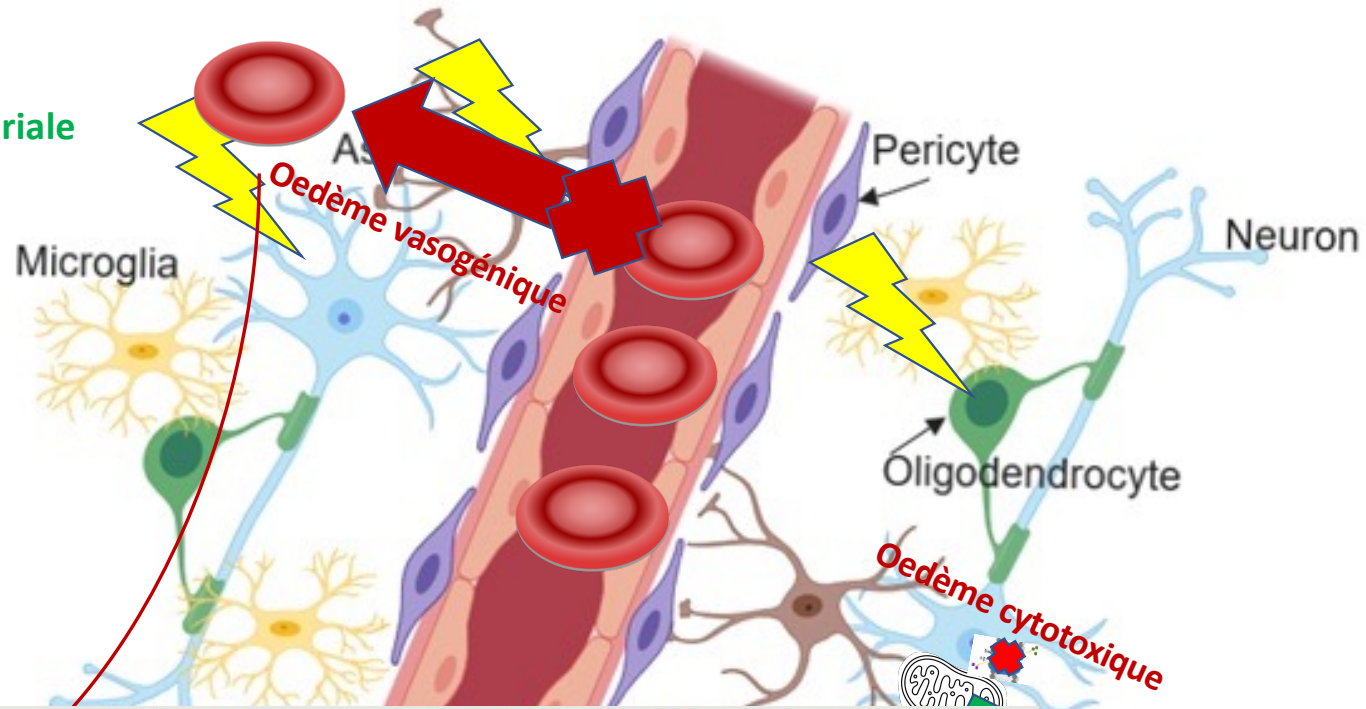


https://www.sciencedirect.com/topics/neuroscience/excitotoxicity

3. Dysfonction mitochondriale

4. Lésions vasculaires

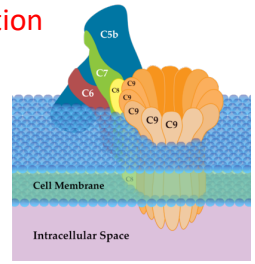




fHB

Complément

Inhibition



Anatibant	• Blocks bradykinin signalling • Prevents BBB disruption	Brain Trial: • Multicentre RCT[148] • 228 adults with GCS score ≤12	Low (10 mg load + 5 mg daily), mid (20 mg load + 10 mg daily), or high (30 mg load + 15 mg daily) versus placebo	No difference in incidence of serious adverse events	Trend towards harm in discharge GCS, DRS, and HIREOS scores	• Recruitment paused due to Data and Safety Monitoring Board concerns • Terminated (withdrawal of funding)
Statins	• Inhibit expression of vascular dhesion molecules and chemokines to reduce leukocyte infiltration of CNS • Associated with reductions in proinflammatory cytokines	• Single-centre RCT[246] • 21 adults with GCS score 9–13	Rosuvastatin 20 mg daily for 10 days versus placebo	Modest decrease in amnesia and disorientation time	No difference in disability at 3 months	Subsequent study[247] showed reduction in plasma TNF at 72 h

Translocation cardiolipines

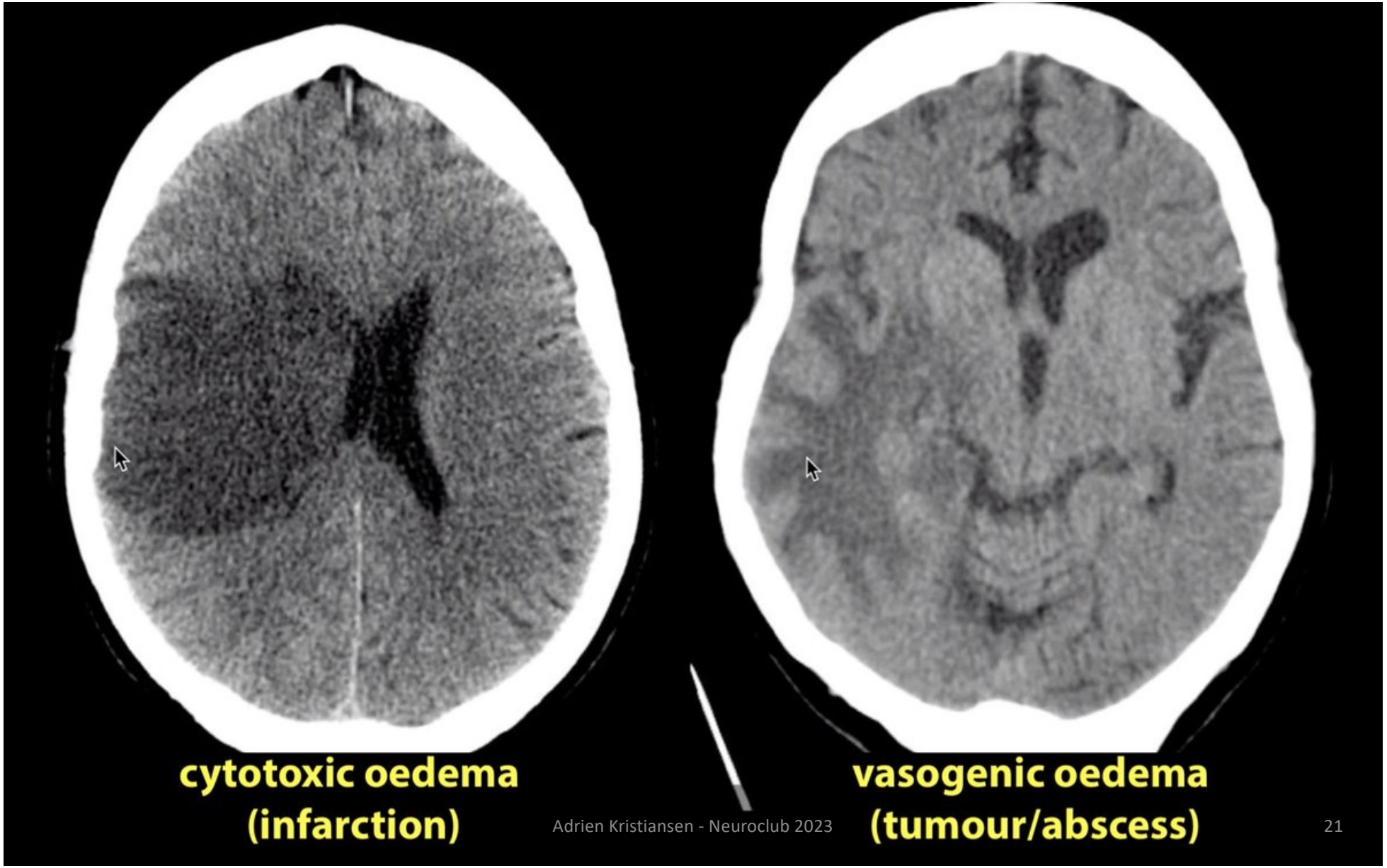

cytotoxic oedema
(infarction)
vasogenic oedema
(tumour/abscess)

Table 1 | **Factors modulating neuroinflammation in patients with TBI**

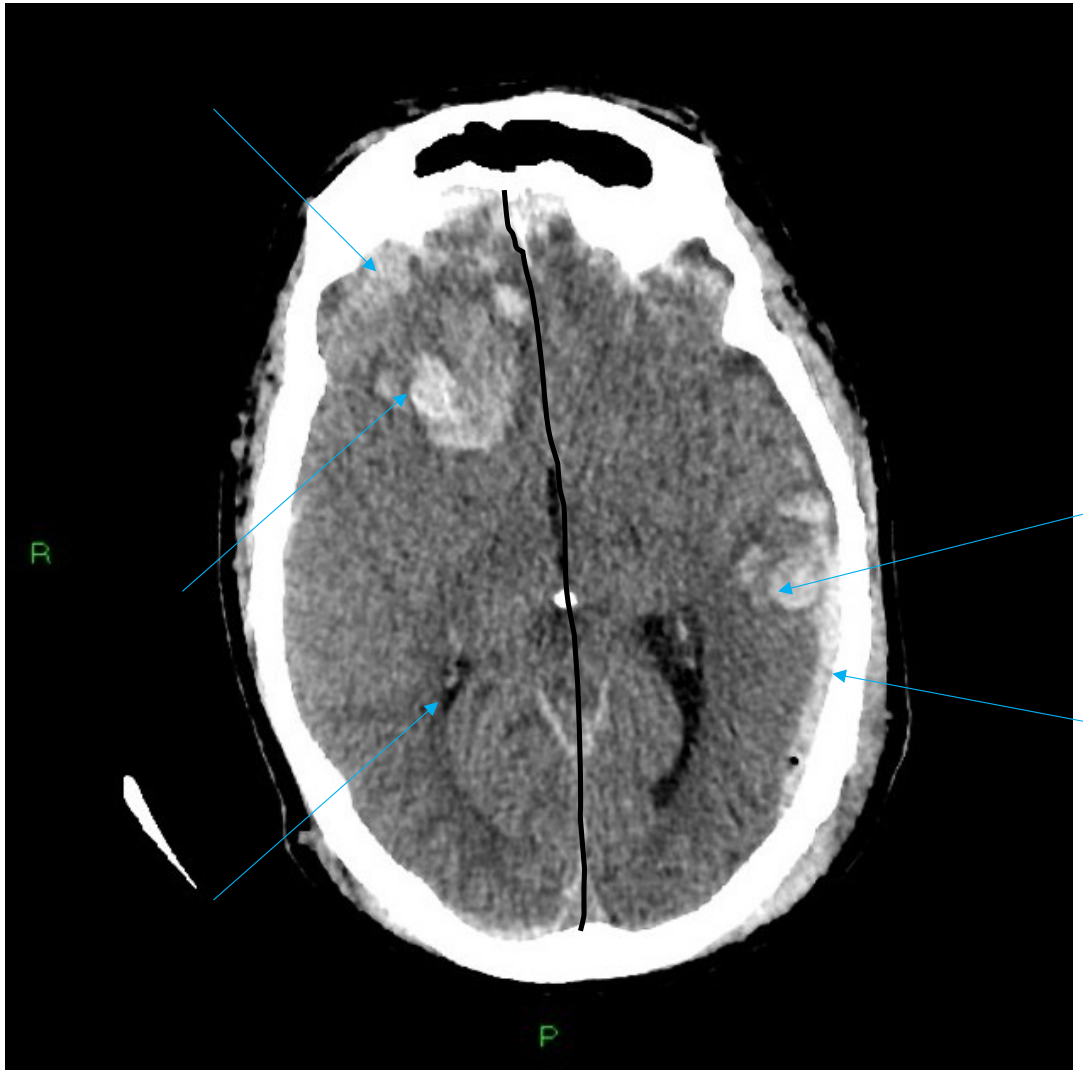
Inflammatory mediator	Tissue or fluid	Time course	Association with clinical outcomes	Other observations	Refs
Cytokines and chemokines					
TNF	CSF, ECF	• Peaks early on day 1 • Prolonged elevation in patients with hypoxia	• Mixed results • Most studies show no association with outcome • High level at 6 h might be associated with ICP and outcome	• Soluble TNF receptor levels peak later (days 4–9) • *TNF* allele variants associated with clinical outcome	5,7,117, 168, 198–203
	Tissue	Increased within 17 min after injury	Unknown	Fourfold increase in mRNA within 17 min	6
IFNγ	Tissue	Increased within 17 min of injury	Unknown	Second-highest cytokine concentration measured (after IL-6)	
IL-1β	CSF, ECF	• Peaks at days 1–2; decreases at days 2–4 • IL-1ra consistently much higher than IL-1β	• Paediatric: mixed results; no correlation with outcome • Adult: mixed results; no correlation with outcome and elevated ICP • Adult: high ECF IL-1ra and IL-1ra:IL-1β ratio associated with good outcome	• *IL1RN* (IL-1ra gene) polymorphisms associated with cerebral haemorrhage after TBI • Principal component analysis of microdialysis data shows close covariance with TNF	117, 203–210
	Tissue	Increased above control 6–122 h after injury	Unknown	Fivefold increase in mRNA at 6–122 h	6
IL-6	CSF, ECF	• Marked increase after TBI • Peaks at day 1, declines at days 2–3	• Paediatric: mixed results; no correlation with outcome • Adult: high CSF or ECF level associated with favorable GOS score	• Paediatric: twofold greater in children with intermittent versus continuous CSF drainage • Adults: associated with NGF level (CSF added to astrocyte culture induced NGF production, blocked by anti-IL-6 antibody)	203–205, 209, 211–217
	Tissue	Increased within 17 min after injury	No relationship with ICP, brain oxygenation or oedema	20-fold increase in mRNA levels at 6–122 h	6,209
IL-10	CSF, ECF	• Peaks at day 1, declines at days 2–3 • May have second or third peak of lower magnitude • Later peak in ECF at days 4–6	• Paediatric: high level associated with mortality in severe TBI • Adult: mixed results; correlation with outcome	• Very young patients (<4 years) have high levels • No change in contused tissue	5,6,117, 203,208, 209,211, 214,218
IL-12p70	CSF, ECF	• Increased at days 2–3 • Peaks at days 3–5	Paediatric: not associated with outcome	35-fold greater in ECF than in plasma	203,204
GM-CSF	Tissue	Increased above control 6–122 h after injury	Unknown	Expression in CSF prolonged by hypoxia	6,219
TGFβ	CSF	Peaks at day 1, gradually decreases over 21 days	Adult: not associated with outcome	Associated with BBB permeability	220
CCL2 (MCP-1)	CSF, ECF	Peaks at day 1, decreases and plateaus by day 4, but remains elevated until day 10	Unknown	Tenfold higher in ECF than in plasma	203,221, 222
	Tissue	mRNA detected 3 h to 15 days after injury	Unknown	The most consistently and strongly expressed chemokine mRNA in evacuated contusion	222
CCL3 (MIP1α)	CSF, ECF	Increased at days 1–3, no clear peak	Paediatric: not associated with outcome	No association with age, sex or GCS score	203,204
	Tissue	mRNA detected 3 h to 15 days after injury	Unknown	Intermediate levels of mRNA detected	222
CXCL8 (IL-8)	CSF, ECF	Peaks at day 1; marked decline at days 2–3; remains elevated up to 108 h after injury	• Paediatric: high level strongly associated with mortality • Adult: high level associated with BBB permeability, but not mortality	• No association with age, sex or GCS score • Tenfold to 20-fold higher in CSF and ECF than in plasma	203,204, 214,223
	Tissue	mRNA detected 3 h to 15 days after injury	Unknown	139-fold increase in mRNA at 6–122 h	6,222

Cytokine	Family	Main sources	Function
IL-1β	IL-1	Macrophages, monocytes	Pro-inflammation, proliferation, apoptosis, differentiation
IL-4	IL-4	Th-cells	Anti-inflammation, T-cell and B-cell proliferation, B-cell differentiation
IL-6	IL-6	Macrophages, T-cells, adipocyte	Pro-inflammation, differentiation, cytokine production
IL-8	CXC	Macrophages, epithelial cells, endothelial cells	Pro-inflammation, chemotaxis, angiogenesis
IL-10	IL-10	Monocytes, T-cells, B-cells	Anti-inflammation, inhibition of the pro-inflammatory cytokines
IL-12	IL-12	Dendritic cells, macrophages, neutrophils	Pro-inflammation, cell differentiation, activates NK cell
IL-11	IL-6	Fibroblasts, neurons, epithelial cells	Anti-inflammation, differentiation, induces acute phase protein
TNF-α	TNF	Macrophages, NK cells, $CD4^+$ lymphocytes, adipocyte	Pro-inflammation, cytokine production, cell proliferation, apoptosis, anti-infection
IFN-γ	INF	T-cells, NK cells, NKT cells	Pro-inflammation, innate, adaptive immunity anti-viral
GM-CSF	IL-4	T-cells, macrophages, fibroblasts	Pro-inflammation, macrophage activation, increase neutrophil and monocyte function
TGF-β	TGF	Macrophages, T cells	Anti-inflammation, inhibition of pro-inflammatory cytokine production

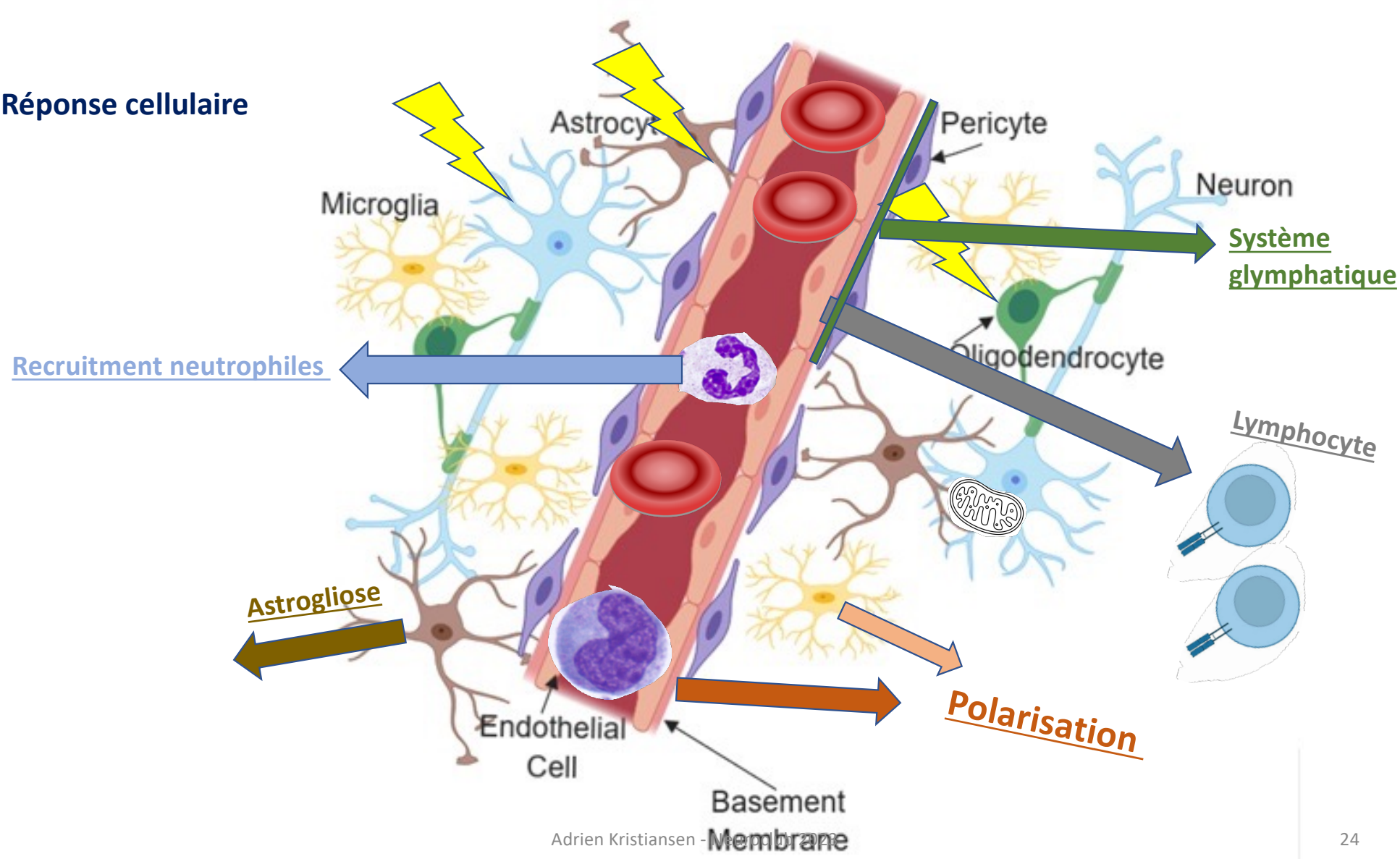
Inflammatory responses and inflammation-associated diseases in organs

Scanner de Gabriel

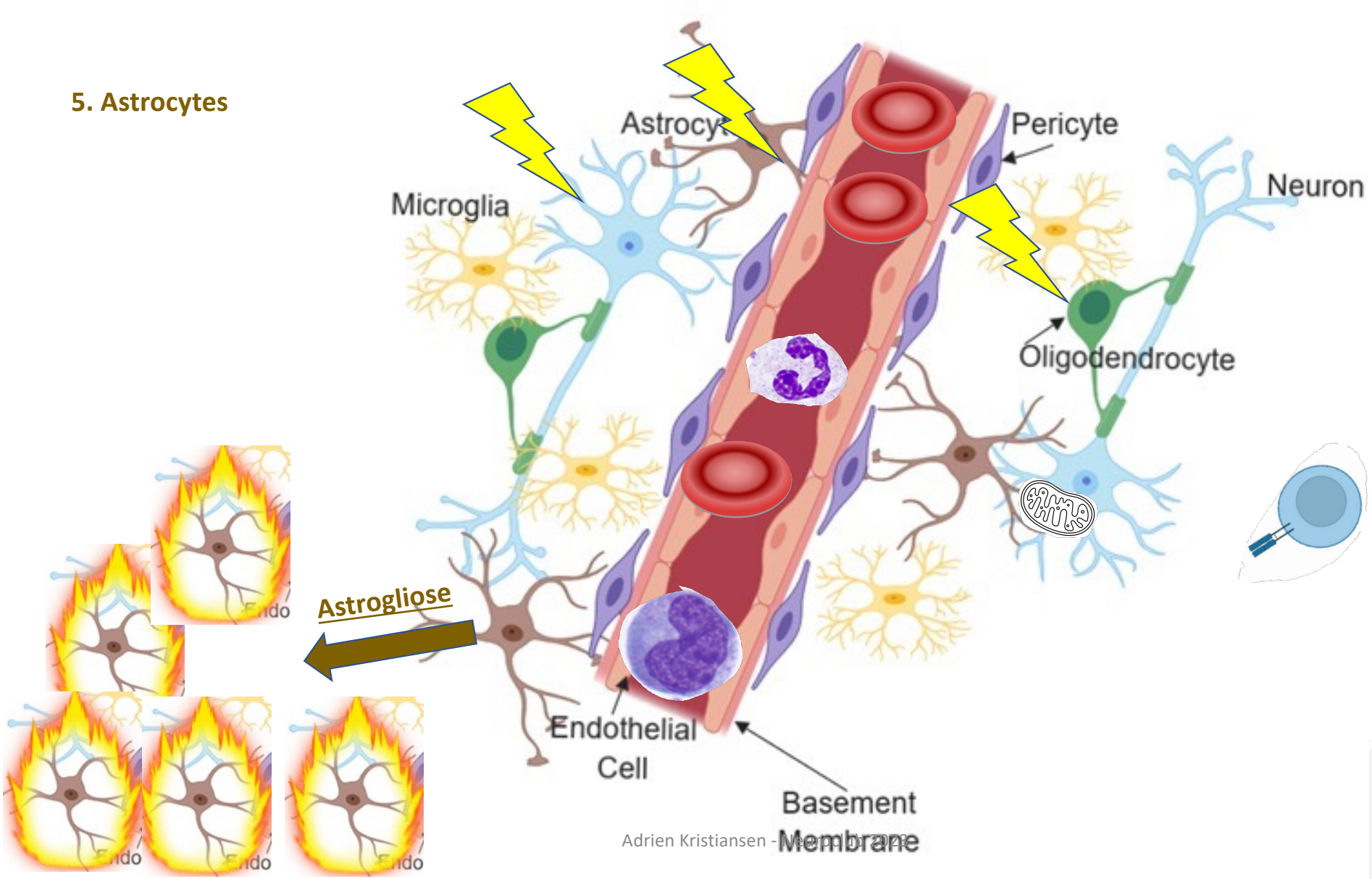
Quelles lésions sont visibles ?



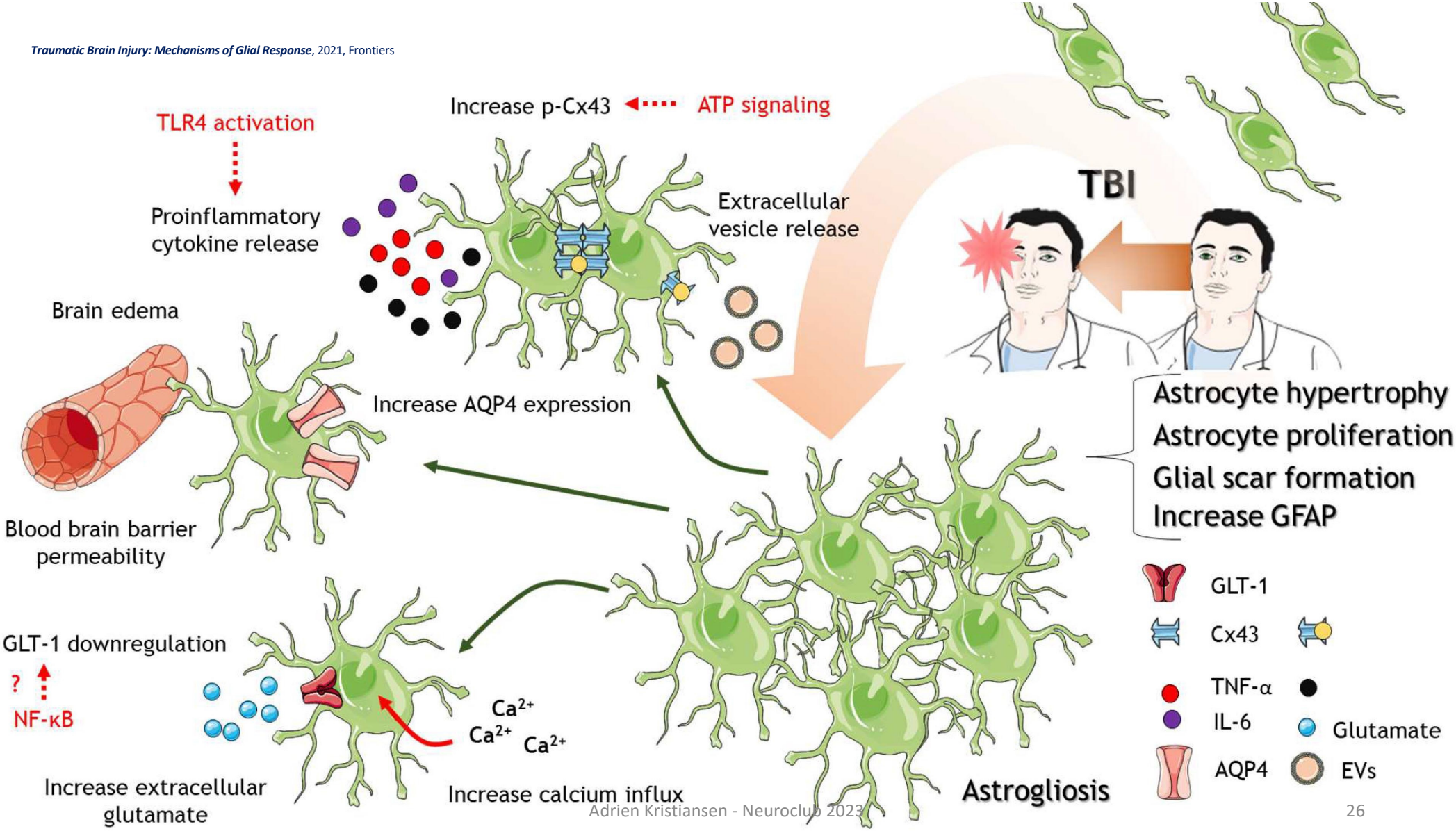
Réponse cellulaire

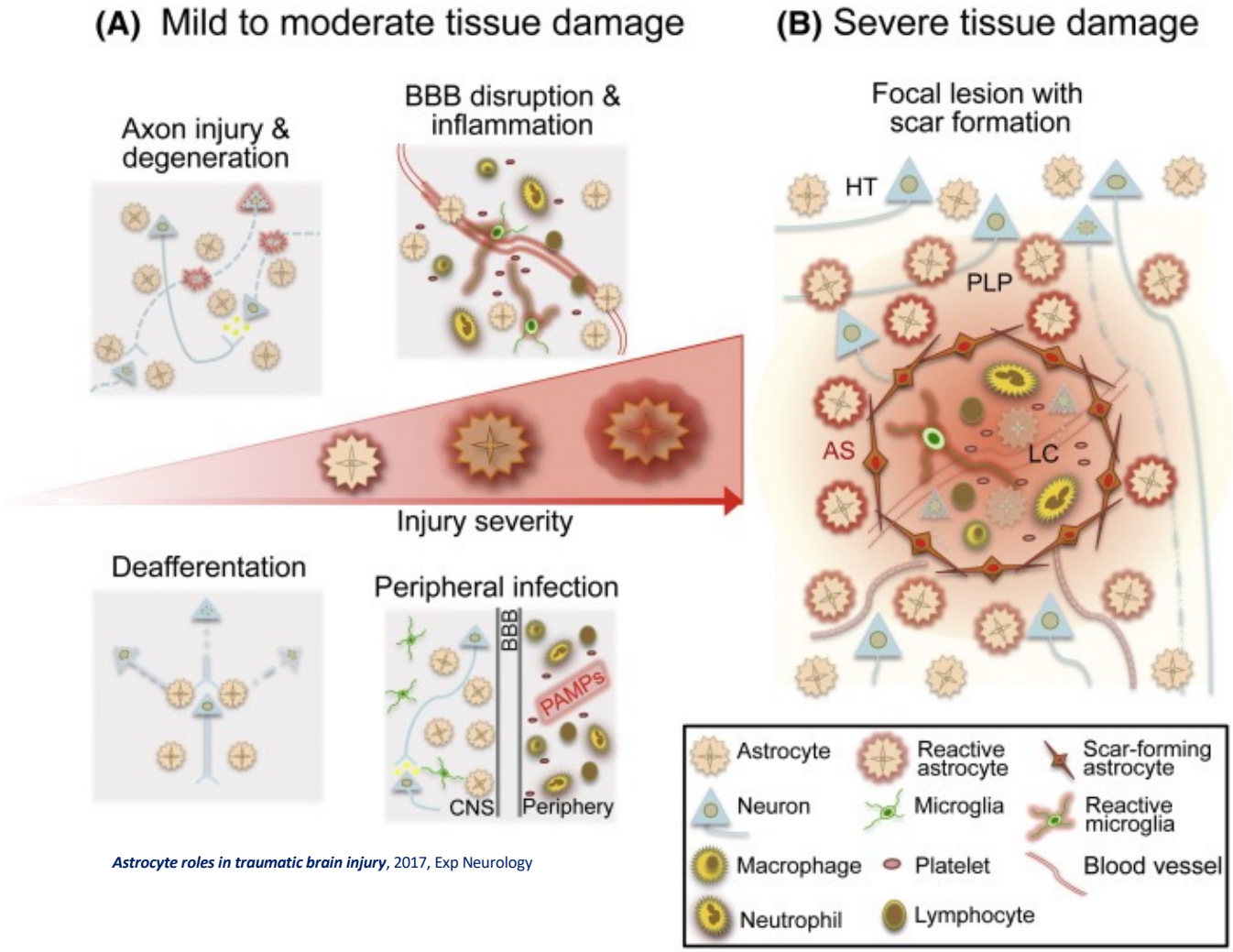


5. Astrocytes



Traumatic Brain Injury: Mechanisms of Glial Response, 2021, Frontiers





Astrocyte roles in traumatic brain injury, 2017, Exp Neurology

Existe-t-il des biomarqueurs utiles en clinique pour les traumatismes crâniens ?

OUI!

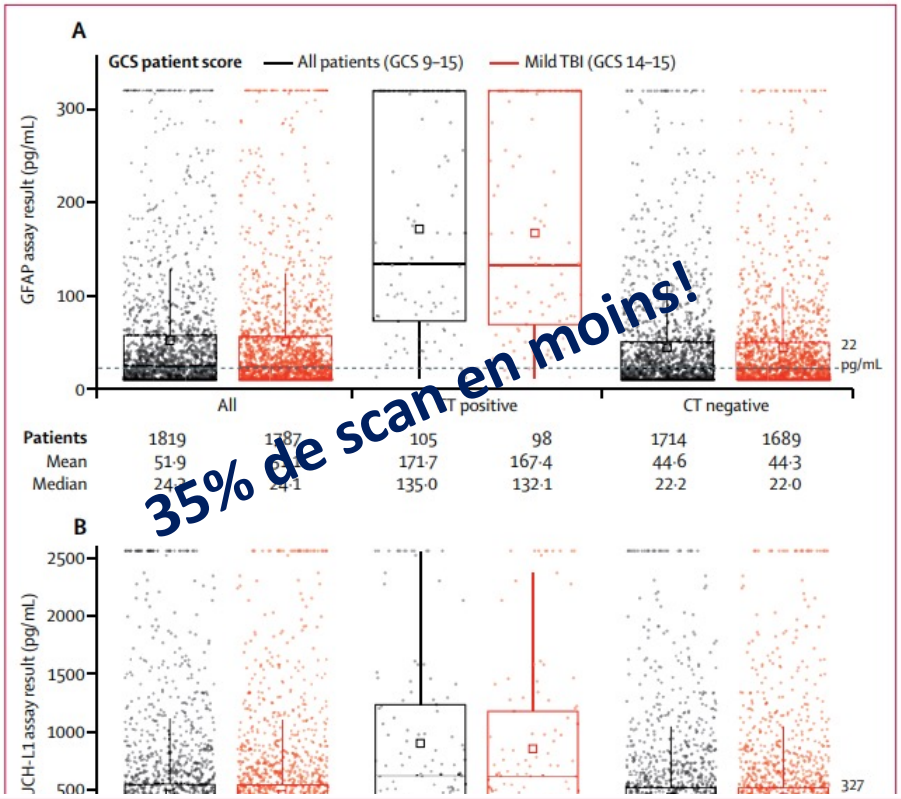
- **GFAP**
- UCTHL1
- S100B
- Nfl

Serum GFAP and UCH-L1 for prediction of absence of intracranial injuries on head CT (ALERT-TBI): a multicentre observational study

GFAP

- **Glial fibrilary acidic protein**
- Filament intermédiaire astrocyes
- Marqueur des astrocytes
- Libéré circulation systémique

>22 pg/mL



	Sensitivity	Specificity	PPV	NPV	LRP	LRN
GCS 9–15 (n=1959)	0·976 (0·931–0·995)	0·364 (0·342–0·387)	0·095 (0·079–0·112)	0·996 (0·987–0·999)	1·5 (1·455–1·616)	0·07 (0·00–0·153)
GCS 14–15 (n=1920)	0·973 (0·924–0·994)	0·367 (0·345–0·390)	0·088 (0·073–0·105)	0·995 (0·987–0·999)	1·5 (1·457–1·618)	0·07 (0·00–0·159)
Neurosurgically manageable lesions (n=8)	1·00 (0·631–1·00)	0·344 (0·323–0·365)	0·006 (0·003–0·012)	1·00 (0·995–1·00)	1·5 (1·447–1·602)	0·0 (0·00–0·093)

Data in parentheses are 95% CIs. PPV=positive predictive value. NPV=negative predictive value. LRP=likelihood ratio positive. LRN=likelihood ratio negative.

Table 3: **Performance of UCH-L1 and GFAP assay for predicting intracranial injury on head CT scan**

27% of patients with a normal CT had positive findings on an MRI
AUC=0.78

	Sensitivity	Specificity	NPV	PPV
4·40 pg/mL	1·000 (1·000–1·000)	0·024 (0·009–0·042)	1·000 (1·000–1·000)	0·271 (0·268–0·275)
12·95 pg/mL	0·958 (0·925–0·992)	0·188 (0·148–0·230)	0·925 (0·863–0·981)	0·300 (0·287–0·313)
25·15 pg/mL	0·908 (0·850–0·958)	0·333 (0·288–0·388)	0·910 (0·861–0·957)	0·332 (0·312–0·354)
71·95 pg/mL	0·825 (0·750–0·892)	0·494 (0·442–0·549)	0·888 (0·845–0·924)	0·373 (0·344–0·407)
282·70 pg/mL	0·642 (0·558–0·733)	0·803 (0·758–0·842)	0·861 (0·832–0·890)	0·543 (0·482–0·603)
848·75 pg/mL	0·233 (0·158–0·308)	0·964 (0·942–0·982)	0·775 (0·760–0·793)	0·698 (0·555–0·842)

The κ-fold cross-validation method was used to select the optimal cutoffs for predicting MRI-positive versus MRI-negative findings in patients with negative CT based on the criteria of adjusted NPV above the level of 0·96, 0·94, 0·92, and 0·90, 0·85, and 0·80, in accordance to data standards for clinical laboratory assays set by the manufacturer. The prevalence of positive MRI scans among patients with negative CT scans was estimated to be 0·27 on the basis of the sample rate to calculate the adjusted NPV. 1000 bootstraps were conducted to determine the optimal cutoffs using the median from each run. The optimal cutoff thresholds were then applied to the full data to calculate the corresponding sensitivity, specificity, NPV, and PPV. GFAP=glial fibrillary acidic protein. NPV=negative predictive value. PPV=positive predictive value.

Table 3: **Cutoff concentrations of plasma GFAP to predict MRI-positive versus MRI-negative findings in patients with negative CT**

	Number of patients	Plasma GFAP concentration (pg/mL)			p value
		Mean (SD)	Median (25–75th percentile)	Range	
Positive CT	199	1400·9 (1598·6)	786·0 (357·0–1863·3)	0–9409·7	<0·0001*
Negative CT	450	308·0 (530·5)	110·3 (22·7–352·3)	0–4095·1	..
Negative CT and positive MRI	120	692·2 (827·6)	414·4 (139·3–813·4)	5·2–4095·1	<0·0001†
Negative CT and negative MRI	330	168·3 (250·9)	74·0 (17·5–214·4)	0–1864·5	..
Orthopaedic trauma controls	122	23·7 (37·2)	13·1 (6·9–20·0)	0–216·8	<0·0001‡§
Healthy controls	209	11·0 (12·7)	8·0 (3·0–14·0)	0–98·0	<0·0001‡§

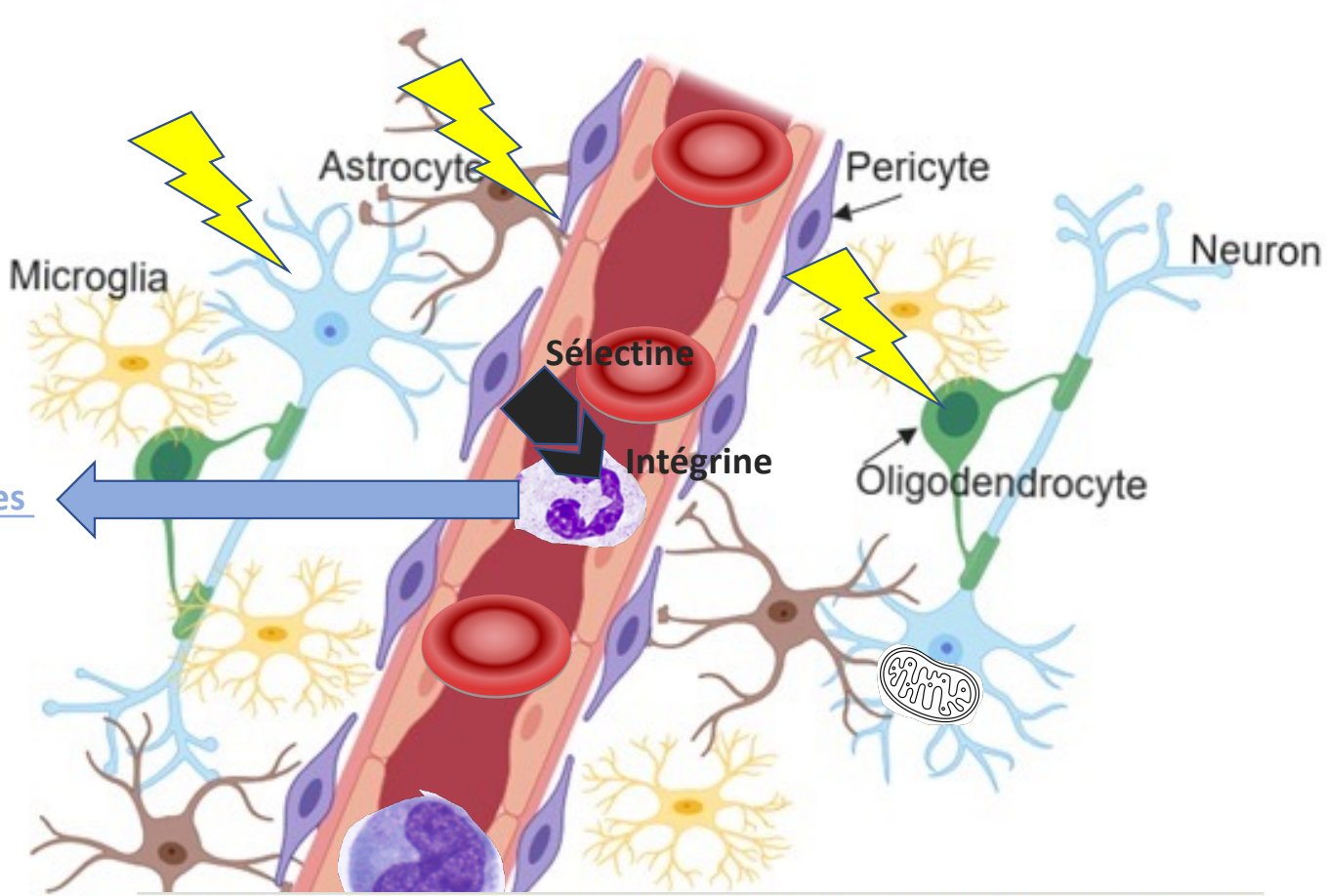
GFAP=glial fibrillary acidic protein. P values were calculated from the Wilcoxon rank sum test for the comparisons, which compares the distributions of the two groups. *Compared with patients with negative CT. †Compared with patients with negative CT and negative MRI findings. ‡Compared with patients with negative CT and positive MRI findings. §Compared with patients with negative CT and negative MRI findings.

Table 2: **Plasma GFAP concentrations by imaging modality and findings**

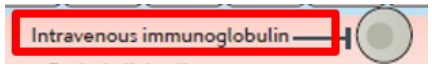
Association between plasma GFAP concentrations and MRI abnormalities in patients with CT-negative traumatic brain injury in the TRACK-TBI cohort: a prospective multicentre study, 2019, The Lancet Neurology

6. Neutrophiles

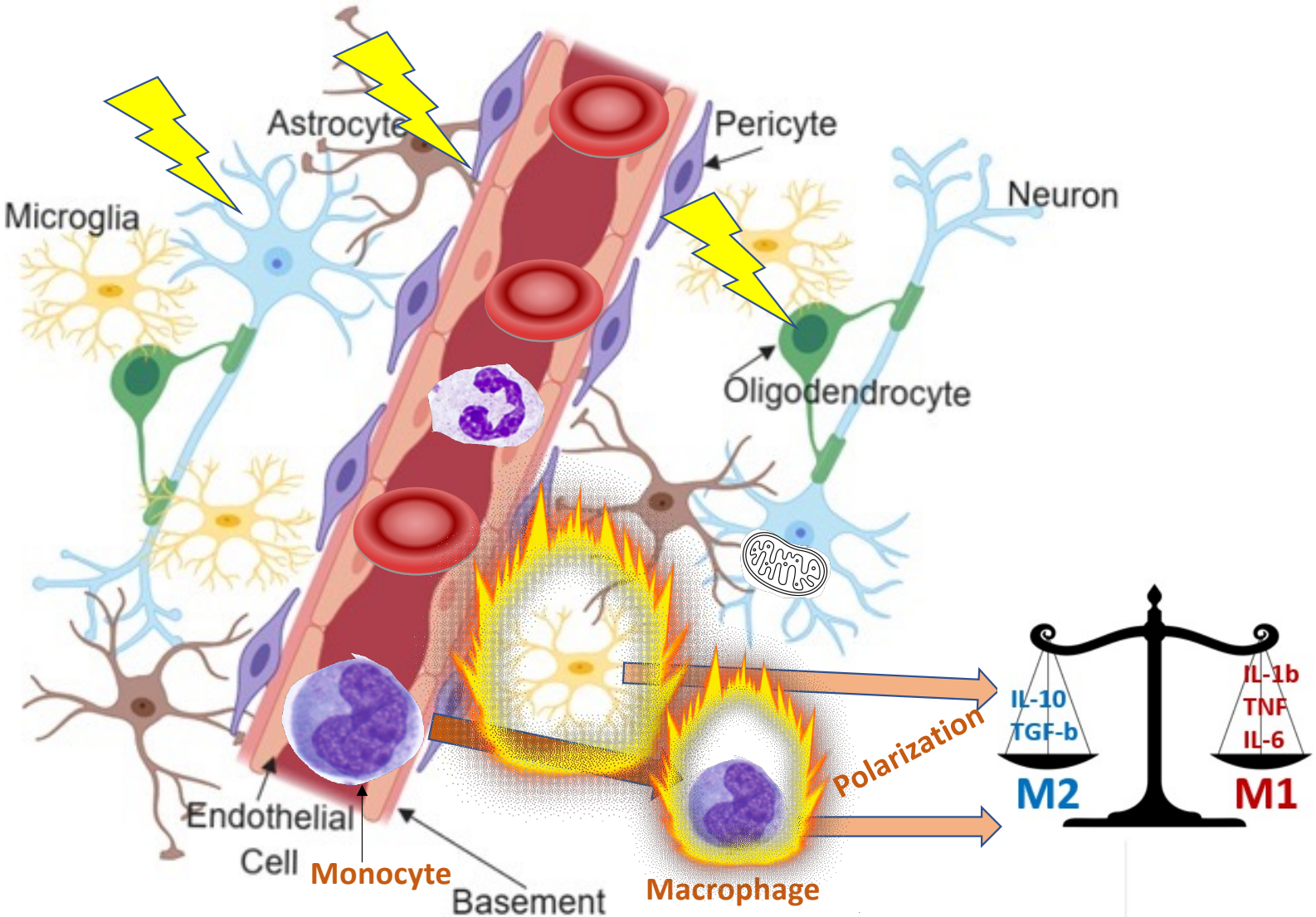
Recruitment neutrophiles

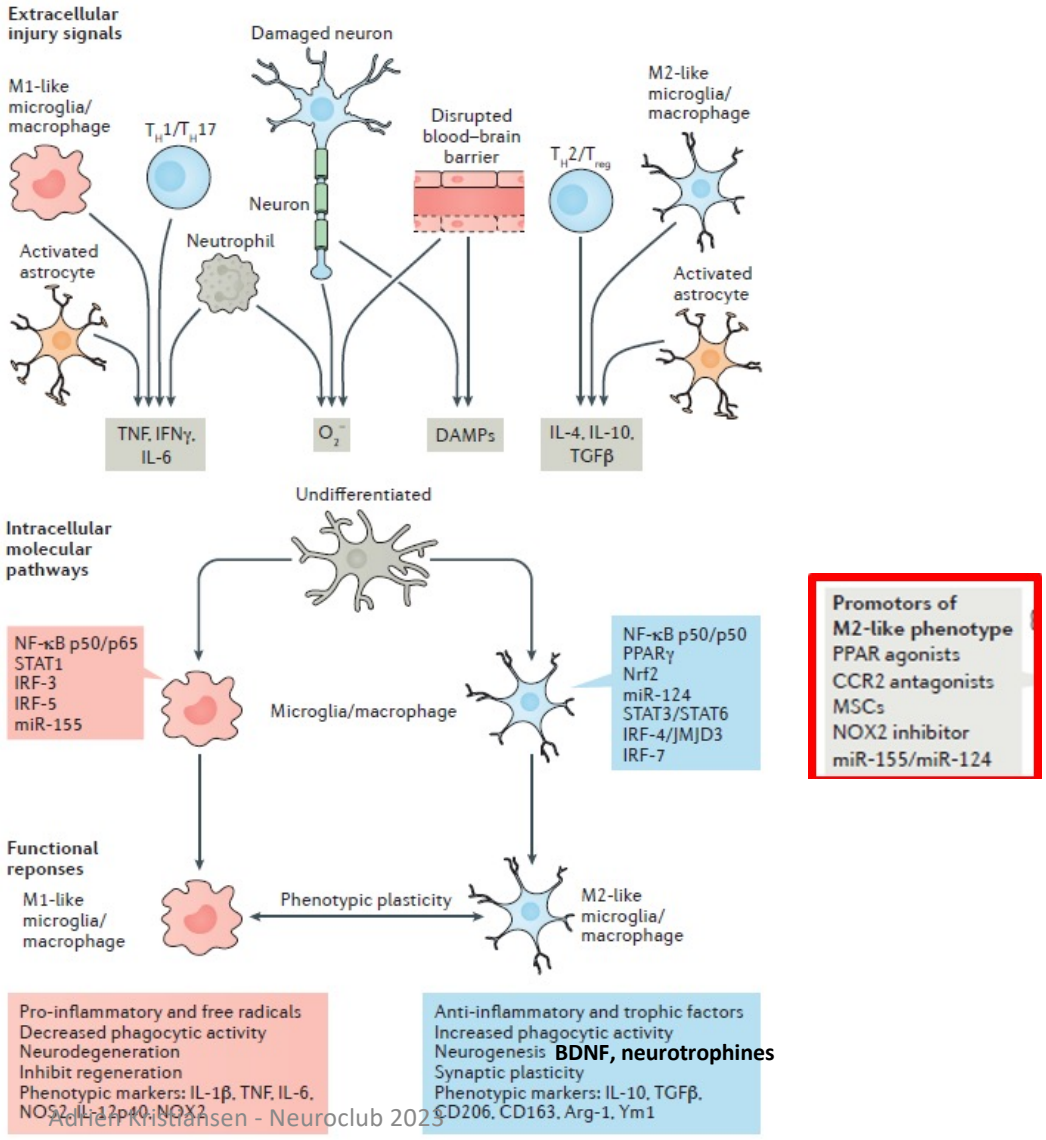


Granulocyte colony-stimulating factor (G-CSF)	Stimulates stem cells to produce granulocytes	• Multicentre RCT[149] • 61 adults with GCS score ≤8, expected to require mechanical ventilation for >3 days	75 µg or 300 µg daily for 10 days versus placebo	Dose-dependent increase in neutrophil count	• No difference in mortality, length of stay, or nosocomial infection • Significant decrease in bacteraemia incidence	• Adverse events similar between groups • Included patients with cerebral haemorrhage as well as TBI

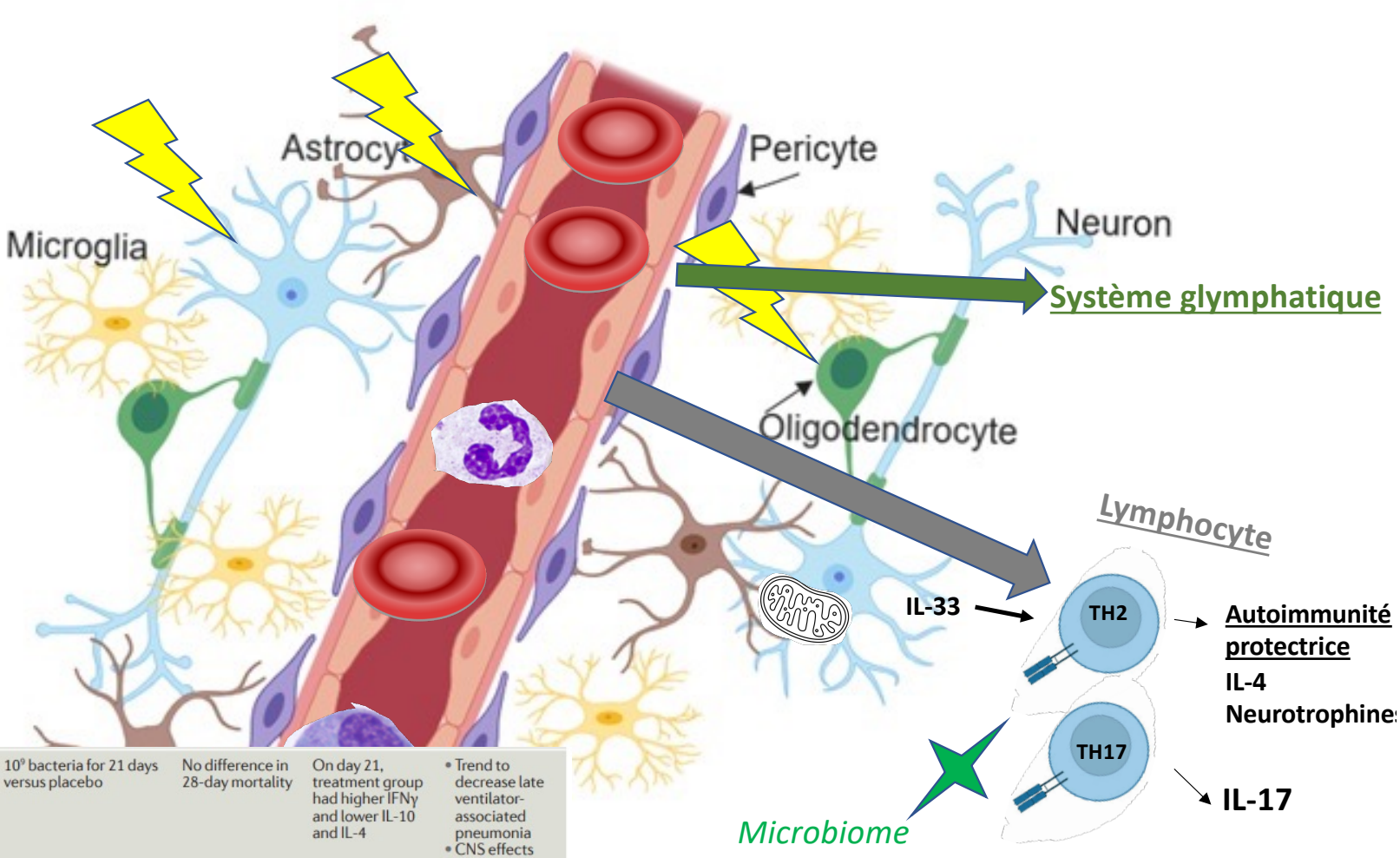


7. Microglie/macrophage




Extracellular injury signals
Damaged neuron
M1-like microglia/ macrophage
T_H1/T_H17
Disrupted blood–brain barrier
T_H2/T_{reg}
M2-like microglia/ macrophage
Neuron
Neutrophil
Activated astrocyte
Activated astrocyte
TNF, IFNγ, IL-6
O_2^-
DAMPs
IL-4, IL-10, TGFβ
Undifferentiated
Intracellular molecular pathways
NF-κB p50/p65
STAT1
IRF-3
IRF-5
miR-155
Microglia/macrophage
NF-κB p50/p50
PPARγ
Nrf2
miR-124
STAT3/STAT6
IRF-4/JMJD3
IRF-7
Promotors of M2-like phenotype
PPAR agonists
CCR2 antagonists
MSCs
NOX2 inhibitor
miR-155/miR-124
Functional reponses
M1-like microglia/ macrophage
Phenotypic plasticity
M2-like microglia/ macrophage
Pro-inflammatory and free radicals
Decreased phagocytic activity
Neurodegeneration
Inhibit regeneration
Phenotypic markers: IL-1β, TNF, IL-6, NOS2, IL-12p40, NOX2
Anti-inflammatory and trophic factors
Increased phagocytic activity
Neurogenesis BDNF, neurotrophines
Synaptic plasticity
Phenotypic markers: IL-10, TGFβ, CD206, CD163, Arg-1, Ym1

9. Lymphocytes
10. Glymphatique



Probiotics	Modify lymphocyte polarization before CNS infiltration	• Single-centre RCT[245] • 52 adults with GCS score 5–8	10^9 bacteria for 21 days versus placebo	No difference in 28-day mortality	On day 21, treatment group had higher IFNγ and lower IL-10 and IL-4	• Trend to decrease late ventilator-associated pneumonia • CNS effects unclear
Cyclosporin A	Reduces T-cell counts and activation	• Single-centre RCT[237] • 38 adults with GCS score ≤8	5 mg/kg over 24 h or 10 mg/kg over 48 h versus placebo	No difference in blood T-cell counts	No difference in incidence of infection	Reduced lymphocyte count on admission associated with worse outcome and increased respiratory infections

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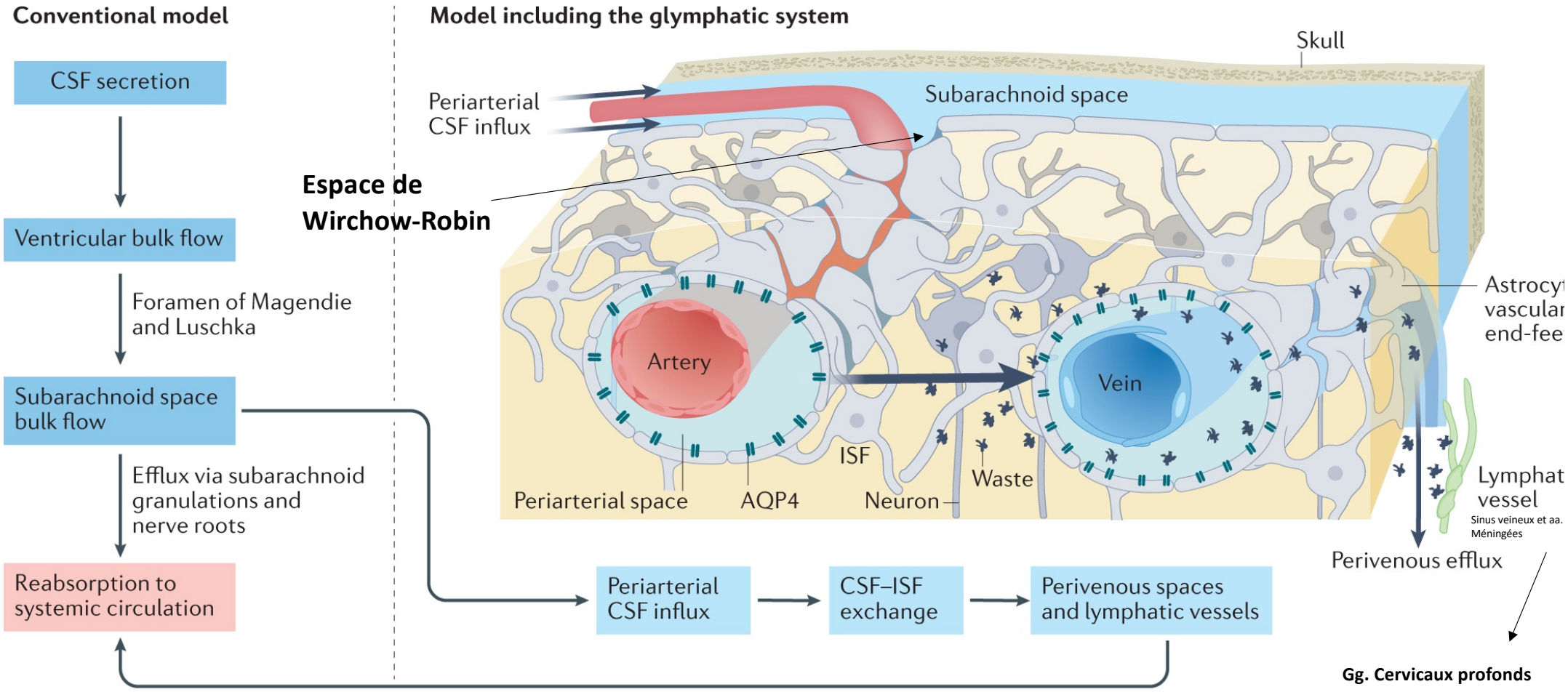
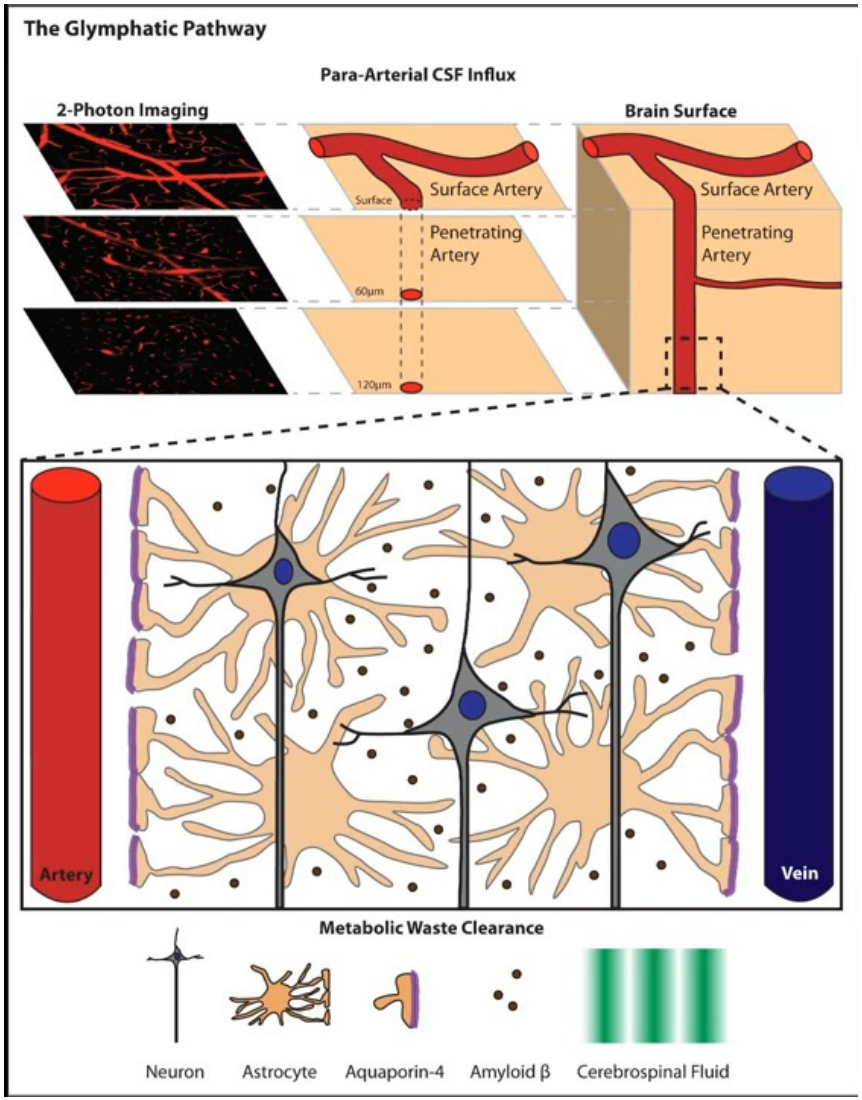


The glymphatic system: implications for drugs for central nervous system diseases



Sleep posture

Corticoïdes ?

Steroids	• Inhibit leukocyte activation and infiltration • Modulate cytokine release • Progesterone decreases upregulation of IL-1β, TNF, and complement factors 3 and 5 • Reduce M1-like microglial activation	CRASH: • Multicentre RCT[142] • 10,008 adults with GCS score ≤14	Methylprednisolone load 2 g over 1 h + maintenance 0.4 g/h for 48 h versus placebo	Higher risk of mortality at 2 weeks in steroid group	Higher risk of mortality at 6 months in steroid group	Terminated early for safety concerns
		• Multicentre RCT[143] • 161 adults with TBI and coma	Dexamethasone 100 mg versus placebo	No difference in survival	No difference in 6-month outcome	–
		• Multicentre RCT[145] • 163 adults with GCS score 9–12 and 957 adults with GCS sc… 4–8	Ti… d 10 mg/k… of in…	No difference in 6-month GOS …core	No difference in mortality	Significant differences in pretreatment hypotension and hypoxia related to intercentre variation
		Corti-TC: • Multicentre RC… • 336 adults w… GCS score ≤…	…difference …ncidence of …ital- …d …onia		No change when analysed according to presence or absence of adrenal insufficiency	Study may have been underpowered owing to lower than expected incidence of hospital-acquired pneumonia
		ProTECT III: • Multicentre RCT[159] • 882 adults with GCS score 4–12	Pro…sterone infus… started within 4 h of injury, duration 96 h	No difference in 6-month GOS score	No difference in mortality	Terminated (futility)
		SyNAPSe: • Multicentre RCT[160] • 1,195 adults with GCS score ≤8	Progesterone 0.71 mg/kg load + 0.5 mg/kg/h infusion for 119 h	No difference in 6-month GOS score	No difference in mortality	–

Table 2 (cont.) | **Selected clinical trials evaluating therapies for neuroinflammation after TBI**

Therapy	Effects on inflammation	Study design and number of patients	Dose	Primary outcome	Secondary outcomes	Comments
Hypertonic saline	• Improves T-cell function • Reduces TNF and IL-10	• Multicentre RCT[241] • 1,331 adults with severe TBI	250 ml bolus of 7.5% saline/6% dextran 70 or 7.5% saline versus 0.9% saline initiated pre-hospital	No difference in GOS-E score at 6 months	No difference in survival at 28 days	Terminated (futility)
Hypothermia	• Humoral and cellular immune response is temperature-dependent • Decreased neutrophil accumulation in CNS • Decreased IL-1β, possibly via reduction in temperature-dependent caspase-1 activity	Cool Kids: • Multicentre RCT[242] • 77 children with GCS score ≤8	32–33 °C versus 36.5–37.5 °C for 48–72 h	No difference in mortality at 3 months	No adverse events	Terminated (futility)
		• Multicentre RCT[11] • 225 children with GCS score ≤8	32.5 °C versus 37 °C for 24 h	No difference in 6-month PCPC score	No difference in mortality	Non-significant trend toward increased mortality, significantly higher incidence of hypotension and vasoactive agent use during rewarming (+0.5 °C every 2 h)
		NABIS: HII • Multicentre RCT[156] • 97 adults with GCS score 4–8, enrolled within 2.5 h of injury	32–34 °C versus 35.5–37 °C for 72 h	No difference in 6-month outcome	No difference in mortality	• Terminated (futility) • Improved outcomes in patients with evacuated haematoma treated with hypothermia
		Eurotherm3235: • Multicentre RCT[155] • 387 adults with severe TBI and ICP >20 mm Hg despite stage 1 treatments	Cooled to 32–35 °C followed by stage 2 if ICP remained high versus stage 2 treatments alone	Lower GOS-E score in hypothermia group	Stage 3 treatments (coma, craniectomy) more often required in the control group than in the hypothermia group	Terminated (safety concerns)
Anakinra	Blocks IL-1 signal transduction	• Single-centre RCT[243] • 20 adults with GCS score ≤8	100 mg subcutaneous every 24 h × 5 doses	Increased IL-1ra in CNS extracellular fluid within 6 h	PCA of 42 cytokine multiplex demonstrated separation between treatment and placebo groups	• Subsequent study[244] showed that patients receiving rIL-1ra had cytokines biasing to M1-like microglial phenotype • Control patients were relatively biased to M2-like phenotype
Probiotics	Modify lymphocyte polarization before CNS infiltration	• Single-centre RCT[245] • 52 adults with GCS score 5–8	10^9 bacteria for 21 days versus placebo	No difference in 28-day mortality	On day 21, treatment group had higher IFNγ and lower IL-10 and IL-4	• Trend to decrease late ventilator-associated pneumonia • CNS effects unclear

Neuroinflammation chronique

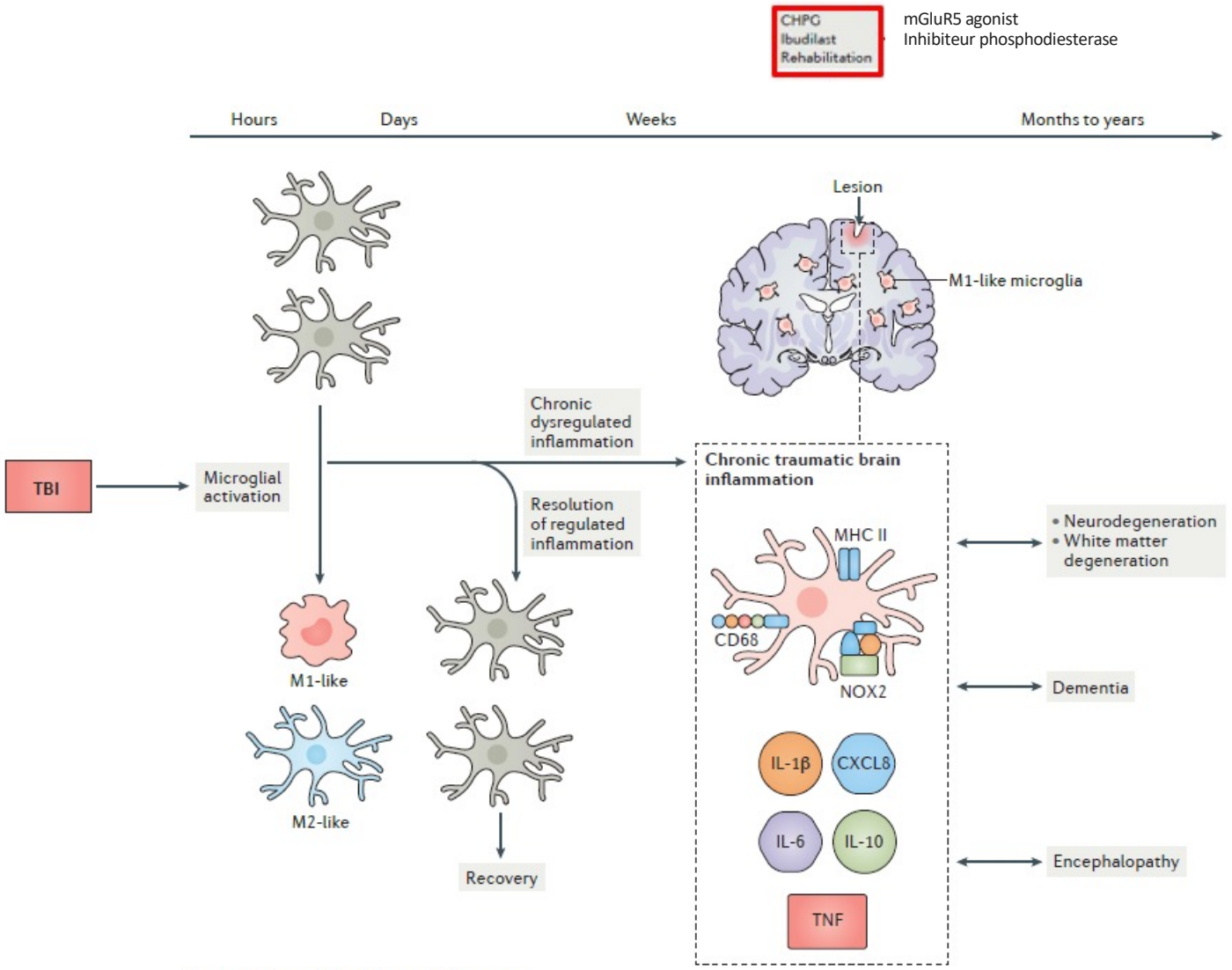
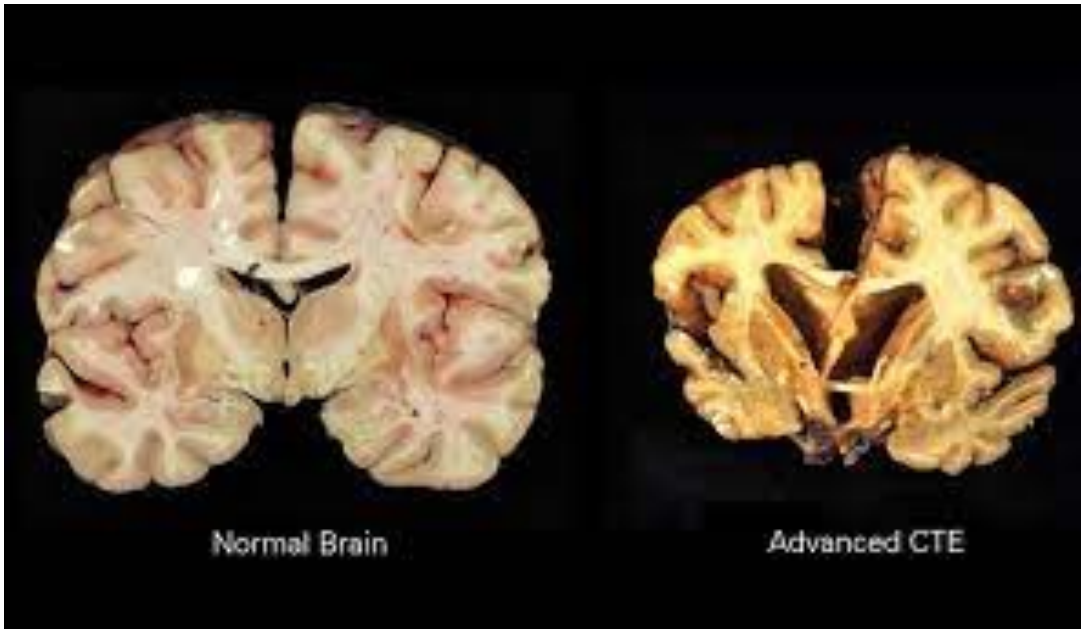


Figure 4 | **Effects of chronic neuroinflammation.**

Chronic traumatic encephalopathy

Tautopathie



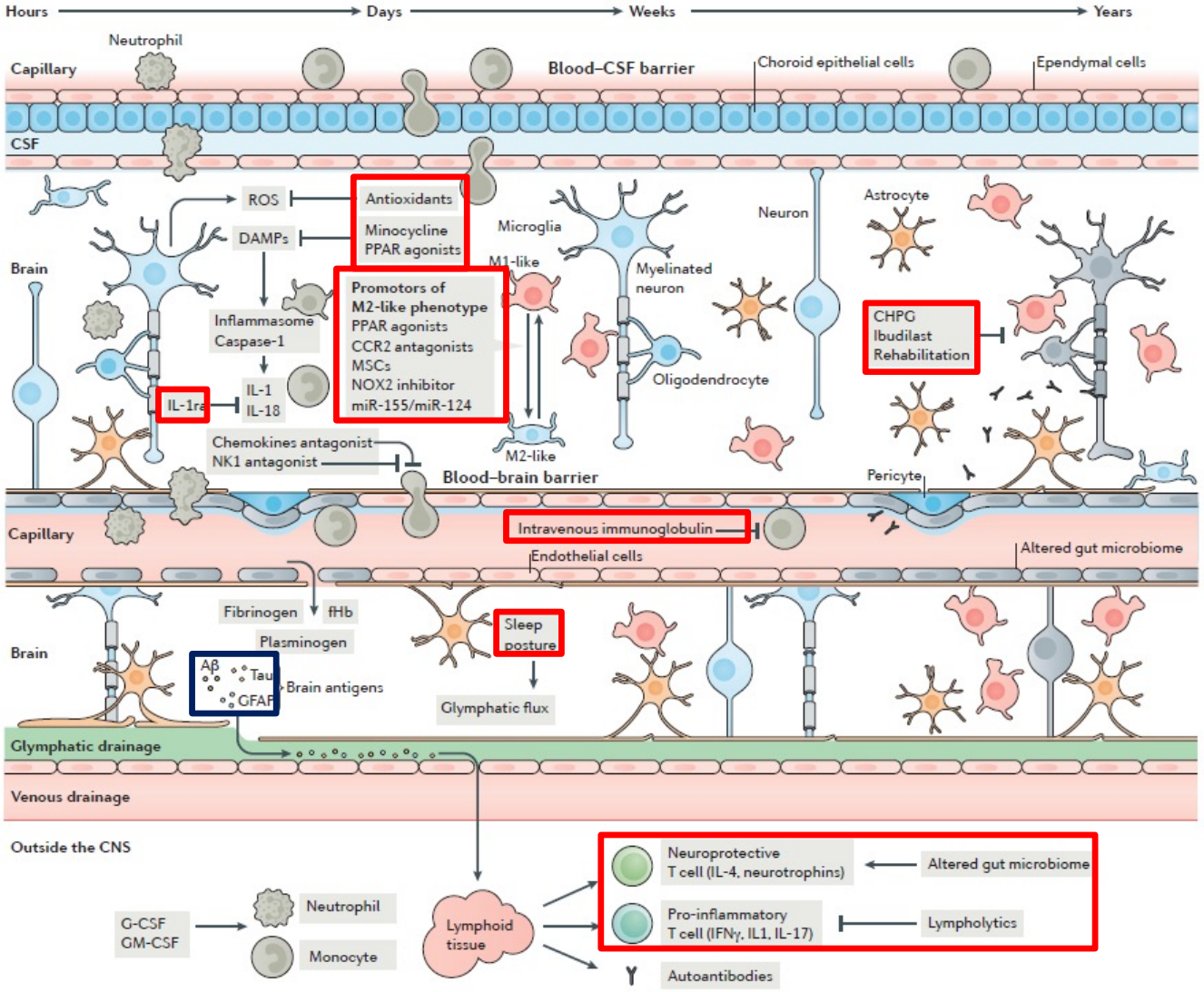
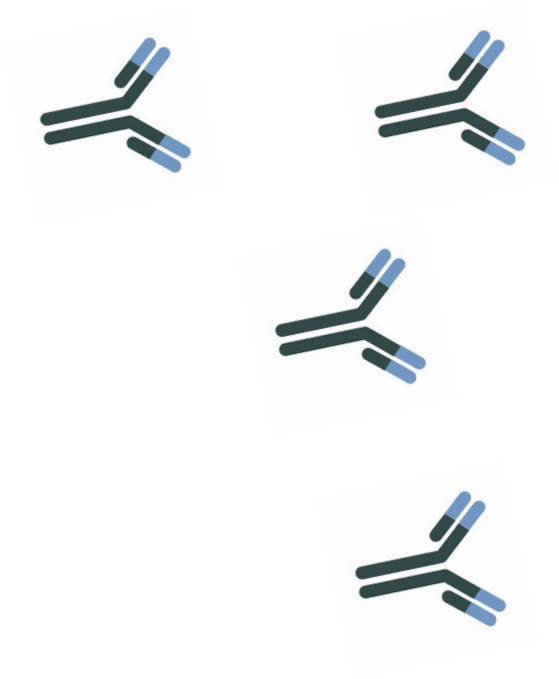


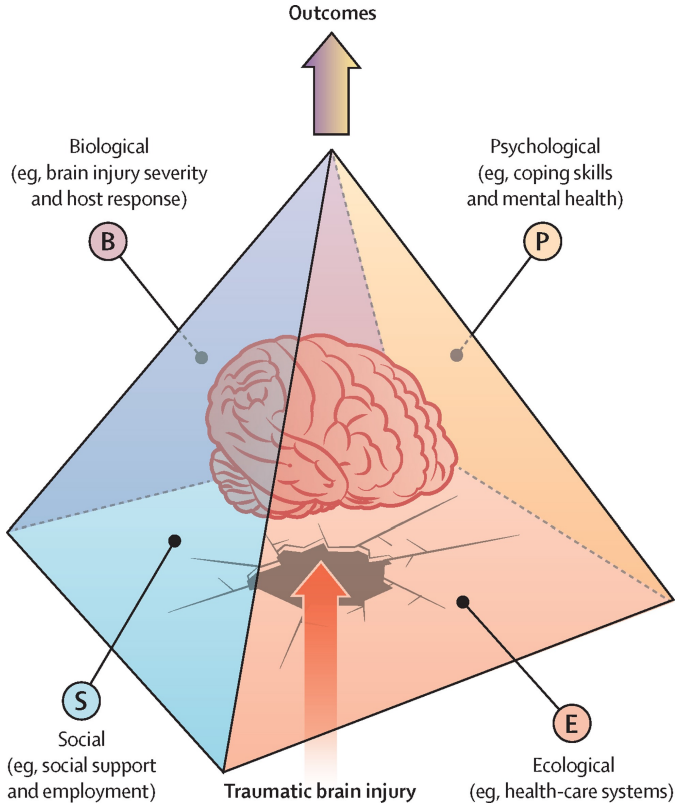
Figure 3 | **Novel TBI therapies targeting inflammation at different time points.**

Retour à Gabriel(le)



Conclusion

- Neuro-inflammation – complexe
  Impliquée dans de nombreuses maladies neurologiques
- Approche large spectre non efficace
- Définir la fenetre thérapeutique, durée du traitement et outcomes
- Phénotypage inflammatoire individualisé du patient
  Patient tailored approach
- Intégrer le patient: approche bio-psycho-socio-écologique

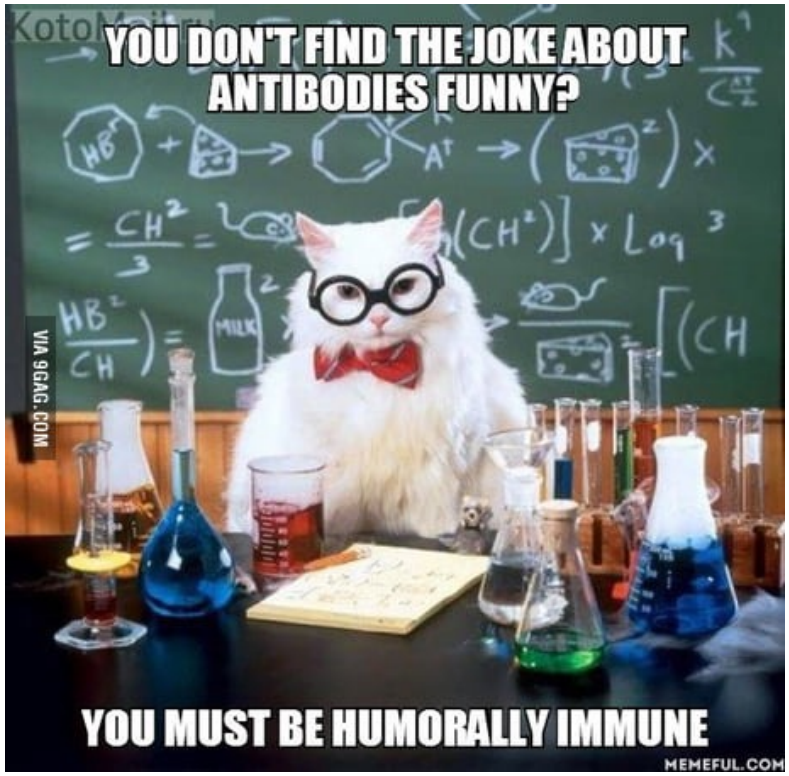


Box 2 | **Outstanding research questions and unmet needs**

- Define the level of acute inflammation needed for clearance of debris, and how it can be determined
- Assess whether the M1-like/M2-like paradigm of microglial polarization translates to human brain injury. Do injury severity-related or regional differences in microglial phenotype exist?
- Investigate the potential of harnessing autoreactive adaptive immune response for the benefit of patients with traumatic brain injury (TBI), and whether T_H17/IL-17 adaptive responses contribute to neurodegeneration in TBI
- Evaluate whether the severity of damage to the CNS lymphatic drainage systems after TBI has a role in defining the magnitude of long-term neuroinflammation
- Investigate the mechanisms that prime reactivity of glia acutely after TBI and sustain their immune activation for weeks, months and years after the initial injury, and the potential of delayed interventions that modulate chronic microglial activation
- Find out how to determine when the reparative processes are no longer beneficial, and how we should facilitate return of the inflammatory process to a normal state
- Could therapeutic trials be stratified to target specific inflammatory phenotypes, reflected by biomarkers?
- New stable and selective PET ligands and/or MRI-based methods to image neuroinflammation are urgently needed

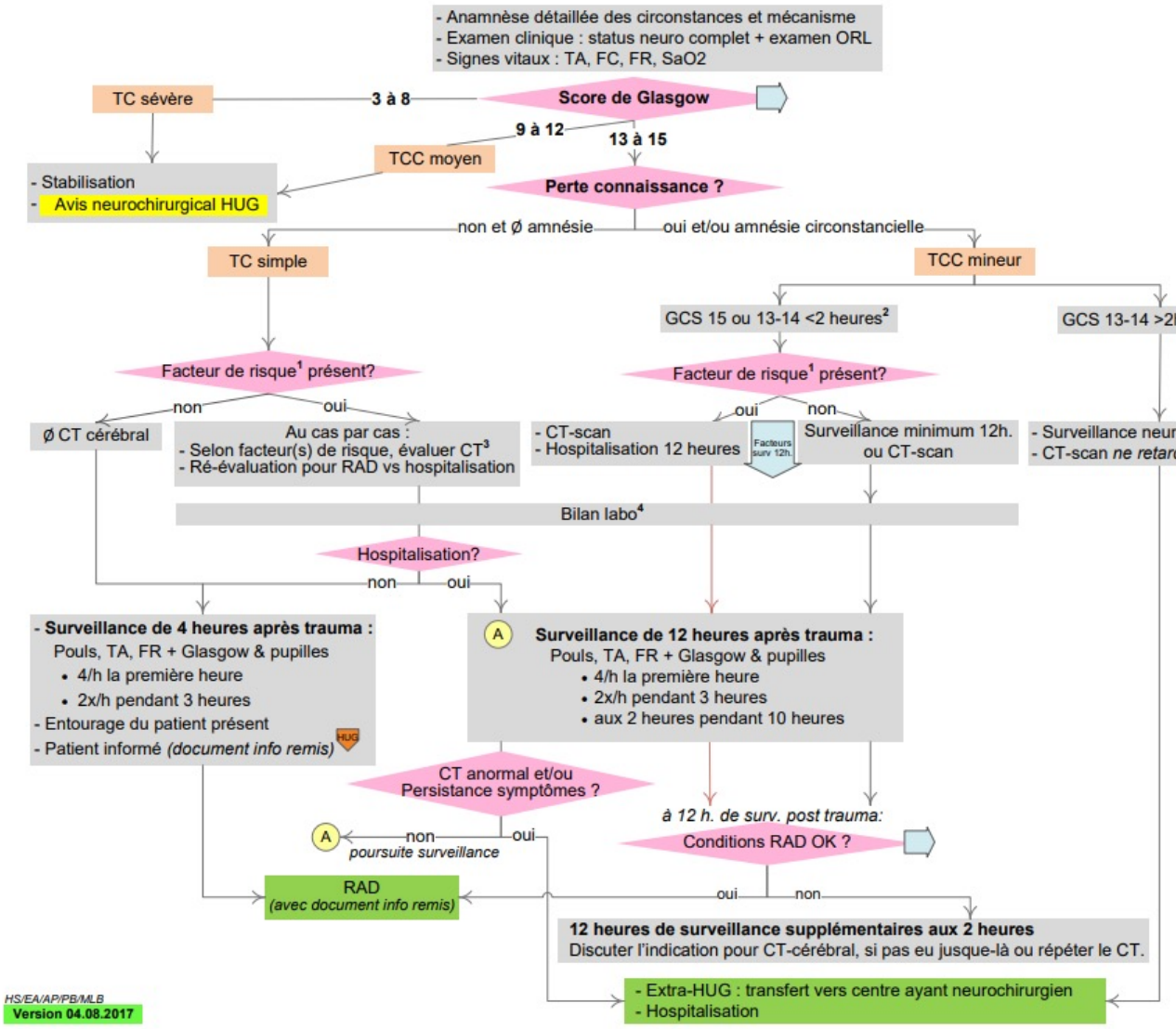
Discussion

- Merci



Prise en charge d'un TRAUMATISME CRANIEN en Urgence

Cet algorithme décisionnel ne se substitue pas au jugement clinique.



HS/EA/AP/PB/MLB
Version 04.08.2017

1 : Facteurs de risque

- Amnésie rétrograde >30 minutes ou antérograde
- Déficit neurologique focal
- OH
- Âge >65 ans
- Prise d'anticoagulant, antiagrégant, coagulopathie connue
- Cinétique (piéton / cycliste / éjection voiture / force impact / chute >1m ou >5 marches)
- Convulsions post-traumatiques
- Vomissements >1 épisode
- Céphalées sévères
- Fracture massif facial, crâne, base du crâne

En cas de doute sur la prise en charge, tél. au neurochirurgien de garde 24h/24h aux HUG : 079 55 33 810

2 : Patient en GCS 13-14 à son arrivée à l'hôpital avec retour à un état de conscience normal <2 heures après l'évènement.

3 : En cas d'amnésie ou d'autres troubles cognitifs, une analyse plus fine peut se faire avec le test MOCA.

Si test anormal, conseiller au médecin traitant un suivi neuropsychologique du patient.

4 : Hb, Ht, Thrombos, Gluc., Na, K, Créat.,
+/- alcoolémie/recherche toxiques
+/- crase selon le contexte clinique

Article de référence:
Traumatisme crânien et cervical : recommandations pour la pratique clinique aux urgences ; B. Vermeulen, A. Reverdin, P.-A. Poletti, Médecine et Hygiène 2003