Calming microglia: a future method for treating multiple sclerosis

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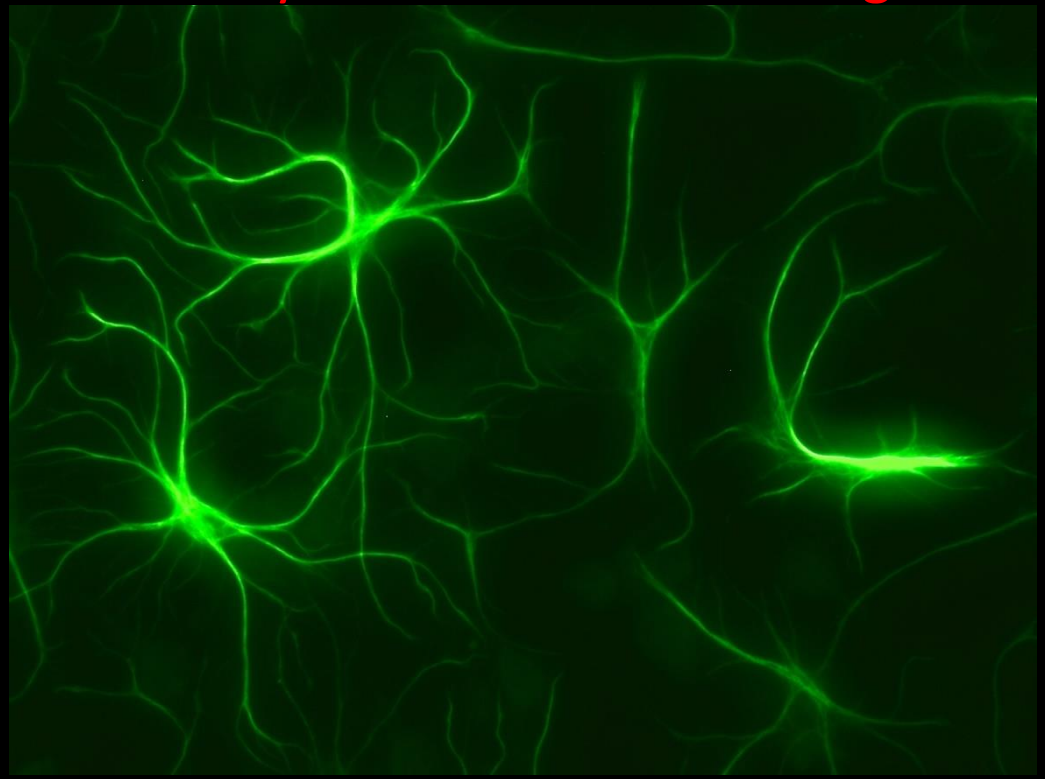

Sonja Paetau, University of Helsinki

Disclosures

Will be discussing off-label use of medications

Will refer only to published scientific data

No conflicts of interest

Overview

Pathophysiology of MS

Actions of LDN in MS

Previous clinical trials of LDN

Future clinical research of LDN

Future clinical use of LDN

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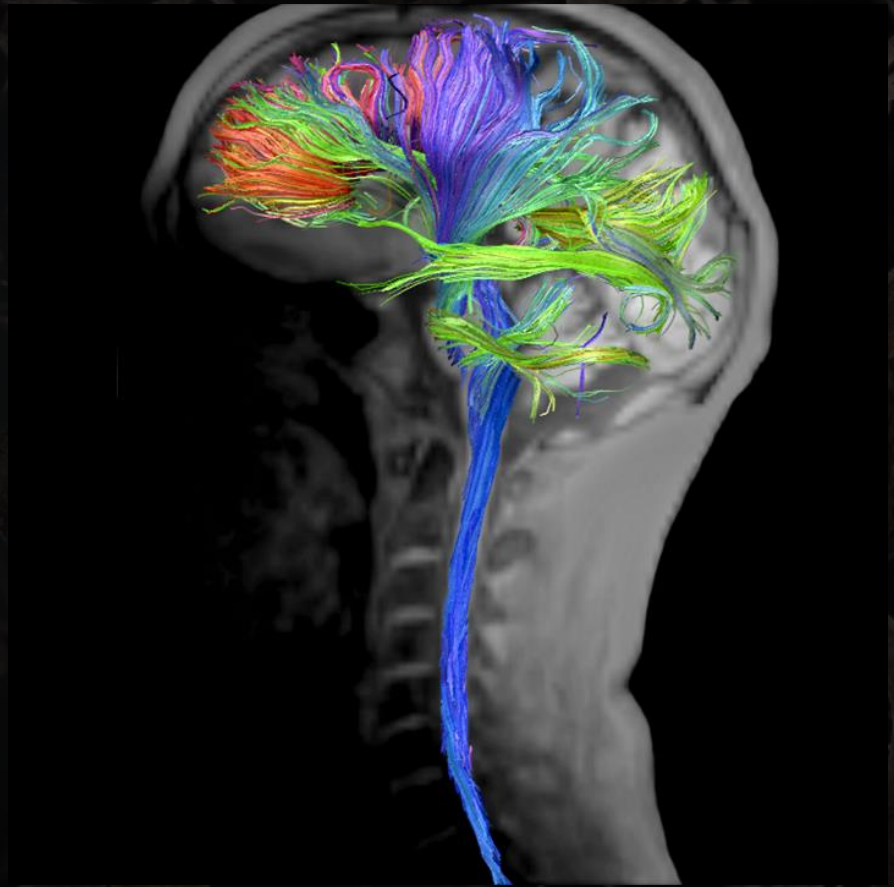
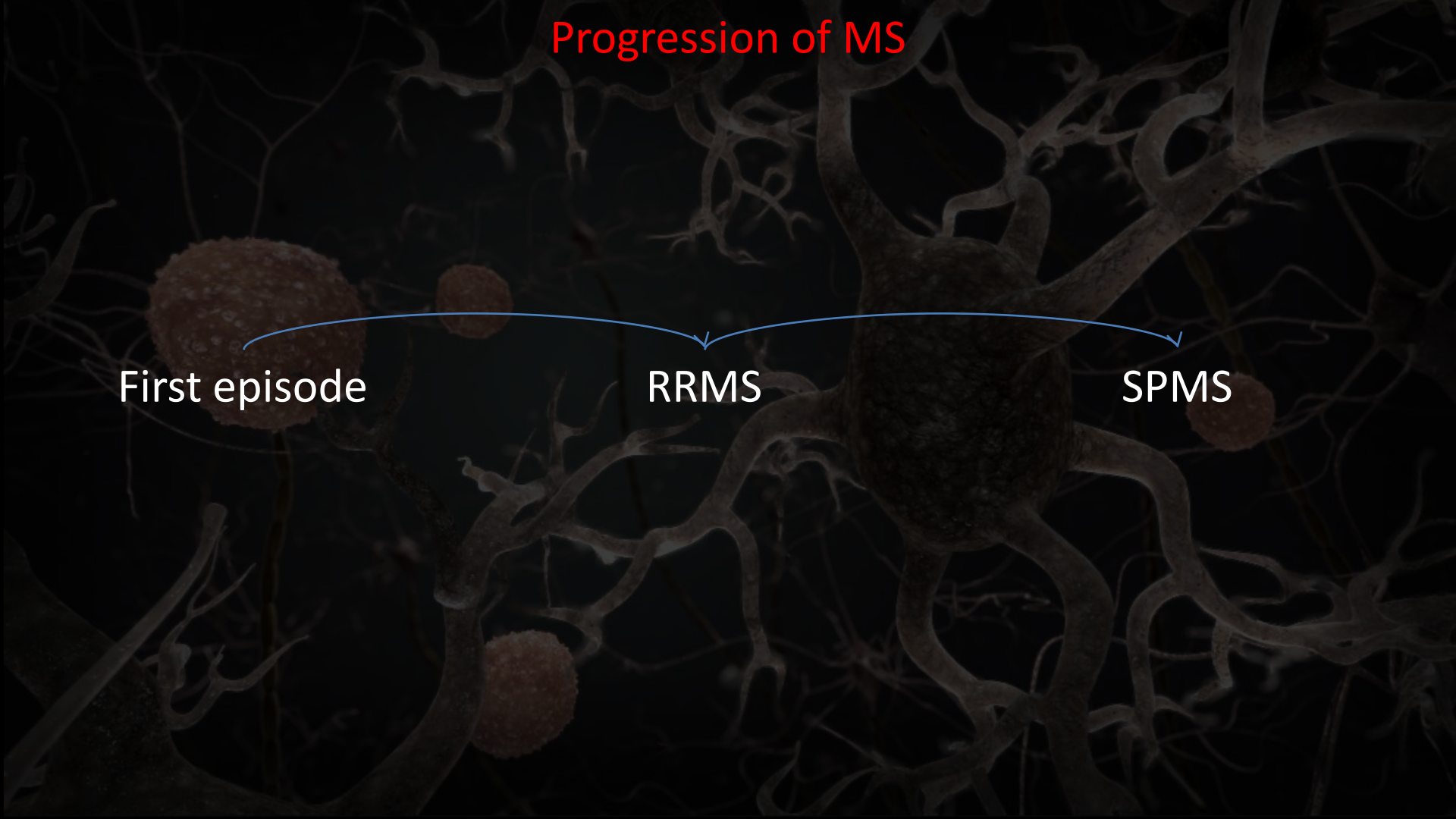
Overview of MS

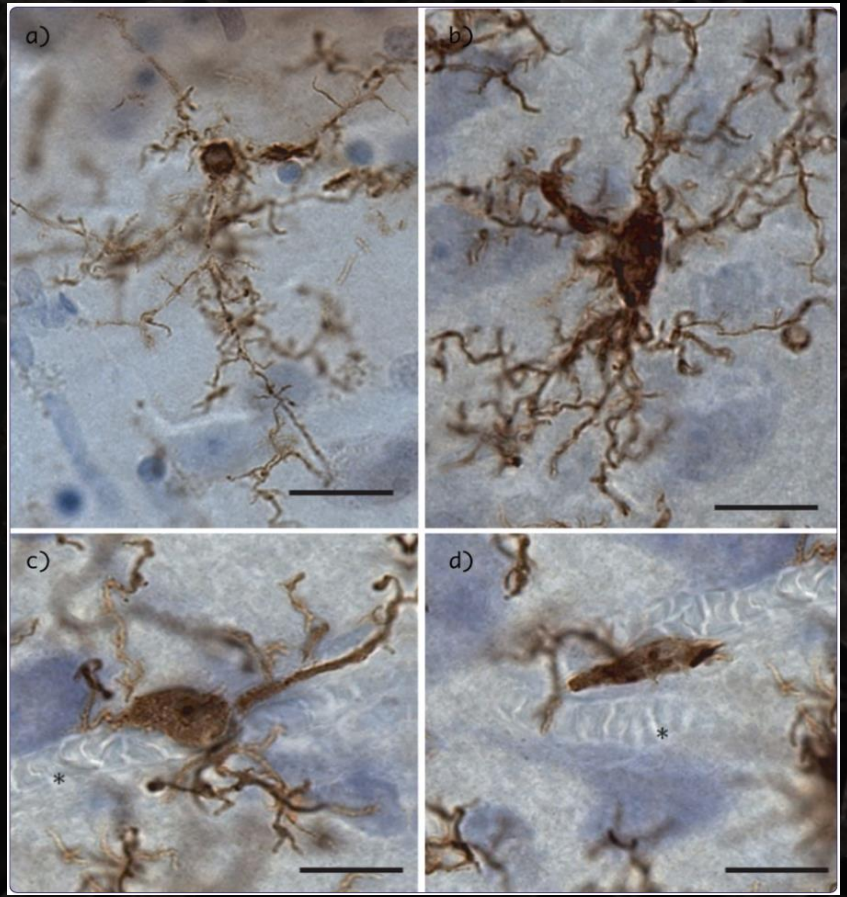


Siemens

Progression of MS

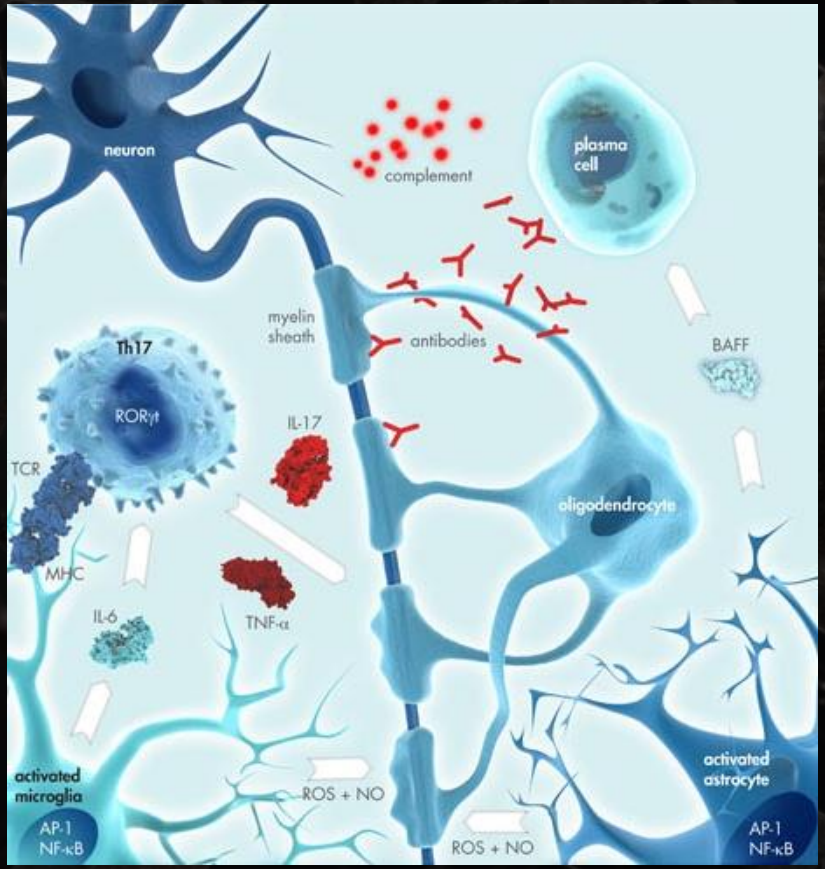


Pathophysiology of MS



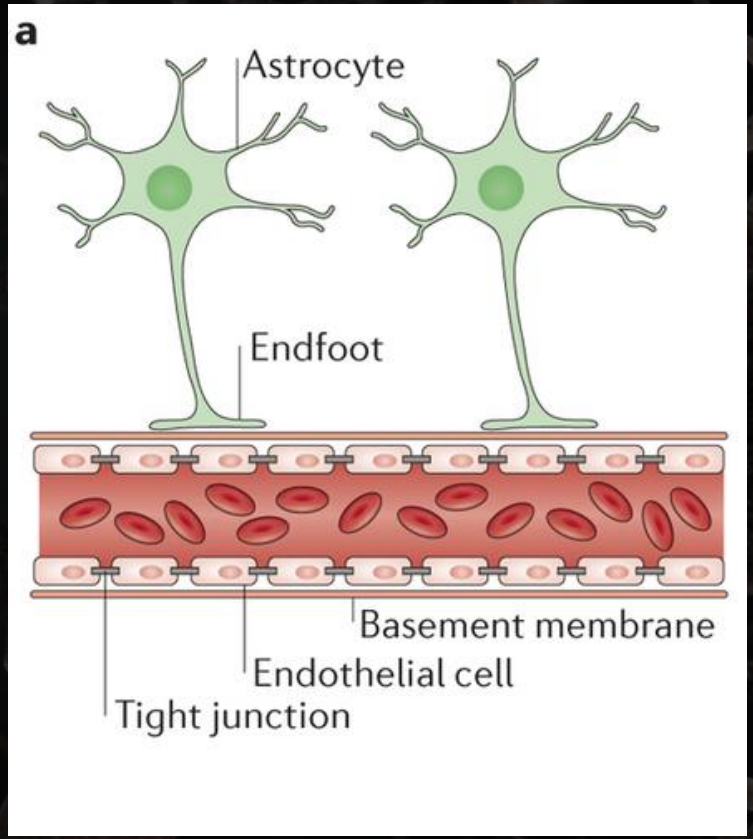
Torres-Platas et al., 2014, *J Neuroinflammation*

Central immune contribution



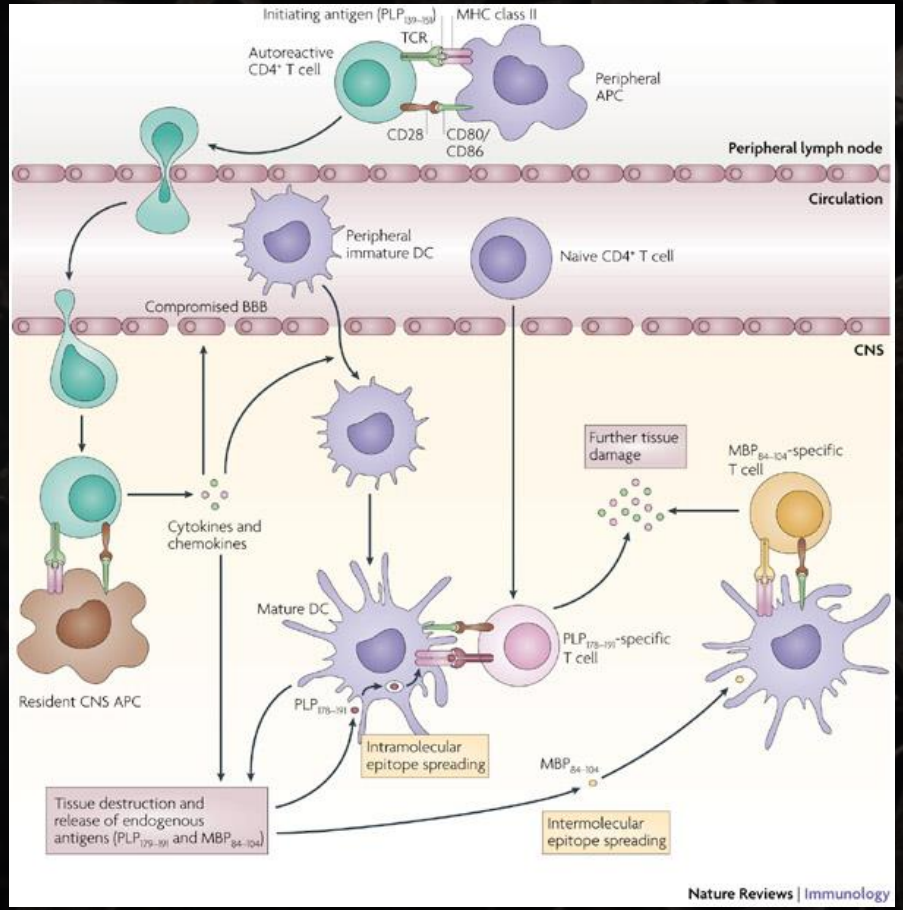
Ehrlich E & Mattiuz K – QIAGEN, sabiosciences.com

Degradation of blood brain barrier



Vishnu et al., 2014; *Nat Rev Neuro*

Peripheral immune contribution



Miller et al., 2007; *Nat Rev Immunol*

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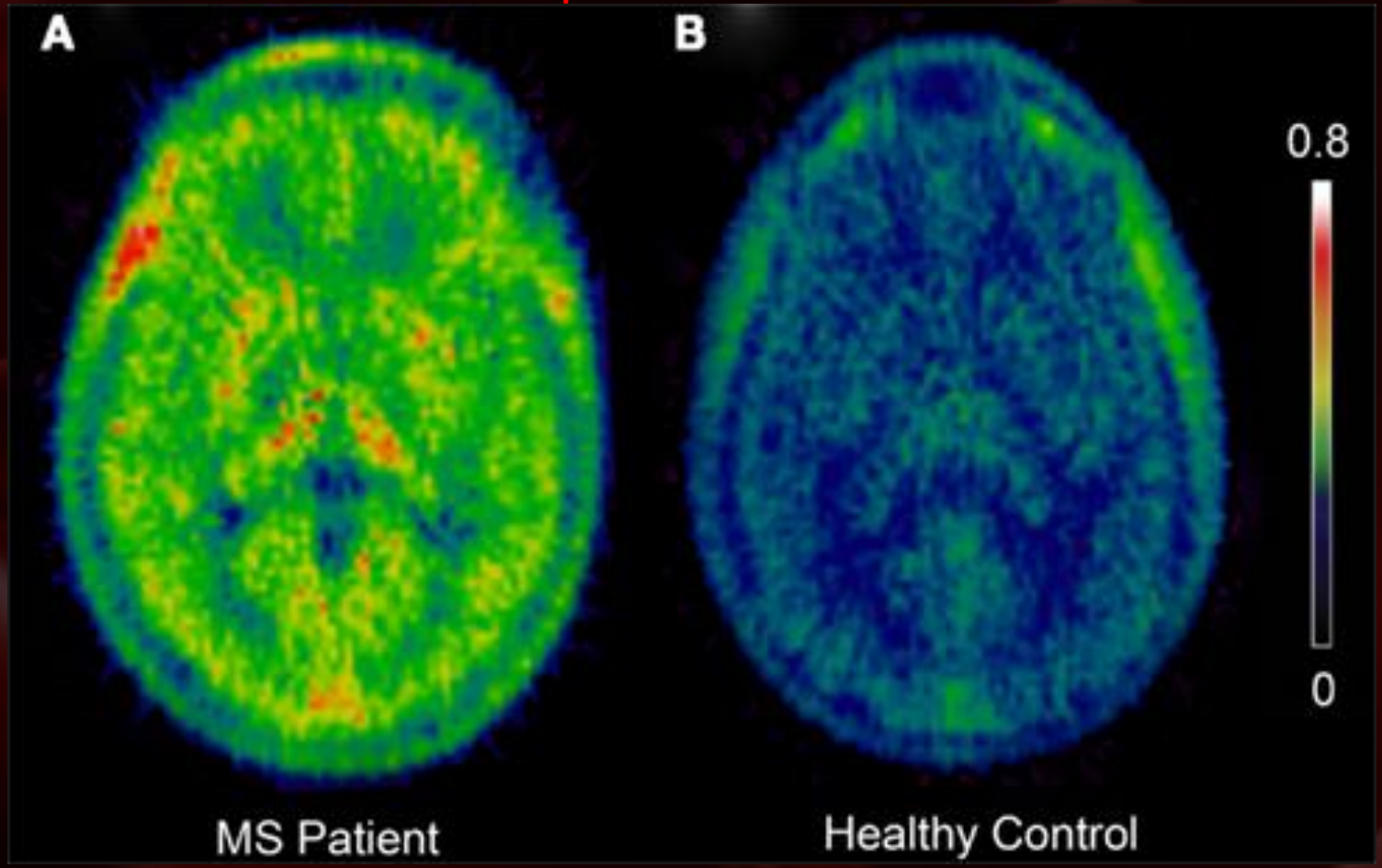
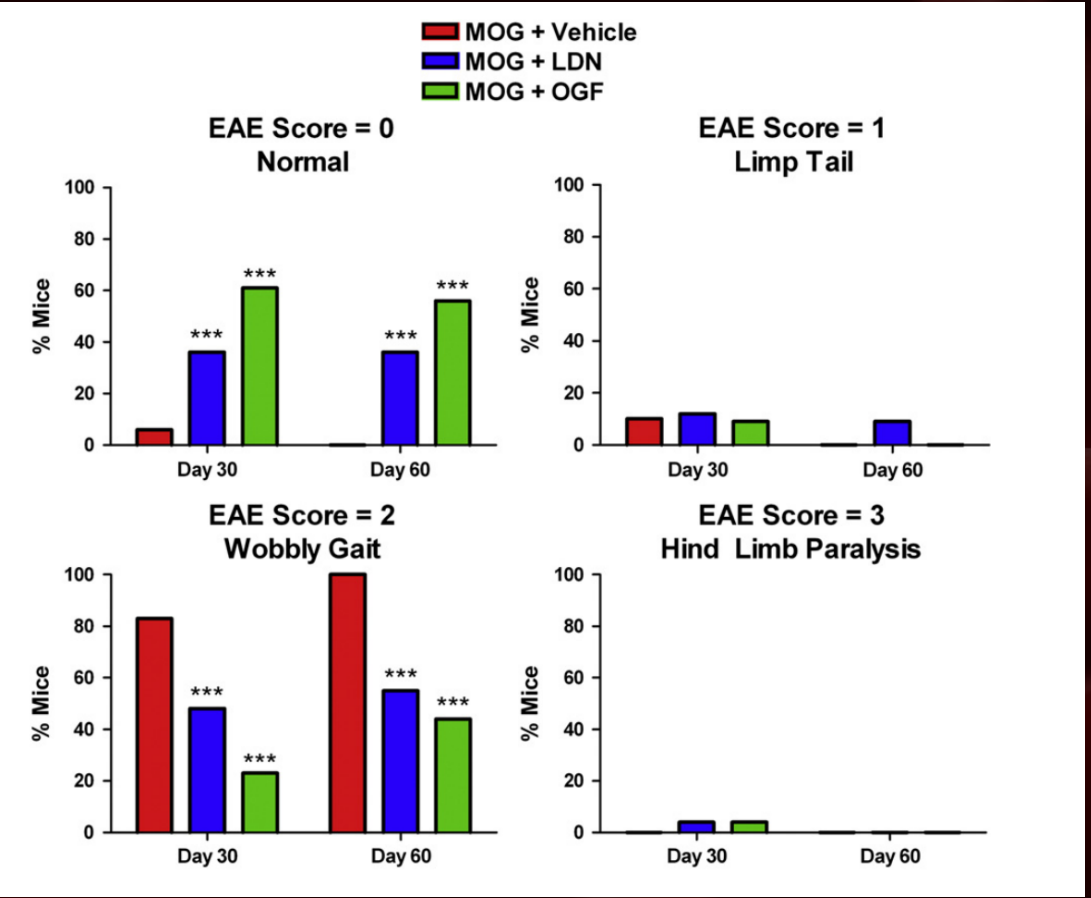
The promise of LDN



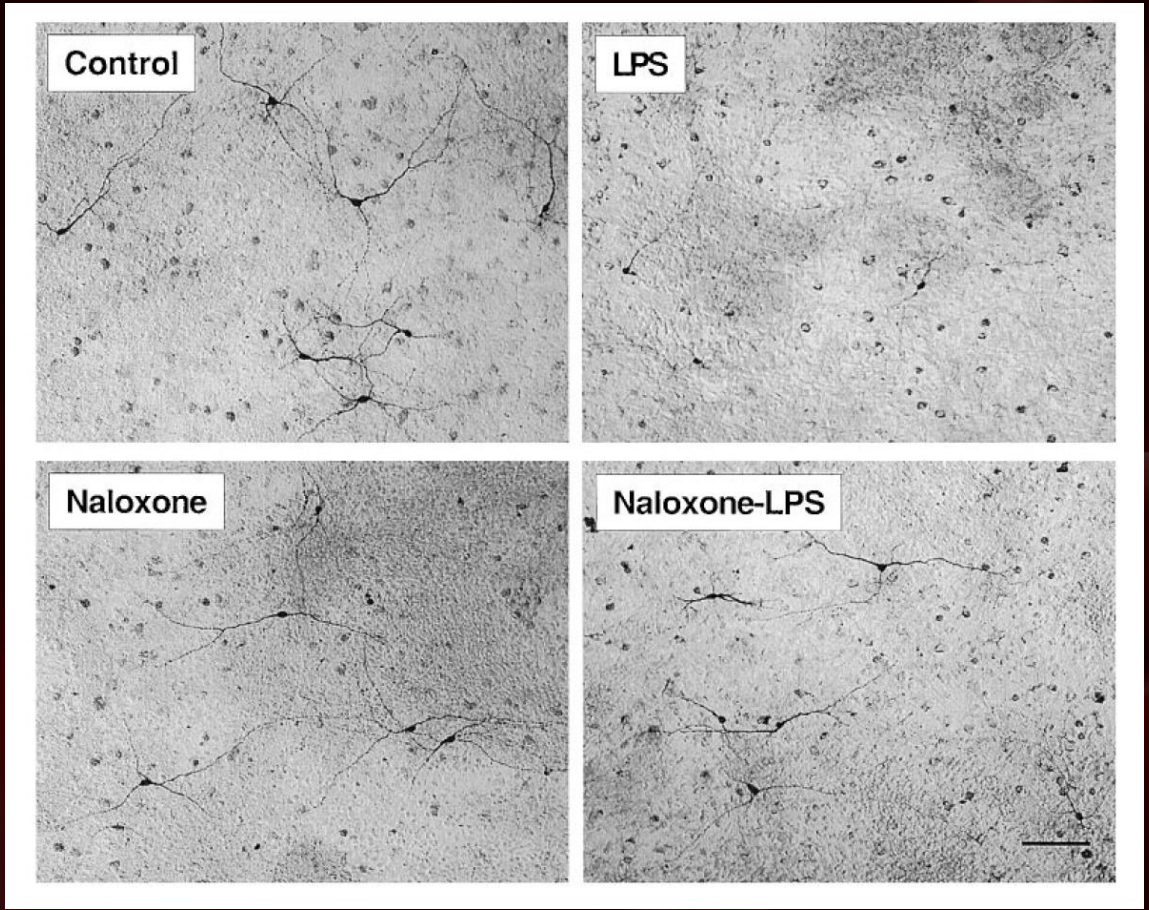
Politis et al., 2012, *Frontiers in Pharmacology*

LDN animal testing



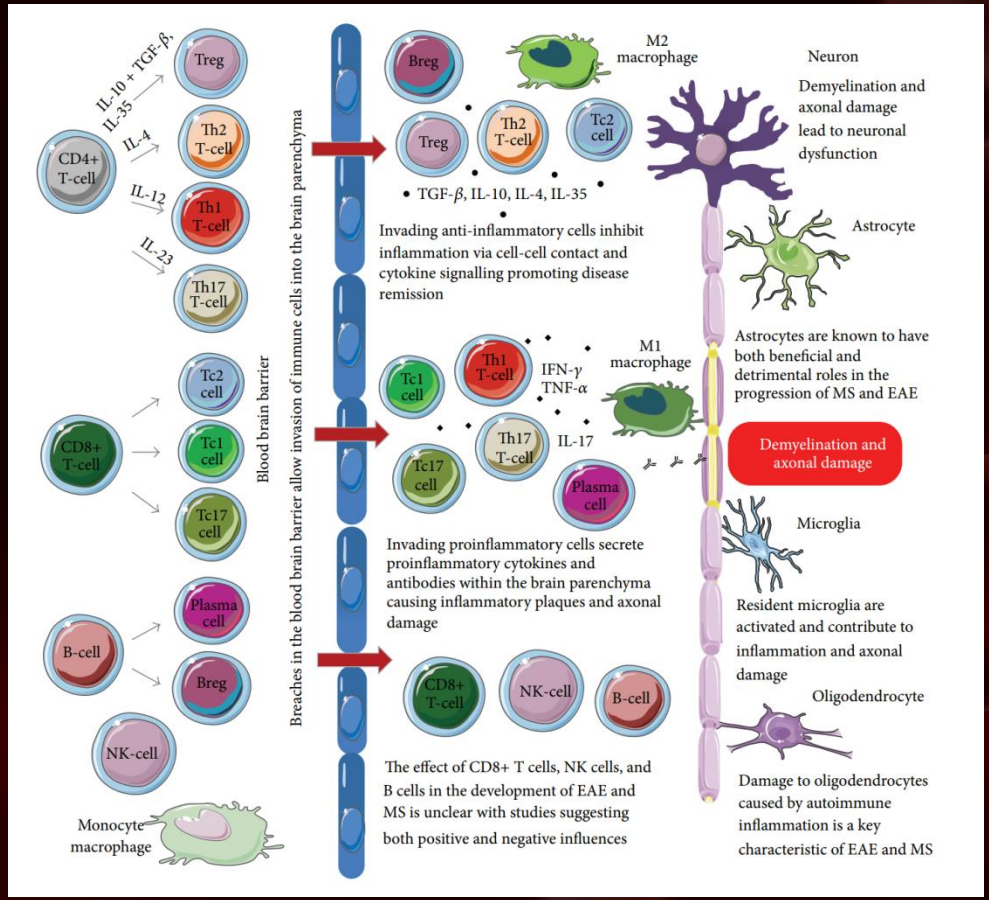
Rahn et al., 2011; *Brain Res*

Central immune-modulating effects of LDN



Liu, B et al. 2000, *JPET*

Peripheral immune-modulating effects of LDN



Duffy et al., 2014; *MS Inter*

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LDN and MS clinical trials to-date

	Size	Length	Type	Outcome
Gironi et al., 2008	40	24 weeks	Primary Progressive	Reduction of spasticity
Cree et al., 2010	60	8 weeks	Relapsing-Remitting or Secondary Progressive	No efficacy
Sharafaddinzadeh et al., 2010	96	17 weeks	Mixed	Improvement mental scores

Gironi M, Martinelli-Boneschi, Sacerdote P, Solaro C, Zaffaroni M, Cavarretta R, Moiola L, Bucello S, Radaelli M, Pilato V, Rodegher M, Cursi M Franchi S, Martinelli V, Nemni R, Comi G, Martino G. A pilot trial of low-dose naltrexone in primary progressive multiple sclerosis. *Mult Scler* 2008, 14: 1076.

Cree B, Kornyeyeva E, Goodin D. Pilot trial of low-dose naltrexone and quality of life in multiple sclerosis. *Ann Neurol* 2010, 68: 145.

Sharafaddinzadeh N, Moghtaderi A, Kashipazha D, Majdinasab N, Shalbafan B. The effect of low-dose naltrexone on quality of life of patients with multiple sclerosis: a randomized placebo-controlled trial. *Mult Scler* 2010, 16: 964.

Problems with previous clinical trials

Not of long enough duration

Varying diagnostic criteria

Varying outcomes

2015 Chart Review

N = 215
3.5mg LDN
Average Tx duration = 804 days
60% reported LDN improved fatigue
60% reported LDN improved disease severity
Minimal side effects

Turel A, Oh K, Zagon I, McLaughlin P. Low dose naltrexone for treatment of multiple sclerosis: a retrospective chart review of safety and tolerability. *J Clin Psychopharmacol* 2015, 35: 609.

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Major goals of future clinical trials

Need to be of much longer duration
Need to use same outcomes as major trials
Need to comprehensively assess outcomes
Need to involve radiologic scans
Need to target early forms of condition
Need larger sample sizes
Need to frequently assess outcomes
Need to do dosage-finding studies

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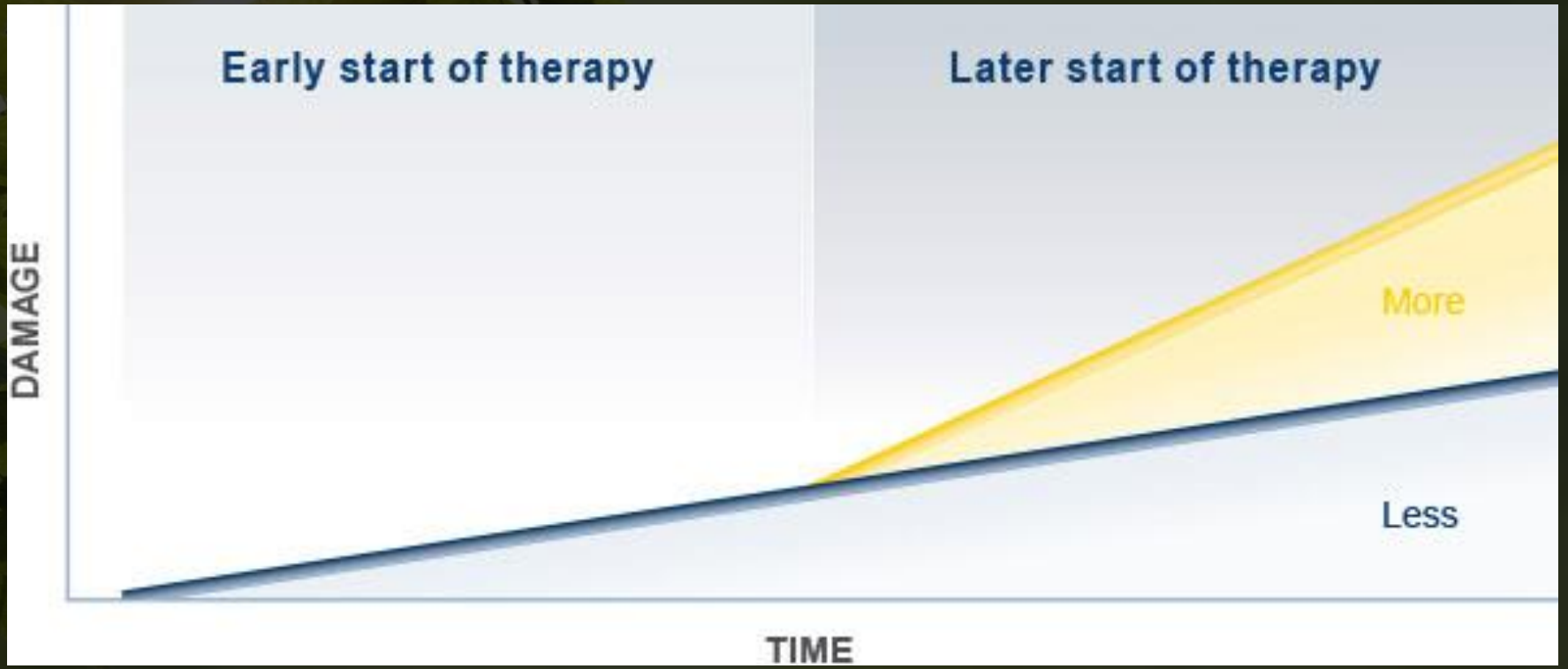
Using LDN early in disease course



Teva

Adjustments of use of LDN

Dosage

Timing

Mode of administration

Future treatments based on LDN

Naltrexone analogs

Other microglia modulators

Botanicals

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