4th International Conference and Exhibition on
Neurology & Therapeutics
July 27-29, 2015 Rome, Italy

Day 2 July 28, 2015

OLIMPCIA 1

Keynote Forum

10:10-10:50

Alessandro Morelli
University of Genova, Italy

www.biochemlab.it

Neural activity is pivotal for myelin growth

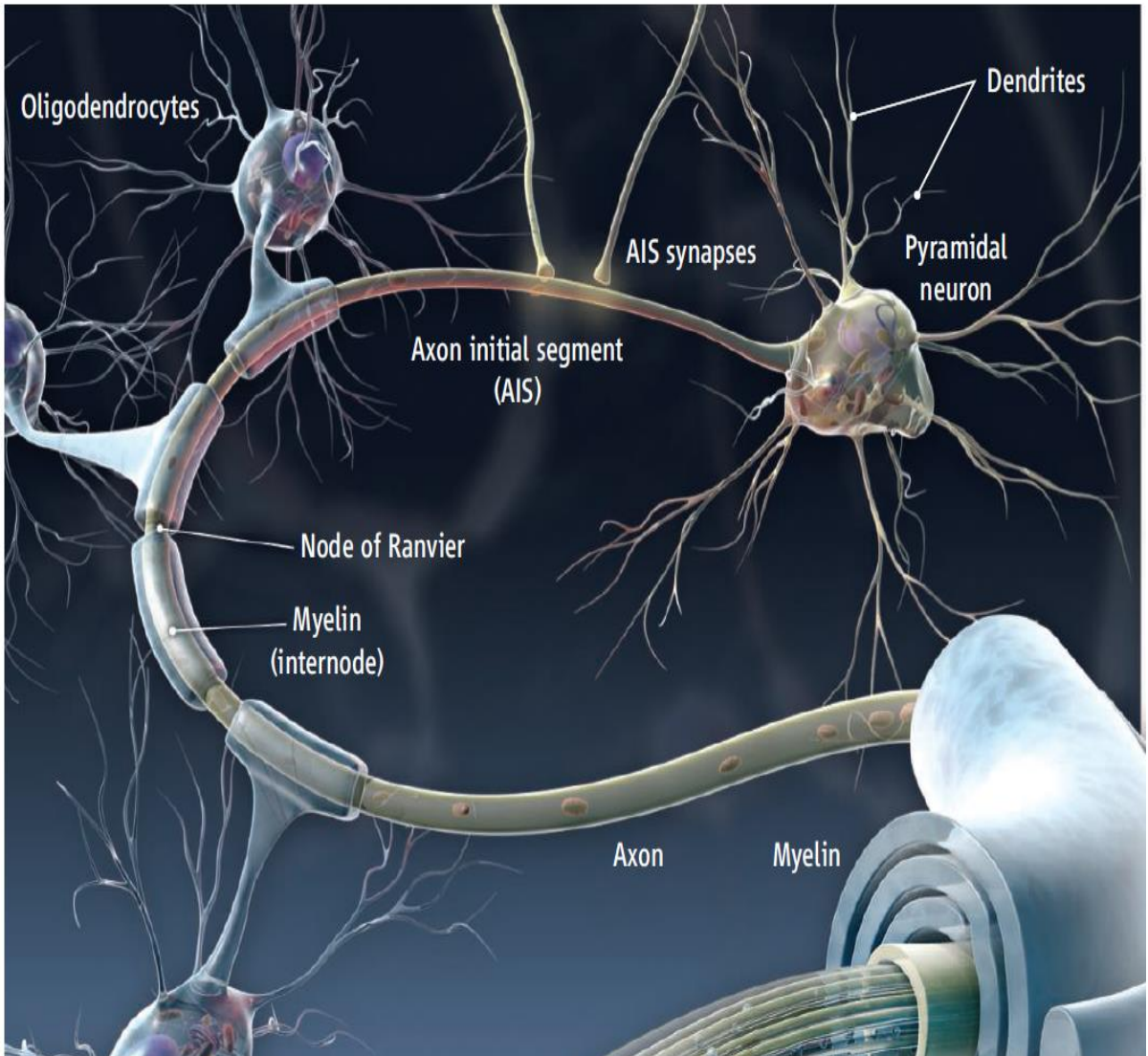
18 APRIL 2014 VOL 344 SCIENCE www.sciencemag.org

NEUROSCIENCE

Myelin—More than Insulation

R. Douglas Fields - NIH, Bethesda

…Myelin organizes the very structure of network connectivity, facilitates modes of nervous system function beyond the neuron doctrine, and regulates the timing of information flow through individual circuits. It is certainly time to set aside the frayed metaphor of myelin as insulation and appreciate the more fascinating reality.



Science
AAAS

Distinct Profiles of Myelin Distribution Along Single Axons of Pyramidal Neurons in the Neocortex

Giulio Srubek Tomassy *et al.*
Science **344**, 319 (2014);
DOI: 10.1126/science.1249766

Giulio Srubek Tomassy,[1] Daniel R. Berger,[2,3] Hsu-Hsin Chen,[1] Narayanan Kasthuri,[2]
Kenneth J. Hayworth,[2] Alessandro Vercelli,[4] H. Sebastian Seung,[3]*
Jeff W. Lichtman,[2] Paola Arlotta[1]†

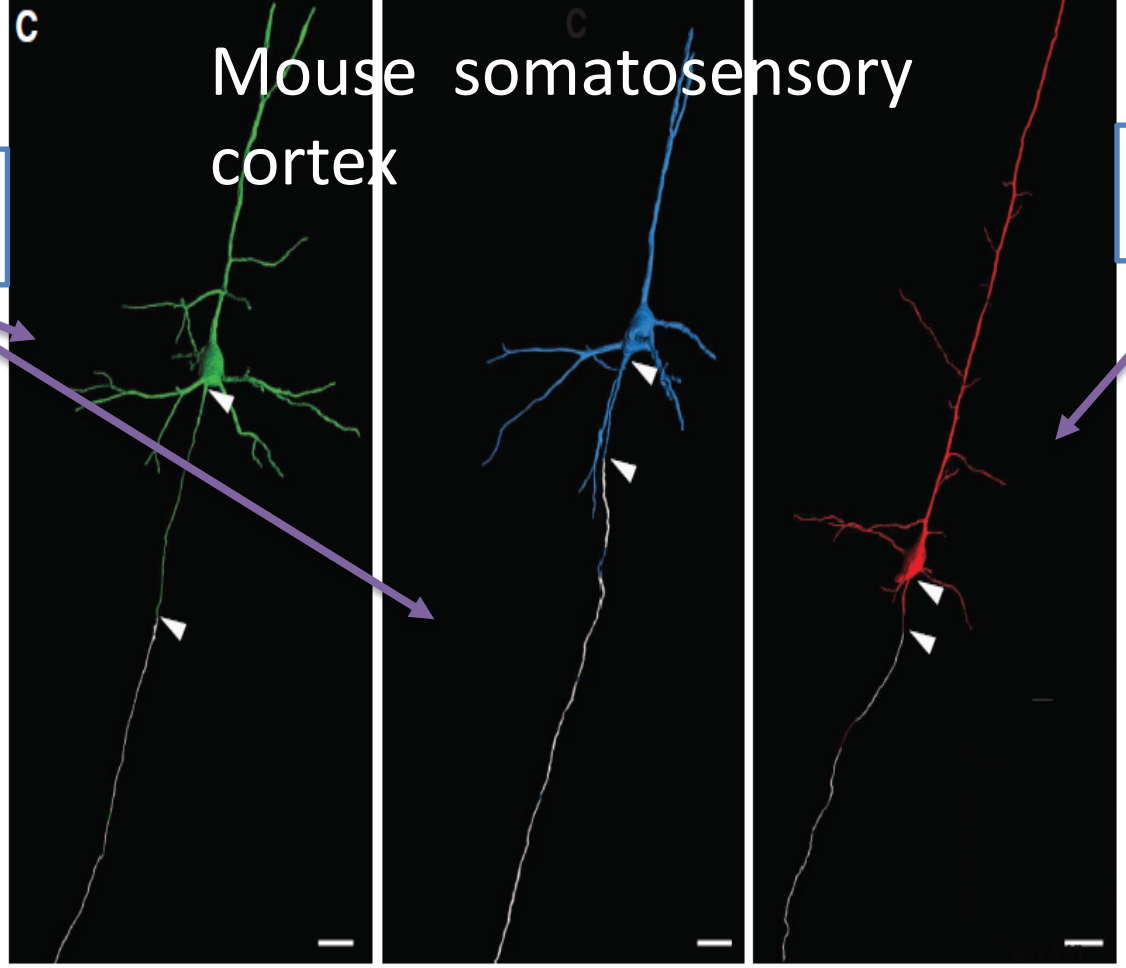
1- Harvard University – Cambridge – USA
4- Neuroscience Institute of Turin - Italy

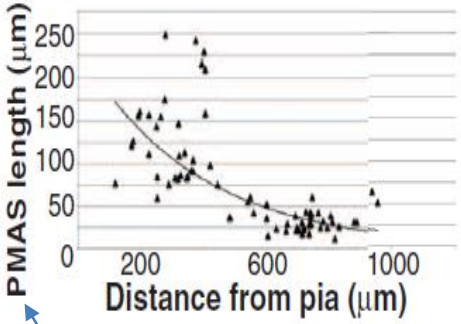
…We find that individual neurons have distinct longitudinal distribution of myelin.
Neurons in the superficial layers displayed the most diversified profiles, including a new pattern where myelinated segments are interspersed with long, unmyelinated tracts…

Mouse somatosensory cortex

Neocortex Layer III-IV

Neocortex Layer V





PMAS: Premyelin Axonal Segment

Fig. 1. Radial distribution of myelin in the adult mouse neocortex. (**A**) Immunohistochemical staining of MBP and Cux1 in coronal sections of wild-type adult neocortex. High magnifications of boxed areas show reduced levels of myelin in layer II/III (brackets). (**B**) PMAS lengths (arrowheads) in Golgi-Cox–labeled adult wild-type cortex. (Top) Representative neurons in layer II/III and layer V. (Bottom) Scatter plot of PMAS length versus distance of neuronal cell bodies from the pia ($n = 72$, $R^2 = 0.61093$). (**C**) Three-dimensional renderings of three representative neurons. The green and blue neurons were located in layer III to IV, and the red neuron was in layer V. Myelin is shown in white. Ctx, cortex; Hip, hippocampus; Th, thalamus. Scale bars: 500 μm (A) low magnification, 100 μm (A) insets, 20 μm (B), and 25 μm (C).

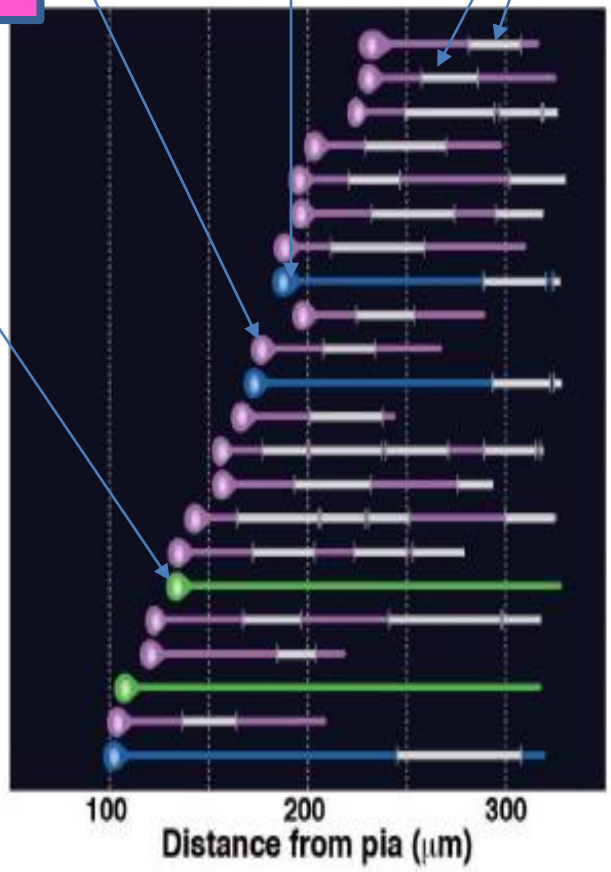
Fig. 2. Layer II/III pyramidal neurons display novel profiles of longitudinal myelination including intermittent myelin. (**A**) High-resolution rendering of myelin distribution along single axons of 22 pyramidal neurons traced and reconstructed in layer II/III of the V1 data set. (Right) Soma position and lengths of axonal tracts for all neurons rendered at left. Magenta, neurons with intermittent myelin; blue, neurons with long PMASs; green, neurons with unmyelinated axons; white, myelinated axonal segments. (**B**) Representative, serial EM reconstructions of neurons with long PMASs (left) or intermittent myelin (right). Unmyelinated axon tracts are highlighted in green and myelinated tracts in magenta. (Insets) EM images and schematic representations of selected regions from each axon. Yellow, selected synapses mapped on the intermittently myelinated axon. Ax, axon; Nu, nucleus; Psd, postsynaptic density. (**C**) High-resolution rendering of three representative neurons displaying different myelination modes. Native positions of these neurons are preserved in the rendering. Arrowheads mark the boundaries of myelinated tracts (white). Scale bars: 50 μm (A), 2 μm (B), 0.5 μm (B) insets, and 20 μm (C).

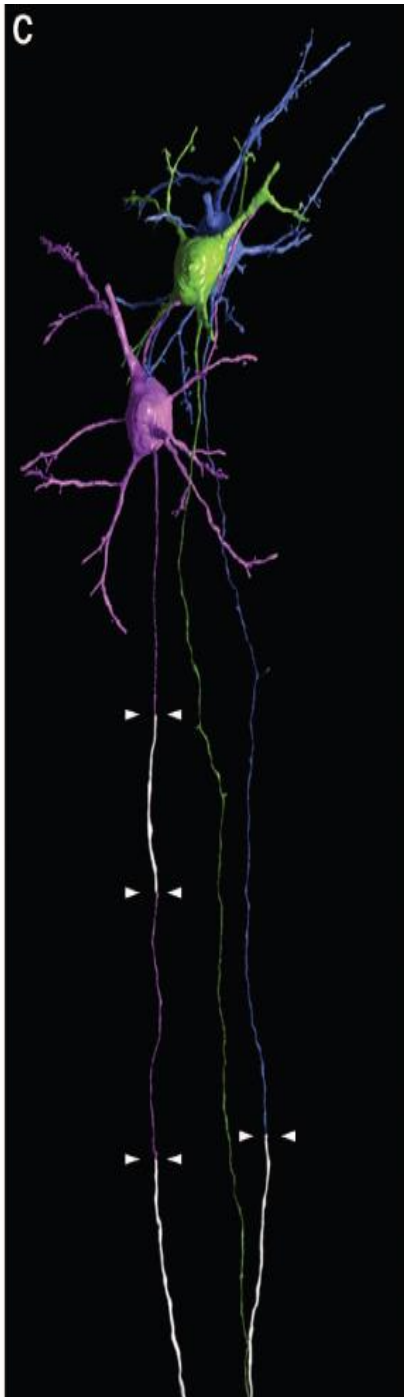
Neuroni con mielina intermittente

Neuroni con esteso PMAS

Tratti mielinati

Neuroni con assone non-mielinato





(2)

Naural activity trigger myelin growth

Report 1

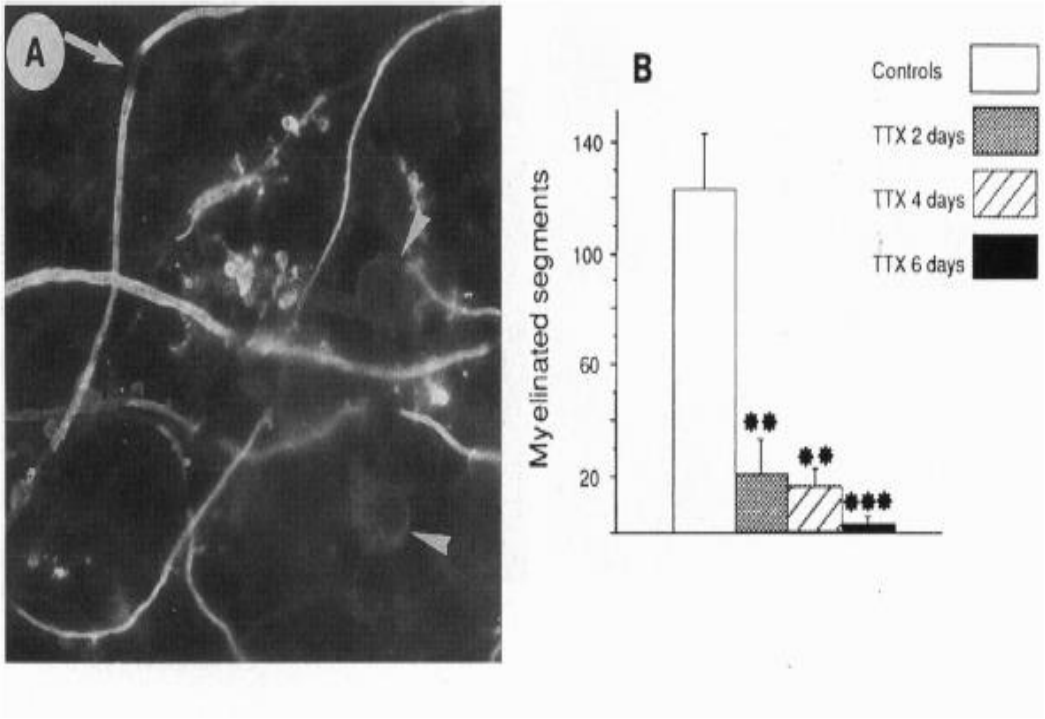
Proc. Natl. Acad. Sci. USA
Vol. 93, pp. 9887–9892, September 1996
Neurobiology

Induction of myelination in the central nervous system by electrical activity

C. DEMERENS*, B. STANKOFF*, M. LOGAK*, P. ANGLADE†, B. ALLINQUANT‡, F. COURAUD§, B. ZALC*¶, AND C. LUBETZKI*

Laboratoire de Neurobiologie Cellulaire, Moléculaire et Clinique, Institut National de la Santé et de la Recherche Médicale, *Unité 134 and †Unité 289, Hôpital de la Salpêtrière, Université Pierre et Marie Curie, 75651 Paris, Cedex 13, France; ‡Ecole Normale Supérieure, Centre National de la Recherche Scientifique, Unité de Recherche Associée 1414, 26 rue d'Ulm, 75005 Paris, France; and §Laboratoire de Neurobiologie des Canaux Ioniques, Institut National de la Santé et de la Recherche Médicale, Unité 374, Faculté de Médecine Nord, 13916 Marseille, Cedex 06, France

tetrodotoxin which can blocks the firing of neurons.



Tetrodotoxin (TTX) blocks the firing of neurons
α-scorpion toxin (α-ScTX) increase the firing o

Table 1. The effect of TTX, α-ScTX, and K^+ on myelination in cultures

Factor added	Time added, DIV	Myelinated segments, % controls	MBP-positive cells, % controls
TTX (10^{-6} M) (n = 3)	9	39.4 ± 16.2	92.6 ± 17.3
TTX (10^{-6} M) (n = 3)	12	2.4 ± 1.1	159.6 ± 13.8
α-ScTX (10^{-8} M) (n = 5)	8	241 ± 44	119.8 ± 22.9
K^+ (15 mM) (n = 3)	12	2.9 ± 1.4	80.1 ± 11.8
TTX + K^+ (15 mM) (n = 3)	12	1.2 ± 0.6	93.8 ± 15.3

Myelinating cultures were as in Fig. 1. At various times after seeding, TTX, α-ScTX (toxin II from *Androctonus australis* Hector), K^+, or TTX plus K^+ were added to the culture media. Treatment lasted 2 days, after which excess reagents were thoroughly eliminated by washing as described (25). The total number of myelinated segments and of MBP-expressing oligodendrocytes per coverslip was evaluated at 21 DIV after immunolabeling with the anti-MBP antibody. Results are expressed as percent of values observed in control cultures (mean ± SEM).

Report 2

Science
AAAS

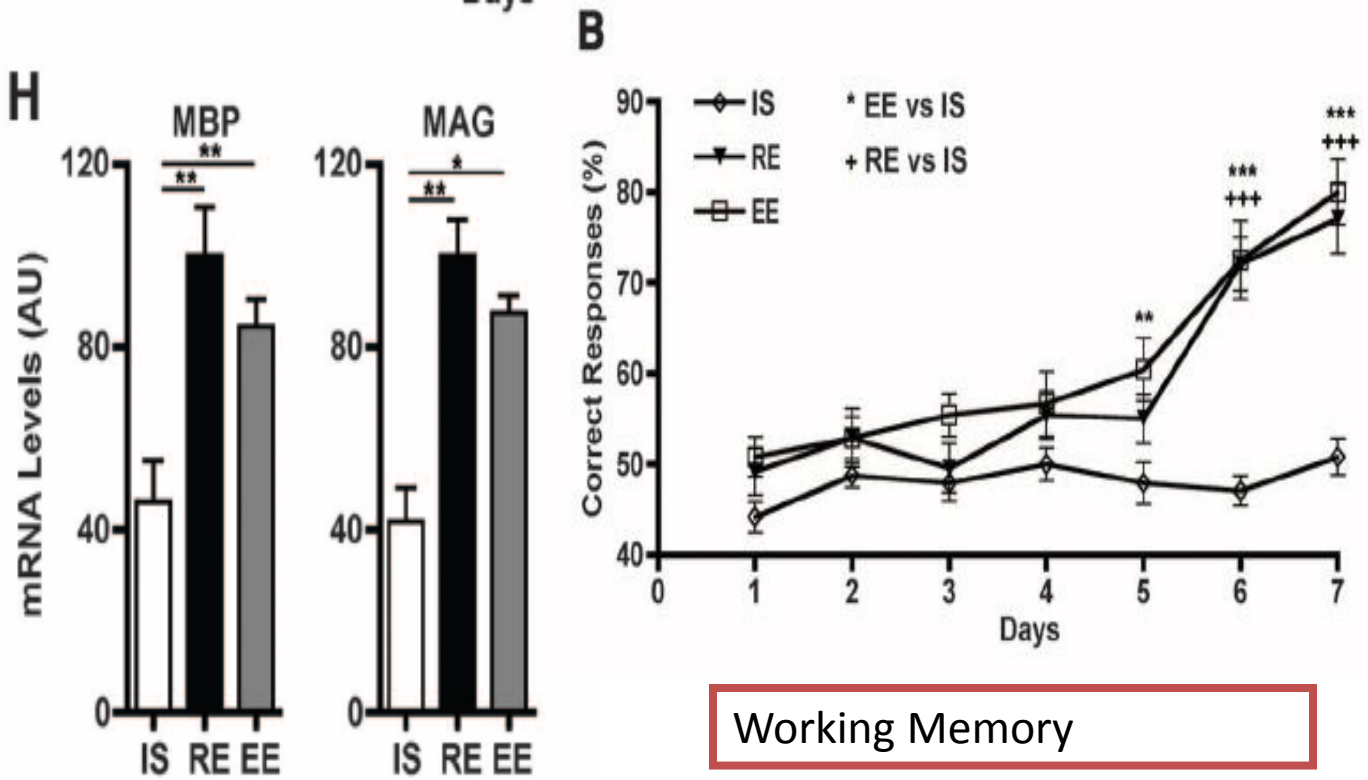
A Critical Period for Social Experience–Dependent Oligodendrocyte Maturation and Myelination
Manabu Makinodan *et al.*
Science **337**, 1357 (2012);
DOI: 10.1126/science.1220845

14 september 2012

A Critical Period for Social Experience–Dependent Oligodendrocyte Maturation and Myelination

Manabu Makinodan,[1,2] Kenneth M. Rosen,[1,3] Susumu Ito,[4] Gabriel Corfas[1,2,3]*

Early social isolation results in adult behavioral and cognitive dysfunction that correlates with white matter alterations. However, how social deprivation influences myelination and the significance of these myelin defects in the adult remained undefined. We show that mice isolated for 2 weeks immediately after weaning have alterations in prefrontal cortex function and myelination that do not recover with reintroduction into a social environment. These alterations, which occur only during this critical period, are phenocopied by loss of oligodendrocyte ErbB3 receptors, and social isolation leads to reduced expression of the ErbB3 ligand neuregulin-1. These findings indicate that social experience regulates prefrontal cortex myelination through neuregulin-1/ErbB3 signaling and that this is essential for normal cognitive function, thus providing a cellular and molecular context to understand the consequences of social isolation.



Working Memory

IS = Insulated Starting at P21;

RE = Regular Environment

EE = Enriched Environment

Report 3

nature neuroscience

VOLUME 15 | NUMBE 12

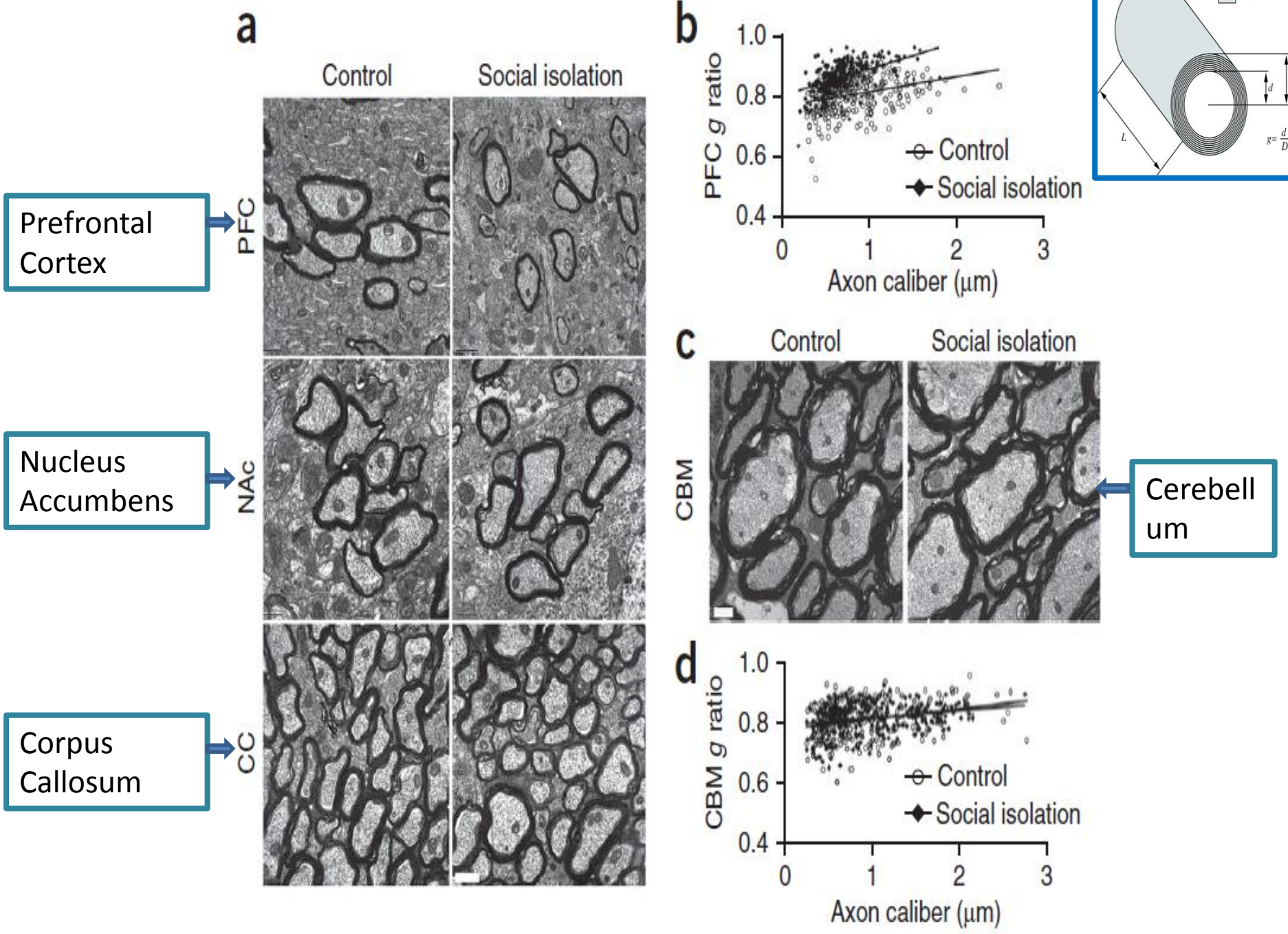
December 2012

Impaired adult myelination in the prefrontal cortex of socially isolated mice

Jia Liu[1,4], Karen Dietz[1,4], Jacqueline M DeLoyht[2], Xiomara Pedre[1], Dipti Kelkar[1], Jasbir Kaur[1], Vincent Vialou[1], Mary Kay Lobo[1,3], David M Dietz[1,3], Eric J Nestler[1], Jeffrey Dupree[2] & Patrizia Casaccia[1]

Protracted social isolation of adult mice induced behavioral, transcriptional and ultrastructural changes in oligodendrocytes of the prefrontal cortex (PFC) and impaired adult myelination. Social re-integration was sufficient to normalize behavioral and transcriptional changes. Short periods of isolation affected chromatin and myelin, but did not induce behavioral changes. Thus, myelinating oligodendrocytes in the adult PFC respond to social interaction with chromatin changes, suggesting that myelination acts as a form of adult plasticity.

Patrizia Casaccia, Mount Sinai Hospital New York


a
Control
Social isolation
PFC
NAc
CC
Prefrontal Cortex
Nucleus Accumbens
Corpus Callosum
b
PFC g ratio
1.0
0.8
0.6
0.4
0
1
2
3
Axon caliber (μm)
Control
Social isolation
Axon
Myelin
c
Control
Social isolation
CBM
Cerebellum
d
CBM g ratio
1.0
0.8
0.6
0.4
0
1
2
3
Axon caliber (μm)
Control
Social isolation

Report 4

Science

AAAS

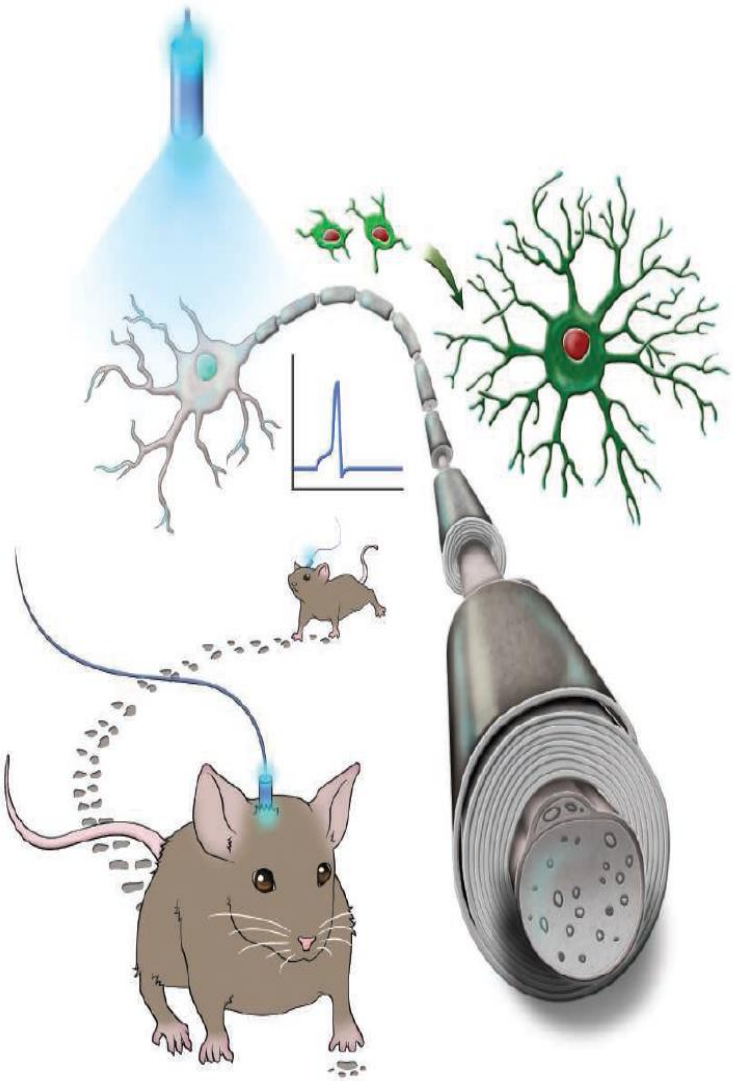
Neuronal Activity Promotes Oligodendrogenesis and Adaptive Myelination in the Mammalian Brain

Erin M. Gibson *et al.* Stanford University – USA

Science **344**, (2014);
DOI: 10.1126/science.125230

Erin M. Gibson, David Purger, Christopher W. Mount, Andrea K. Goldstein, Grant L. Lin, Lauren S. Wood, Ingrid Inema, Sarah E. Miller, Gregor Bieri, J. Bradley Zuchero, Ben A. Barres, Pamelyn J. Woo, Hannes Vogel, Michelle Monje*

- → We use in vivo optogenetic techniques in awake, behaving mice to provide direct evidence that neuronal activity regulates changes in myelinforming cells within an active circuit.
- → We used an optogenetic mouse model in which 470-nm light delivered near the brain surface stimulates the excitatory opsin channelrhodopsin expressed by cortical layer V projection neurons.
- → **Results:** Optogenetic stimulation of cortical layer V projection neurons resulted in robust proliferation of OPCs within the premotor circuit, from the deep layers of the premotor cortex to the subcortical projections through the corpus callosum.



Conclusion: Neuronal activity regulates OPC proliferation, differentiation, and myelin remodeling in the murine brain with accompanying changes in behavioral function.

Taken together, these findings suggest that adaptive changes in myelin-forming cells represent a type of behaviorally relevant neural plasticity, raising numerous conceptual and mechanistic questions.

Mechanisms regulating myelin plasticity may be important for adaptive neural function.

Morelli A et al - 07/21/2014 –Science

Comment to a papers of Field, Tomassy, Gibson:

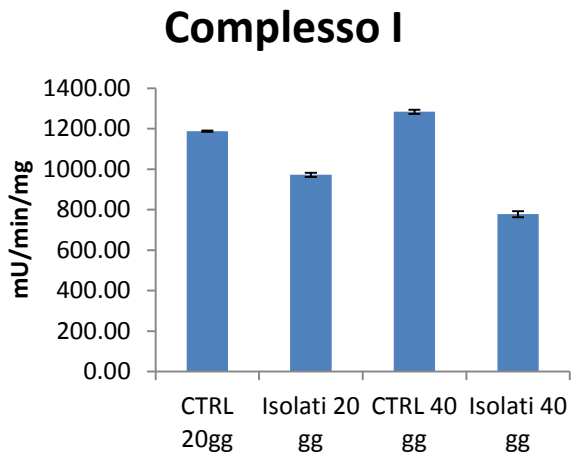
In his comment on the paper by Tomassy et al.(1), Douglas Fields (2) said:" It is certainly time to set aside the frayed metaphor of myelin as insulation and appreciate the more fascinating reality". The revolutionary data demonstrated that myelination is not homogeneous: there appear to exist large tracts of bare axons and the length of the axonal initial segment was unexpectedly long. This does not fall in the "neuron doctrine". Fields (2) associates this anomaly to a possible amplification of connectivity. However, it is difficult to imagine that the fine and behaviourally relevant neural plasticity and "complex forms of network integration" should be accompanied by a slowing down of conduction. This is in fact what we should expect with a too long node of Ranvier, which may hinder the progression of the action potential. The time seems ripe to abandon a vision of myelin based on a metaphor and accept a new epistemological paradigm more consistent with the observational data, and less theory laden. (i) chronically demyelinated axons eventually degenerate, which prompted (3) to propose a new trophic role for myelin; (ii) myelin conducts aerobic respiration, which rose the idea that the trophic role for myelin is to energetically support the axon (4). Symptoms in Multiple Sclerosis (3) would be a consequence of the loss of this support (5). In your perspective on a recent optogenetic approach on cortical neurons of freely moving mouse (6) you suggested that neuronal activity regulates myelin remodelling. Cognitive activity stimulates myelin deposition (7,8). The idea of the "electrical insulator" and of a closed electrical circuit (9) in the axon dates nearly a century Fields himself observed: "nerve impulses are not transmitted as electrons are conducted through a copper wire".

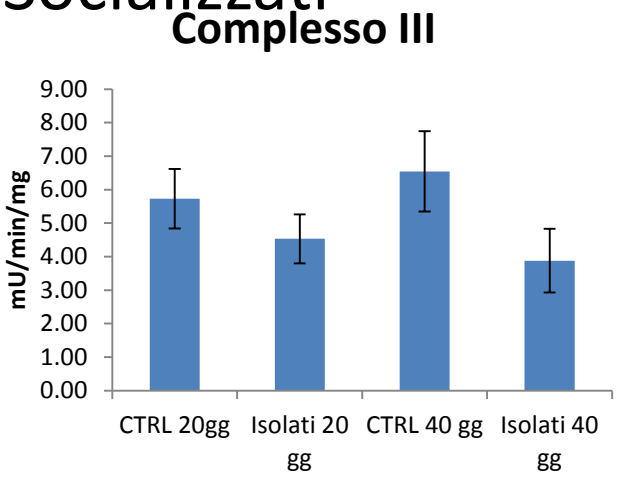
→ Do you think that we are in view of a new paradigm for Myelin function? ←

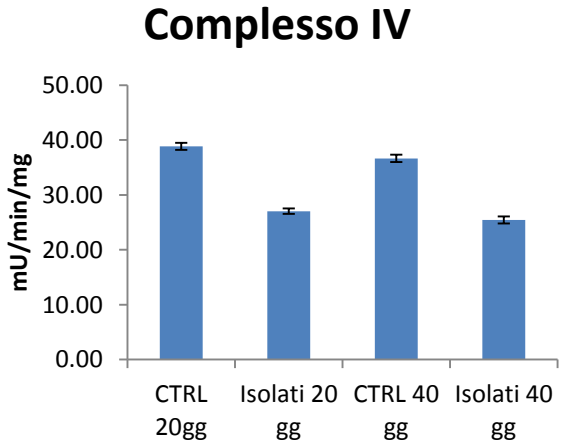
A. MORELLI, S. RAVERA, D. CALZIA, M. BARTOLUCCI, C. ROSANO, D. SERPICO, M. BALESTRINO, I. PANFOLI

Preliminar date on growth and OXPHOS function of myelin trigger by sociality

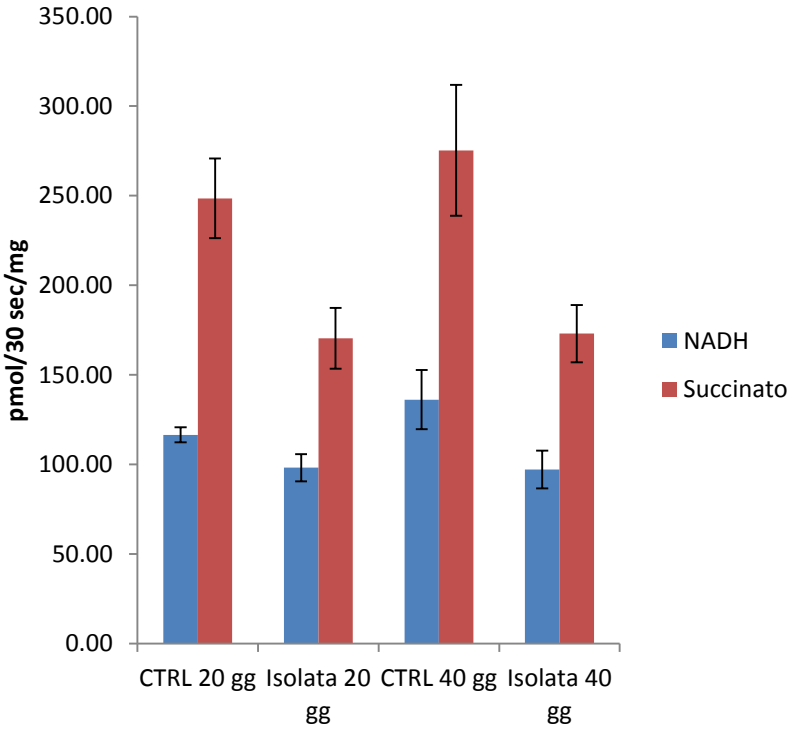
Attività Complessi Respiratori Mielina Topi Isolati /Socializzati



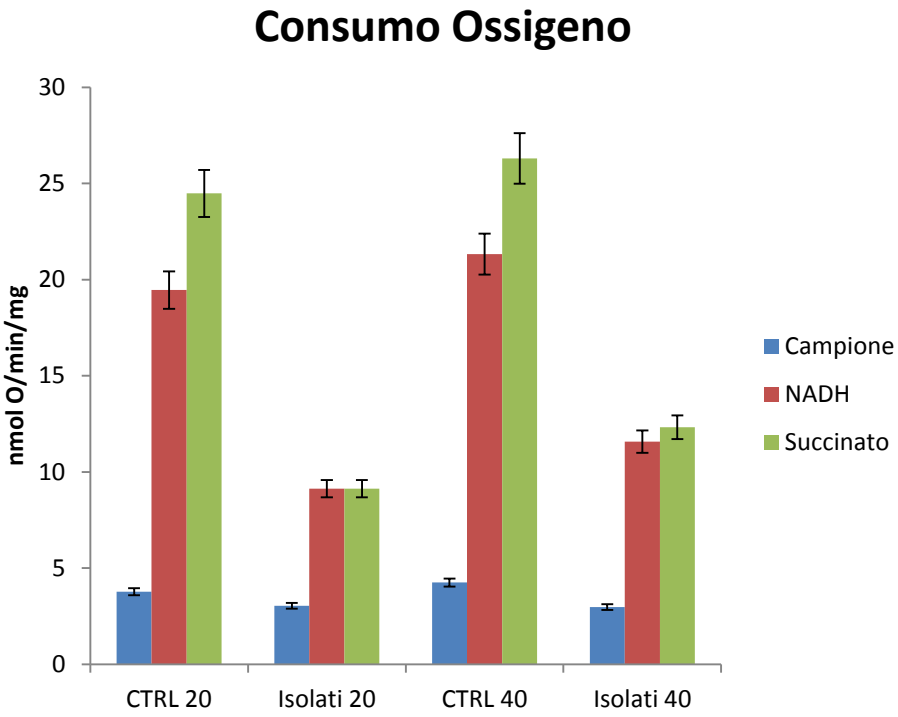


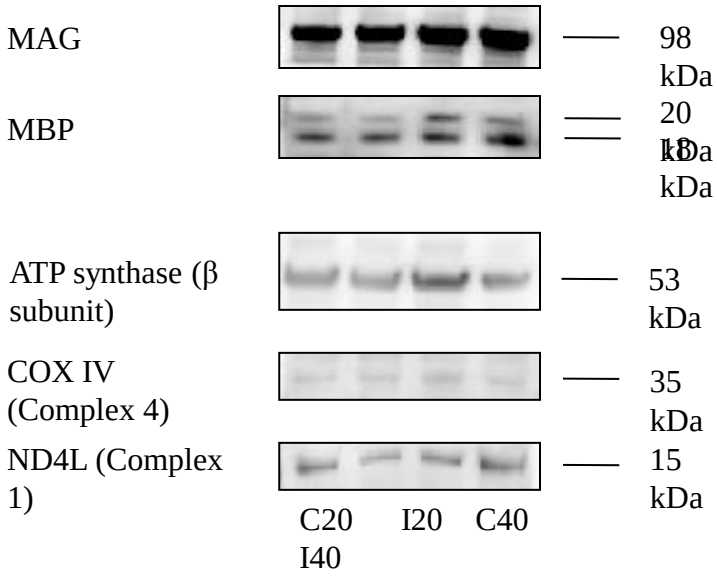


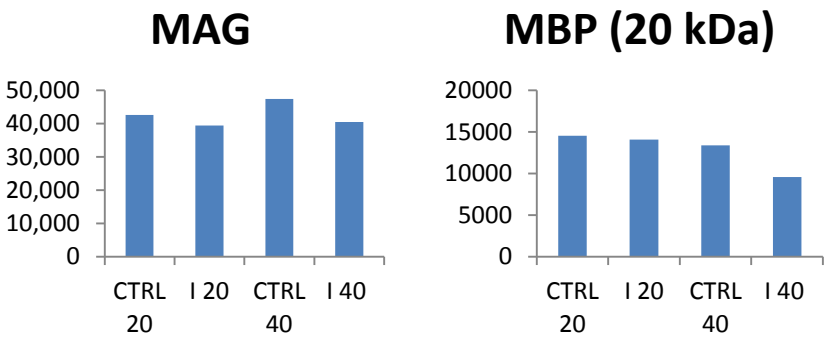
Produzione ATP da mielina topi isolati/socializzati



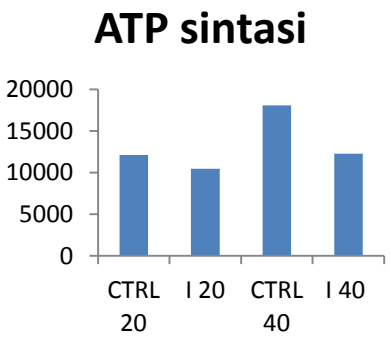
Consumo Ossigeno da mielina topi isolati/socializzati

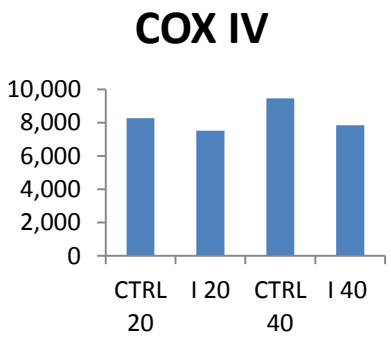


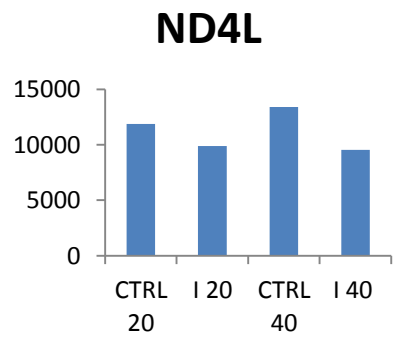

MAG
98 kDa
MBP
20 kDa
18 kDa
ATP synthase (β subunit)
53 kDa
COX IV (Complex 4)
35 kDa
ND4L (Complex 1)
15 kDa
C20
I20
C40
I40


MAG
50,000
40,000
30,000
20,000
10,000
0
CTRL 20
I 20
CTRL 40
I 40

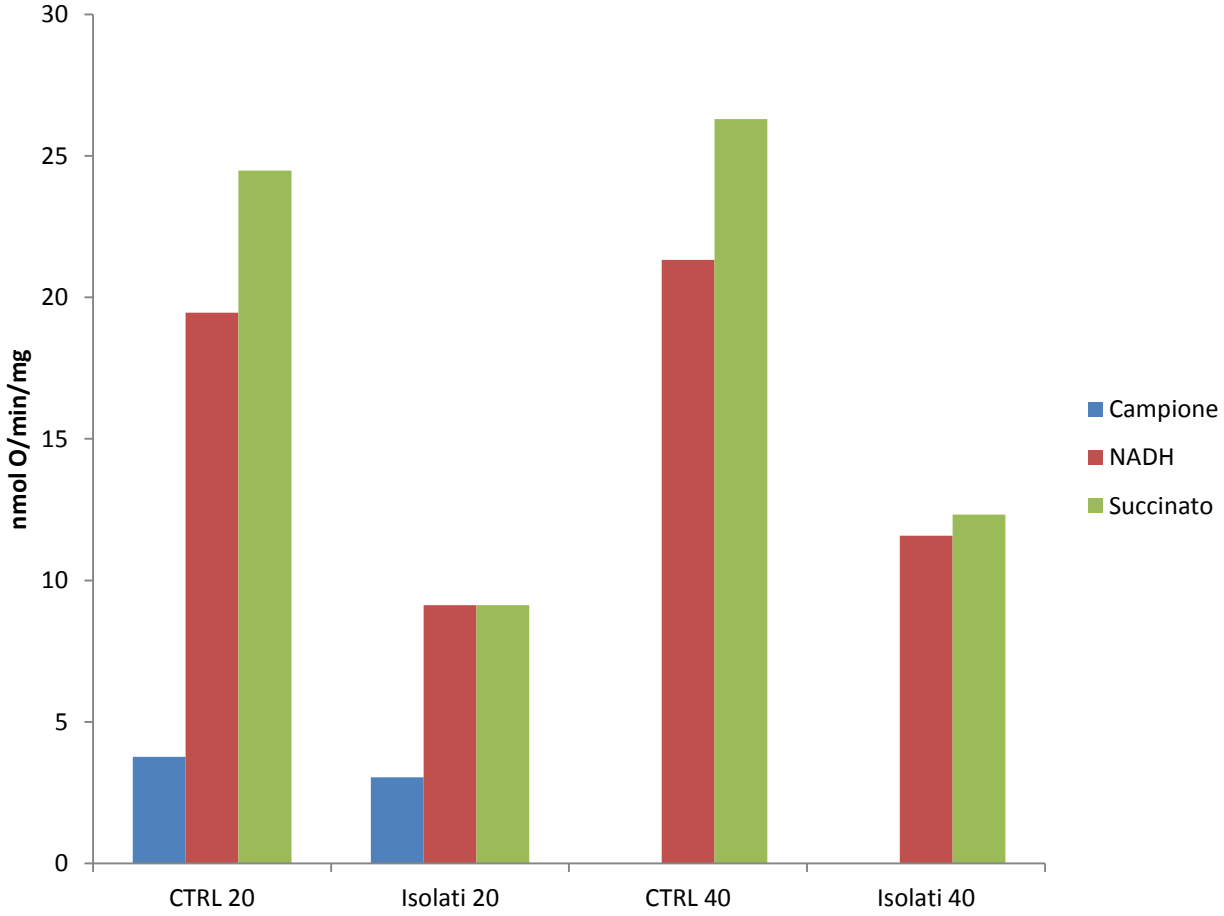
MBP (20 kDa)
20000
15000
10000
5000
0
CTRL 20
I 20
CTRL 40
I 40


ATP sintasi
20000
15000
10000
5000
0
CTRL 20
I 20
CTRL 40
I 40

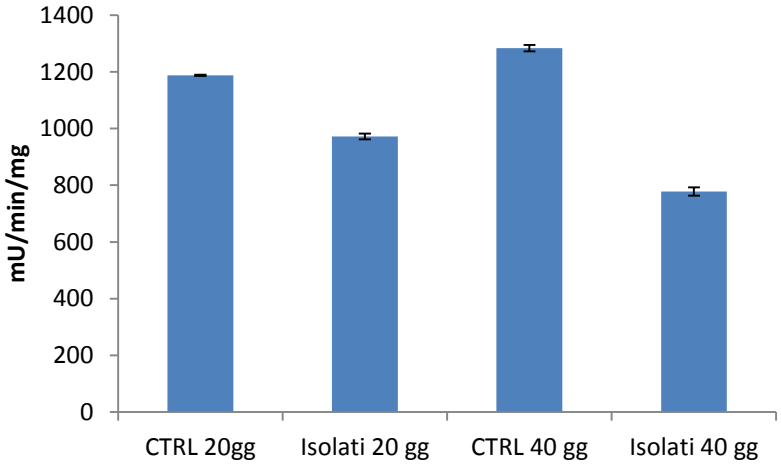

COX IV
10,000
8,000
6,000
4,000
2,000
0
CTRL 20
I 20
CTRL 40
I 40


ND4L
15000
10000
5000
0
CTRL 20
I 20
CTRL 40
I 40

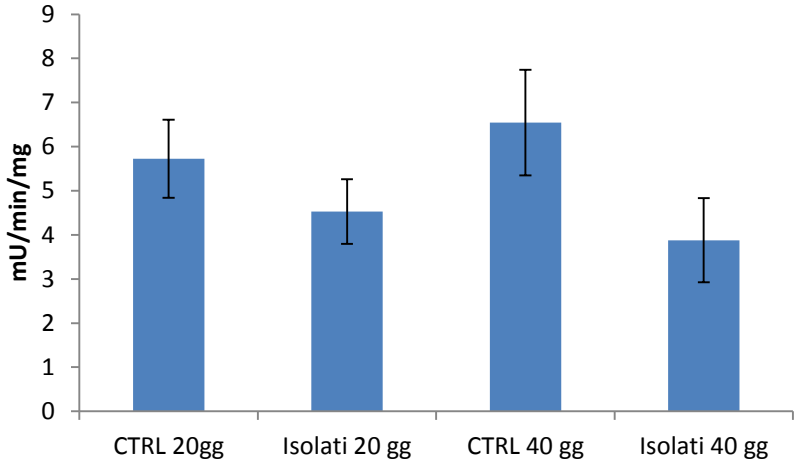
Consumo di ossigeno in mielina isolate da encefali di topi controllo e isolati 20 e 40 giorni da p10



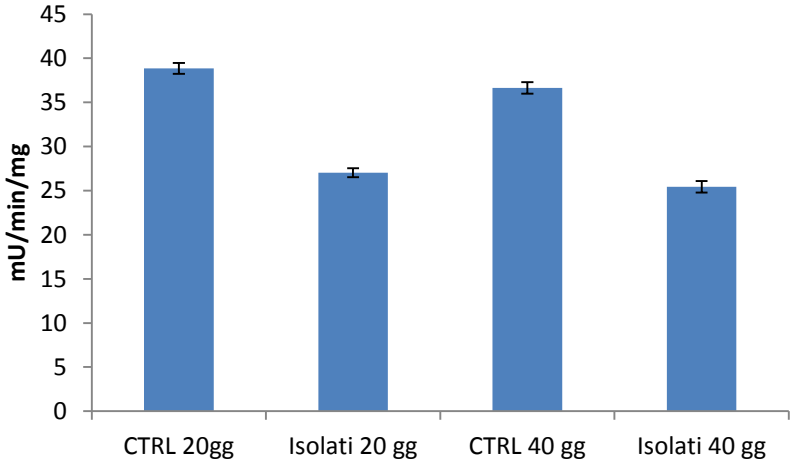
Complesso I

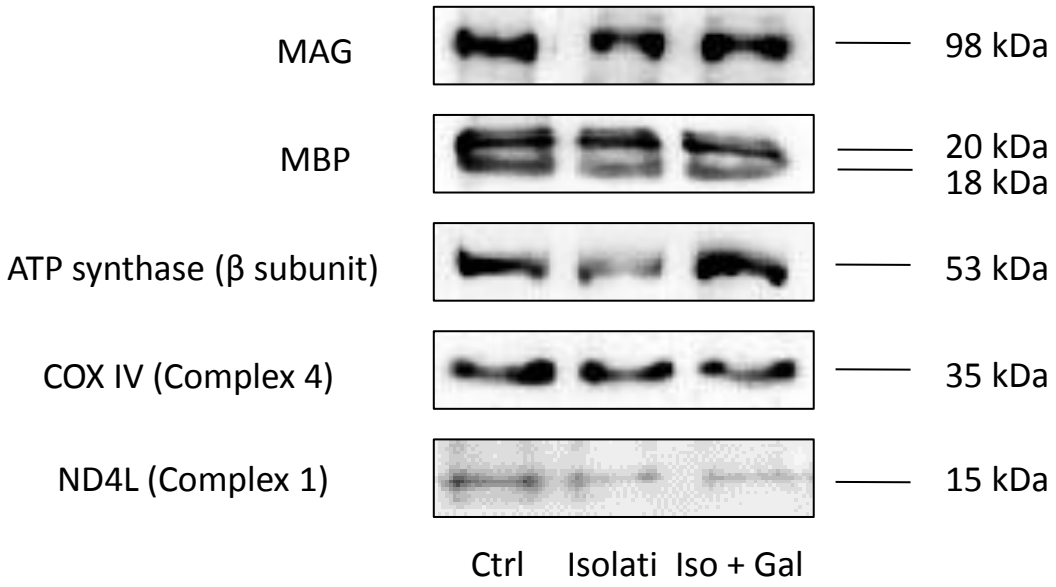


Complesso III

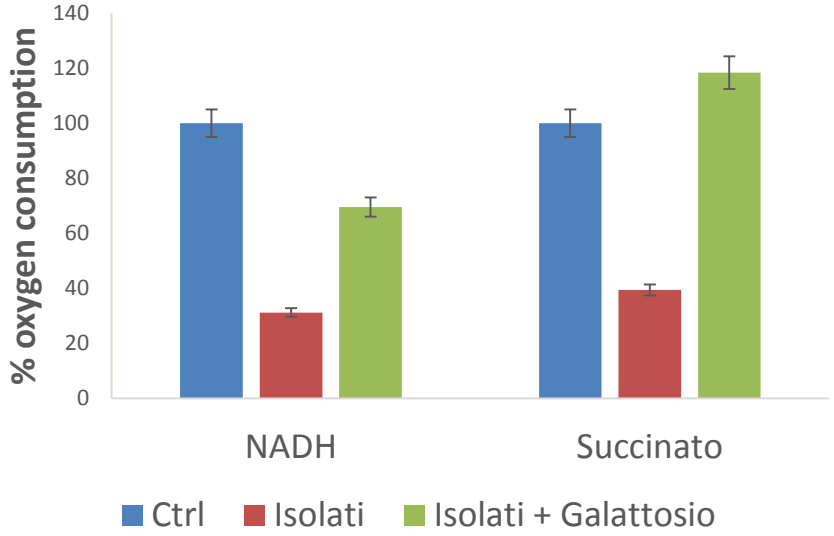


Complesso IV

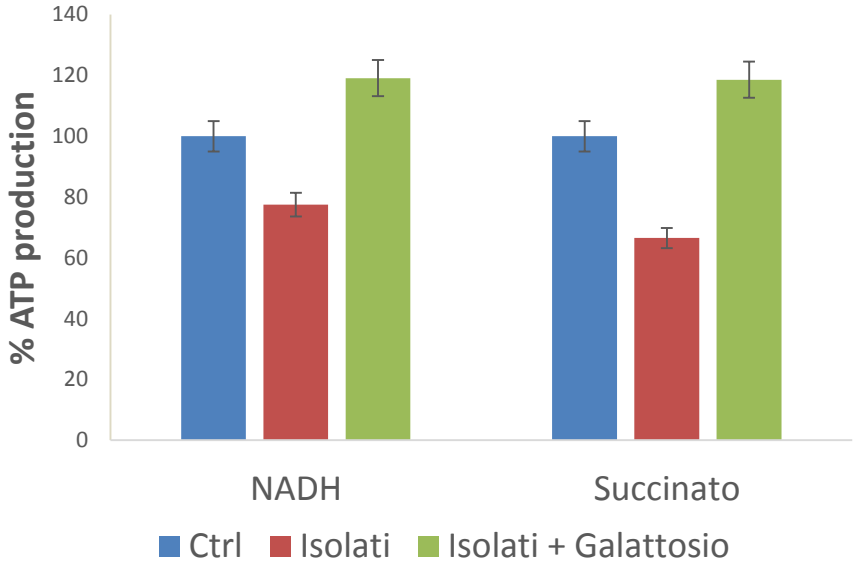




	MAG	MBP (20 KD)	MBP (18 KD)	ATP synthase	COX IV	ND4L
Ctrl	13,5	19,6	16	10,6	8,8	7,9
Isolati	10,8	15,6	9,7	4,9	6,7	4
Isolati + Galattosio	13,8	15,5	10,7	13,2	5,9	4,5


% oxygen consumption
140
120
100
80
60
40
20
0
NADH
Succinato
Ctrl
Isolati
Isolati + Galattosio

A


% ATP production
140
120
100
80
60
40
20
0
NADH
Succinato
Ctrl
Isolati
Isolati + Galattosio

B

Hypothesis on neuron survival by means of myelination:

→ In most of vertebrate, at birth, neuron have not myelin.

→ An intense firing depletes ATP and Adenosine store up triggering oligodendrocyte development (by means of purinergic receptor P1) and myelin production. Myelin makes ATP by OXPHOS and may deliver it to axon through the gap-junctions.

→ With ATP neurons survive.

→ Without ATP neurons degenerate.

(3)

Myelin and memory

Molecular Brain December 2008

BioMed Ce

Research

Open Acc

Normal mitochondrial respiratory function is essential for spatial remote memory in mice

Daisuke Tanaka[†1], Kazuto Nakada[†1], Keizo Takao[2,3], Emi Ogasawara[1], Atsuko Kasahara[1,4], Akitsugu Sato[1], Hiromichi Yonekawa[1,5], Tsuyoshi Miyakawa[2,3] and Jun-Ichi Hayashi[*1]

Address: [1]Graduate School of Life and Environmental Sciences, University of Tsukuba, Tsukuba, Ibaraki 305-8572, Japan, [2]Division of Systems Medical Science, Institute for Comprehensive Medical Science, Fujita Health University, 1-98 Dengakugakubo, Kutsukake-cho, Toyoake, Aichi 470-1192, Japan, [3]Genetic Engineering and Functional Genomics Group, Frontier Technology Center, Graduate School of Medicine, Kyoto University, Yoshida-Konoe-cho, Sakyo-ku, Kyoto 606-8501, Japan, [4]Department of Cell Physiology and Metabolism, University of Geneva Medical School, Rue Michel Servet 1, 1211 Geneva 4-CH, Switzerland and [5]Department of Laboratory Animal Science, The Tokyo Metropolitan Institute of Medical Science, 3-18-22 Honkomagome, Bunkyo-ku, Tokyo 113-8613, Japan

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* Corresponding author †Equal contributors

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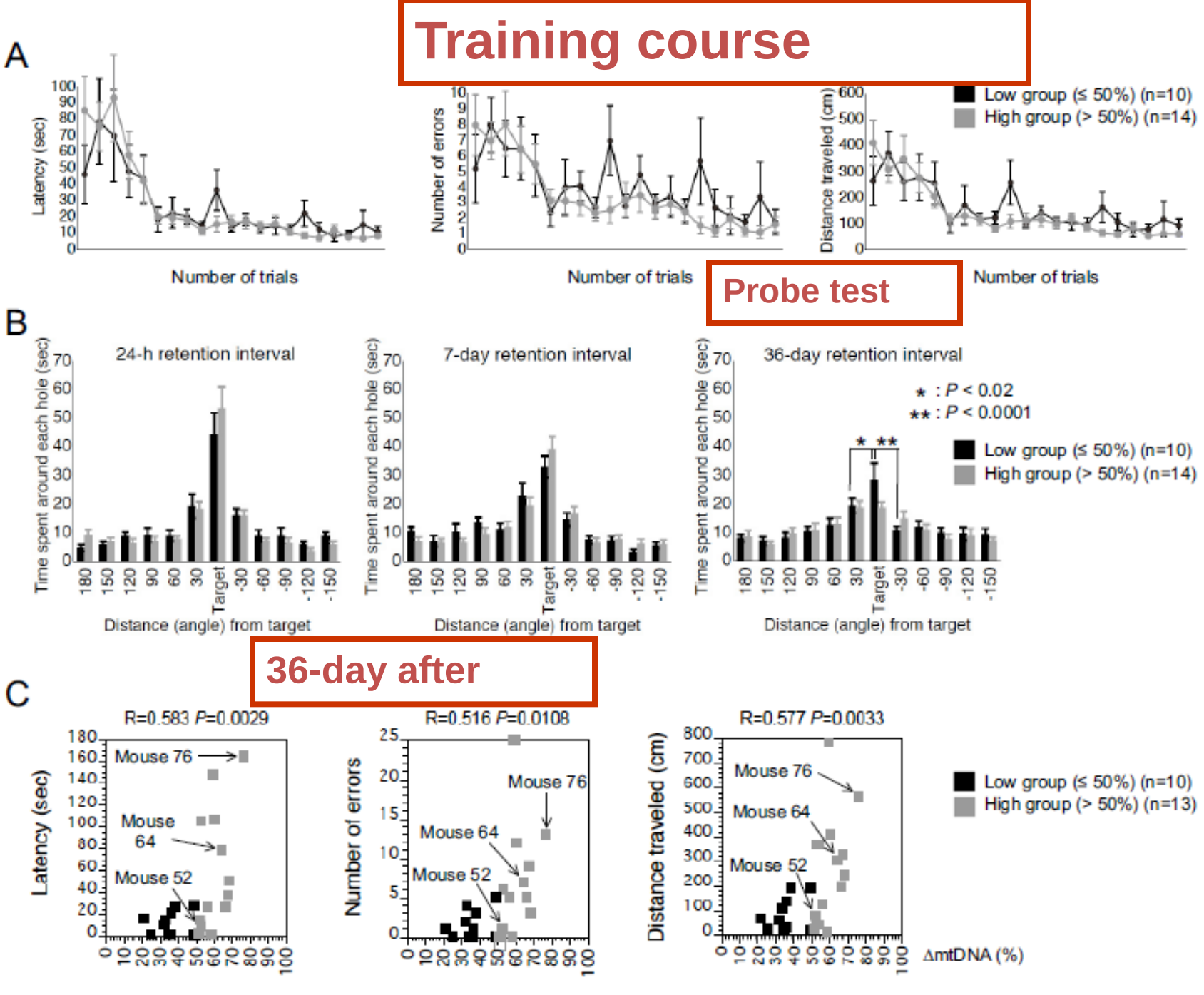
Accepted: 16 December 2008

Figure 3

Spatial learning and memory analyses using Barnes circular maze test in mito-mice. (A) Training course. Latency ($P = 0.7381$), number of errors ($P = 0.5051$), and distance traveled ($P = 0.7885$) to target hole for low (black) and high (gray) groups were plotted. (B) Probe tests at 24-h, 7-day, and 36-day after the last training. There was no significant difference in the probe test at 24-h (between the target hole and right side hole, $P < 0.005$ in the low and $P < 0.001$ in the high groups; between the target hole and left side hole, $P < 0.05$ in the low and $P < 0.002$ in the high groups) and 7-day retention intervals (between the target and right side holes, $P < 0.001$ in the low and $P < 0.001$ in the high groups; between the target and left side holes, $P < 0.05$ in the low and $P < 0.002$ in the high groups). In the probe test at the 36-day retention interval, single and double asterisks indicate significant differences between the target and right side holes in the low group ($P < 0.02$ in the low and $P = 0.9804$ in the high groups) and between the target and left side holes in the low group ($P < 0.0001$ in the low and $P = 0.2106$ in the high groups), respectively. (C) A single retraining after the probe test at the 36-day retention interval. Each score of individual mito-mice in the low (black) and high (gray) groups were plotted against the proportion of ΔmtDNA in the tails at age 4 weeks. Mice 52, 64, and 76 carried 52%, 64%, and 76% ΔmtDNA, respectively. Pearson's product-moment correlation coefficients and the associated probabilities are indicated as R and *P*, respectively. All values are means ± SE.

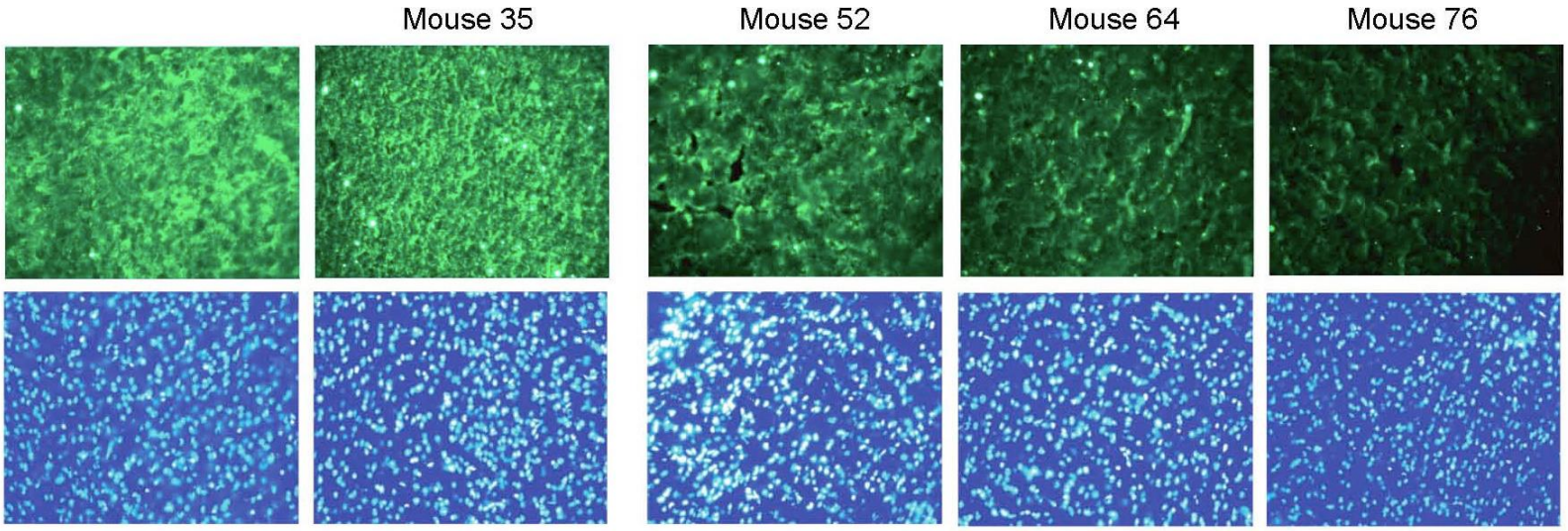

Training course
A
Latency (sec)
Number of trials
Number of errors
Number of trials
Distance traveled (cm)
Number of trials
Low group (≤ 50%) (n=10)
High group (> 50%) (n=14)
Probe test
B
24-h retention interval
7-day retention interval
36-day retention interval
Time spent around each hole (sec)
Target
Distance (angle) from target
* : P < 0.02
** : P < 0.0001
Low group (≤ 50%) (n=10)
High group (> 50%) (n=14)
36-day after
C
R=0.583 P=0.0029
R=0.516 P=0.0108
R=0.577 P=0.0033
Latency (sec)
Number of errors
Distance traveled (cm)
Mouse 76
Mouse 64
Mouse 52
Low group (≤ 50%) (n=10)
High group (> 50%) (n=13)
ΔmtDNA (%)

http://en.wikipedia.org/wiki/Barnes_maze

The Barnes maze is a tool used in psychological laboratory experiments to measure spatial learning and memory. The test subjects are usually rodents such as mice or lab rats, which either serve as a control or may have some genetic variable or deficiency present in them which will cause them to react differently to the maze.

Video: http://www.youtube.com/watch?v=MBwoYJ7Mdl8

	Low group (n=10)			High group (n=12)		
Tissue	Tail (4 weeks)	Brain (8.5 months)	Skeletal muscle (8.5 months)	Tail (4 weeks)	Brain (8.5 months)	Skeletal muscle (8.5 months)
ΔmtDNA load	35.3% ± 2.8%	36.9% ± 3.3%	64.5% ± 3.5%	60.4% ± 2.8%	57.4% ± 2.0%	82.5% ± 0.9%
Increased proportion	n.d.	1.6% ± 2.8%	29.2% ± 3.7%	n.d.	- 3.0% ± 1.6%	22.1% ± 2.7%



	Average in low group (n=10)	Mouse 52	Mouse 64	Mouse 76	Average in high group (n=12)
Latency (sec)	12.6	15	79	165	59.8
Number of errors	1.6	1	7	13	6.7
Distance traveled (cm)	86.6	81	303	567	269.3

B) Relationship between mitochondrial respiratory function and phenotypic expression of impaired spatial remote memory

These researches conclude that the spatial memory is very compromized, because the proteins codified by mitochondrial DNA are loose.

We therefore succeeded for the first time in showing experimental evidence that a high load of pathogenically mutated mtDNA and the resultant mitochondrial respiration deficiencies, in the absence of severe mitochondrial disease phenotypes, are responsible for the impairment of spatial remote memory.

Parental trasmission of behaviour

Anim. Behav., 1997, **54**, 559–570

Genetic correlates of social behaviour in wild chimpanzees: evidence from mitochondrial DNA

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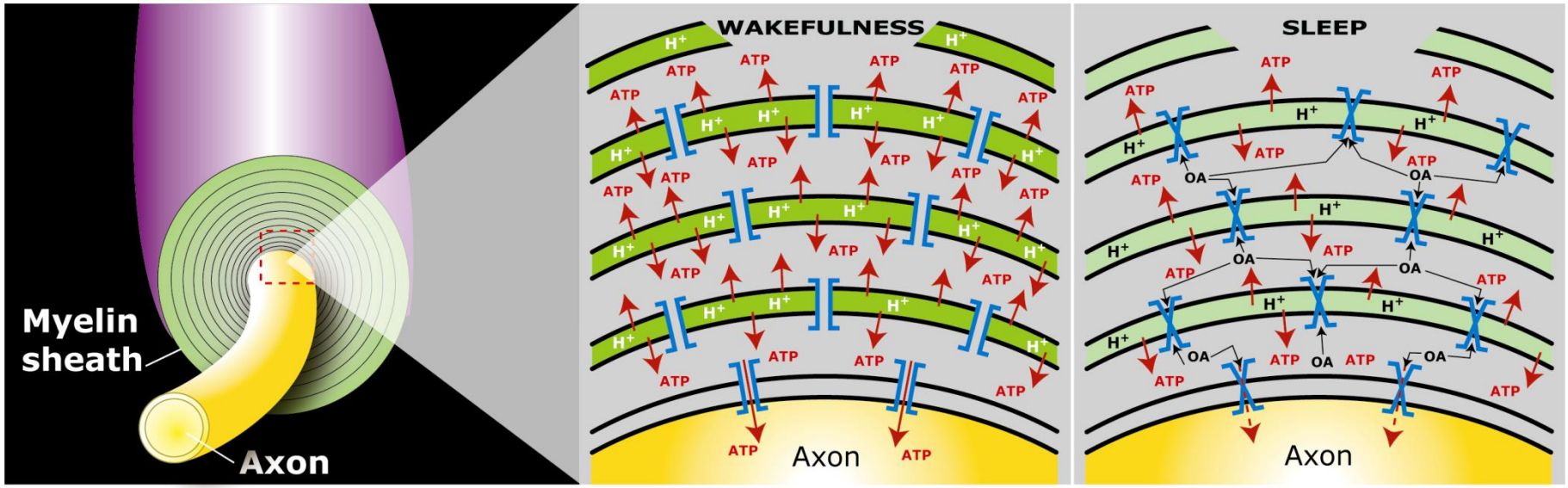
www.sjoert.com

(4)

Assumptions on the energetic basis of sleep

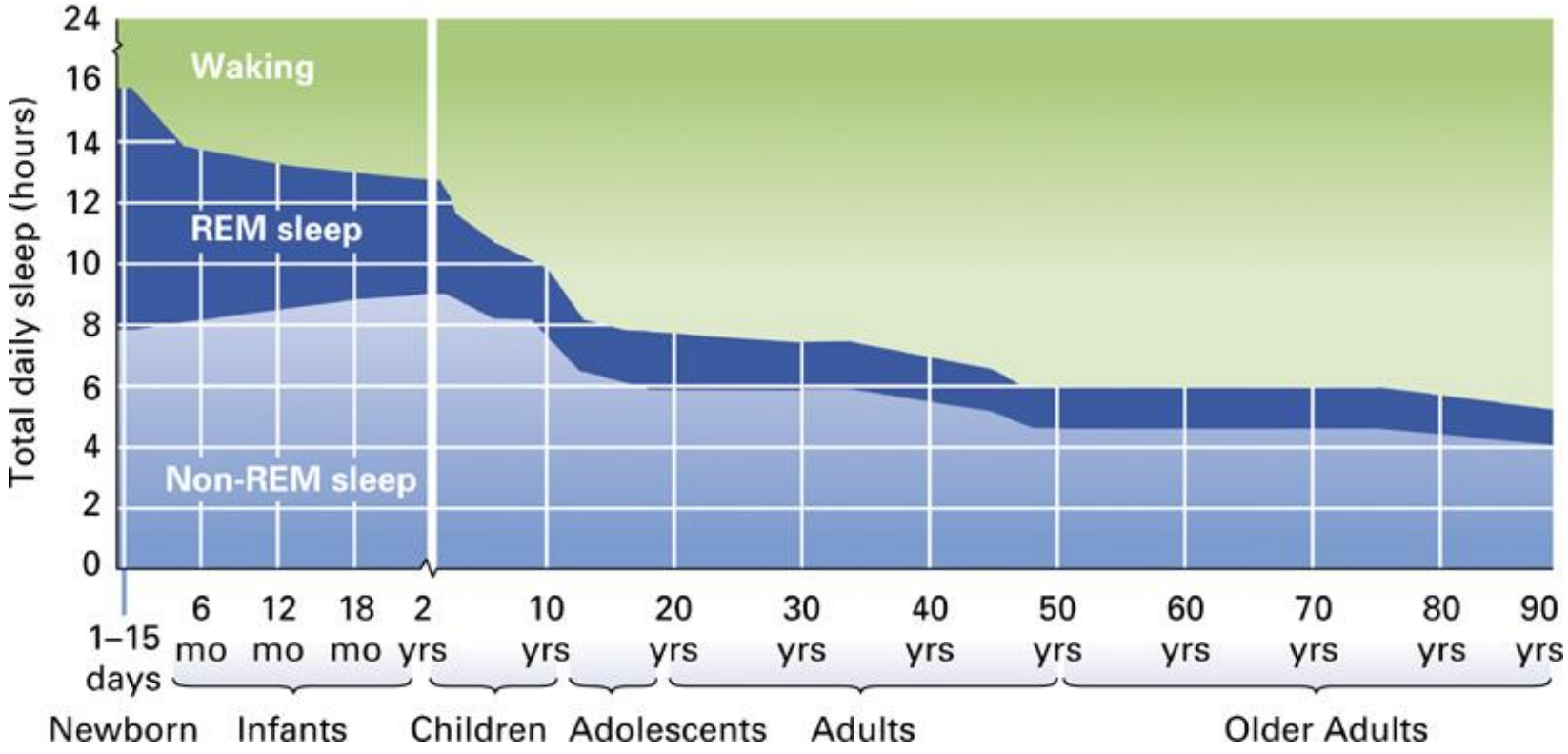
Does sleep serve to "recharge“ myelin?

Model of myelin sheath containing Myelin Basic Protein with function of laminar chemiosmotic buffer: a hypothesis on the role of MBP in the basic mechanisms of sleep / wake

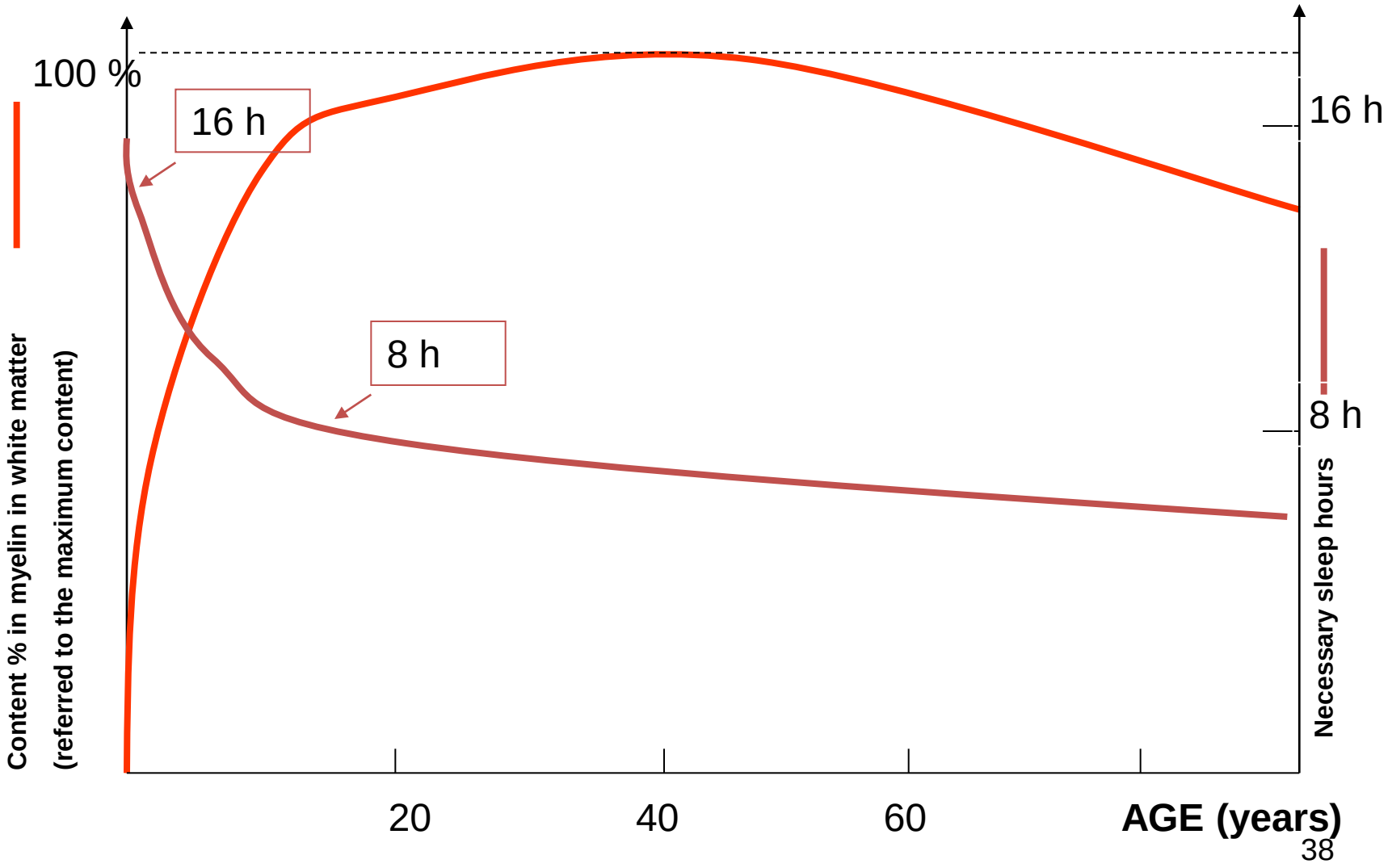


OA = Oleammide

Sleep Across the Human Life Span



- **The cognitive ability increases with myelin**
- **The hours of sleep decrease as the myelin increases**



The sleep:

For the vast majority of biological functions, there is a satisfactory explanation, connecting the structure of the organ to its function and vice versa. For i.e. a muscle exerts a mechanical action, as there are molecules that slide over each other and receive chemical energy from other molecules and clearly identified

For the brain we do not know how it used the considerable energy it uses. About sleep, which is one of the most striking features of the brain, we have no explanation to date.

It 'been said that if sleep did not have a solid functional justification, it would be an extravagance of evolution and / or nature itself.

Among the many theories about sleep, the energetic one is still considered the most, but its molecular and functional evidence, if any, is absolutely to define and / or to discover.

- **During sleep, glucose burning is almost the same as during wakefulness.**

- It's known that during sleep the nervous system as a whole consumes less energy.

- **It's possible that the excess energy is accumulated in the form of protons stored in solution in neutral lipid and/or in myelin basic protein**

Sleep Neuro-energetics

Kalinchuk AV, ei al. Local energy depletion in the basal forebrain increases sleep.

Eur J Neurosci 2003;17(4):863-9.

Energy depletion in localized brain areas seems to mimick sleep need[31]: interestingly, infusion of 2,4-dinitrophenol (DNP), an uncoupler which prevents the synthesis of ATP, in the basal forebrain of rats induced increases in non-REM sleep that was comparable to those induced by sleep deprivation.

Oleamide Synthesizing Activity from Rat Kidney

IDENTIFICATION AS CYTOCHROME C

William J. Driscoll, Shalini Chaturvedi, and Gregory P. Mueller

THE JOURNAL OF BIOLOGICAL CHEMISTRY , August 3, 2007

Naturally occurring oleamide was shown to accumulate in the cerebrospinal fluid of sleep deprived cats and to produce a profound sleep-like state when administered to rodents.. **These findings led to the proposal that oleamide directly contributes to the biochemical mechanisms underlying the drive to sleep** . More recently, oleamide was reported to modulate gap junctions.

Soleep-Memory: Conclusions

- During the conscious waking the energy demand exceeds that mechanically possible. There is a conscious activity in neocortical gray matter that utilizes most of the energy produced at the time by burning / breathing. Then there is a discernible physical activity of the unconscious in the white matter that extabilishes a huge number of connections between different sites of the cortex

- This activity during waking consumes the energy reserves represented by the accumulation of protons in the chemiosmotic laminar buffer of myelin and the feeling of sleep is due to poor energy supply fed by the axon myelin.

- neuronal activity requires a lot of energy intake. Biological systems use chemical energy in the form of ATP.

- With sleep we refill the proton and the myelin is energized, because the available energy is almost equal to that of wakefulness but during sleep it is mostly devoted to recharging, since the needs of the conscious system have decreased significantly.

- **It can be assumed that the memory is an energization of axonal connections by the white matter, in light of the fact that sleep strengthens the memory.**

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Letter to the Editor

from Morelli, Ravera & Panfoli

Myelin sheath: A new possible role in sleep mechanism

pivotal role in the axon surrounding, allowing the nerve to transmit its impulses rapidly. However, there is growing evidence
that myelin has also an as yet unexplained neuro-trophic role. We reported that the respiratory chain components are expressed in myelin, outside of mitochondria [1]. These components would generate a proton gradient across myelin membranes to support ATP synthesis by an Fo-F1 ATP synthase. This may explain how in demyelinising diseases, as Multiple Sclerosis (MS), myelin loss causes an axonal necrosis.

Recently, Gallup et al [2] described sleep problems and frequent yawning in MS patients. During sleep, the glucose consumption by brain is very similar to that in wakefulness, even though the neuronal energetic demand is low. We have envisaged an involvement of myelin sheath. Imagine that myelin sheath acts as a proton (H+) buffer capacitor, thank to the abundance of myelin basic protein (MBP) and phospholipids, whose exceptional buffering capacity of phospholipids was demonstrated [3].

junctions, formed by connexins 32 [5], that seems to transport mainly ATP [6], likely from myelin to the axon.

This potential would be used by myelin to produce energy, during the wake period. In turn, sleep would be induced by a “discharge” of H+ in myelin sheath and wakefulness by a “complete recharge” of myelin sheath. The sleep need correlates to age. In fact, newborn and children have a higher sleep need than the adults. This may depend on myelinogenesis, that begins after born and goes on until 22-25 years age. Under these conditions, myelin may be less competent in accumulating energy= H+ and generate the need for sleep. Interestingly, sleep is also regulated by oleamide, an endogenous hypnotic compound that increases before the sleep, decreases before the wake up and is accumulated in cerebral spinal fluid of sleep-deprived animals [4]. Interestingly, oleamide closes the myelin gap junction, formed by connexin 32 [5], that seem to transport mainly ATP [6], likely from myelin to the axon.

The Journal of Neuroscience, September 4, 2013 • 33(36):14288 –14300

Effects of Sleep and Wake on Oligodendrocytes and Their Precursors

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Previous studies of differential gene expression in sleep and wake pooled transcripts from all brain cells showed that several genes expressed at higher levels during sleep are involved in the synthesis/maintenance of membranes in general and of myelin in particular, a surprising finding given the reported slow turnover of many myelin components…