UNIVERSITÄT BERN

17° corso di aggiornamento per il medico di base

25, 26 e 27 settembre 2019
Mercato coperto Giubiasco

INSELSPITAL
UNIVERSITÄTSSPITAL BERN
HÔPITAL UNIVERSITAIRE DE BERNE

Novità terapeutiche in neurologia

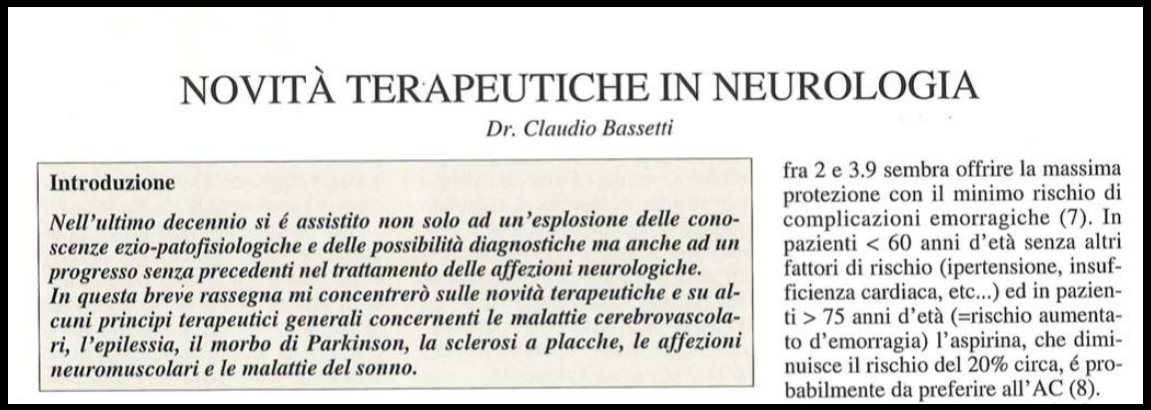
Prof. Claudio L. Bassetti
Neurology Department
University Hospital, Bern
Switzerland

La neurologie en marche[1]

par

F. REGLI

Revue Med Suisse Romande
1975



NOVITÀ TERAPEUTICHE IN NEUROLOGIA

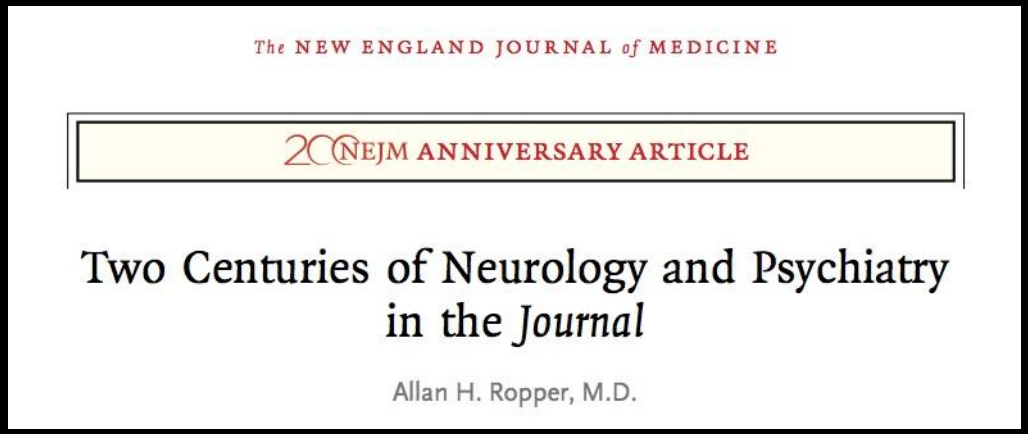
Dr. Claudio Bassetti

Introduzione

Nell'ultimo decennio si é assistito non solo ad un'esplosione delle conoscenze ezio-patofisiologiche e delle possibilità diagnostiche ma anche ad un progresso senza precedenti nel trattamento delle affezioni neurologiche.
In questa breve rassegna mi concentrerò sulle novità terapeutiche e su alcuni principi terapeutici generali concernenti le malattie cerebrovascolari, l'epilessia, il morbo di Parkinson, la sclerosi a placche, le affezioni neuromuscolari e le malattie del sonno.

fra 2 e 3.9 sembra offrire la massima protezione con il minimo rischio di complicazioni emorragiche (7). In pazienti < 60 anni d'età senza altri fattori di rischio (ipertensione, insufficienza cardiaca, etc...) ed in pazienti > 75 anni d'età (=rischio aumentato d'emorragia) l'aspirina, che diminuisce il rischio del 20% circa, é probabilmente da preferire all'AC (8).

Rivista medica ticinese
1995



The NEW ENGLAND JOURNAL of MEDICINE

200 NEJM ANNIVERSARY ARTICLE

Two Centuries of Neurology and Psychiatry in the *Journal*

Allan H. Ropper, M.D.

New Engl J Med
2012

Introduzione
Principi terapeutici
Malattie neurologiche
Conclusioni e futuro

Introduzione

Principi terapeutici

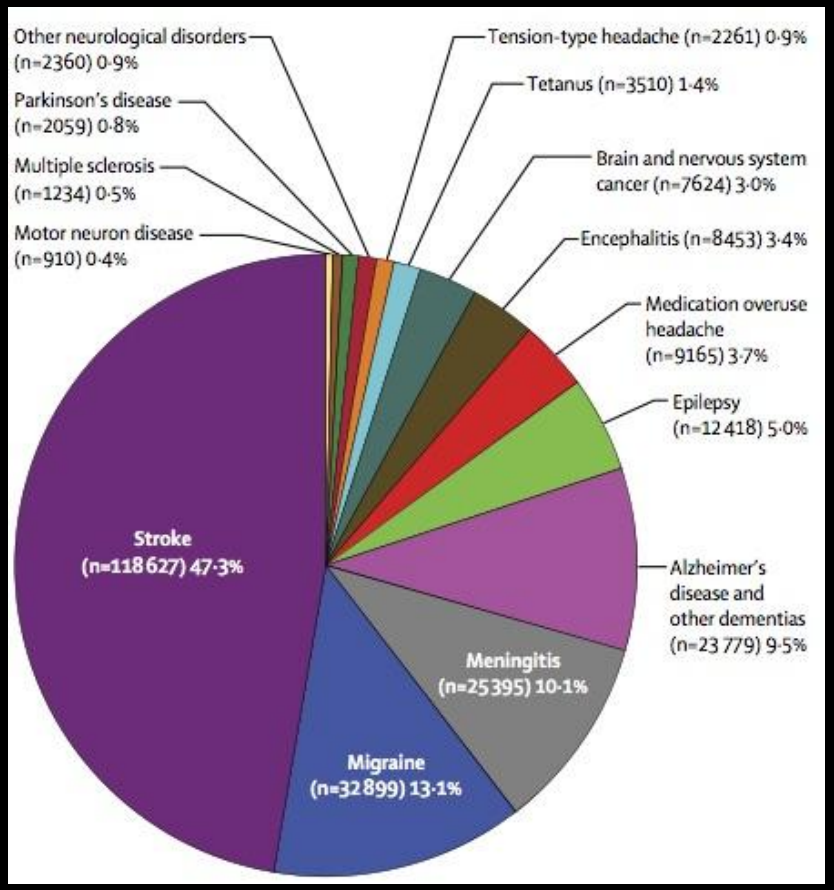
Malattie neurologiche

Conclusioni e futuro

Global, regional, and national burden of neurological disorders during 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015

GBD 2015 Neurological Disorders Collaborator Group*

Lancet Neurol 2017



Affezioni neurologiche, 2015
195 paesi, 395 patologie

10% disabilità (disability adjusted life-years)
17% decessi

Frequenza: cefalee, demenze

in aumento negli ultimi 25 anni

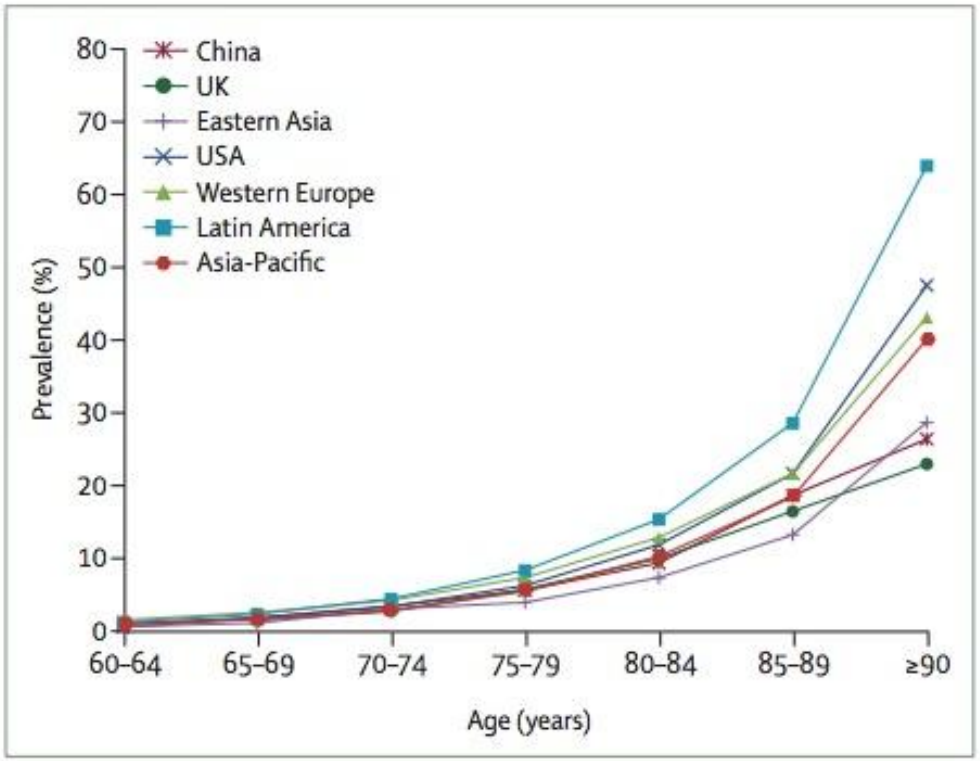


***Figure 3*: Age-specific prevalence of dementia by world region and in major countries**

Patterns of age-specific prevalence of dementia are similar across worldwide regions, but vary substantially among the oldest old (age ≥90 years).[72–75]

M. Alzheimer

2-5 % della popolazione

>10% sopra 80 anni
>20% sopra i 90 anni

Winblad, Lancet Neurol 2016

Neurologist ambulatory care, health care utilization, and costs in a large commercial dataset

Neurology 2016

Figure 2 Average annual episode treatment group (ETG) costs (allowed third-party payments, in 2012 US dollars) by neurologist involvement

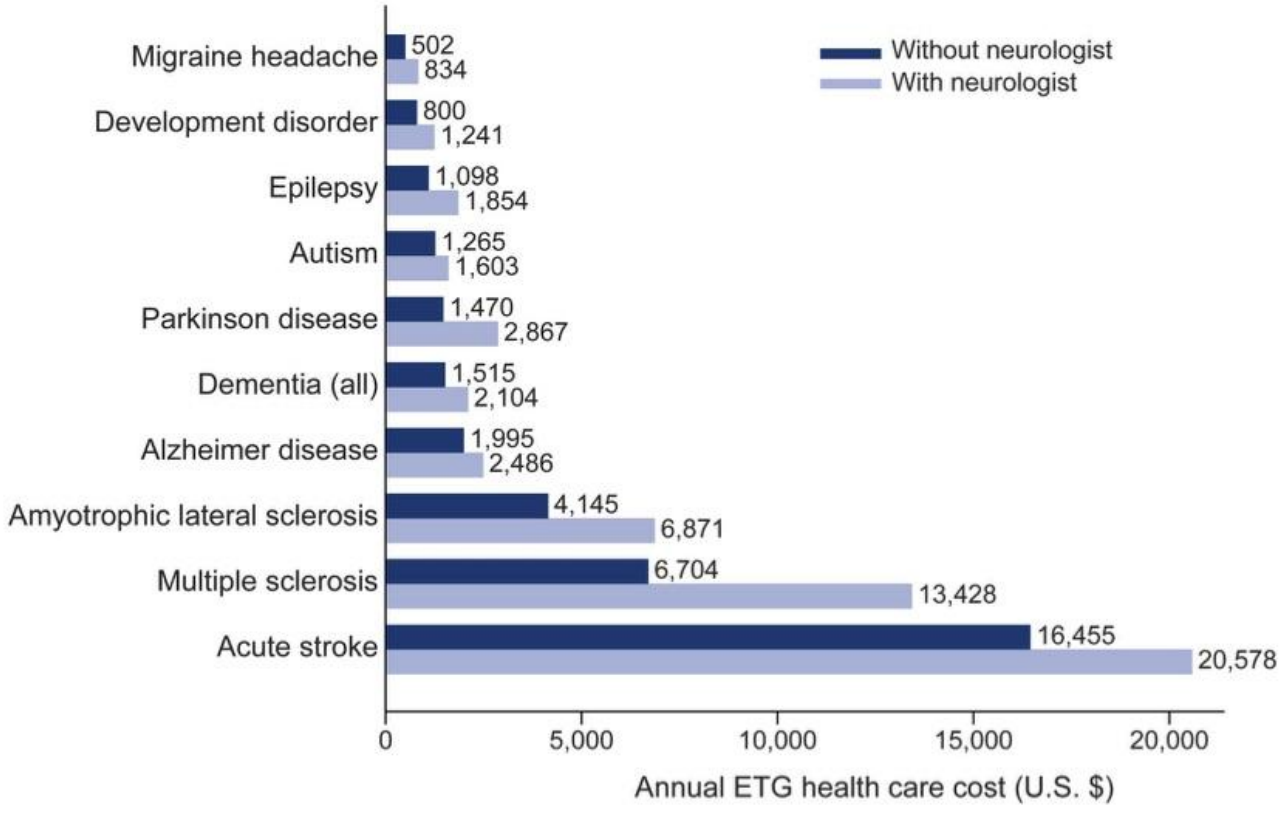
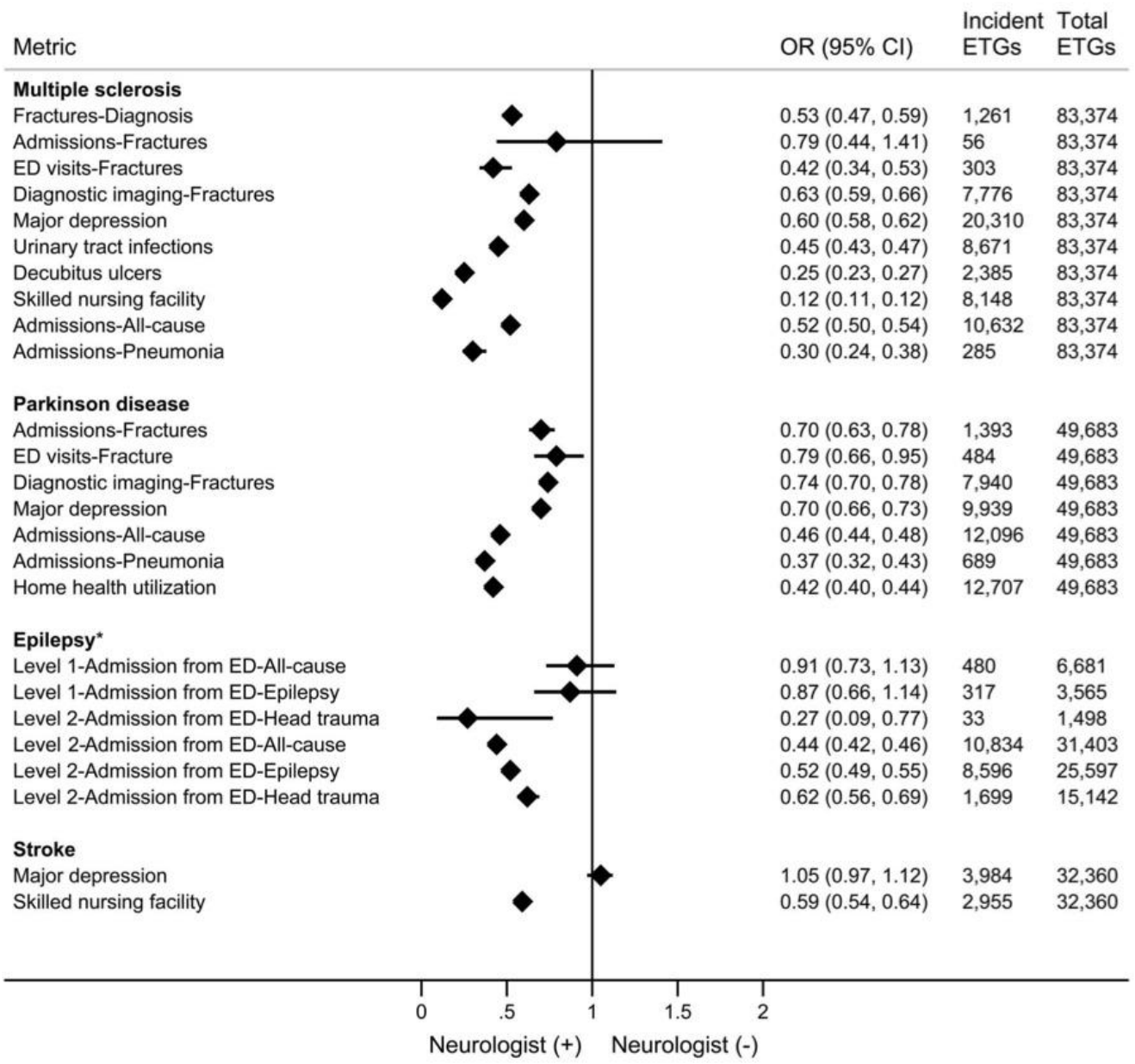


Figure 3 Adverse events and health care utilization metrics, and association with neurologist ambulatory care, by condition



Introduzione

Principi terapeutici

Malattie neurologiche
Conclusioni e futuro

Principi terapeutici

- interventistica/“time is brain“
- neuroimmunologia/anticorpi monoclonali
- neuro-modulazione/“closed-loop“
- terapie genetiche

- prevenzione/diagnosi precoce
- neuroriabilitazione
- trattamenti sintomatici/palliativi
- terapie enzimatiche

Principi terapeutici

Ictus: nuovo servizio al Neurocentro

Sarà presentato in una conferenza pubblica da NSI e CdT il 19 maggio

CdT 2010

- interventistica/“time is brain“
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- trattamenti sintomatici/palliativi
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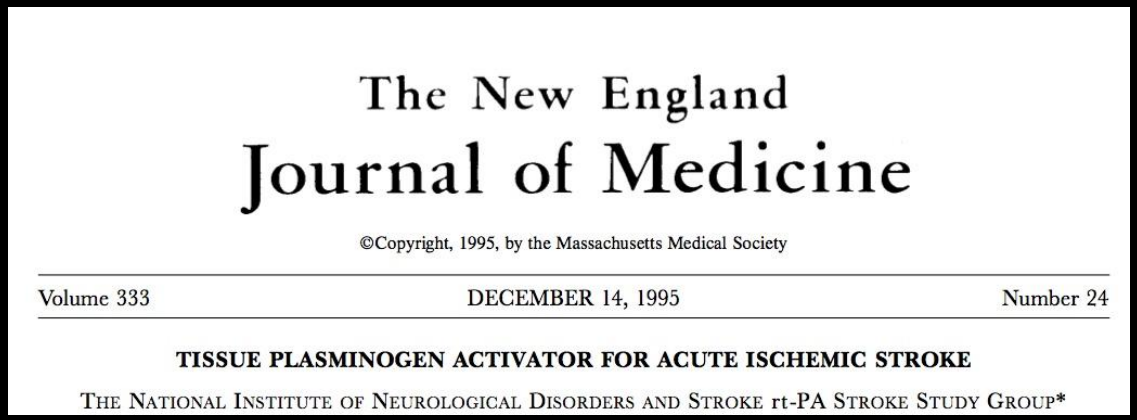

The New England
Journal of Medicine

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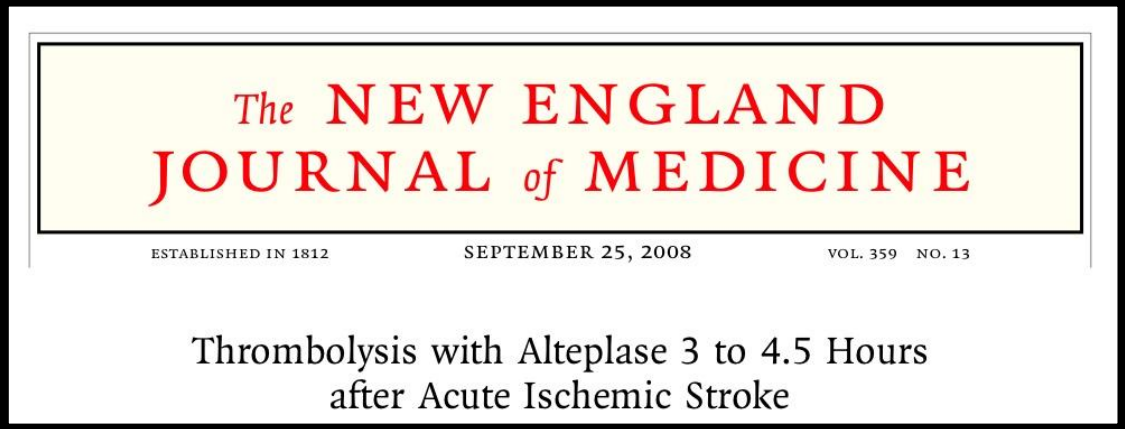
Volume 333 DECEMBER 14, 1995 Number 24

TISSUE PLASMINOGEN ACTIVATOR FOR ACUTE ISCHEMIC STROKE

THE NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE rt-PA STROKE STUDY GROUP*

N Engl J Med 1995



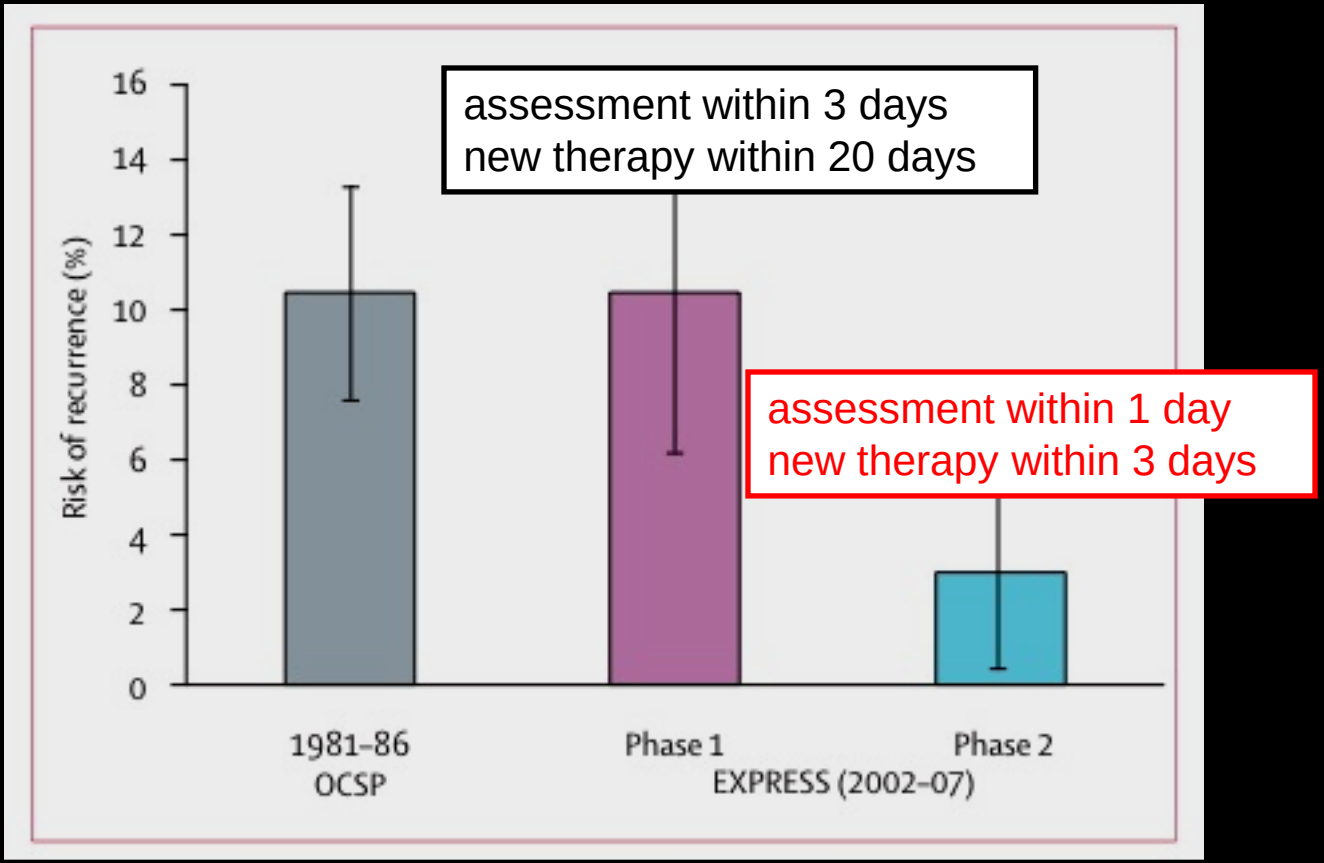
The NEW ENGLAND
JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 25, 2008 VOL. 359 NO. 13

Thrombolysis with Alteplase 3 to 4.5 Hours
after Acute Ischemic Stroke

N Engl J Med 2008

Risk of stroke after TIA



Rothwell, Lancet Neurol 2007 (Express Study)

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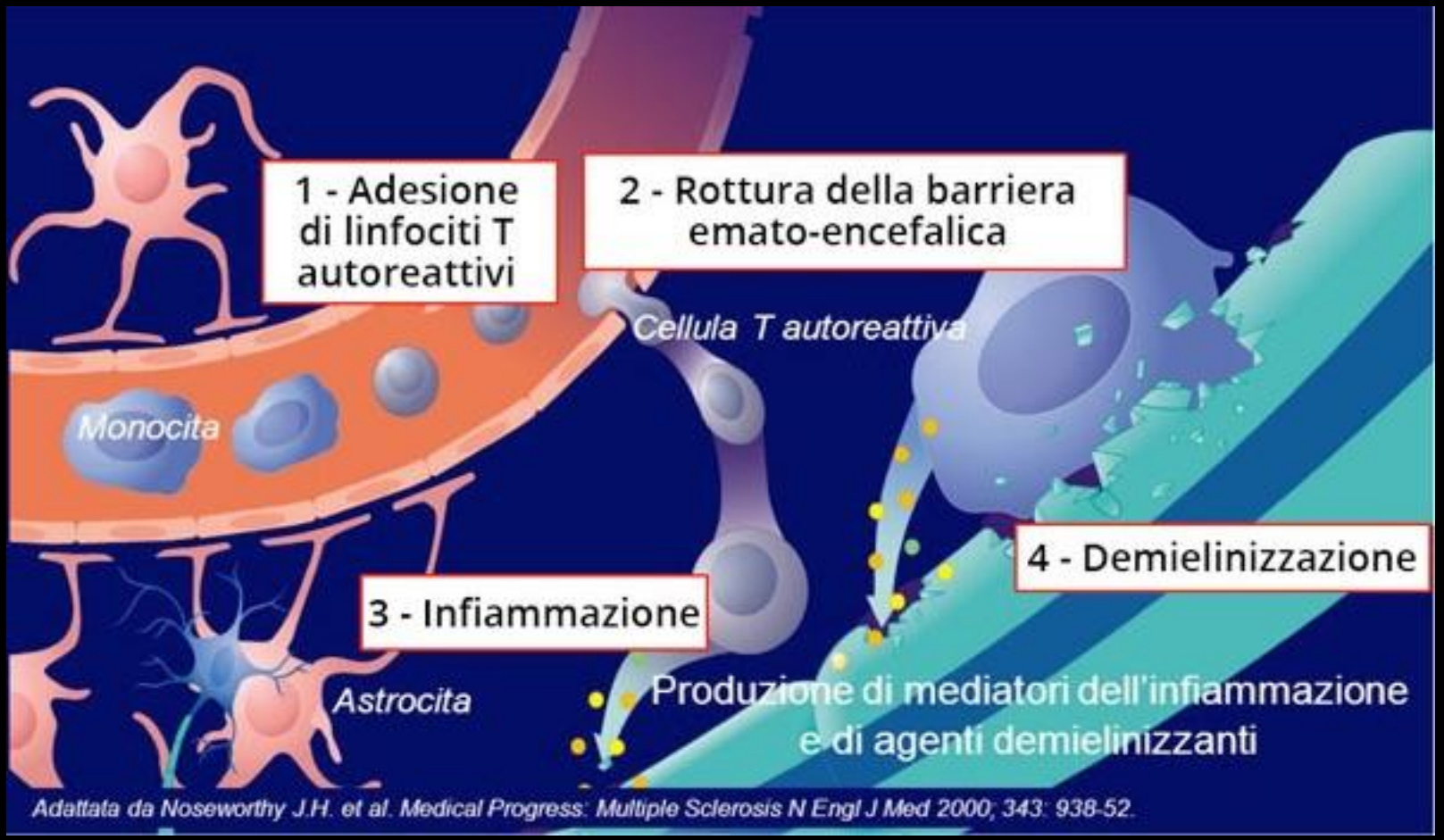
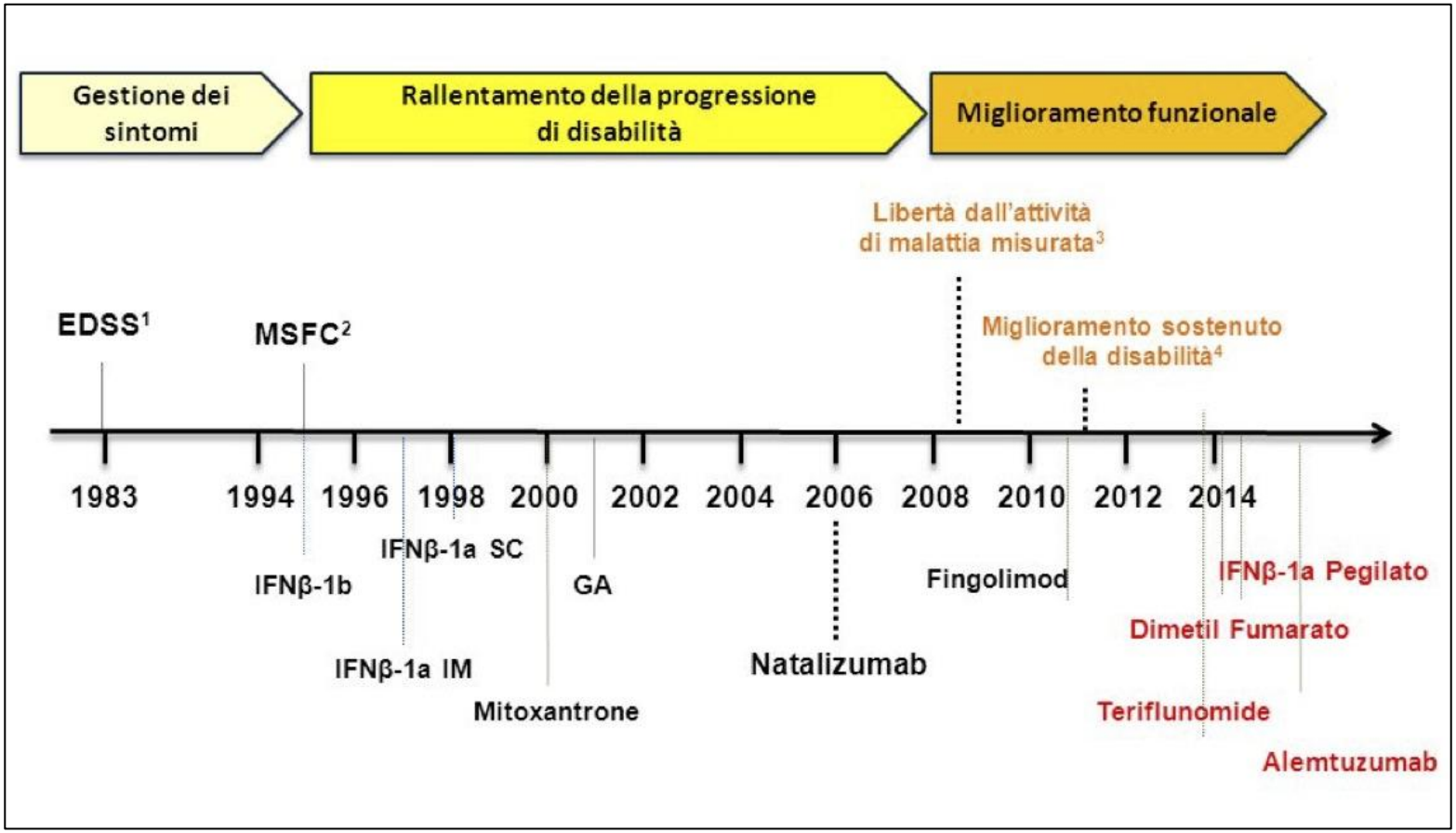
Sclerosi multipla ed auto-immunità



Sclerosi multipla: Trattamenti immunomodulanti



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Controlled Trial of Natalizumab for Relapsing Multiple Sclerosis

David H. Miller, M.D., Omar A. Khan, M.D., William A. Sheremata, M.D., Lance D. Blumhardt, M.D., George P.A. Rice, M.D., Michele A. Libonati, M.S., Allison J. Willmer-Hulme, Ph.D., Catherine M. Dalton, M.B., Katherine A. Miszkiel, M.B., and Paul W. O'Connor, M.D., for the International Natalizumab Multiple Sclerosis Trial Group*

N Engl J Med 2003

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Oral Fingolimod or Intramuscular Interferon for Relapsing Multiple Sclerosis

Jeffrey A. Cohen, M.D., Frederik Barkhof, M.D., Giancarlo Comi, M.D., Hans-Peter Hartung, M.D., Bhupendra O. Khatri, M.D., Xavier Montalban, M.D., Jean Pelletier, M.D., Ruggero Capra, M.D., Paolo Gallo, M.D., Guillermo Izquierdo, M.D., Klaus Tiel-Wilck, M.D., Ana de Vera, M.D., James Jin, Ph.D., Tracy Stites, Ph.D., Stacy Wu, M.D., Shreeram Aradhye, M.D., and Ludwig Kappos, M.D., for the TRANSFORMS Study Group*

N Engl J Med 2010

Principi terapeutici

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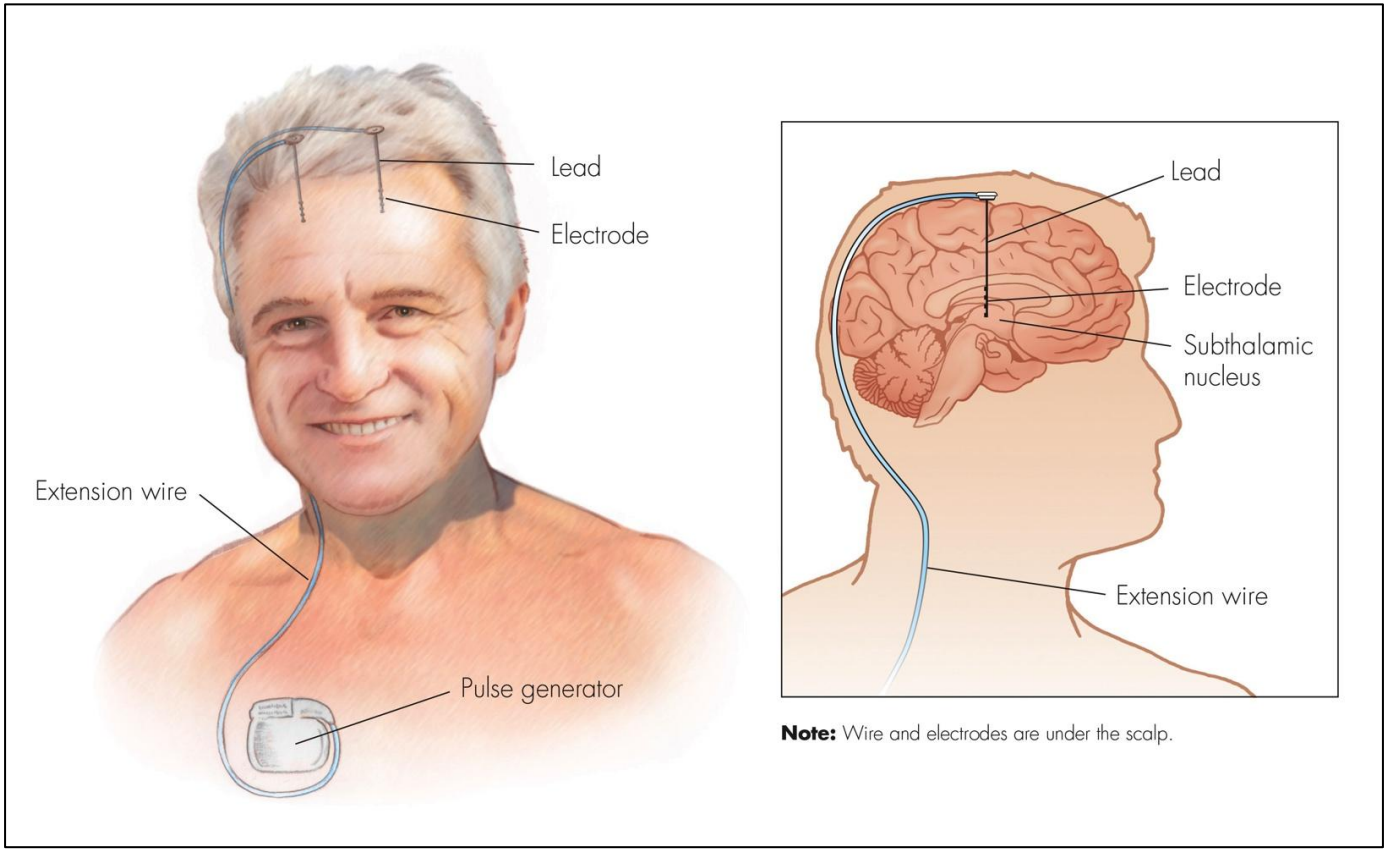
- trattamenti sintomatici/palliativi
- terapie enzimatiche

M. Parkinson: Terapia con stimolazione cerebrale profonda (DBS)

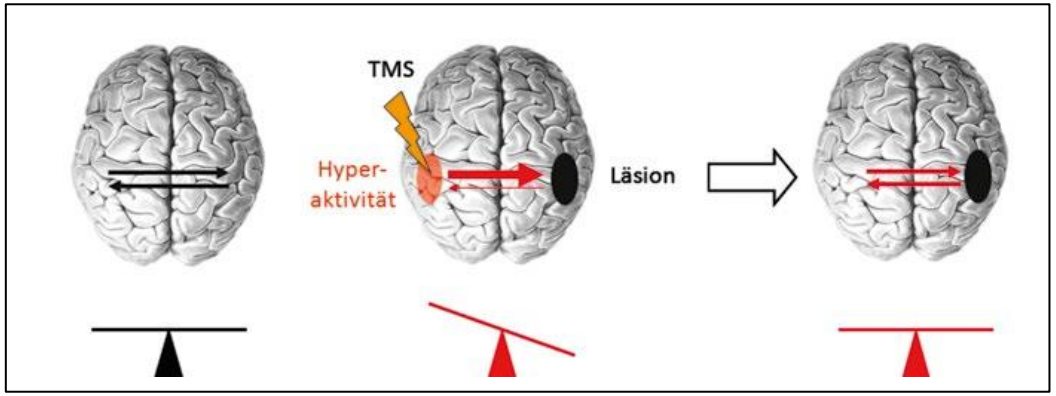


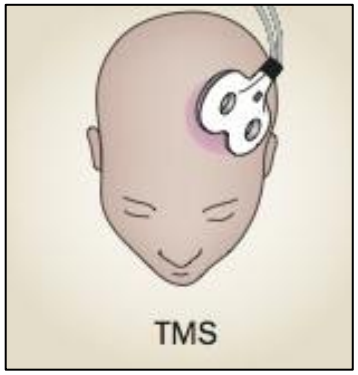
M. Parkinson: Terapia con DBS

Deuschl NEJM 2006, Weaver, JAMA 2009

M.Z., 52a

Stimolazione transcranica (TMS) e recupero da neglect





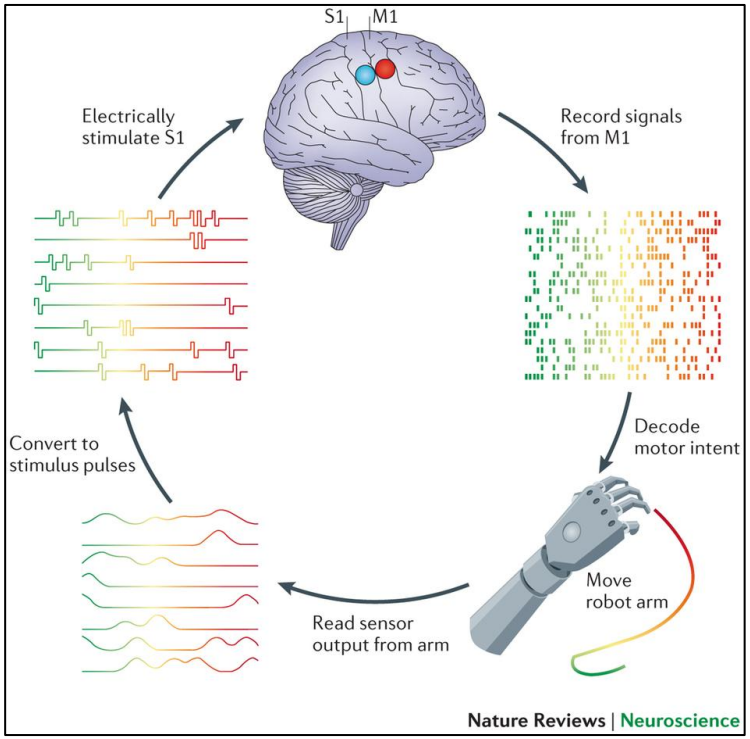
doi:10.1093/brain/aws182 Brain 2012: 135; 3426–3439 | 3426

BRAIN
A JOURNAL OF NEUROLOGY

Theta burst stimulation reduces disability during the activities of daily living in spatial neglect

Dario Cazzoli,[1,2] René M. Müri,[2] Rahel Schumacher,[2] Sebastian von Arx,[2] Silvia Chaves,[2] Klemens Gutbrod,[2] Stephan Bohlhalter,[2,3] Daniel Bauer,[3] Tim Vanbellingen,[2] Manuel Bertschi,[2] Stefan Kipfer,[2] Clive R. Rosenthal,[1] Christopher Kennard,[1] Claudio L. Bassetti[2] and Thomas Nyffeler[2,3]

Interfaccia cervello-computer/Closed-loop systems

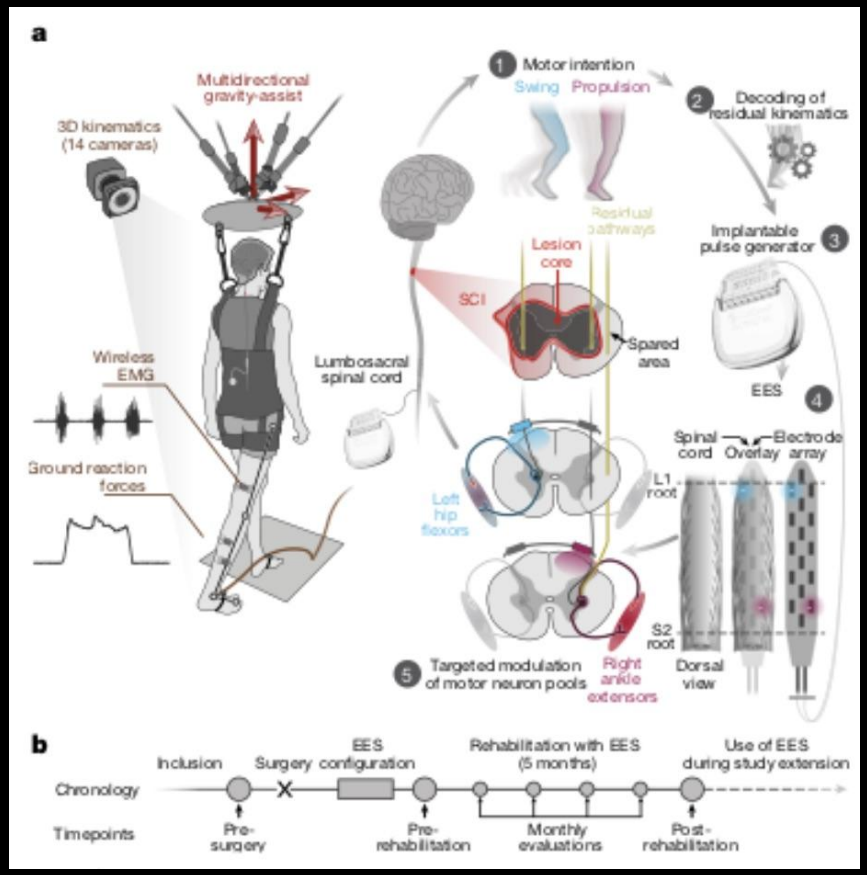


Bensmaia and Miller, Nature Rev Neurosci 2014

Targeted neurotechnology restores walking in humans with spinal cord injury

Fabien B. Wagner[1,2,15], Jean-Baptiste Mignardot[1,2,15], Camille G. Le Goff-Mignardot[1,2,15], Robin Demesmaeker[1,2], Salif Komi[1,2], Marco Capogrosso[3], Andreas Rowald[1,2], Ismael Seáñez[1,2], Miroslav Caban[4,5], Elvira Pirondini[1,2,6], Molywan Vat[7], Laura A. McCracken[1,2], Roman Heimgartner[1,2], Isabelle Fodor[2], Anne Watrin[4], Perrine Seguin[1,2], Edoardo Paoles[4], Katrien Van Den Keybus[2], Grégoire Eberle[2], Brigitte Schurch[2], Etienne Pralong[7], Fabio Becce[8], John Prior[9], Nicholas Buse[10], Rik Buschman[10], Esra Neufeld[11], Niels Kuster[11,12], Stefano Carda[2], Joachim von Zitzewitz[4], Vincent Delattre[4], Tim Denison[10,13], Hendrik Lambert[4], Karen Minassian[1,2,16], Jocelyne Bloch[2,7,14,16] & Grégoire Courtine[1,2,7,14,16]*

Nature 2018



Principi terapeutici

- interventistica/“time is brain“
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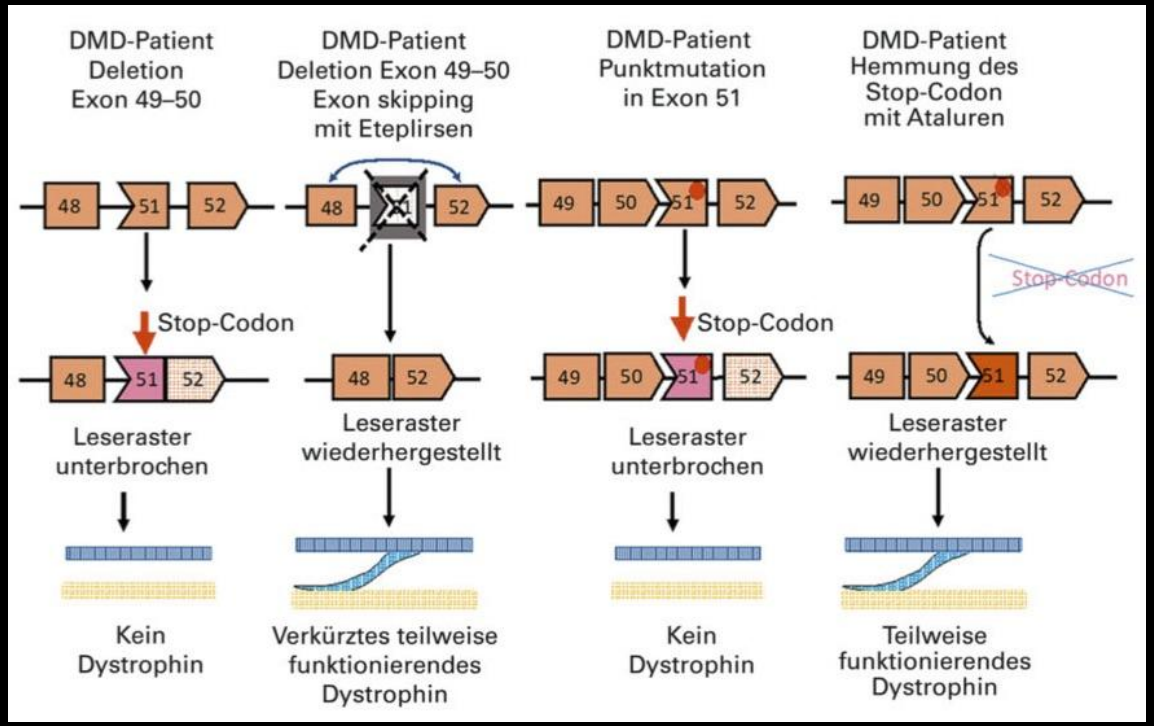
- neuroriabilitazione
- trattamenti sintomatici/palliativi
- terapie enzimatiche

Read through and exon skipping nella Distrofia Duchenne



Lütschg, SMF 2017

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Malattie neurologiche

Ictus

Epilessia

Parkinson

Sclerosi multipla

Malattie neuromuscolari

Cefalee

Malattie sonno

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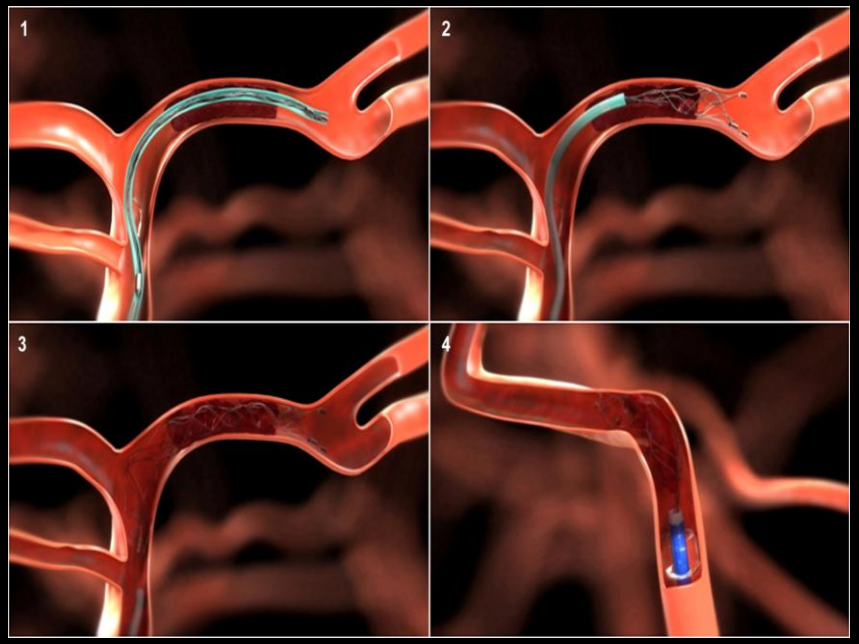
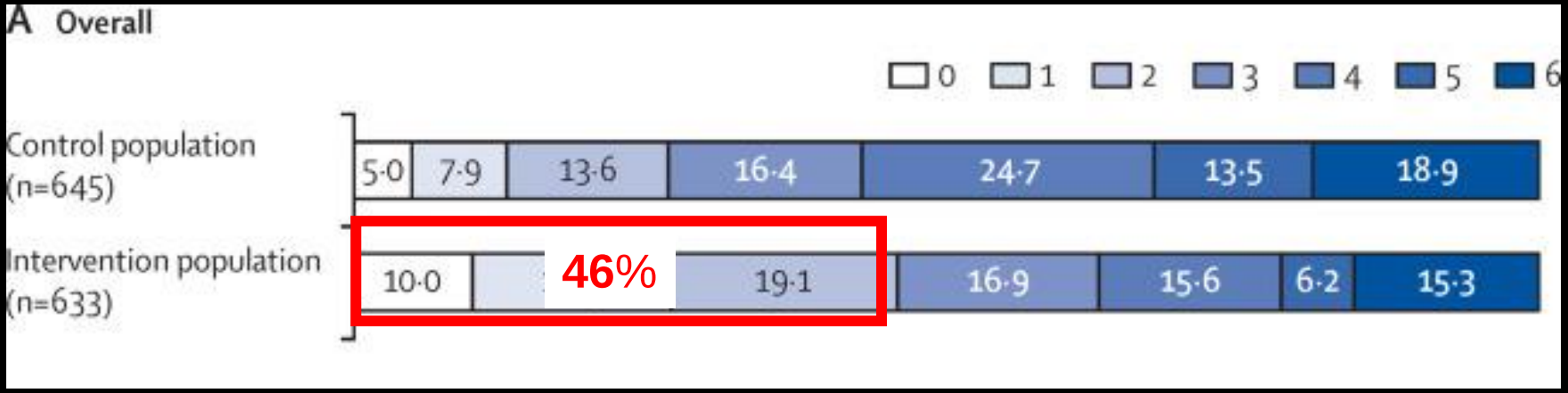

1
2
3
4

Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials

Mayank Goyal, Bijoy K Menon, Wim H van Zwam, Diederik W J Dippel, Peter J Mitchell, Andrew M Demchuk, Antoni Dávalos, Charles B L M Majoie, Aad van der Lugt, Maria A de Miquel, Geoffrey A Donnan, Yvo B W E M Roos, Alain Bonafe, Reza Jahan, Hans-Christoph Diener, Lucie A van den Berg, Elad I Levy, Olvert A Berkhemer, Vitor M Pereira, Jeremy Rempel, Mònica Millán, Stephen M Davis, Daniel Roy, John Thornton, Luis San Román, Marc Ribó, Debbie Beumer, Bruce Stouch, Scott Brown, Bruce C V Campbell, Robert J van Oostenbrugge, Jeffrey L Saver, Michael D Hill, Tudor G Jovin, for the HERMES collaborators

Lancet 2016



NNT 2.6

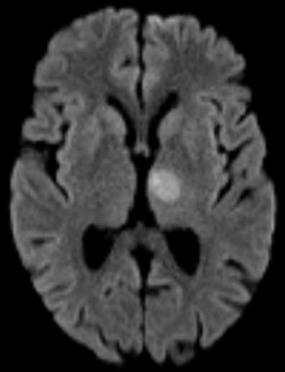
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 16, 2018 VOL. 379 NO. 7

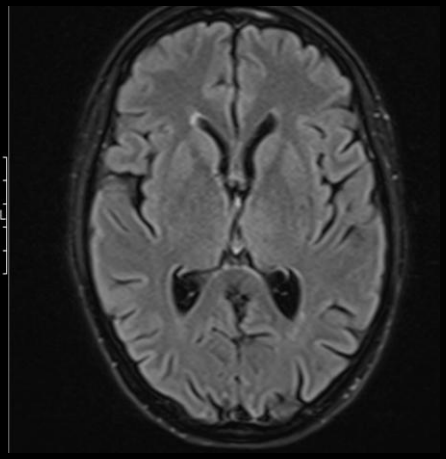
MRI-Guided Thrombolysis for Stroke with Unknown Time of Onset

G. Thomalla, C.Z. Simonsen, F. Boutitie, G. Andersen, Y. Berthezene, B. Cheng, B. Cheripelli, T.-H. Cho, F. Fazekas, J. Fiehler, I. Ford, I. Galinovic, S. Gellissen, A. Golsari, J. Gregori, M. Günther, J. Guibernau, K.G. Häusler, M. Hennerici, A. Kemmling, J. Marstrand, B. Modrau, L. Neeb, N. Perez de la Ossa, J. Puig, P. Ringleb, P. Roy, E. Scheel, W. Schonewille, J. Serena, S. Sunaert, K. Villringer, A. Wouters, V. Thijs, M. Ebinger, M. Endres, J.B. Fiebach, R. Lemmens, K.W. Muir, N. Nighoghossian, S. Pedraza, and C. Gerloff, for the WAKE-UP Investigators*

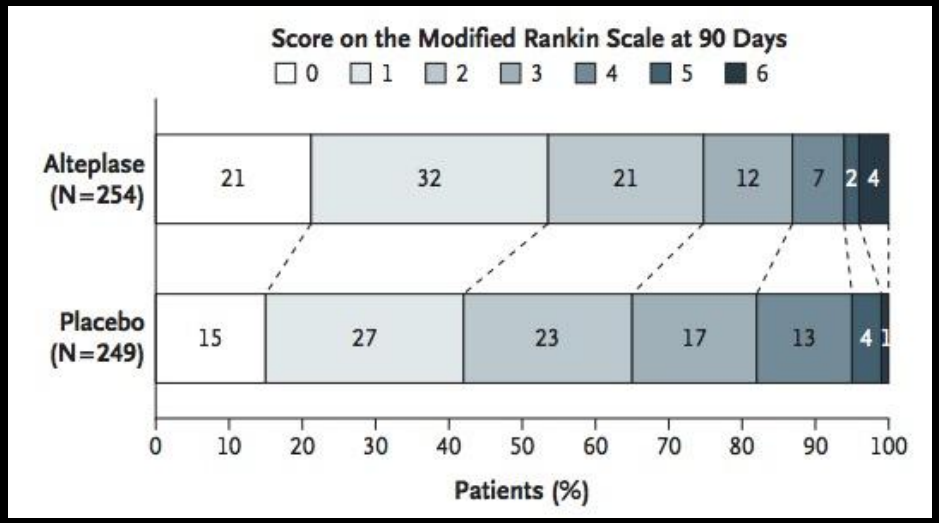
N Engl J Med 2018



DWI



FLAIR



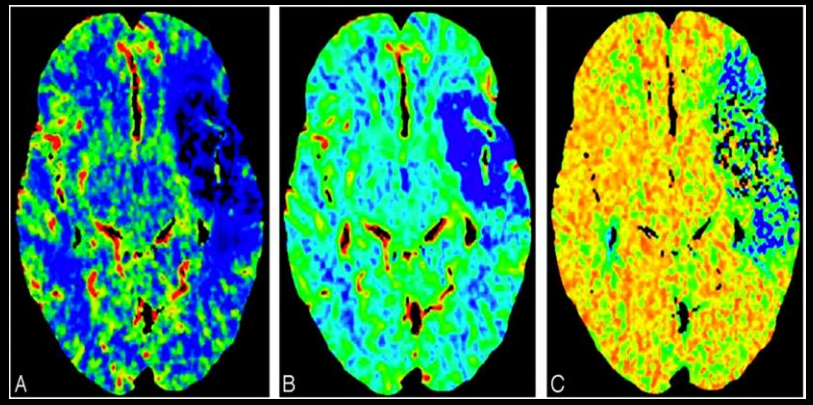
The NEW ENGLAND JOURNAL of MEDICINE

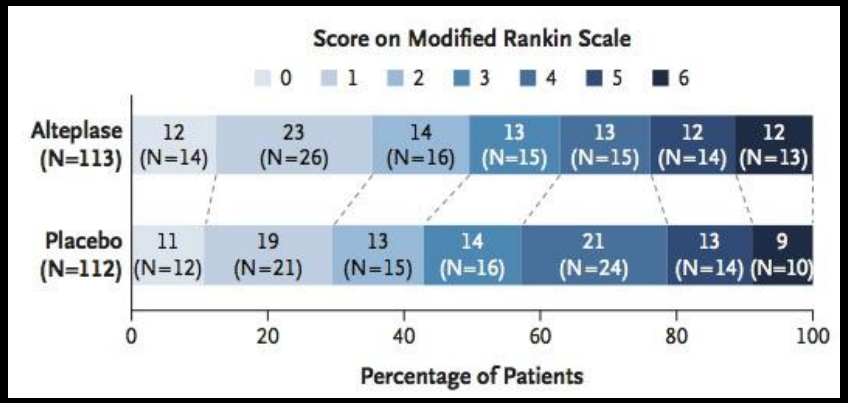
ESTABLISHED IN 1812 MAY 9, 2019 VOL. 380 NO. 19

Thrombolysis Guided by Perfusion Imaging up to 9 Hours after Onset of Stroke

H. Ma, B.C.V. Campbell, M.W. Parsons, L. Churilov, C.R. Levi, C. Hsu, T.J. Kleinig, T. Wijeratne, S. Curtze, H.M. Dewey, F. Miteff, C.-H. Tsai, J.-T. Lee, T.G. Phan, N. Mahant, M.-C. Sun, M. Krause, J. Sturm, R. Grimley, C.-H. Chen, C.-J. Hu, A.A. Wong, D. Field, Y. Sun, P.A. Barber, A. Sabet, J. Jannes, J.-S. Jeng, B. Clissold, R. Markus, C.-H. Lin, L.-M. Lien, C.F. Bladin, S. Christensen, N. Yassi, G. Sharma, A. Bivard, P.M. Desmond, B. Yan, P.J. Mitchell, V. Thijs, L. Carey, A. Meretoja, S.M. Davis, and G.A. Donnan, for the EXTEND Investigators*

N Engl J Med 2019





Introduzione

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Cefalee

Malattie sonno

Neuroriabilitazione

Conclusioni e futuro

Status epilepticus in adults

John P Betjemann, Daniel H Lowenstein

Lancet Neurol 2015

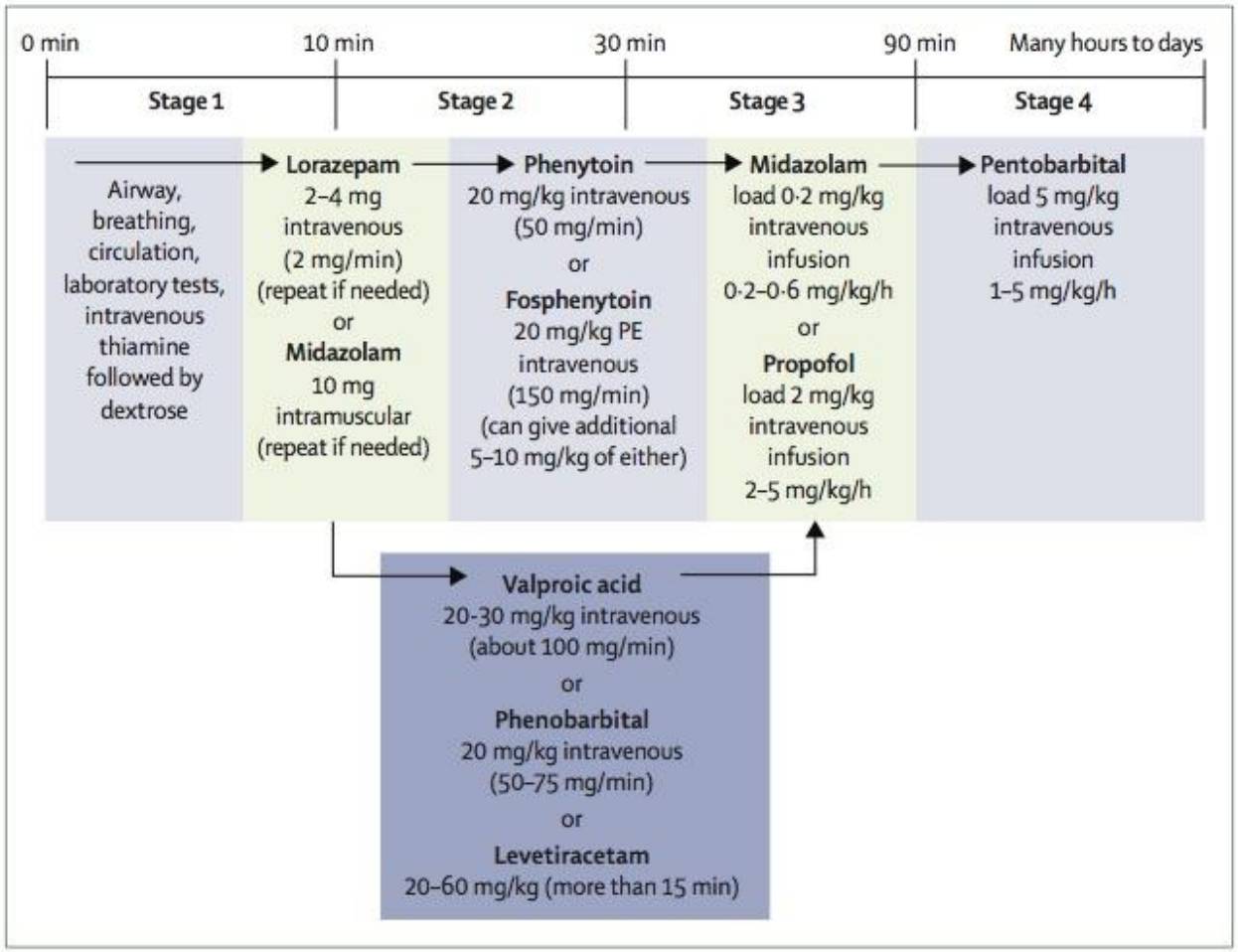
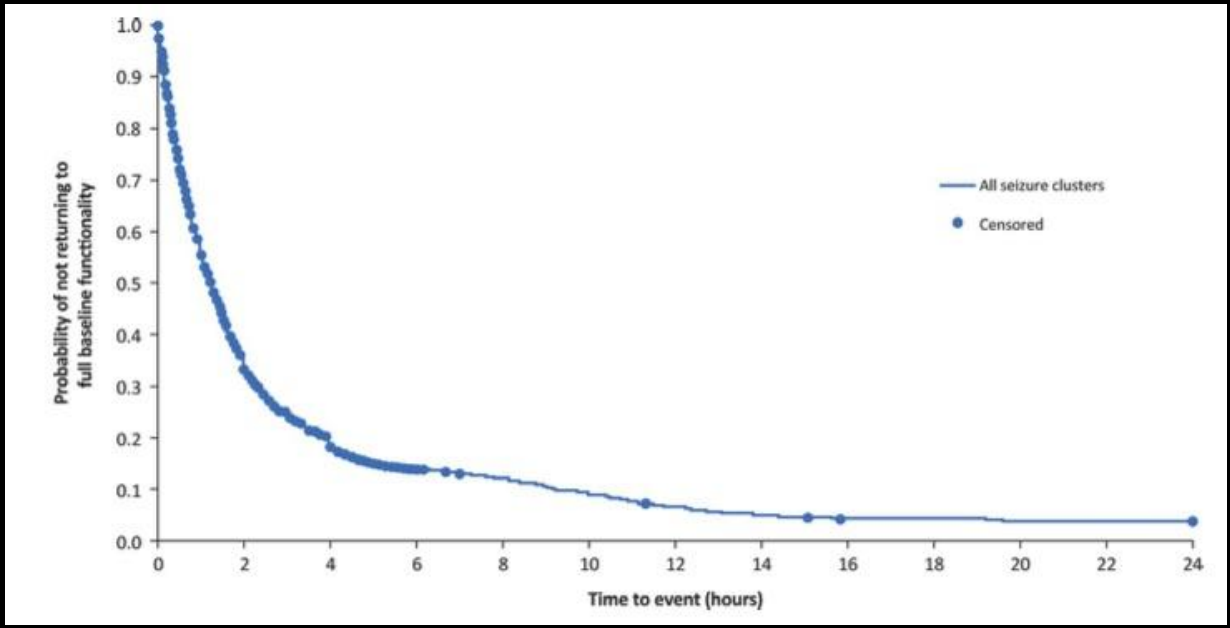


Figure 3: **Updated treatment algorithm for generalised convulsive status epilepticus in adults and older children**
PE=phenytoin equivalents.

Safety and efficacy of midazolam nasal spray in the outpatient treatment of patients with seizure clusters: An open-label extension trial

James W. Wheless[1,2] | Tze-Chiang Meng[3] | Peter J. Van Ess[3] | Kamil Detyniecki[4] | David J. Sequeira[3] | William E. Pullman[3]

Epilepsia 2019



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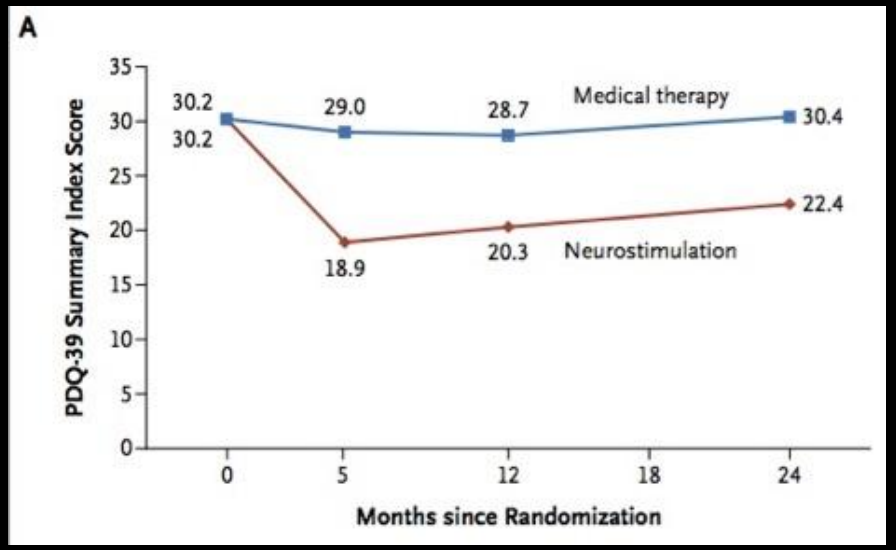
The NEW ENGLAND JOURNAL of MEDICINE

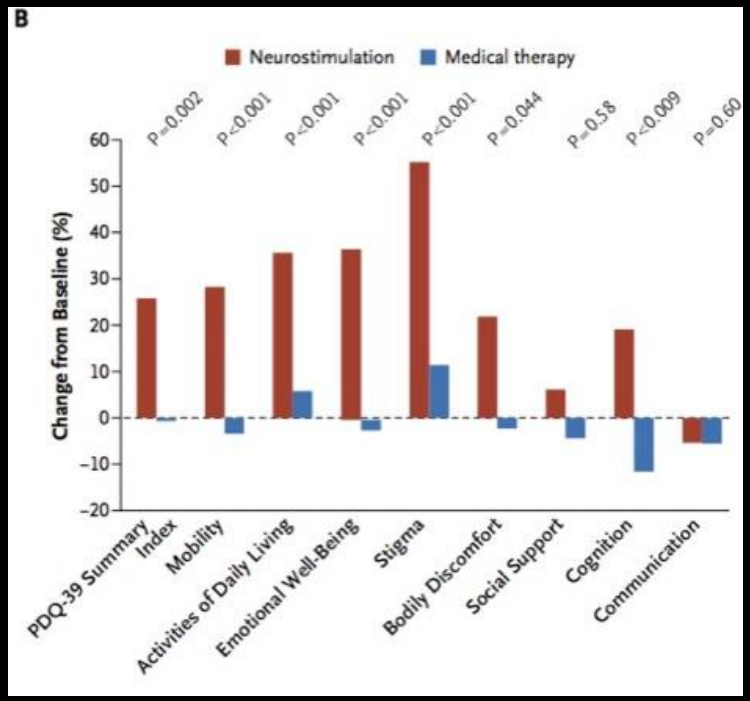
ORIGINAL ARTICLE

Neurostimulation for Parkinson's Disease with Early Motor Complications

W.M.M. Schuepbach, J. Rau, K. Knudsen, J. Volkmann, P. Krack, L. Timmermann, T.D. Hälbig, H. Hesekamp, S.M. Navarro, N. Meier, D. Falk, M. Mehdorn, S. Paschen, M. Maarouf, M.T. Barbe, G.R. Fink, A. Kupsch, D. Gruber, G.-H. Schneider, E. Seigneuret, A. Kistner, P. Chaynes, F. Ory-Magne, C. Brefel Courbon, J. Vesper, A. Schnitzler, L. Wojtecki, J.-L. Houeto, B. Bataille, D. Maltête, P. Damier, S. Raoul, F. Sixel-Doering, D. Hellwig, A. Gharabaghi, R. Krüger, M.O. Pinsker, F. Amtage, J.-M. Régis, T. Witjas, S. Thobois, P. Mertens, M. Kloss, A. Hartmann, W.H. Oertel, B. Post, H. Speelman, Y. Agid, C. Schade-Brittinger, and G. Deuschl, for the EARLYSTIM Study Group*



- 251 pts with idiopathic PD
- motor fluctuations< 3 y
- age<60
- DBS vs medication



Schüpbach, NEJM 2014

ORIGINAL ARTICLE

A Pilot Study of Focused Ultrasound Thalamotomy for Essential Tremor

W. Jeffrey Elias, M.D., Diane Huss, P.T., D.P.T., N.C.S., Tiffini Voss, M.D., Johanna Loomba, B.S., Mohamad Khaled, M.D., Eyal Zadicario, M.Sc., Robert C. Frysinger, Ph.D., Scott A. Sperling, Psy.D., Scott Wylie, Ph.D., Stephen J. Monteith, M.D., Jason Druzgal, M.D., Ph.D., Binit B. Shah, M.D., Madaline Harrison, M.D., and Max Wintermark, M.D.

N Engl J Med 2013

Focused ultrasound subthalamotomy in patients with asymmetric Parkinson's disease: a pilot study

Raul Martínez-Fernández, Rafael Rodríguez-Rojas, Marta del Álamo, Frida Hernández-Fernández, Jose A Pineda-Pardo, Michele Dileone, Fernando Alonso-Frech, Guglielmo Foffani, Ignacio Obeso, Carmen Gasca-Salas, Esther de Luis-Pastor, Lydia Vela, José A Obeso

Lancet Neurol 2018

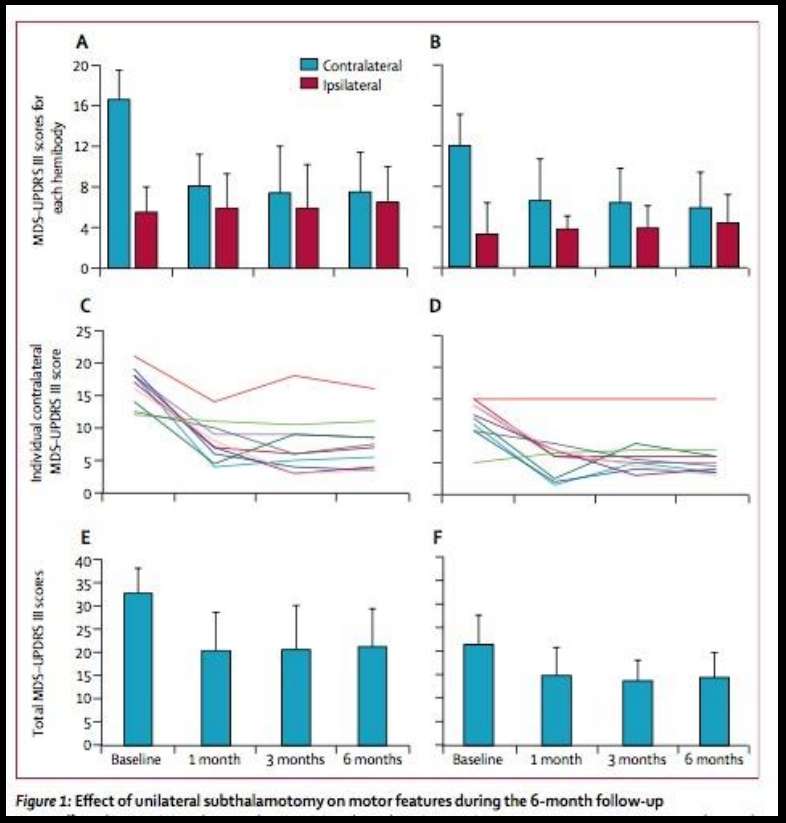


Figure 1: Effect of unilateral subthalamotomy on motor features during the 6-month follow-up

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The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 19, 2017 VOL. 376 NO. 3

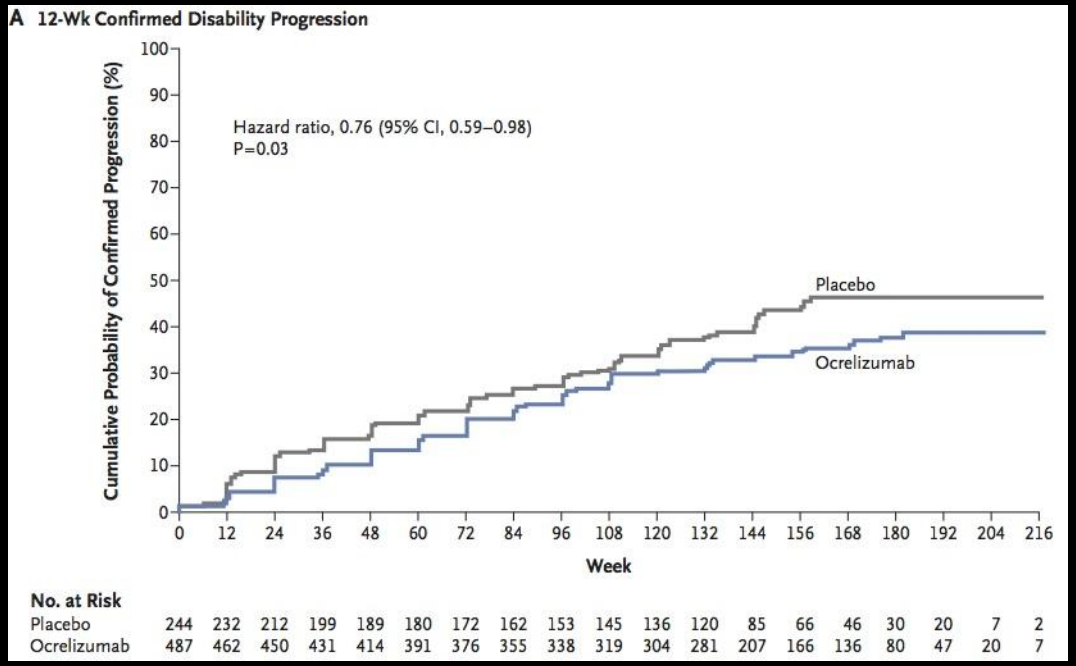
Ocrelizumab versus Placebo in Primary Progressive Multiple Sclerosis

X. Montalban, S.L. Hauser, L. Kappos, D.L. Arnold, A. Bar-Or, G. Comi, J. de Seze, G. Giovannoni, H.-P. Hartung, B. Hemmer, F. Lublin, K.W. Rammohan, K. Selmaj, A. Traboulsee, A. Sauter, D. Masterman, P. Fontoura, S. Belachew, H. Garren, N. Mairon, P. Chin, and J.S. Wolinsky, for the ORATORIO Clinical Investigators*

New Engl J 2017

Ocrevus, CH 2018

Prevalenza: 10-15/100‘000
(10-15% paz. con SM)



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

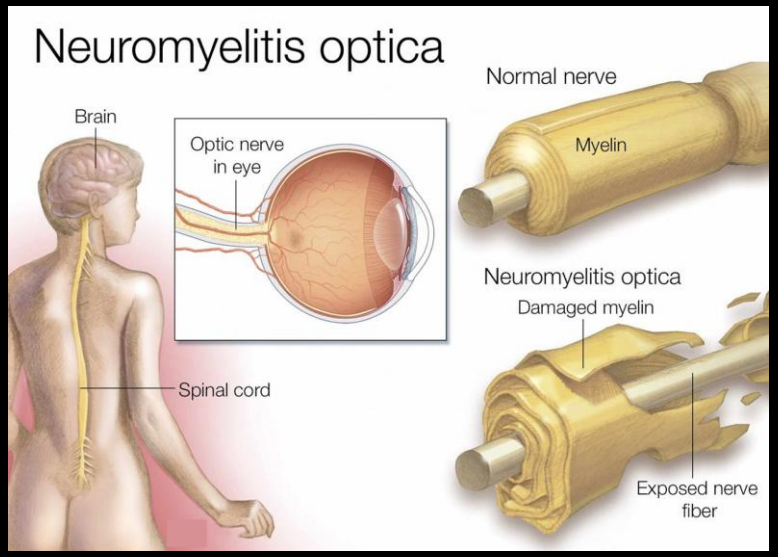
Eculizumab in Aquaporin-4–Positive Neuromyelitis Optica Spectrum Disorder

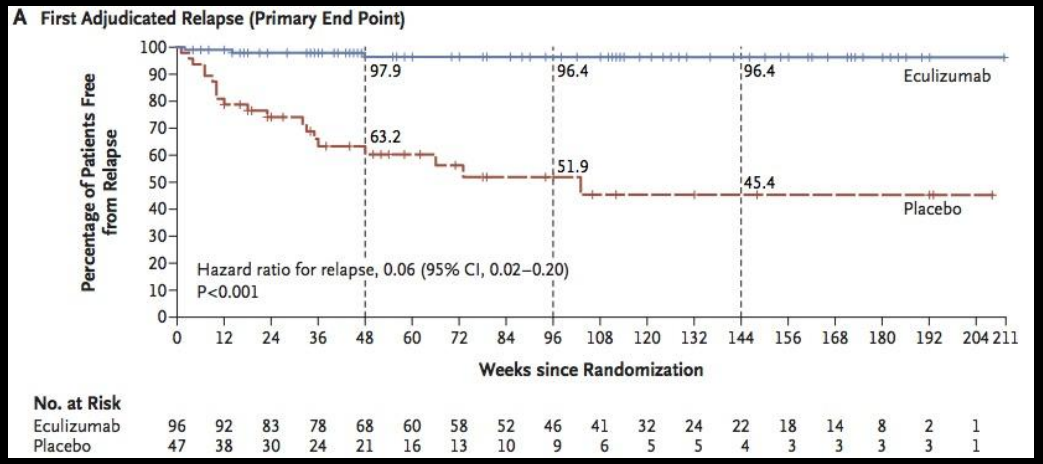
S.J. Pittock, A. Berthele, K. Fujihara, H.J. Kim, M. Levy, J. Palace, I. Nakashima, M. Terzi, N. Totolyan, S. Viswanathan, K.-C. Wang, A. Pace, K.P. Fujita, R. Armstrong, and D.M. Wingerchuk

New Engl J 2019

Soliris, CH 2018

Myasthenia gravis generalizzata refrattaria





Prevalenza: 0.5-10/100‘000

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Trattamenti immunologici nelle malattie neuromuscolari

- IVIG/plasmaferesi e sindrome di Guillain-Barré acuta
- IVIG/plasmaferesi e CIDP
- steroidi e CIDP
- IVIG neuropatia motoria multifocale (MMN)
- IVIG/plasmaferesi e miastenia gravis
- timectomia e miastenia gravis
- ....

SPINAL MUSCULAR ATROPHY - OVERVIEW

Spinal muscular atrophy (SMA) is an autosomal recessive neurodegenerative disease.It is caused by mutations in the survival motor neuron 1 (SMN1) gene. The disease is classified on the basis of age of onset and clinical course.

SMA type 0 (prenatal SMA)
The most severe form. Children usually succumb to the disease before the age of 6 months.

SMA type 2 (chronic infantile SMA)
Serious muscle weakness (assisted sitting and walking). Symptoms usually appear between 7-18 months of age.

SMA type 1 (Werdnig-Hoffman disease)
Symptoms appear within the first few months of life. Children rarely survive passed their 2nd birthday.

SMA type 4 (adult onset SMA)
Not a life-threatening condition. Symptoms appear in adulthood.

SMA type 3 (Kugelberg Welander disease)
Children are able to stand and walk, but worsen with time. Symptoms usually appear after 18 months of age.

Finkel type SMA
Also an adult onset disease, it is caused by mutations in another gene called VAPB.

SMARD1 (Distal SMA)
Clinically and genetically distinct and uncommon form of SMA.

SMA NEWS TODAY
www.smanewstoday.com

Prevalenza: 10-50/100‘000

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Nusinersen versus Sham Control in Infantile-Onset Spinal Muscular Atrophy

R.S. Finkel, E. Mercuri, B.T. Darras, A.M. Connolly, N.L. Kuntz, J. Kirschner, C.A. Chiriboga, K. Saito, L. Servais, E. Tizzano, H. Topaloglu, M. Tulinius, J. Montes, A.M. Glanzman, K. Bishop, Z.J. Zhong, S. Gheuens, C.F. Bennett, E. Schneider, W. Farwell, and D.C. De Vivo, for the ENDEAR Study Group*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Nusinersen versus Sham Control in Later-Onset Spinal Muscular Atrophy

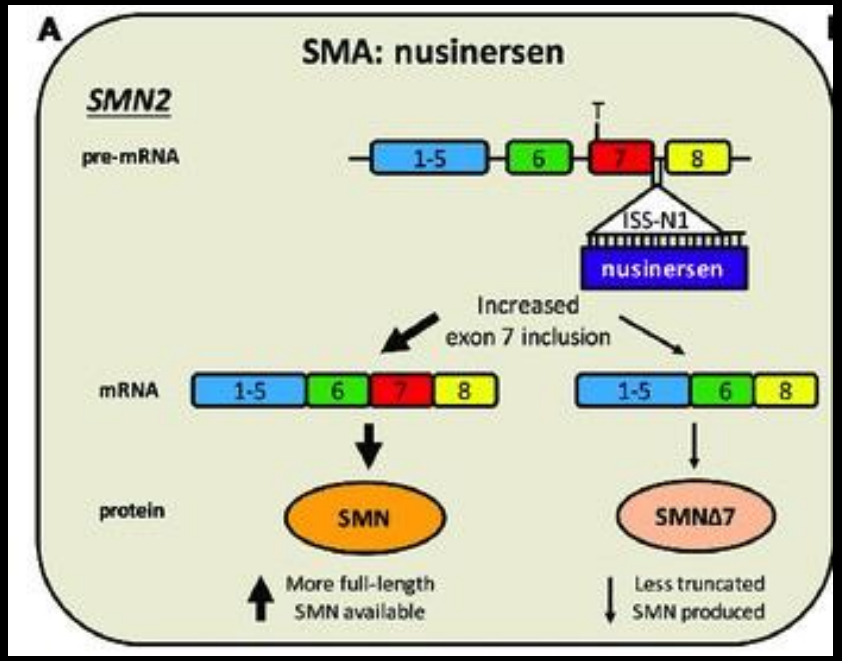
E. Mercuri, B.T. Darras, C.A. Chiriboga, J.W. Day, C. Campbell, A.M. Connolly, S.T. Iannaccone, J. Kirschner, N.L. Kuntz, K. Saito, P.B. Shieh, M. Tulinius, E.S. Mazzone, J. Montes, K.M. Bishop, Q. Yang, R. Foster, S. Gheuens, C.F. Bennett, W. Farwell, E. Schneider, D.C. De Vivo, and R.S. Finkel, for the CHERISH Study Group*

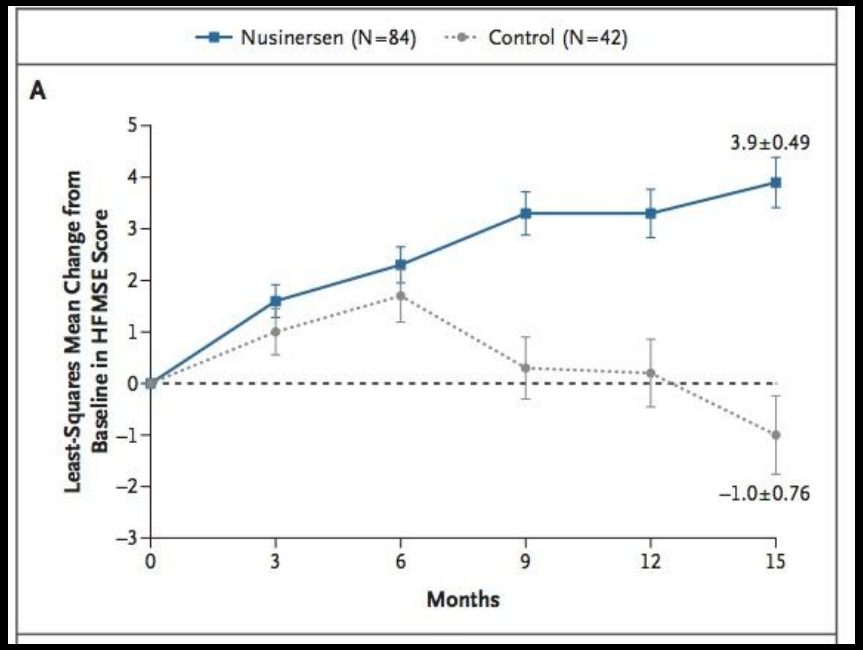
New Engl J Med 2017

Spinraza, CH 2017

alle 4 Monate intrathekal

Prevalenza: 10-50/100‘000

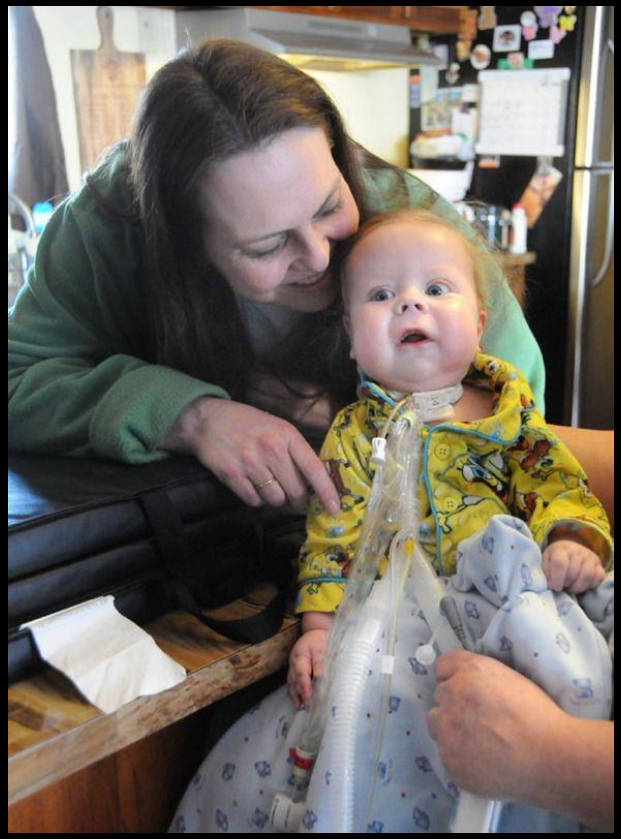




oligonucleotide antisense therapy

Zolgensma, FDA 2019

1x i.v., gene therapy, SMA type 1



Safety and efficacy of edaravone in well defined patients with amyotrophic lateral sclerosis: a randomised, double-blind, placebo-controlled trial

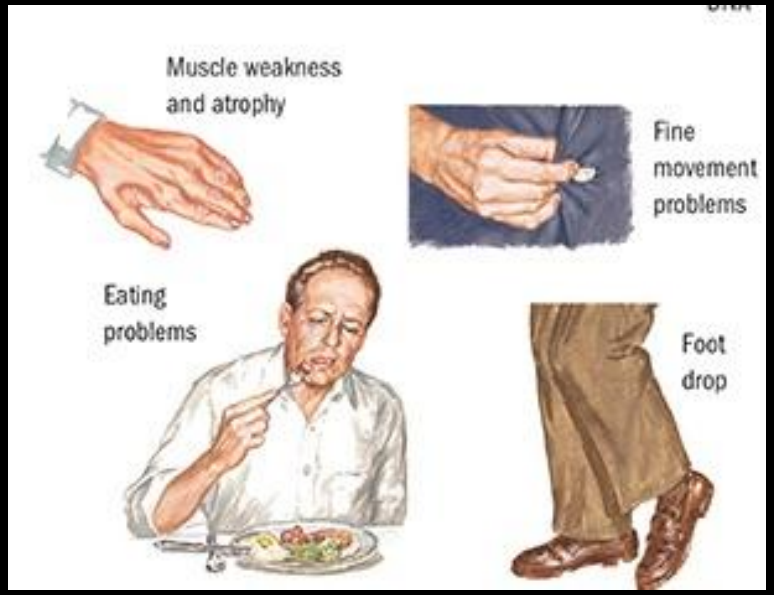
The Writing Group on behalf of the Edaravone (MCI-186) ALS 19 Study Group†*

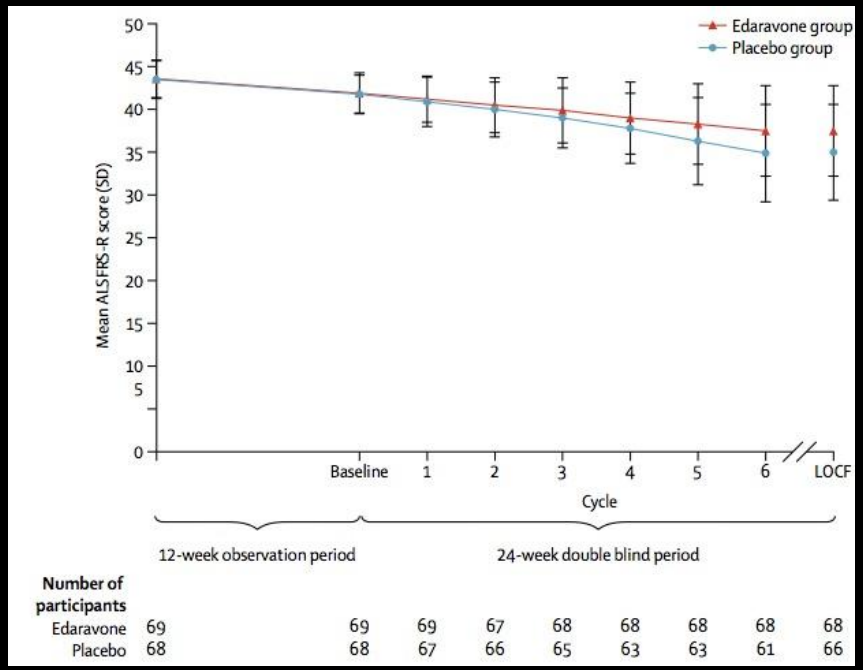
Lancet Neurol 2017

Radicava, CH 2019

14 Tage/Monat i.v.

Prevalenza: 4/100‘000





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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Controlled Trial of Erenumab for Episodic Migraine

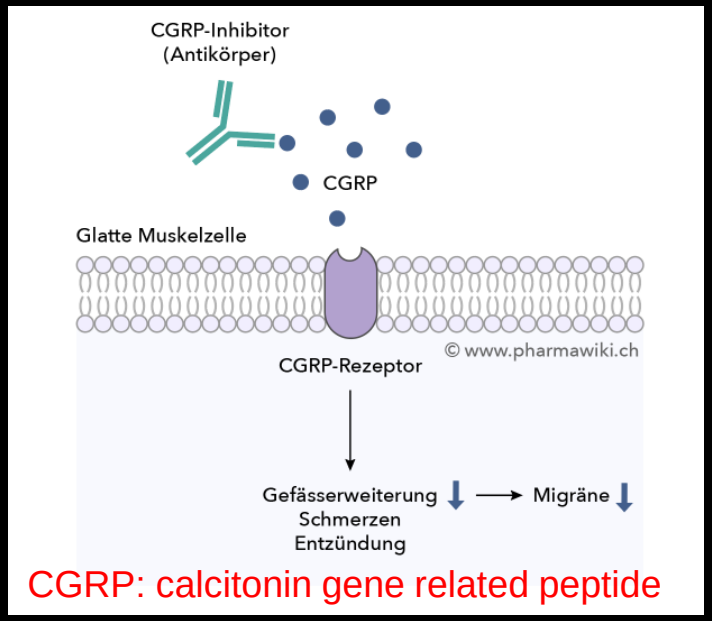
Peter J. Goadsby, M.D., Ph.D., Uwe Reuter, M.D., Yngve Hallström, M.D., Gregor Broessner, M.D., Jo H. Bonner, M.D., Feng Zhang, M.S., Sandhya Sapra, Ph.D., Hernan Picard, M.D., Ph.D., Daniel D. Mikol, M.D., Ph.D., and Robert A. Lenz, M.D., Ph.D.

New Engl J 2017

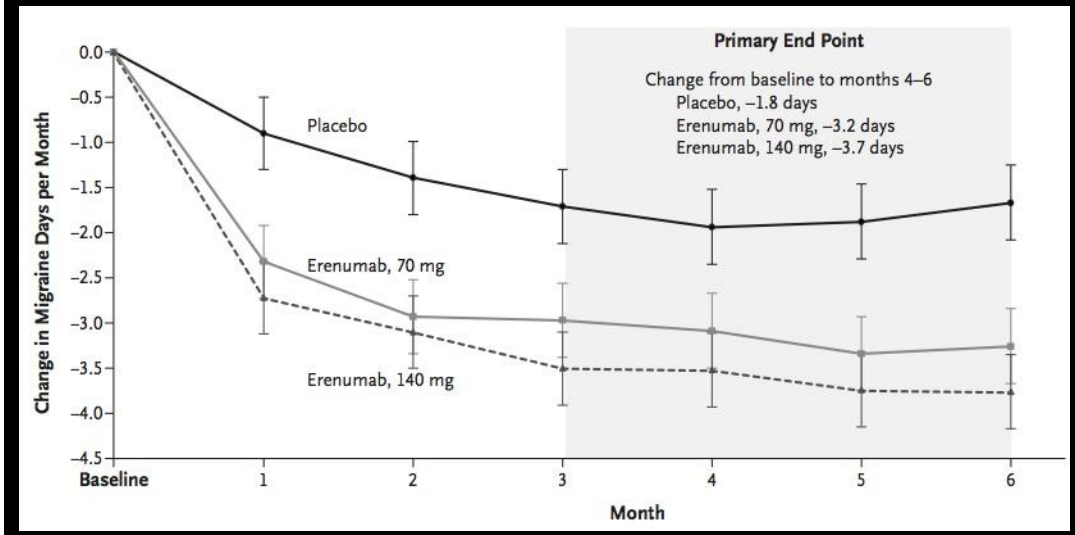
Aimovig, CH 2017

1x/Monat s.c.

Prevalenza: 12‘000/100‘000



CGRP: calcitonin gene related peptide



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Trial of Galcanezumab in Prevention of Episodic Cluster Headache

Peter J. Goadsby, M.D., Ph.D., David W. Dodick, M.D., Massimo Leone, M.D., Jennifer N. Bardos, Pharm.D., Tina M. Oakes, Ph.D., Brian A. Millen, Ph.D., Chunmei Zhou, M.S., Sherie A. Dowsett, Ph.D., Sheena K. Aurora, M.D., Andrew H. Ahn, M.D., Ph.D., Jyun-Yan Yang, M.D., Robert R. Conley, M.D., and James M. Martinez, M.D.

New Engl J 2019

Emgality, CH 2019 (emicrania)

1x/Monat s.c.

Prevalenza: 100/100‘000

Table 2. Primary and Key Secondary End Points.*

End Point	Placebo (N=57)	Galcanezumab (N=49)	P Value
Least-squares mean change from baseline in weekly frequency of cluster headache attacks across wk 1–3	−5.2±1.3	−8.7±1.4	0.04
Percentage of patients with a response at wk 3†	53	71	0.046

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Sleep Medicine Reviews 38 (2018) 3–16

Contents lists available at ScienceDirect

Sleep Medicine Reviews

journal homepage: www.elsevier.com/locate/smrv

CLINICAL REVIEW

Cognitive and behavioral therapies in the treatment of insomnia: A meta-analysis

Annemieke van Straten [a, *], Tanja van der Zweerde [a], Annet Kleiboer [a], Pim Cuijpers [a], Charles M. Morin [b], Jaap Lancee [c]

[a] Department of Clinical Psychology & EMGO Institute for Health and Care Research, VU University, Amsterdam, The Netherlands
[b] Université Laval, École de Psychologie, Québec City, QC, Canada
[c] Department of Clinical Psychology, University of Amsterdam, The Netherlands

Sleep Med Rev 2018

Pitolisant versus placebo or modafinil in patients with narcolepsy: a double-blind, randomised trial

Yves Dauvilliers, Claudio Bassetti, Gert Jan Lammers, Isabelle Arnulf, Geert Mayer, Andrea Rodenbeck, Philippe Lehert, Claire-Li Ding, Jeanne-Marie Lecomte, Jean-Charles Schwartz, for the HARMONY I study group*

Lancet Neurol 2013

Safety and efficacy of pitolisant on cataplexy in patients with narcolepsy: a randomised, double-blind, placebo-controlled trial

Zoltan Szakacs, Yves Dauvilliers, Vladimir Mikhaylov, Irina Poverennova, Sergei Krylov, Slavko Jankovic, Karel Sonka, Philippe Lehert, Isabelle Lecomte, Jeanne-Marie Lecomte, Jean-Charles Schwartz, for the HARMONY-CTP study group*

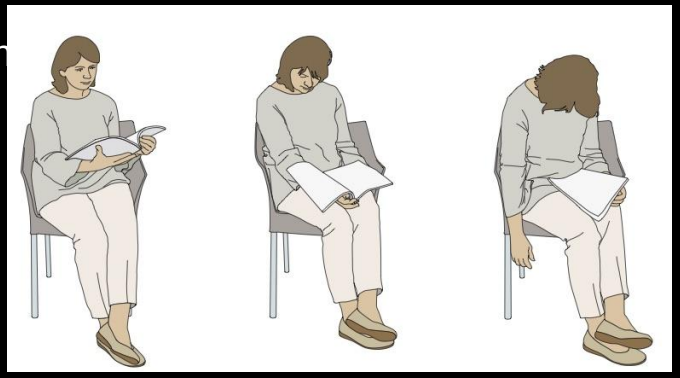
Lancet Neurol 2017

Wakix, CH 2019?

A Randomized Study of Solriamfetol for Excessive Sleepiness in Narcolepsy

Michael J. Thorpy, MB, ChB,[1] Colin Shapiro, MBBCh, PhD,[2] Geert Mayer, MD,[3] Bruce C. Corser, MD,[4] Helene Emsellem, MD,[5] Giuseppe Plazzi, MD,[6,7] Dan Chen, MD, PhD,[8] Lawrence P. Carter, PhD,[8,9] Hao Wang, PhD,[10] Yuan Lu, MS,[9] Jed Black, MD,[8,11] and Yves Dauvilliers, MD, PhD[12]

An



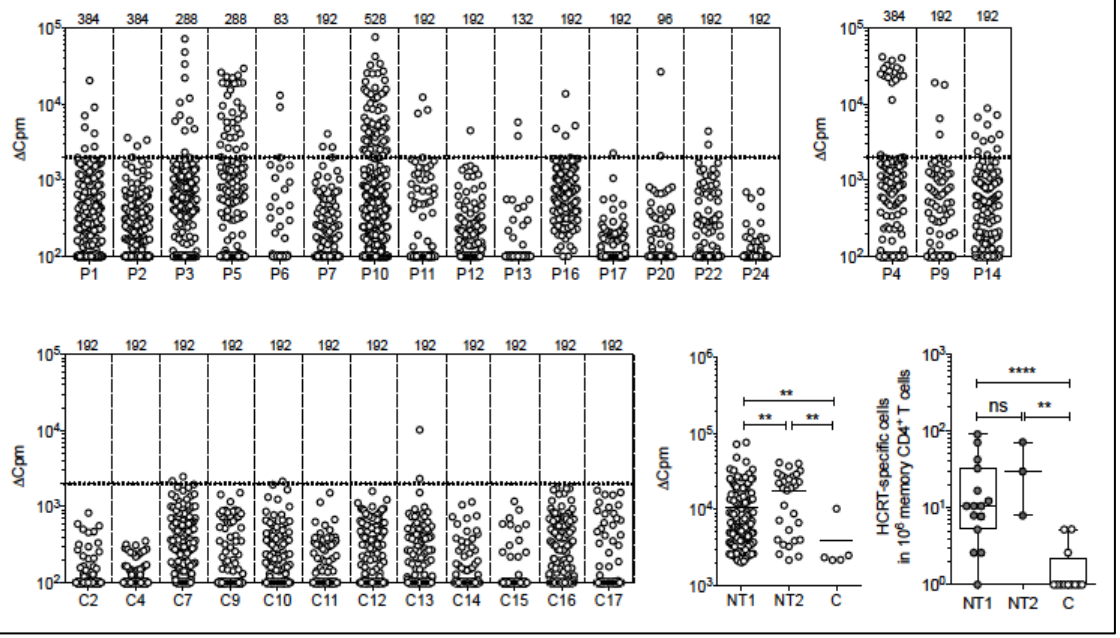
Prevalenza: 20-50/100‘000

T cells in patients with narcolepsy target self–antigens of hypocretin neurons

Daniela Latorre[1,2,10], Ulf Kallweit[3,4,10], Eric Armentani[1], Mathilde Foglierini[1,5], Federico Mele[1], Antonino Cassotta[1,2], Sandra Jovic[1], David Jarrossay[1], Johannes Mathis[3], Francesco Zellini[6], Burkhard Becher[7], Antonio Lanzavecchia[1], Ramin Khatami[8], Mauro Manconi[3,6], Mehdi Tafti[9], Claudio L. Bassetti[3]* & Federica Sallusto[1,2]*

Nature 2018

CD4+ T-cells



narcoleptics
with/without cataplexy

controls
HLA+

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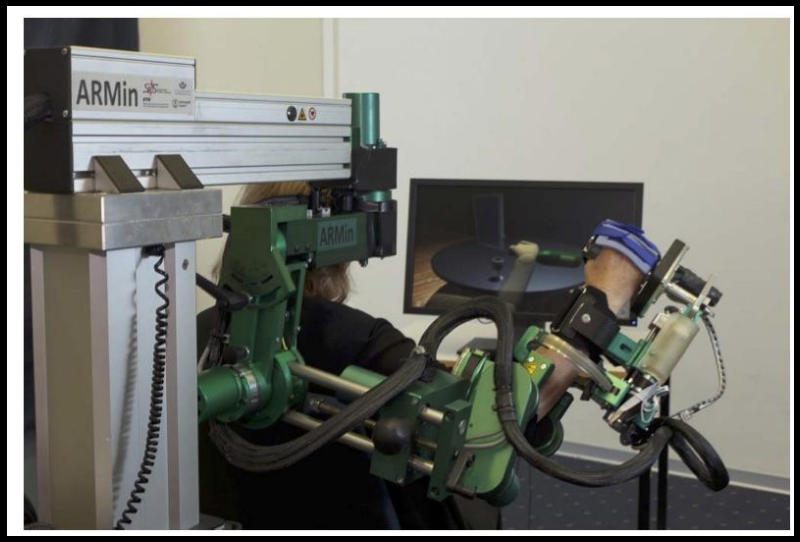
Three-dimensional, task-specific robot therapy of the arm after stroke: a multicentre, parallel-group randomised trial

Verena Klamroth-Marganska, Javier Blanco, Katrin Campen, Armin Curt, Volker Dietz, Thierry Ettlin, Morena Felder, Bernd Fellinghauer, Marco Guidali, Anja Kollmar, Andreas Luft, Tobias Nef, Corina Schuster-Amft, Werner Stahel, Robert Riener

Lancet Neurol 2014



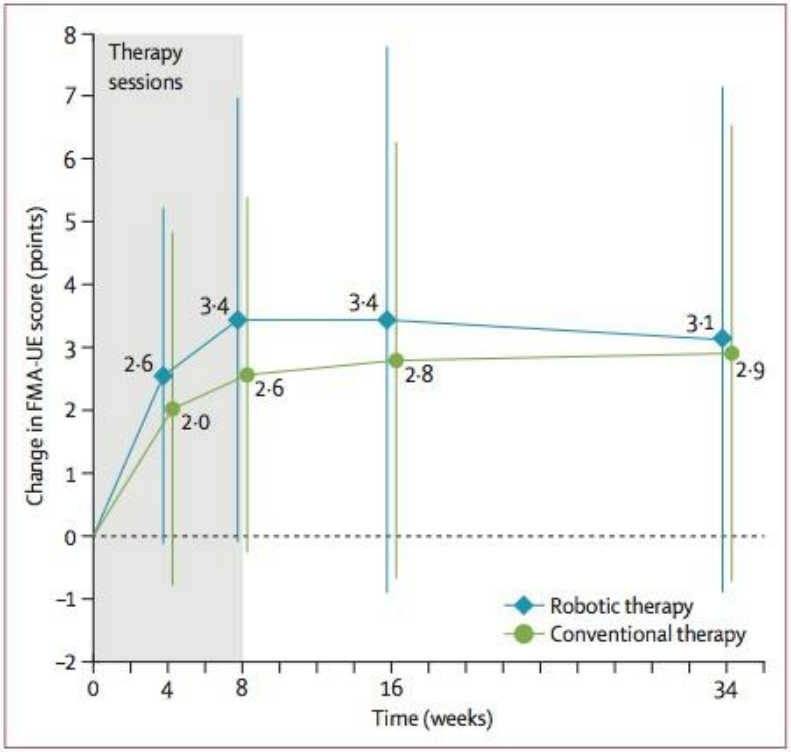
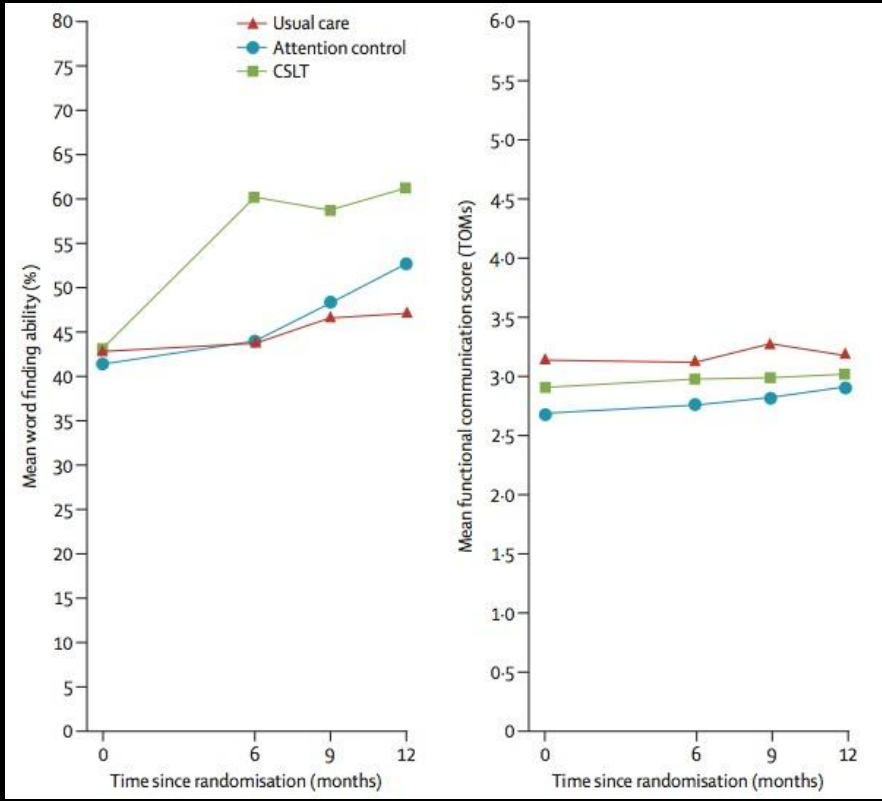


Figure 3: **Change in FMA-UE score from baseline**
Error bars are SD. FMA-UE=arm (upper extremity) section of Fugl-Meyer assessment.

Self-managed, computerised speech and language therapy for patients with chronic aphasia post-stroke compared with usual care or attention control (Big CACTUS): a multicentre, single-blinded, randomised controlled trial

Rebecca Palmer, Munyaradzi Dimairo, Cindy Cooper, Pam Enderby, Marian Brady, Audrey Bowen, Nicholas Latimer, Steven Julious, Elizabeth Cross, Abualbishr Alshreef, Madeleine Harrison, Ellen Bradley, Helen Witts, Tim Chater

Lancet Neurol 2019



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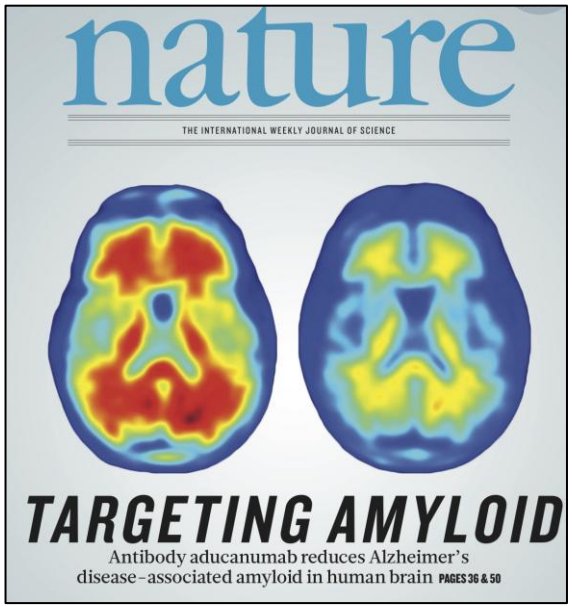
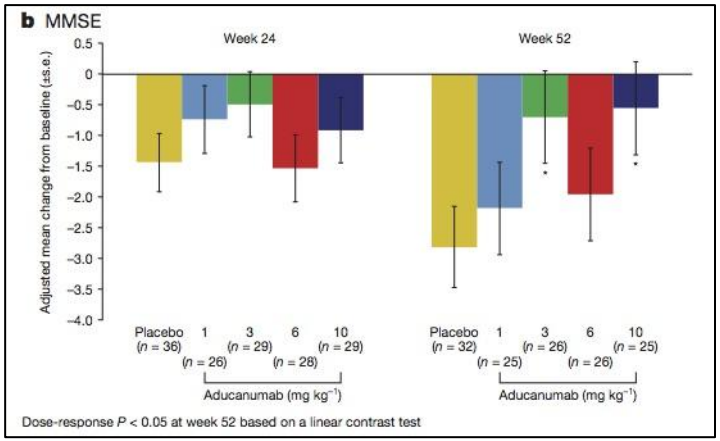




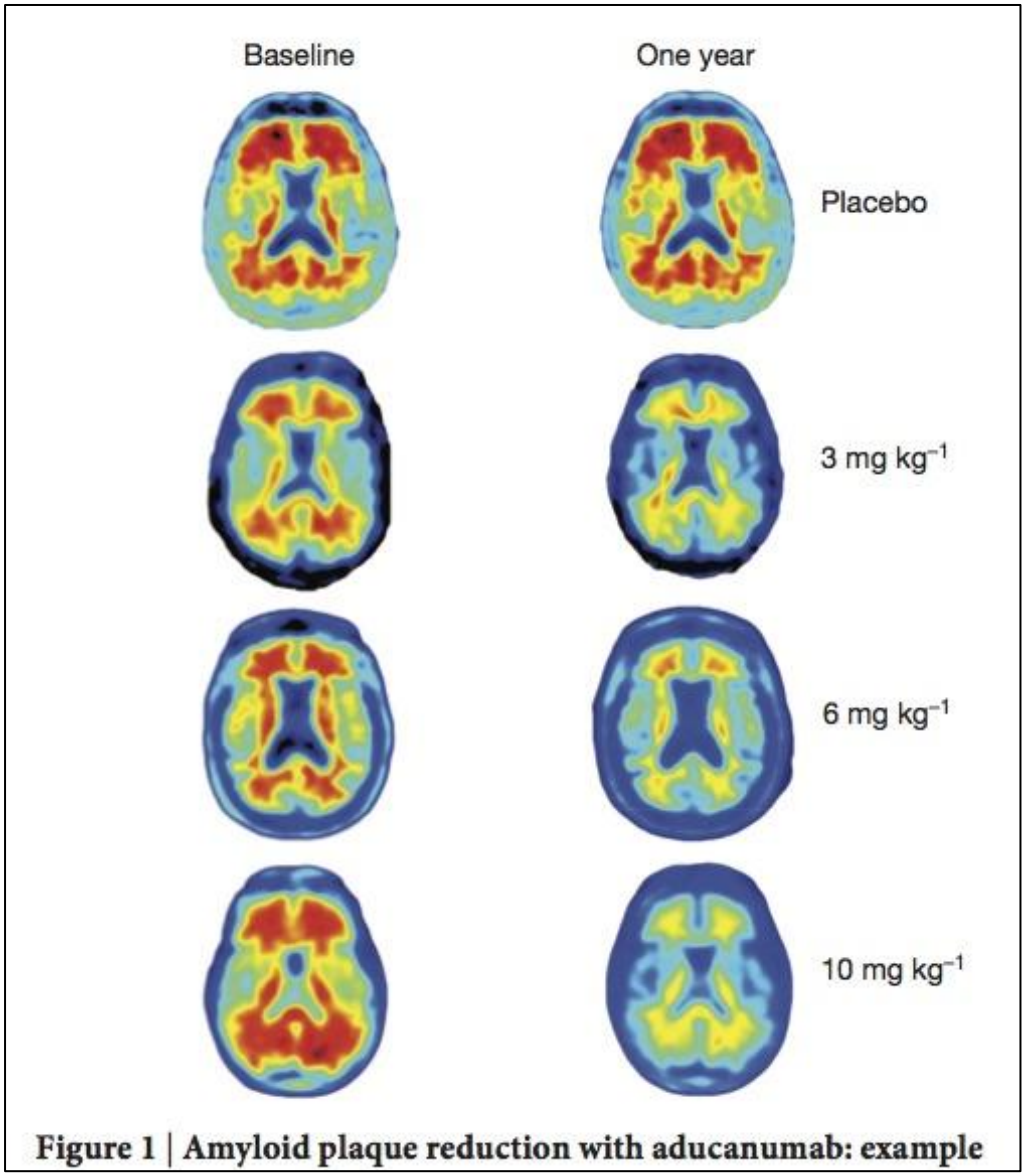
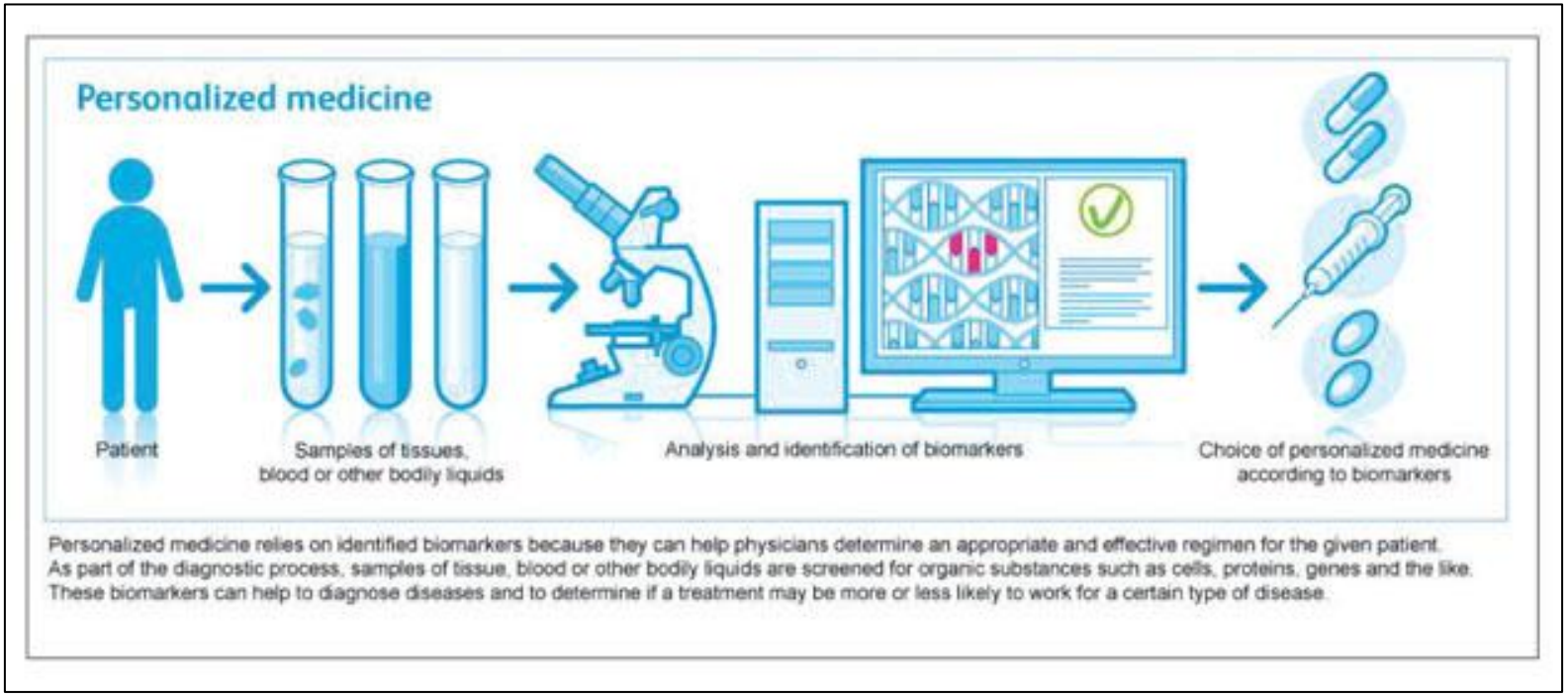


Figure 1 | Amyloid plaque reduction with aducanumab: example

Sevigny, Nature 2016

Medicina personalizzata



The NEW ENGLAND JOURNAL of MEDICINE

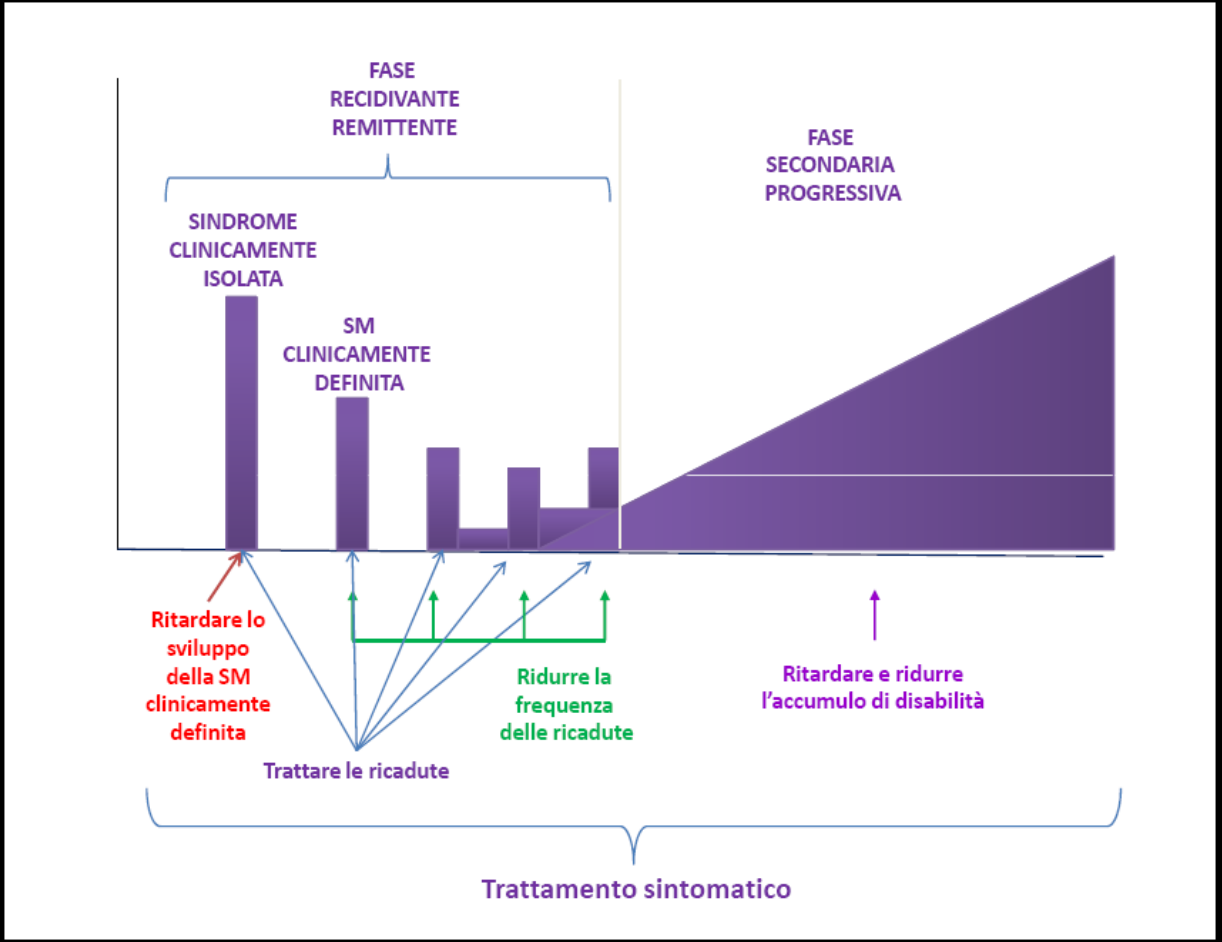
ESTABLISHED IN 1812 NOVEMBER 30, 2017 VOL. 377 NO. 22

Fremanezumab for the Preventive Treatment of Chronic Migraine

Stephen D. Silberstein, M.D., David W. Dodick, M.D., Marcelo E. Bigal, M.D., Ph.D., Paul P. Yeung, M.D., M.P.H., Peter J. Goadsby, M.D., Ph.D., Tricia Blankenbiller, M.A., Melissa Grozinski-Wolff, B.S., Ronghua Yang, Ph.D., Yuju Ma, M.S., and Ernesto Aycardi, M.D.

New Engl J 2017

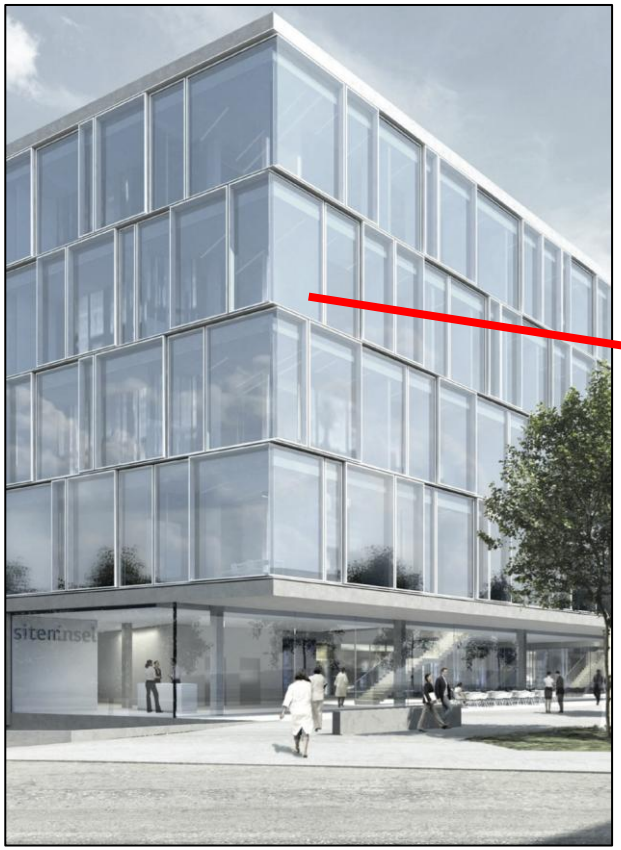
Sclerosi multipla: Trattamento precoce



SITEM

Swiss Institute Translational and Entrepreneurial Medicine (SITEM)

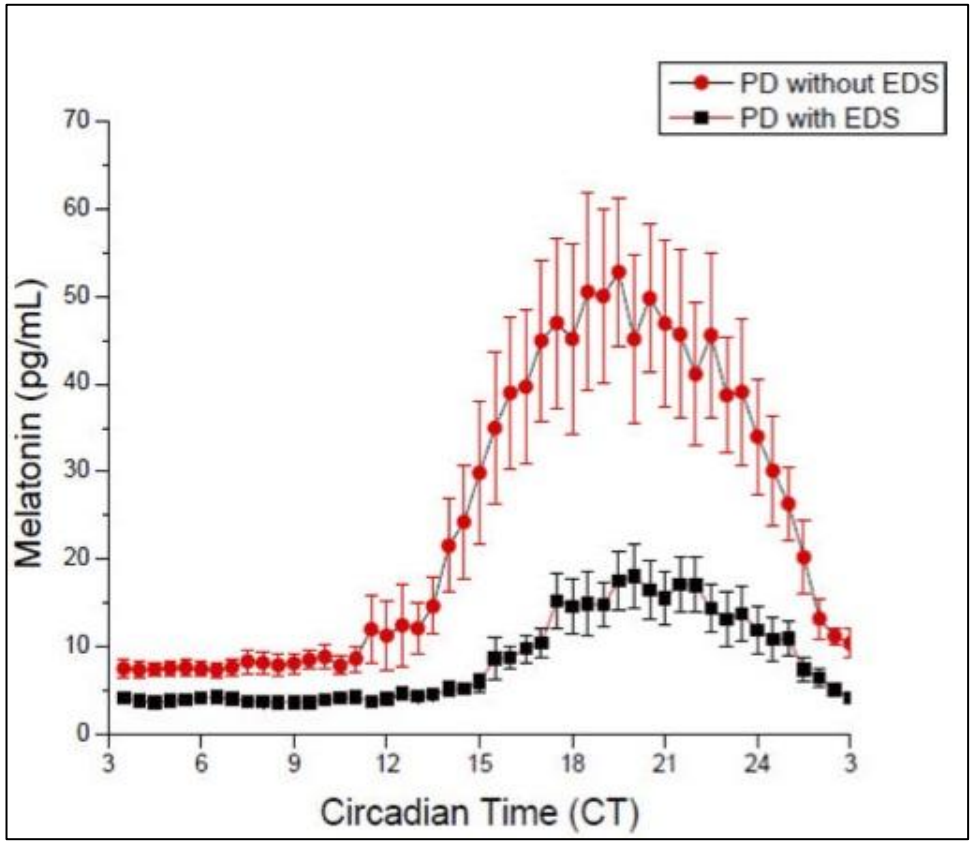
130 Mio, 20‘000 m^2
Apertura 8.2019



Tele-Neuromedicina

Stucki, J Internet Res 2014

M. Parkinson: Sleepiness and circadian dysfunction

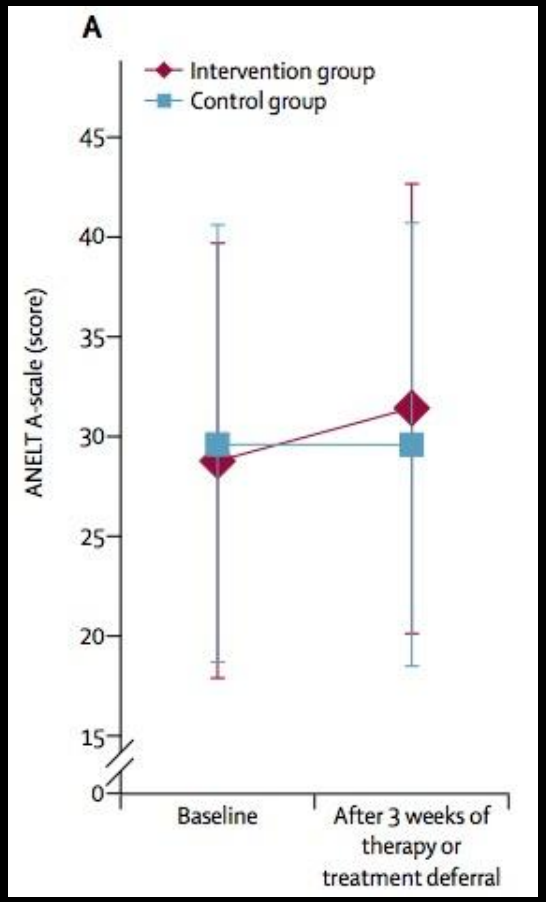


Videnovich, JAMA Neurol 2014

Intensive speech and language therapy in patients with chronic aphasia after stroke: a randomised, open-label, blinded-endpoint, controlled trial in a health-care setting

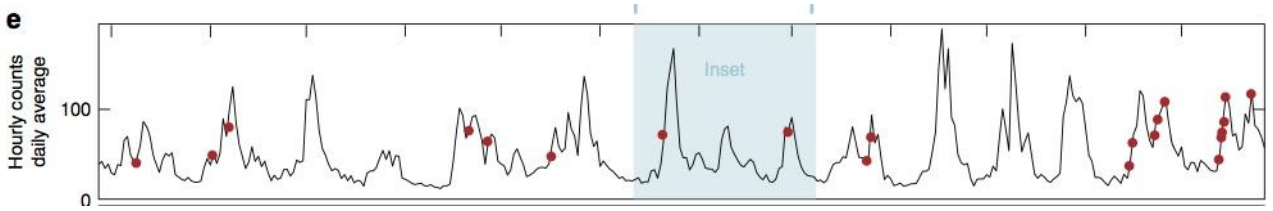
Caterina Breitenstein, Tanja Grewe, Agnes Flöel, Wolfram Ziegler, Luise Springer, Peter Martus, Walter Huber, Klaus Willmes, E Bernd Ringelstein, Karl Georg Haeusler, Stefanie Abel, Ralf Glindemann, Frank Domahs, Frank Regenbrecht, Klaus-Jürgen Schlenck, Marion Thomas, Hellmuth Obrig, Ernst de Langen, Roman Rocker, Franziska Wigbers, Christina Rühmkorf, Indra Hempen, Jonathan List, Annette Baumgaertner, for the FCET2EC study group†*

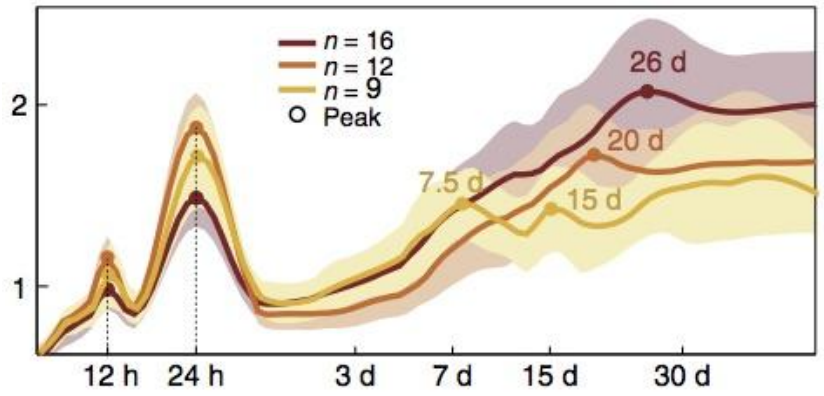
Lancet 2017



Chronobiology of epileptiform activity

subcutaneous
long-term
EEG monitoring

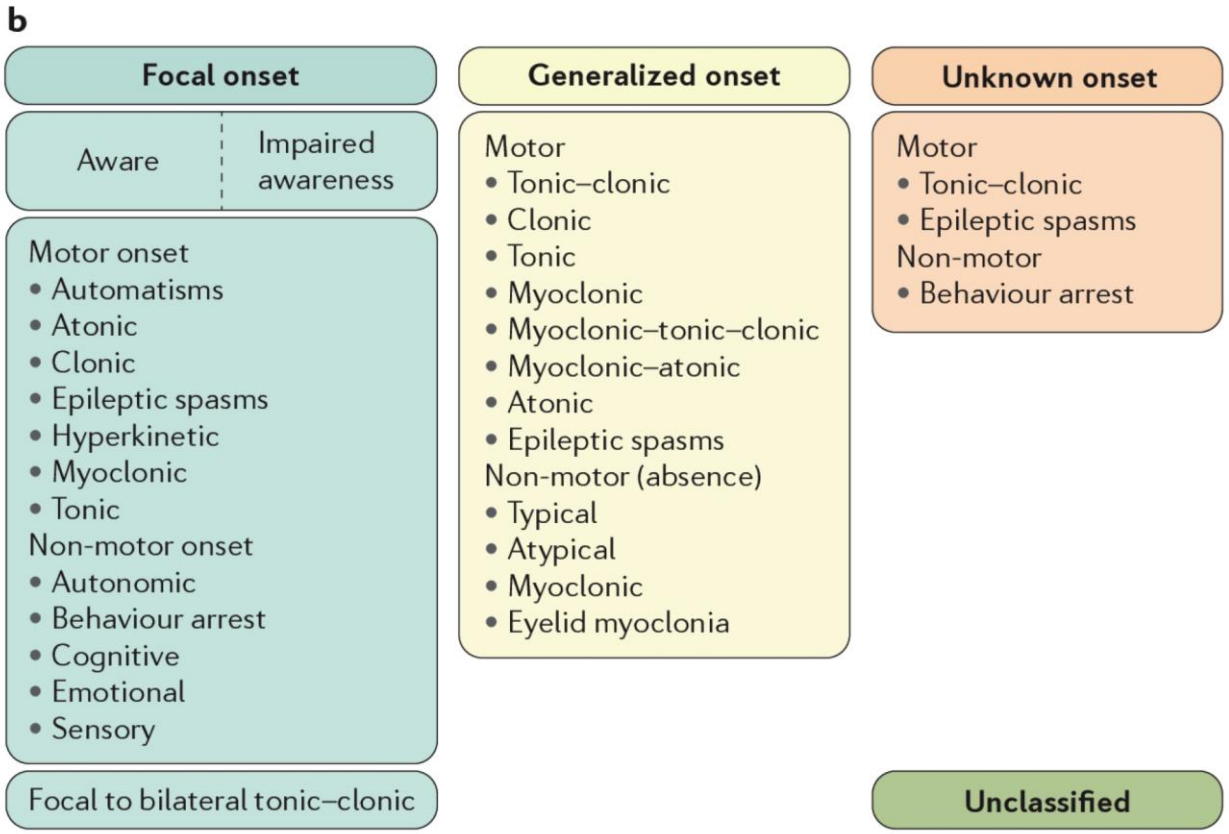




Baud, Nature Commun 2018

2017 Epilepsy Classification

clinical features
EEG
neuroimaging



Devinsky
Nature Review Dis Prim 2018