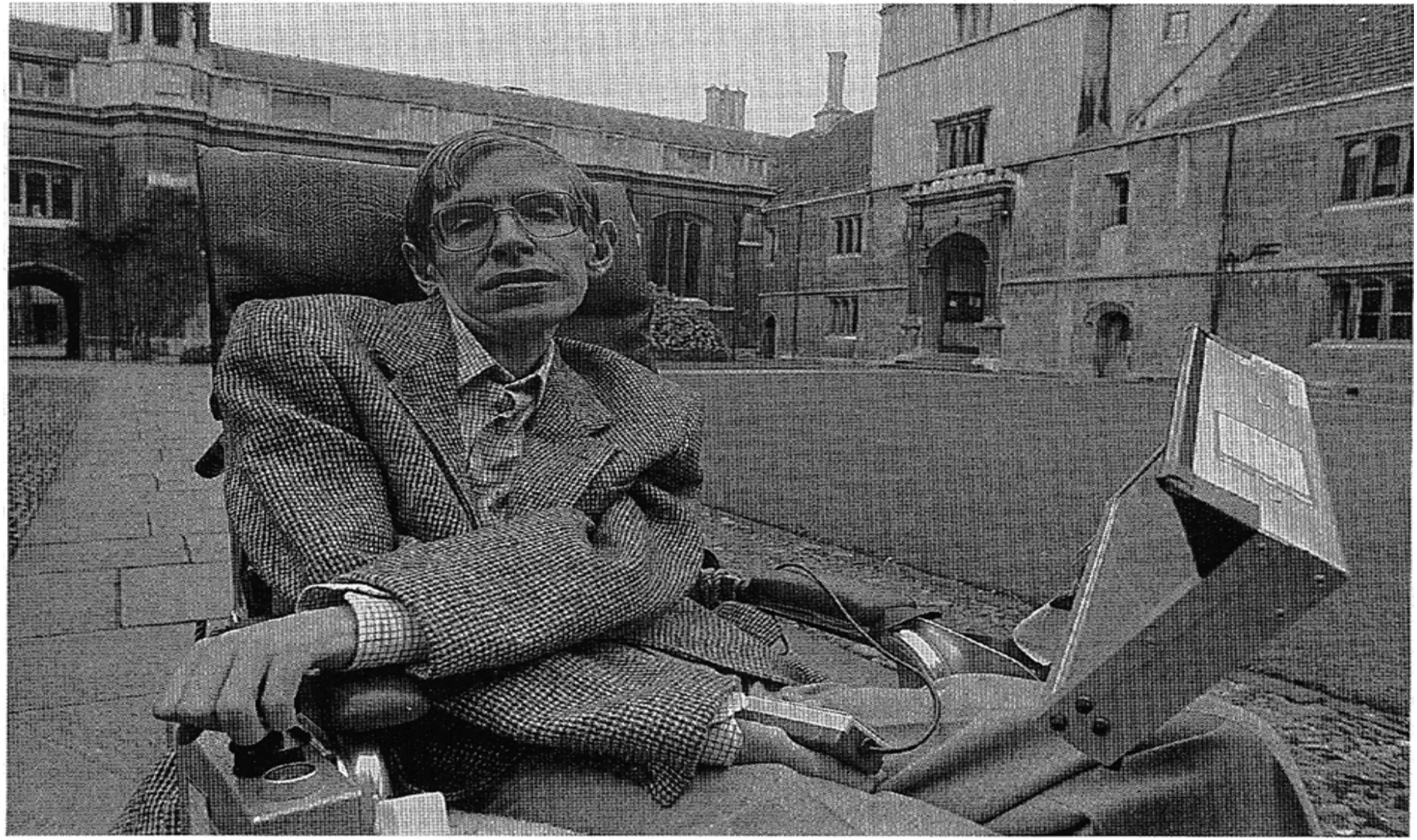
AMYOTROPHE LATERALSKLEROSE (ALS)

Überblick und Neues

Prof. Dr. Markus Weber

5. ALS Tag 26. Oktober 2012

Stephen Hawking



Mao Tse-tung

Charles Mingus

Dimitri Schostakovisch

Fussballspieler

gesundheit

Von **GIUSEPPE DI GRAZIA** und **JAN SCHWEITZER**

Raffaele Guariniello spricht leise, für einen Italiener unfassbar leise. Er ist ein zierlicher kleiner Mann mit Brille, Staatsanwalt am Turiner Gericht, zuständig für Umwelt und Gesundheit. „Großinquisitor" nannte der „Corriere della sera" den 62-Jährigen wegen seiner gestrengen Verhöre italienischer Sportler.

Seit fünf Jahren ermittelt Guariniello in der Welt der Kicker wegen Betrugsverdachts. Dabei stieß er auf die Nervenkrankheit ALS. Es schien eine mysteriöse Häufung von Fällen zu geben. Vom Forschungsinstitut des italienischen Gesundheitsministeriums hatte der Ermittler die Biografien von 24 000 Spielern der drei Profi-Ligen aus den Jahren 1960 bis 1996 sichten lassen. Spezialisten stöberten in Krankenakten und Spielberichten, sogar in Fußball-Sammelheften, die sie auf Flohmärkten erstanden.

„Die Ergebnisse waren fürchterlich", erzählt Guariniello. Demnach sind Fußballer für gewisse Krankheiten weit anfälliger als der Durchschnitt der Bevölkerung. Die Forscher fanden 420 anormale Todesfälle – darunter acht ALS-Opfer. „Laut Statistik hätten es aber nur 0,61 sein dürfen", sagt Guariniello, „nicht einmal einer." In ganz Italien leiden 4000 Patienten an ALS.

Die Experten beschlossen, auch die Zeit nach 1996 zu untersuchen. „Bis heute sind 28 weitere Fußballer an ALS erkrankt, acht davon sind gestorben", sagt Guariniello. Zu den Opfern zählen Giorgio Rognoni, er

In den italienischen Profi-Ligen erkrankten auffällig viele Fußballer an **ALS**. Ihre Vereine müssen jetzt mit einem juristischen Nachspiel rechnen

Gianluca Signorini (vordere Reihe links), hier 1993 mit seiner Mannschaft Sampdoria Genua, starb 2002

FOTOS: RICHARD/SPORTIMAGE; OMEGA; OLYMPIA(2); STEFANO G. PAYES/CONTRASTO

Das Rätsel um die toten Kicker

39. Leben
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FAKTEN

- Lebenszeitrisiko
  - Frauen 1:1200
  - Männer 1:800
- Erkrankungsgipfel um das 60. Lebensjahr
- Sporadische ALS
- Familiäre ALS (5-10%)
- Beginn:
  - Extremitäten (spinal) oder
  - Sprech/Schkluckstörung (bulbär)
- Neuerkrankungen pro Jahr: 2/100000
- Krankenstand: 5-9/ 100000
  - 20.000 USA
  - 28.000 Europa

150 Neudiagnosen pro Jahr

Krankenstand: 400-600

AMYOTROPHE LATERALSKLEROSE (ALS)

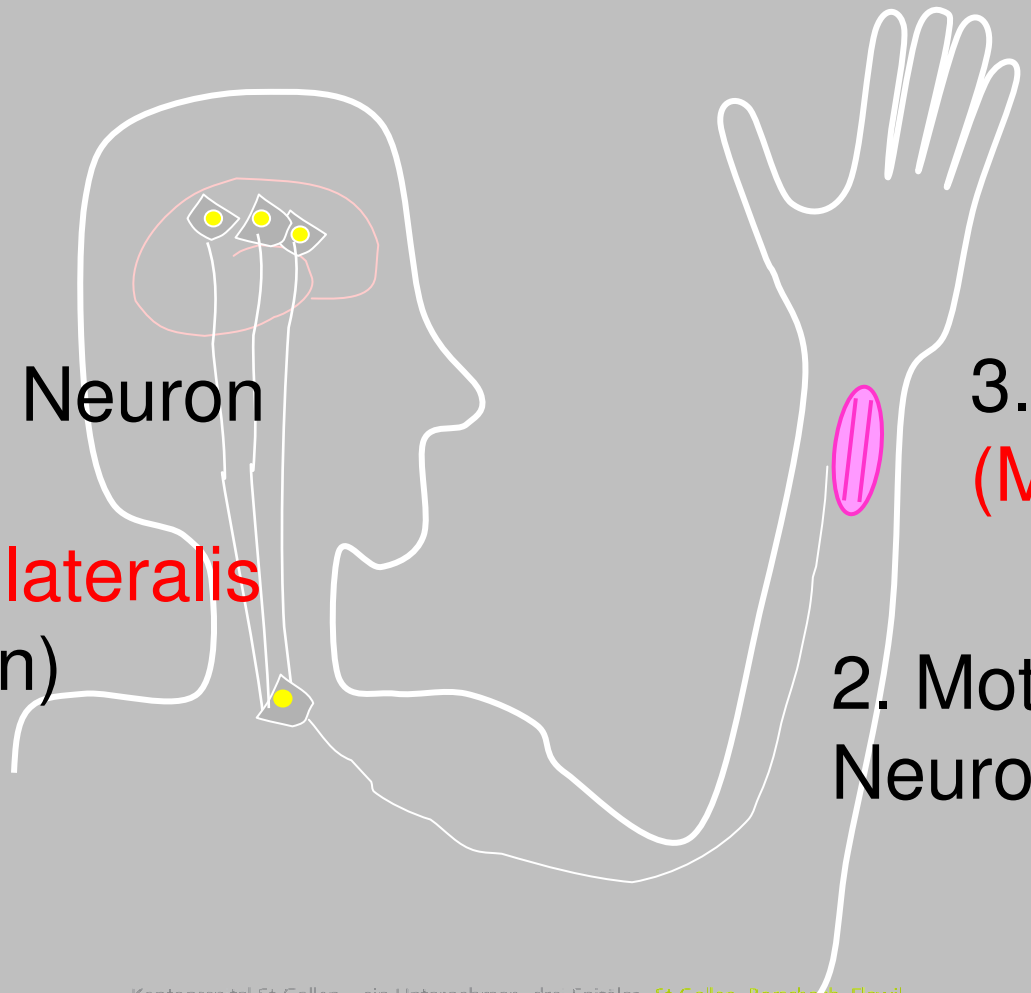
-

eine neuromotorische Erkrankung

NEURON=NERVENZELLE
MOTORIK= BEWEGLICHKEIT

DAS MOTORISCHE SYSTEM

1. Motorisches Neuron (Tractus corticospinalis lateralis Pyramidenbahn)



3. Muskel (Myos)

2. Motorisches Neuron

いろた

UNSPEZIFISCHE SYMPTOME

- Gewichtsverlust
- vegetative Symptomatik (Schwitzen, Jucken)
- Kein Dekubitus
- Selten Parkinsonsymptome
- Demenz (10%)
- kognitive Störungen (60%)
  - Verlust an Wortgewandtheit
  - Emotionale „Abgestumpftheit“
  - Gestörte Entscheidungsfähigkeit
  - Verlust an Planungsfähigkeit
  - Verlust der Einsichtsfähigkeit

Neues = Forschung

- Ursache
  - Modelle
    - Zellkulturen
    - Tiermodelle
    - Klinische Forschung
- Therapie
  - Tiermodelle
  - klinische Studien
    - Symptomatische Therapie = Symptomkontrolle
    - Krankheitsverzögerung/-stop
- Verschiedenes
  - Epidemiologie
  - Lebensqualität
  - Spiritualität

Amyotrophic Lateral Sclerosis, 2012; 13: 351–356

informa healthcare

REVIEW ARTICLE

Is head trauma a risk factor for amyotrophic lateral sclerosis? An evidence based review

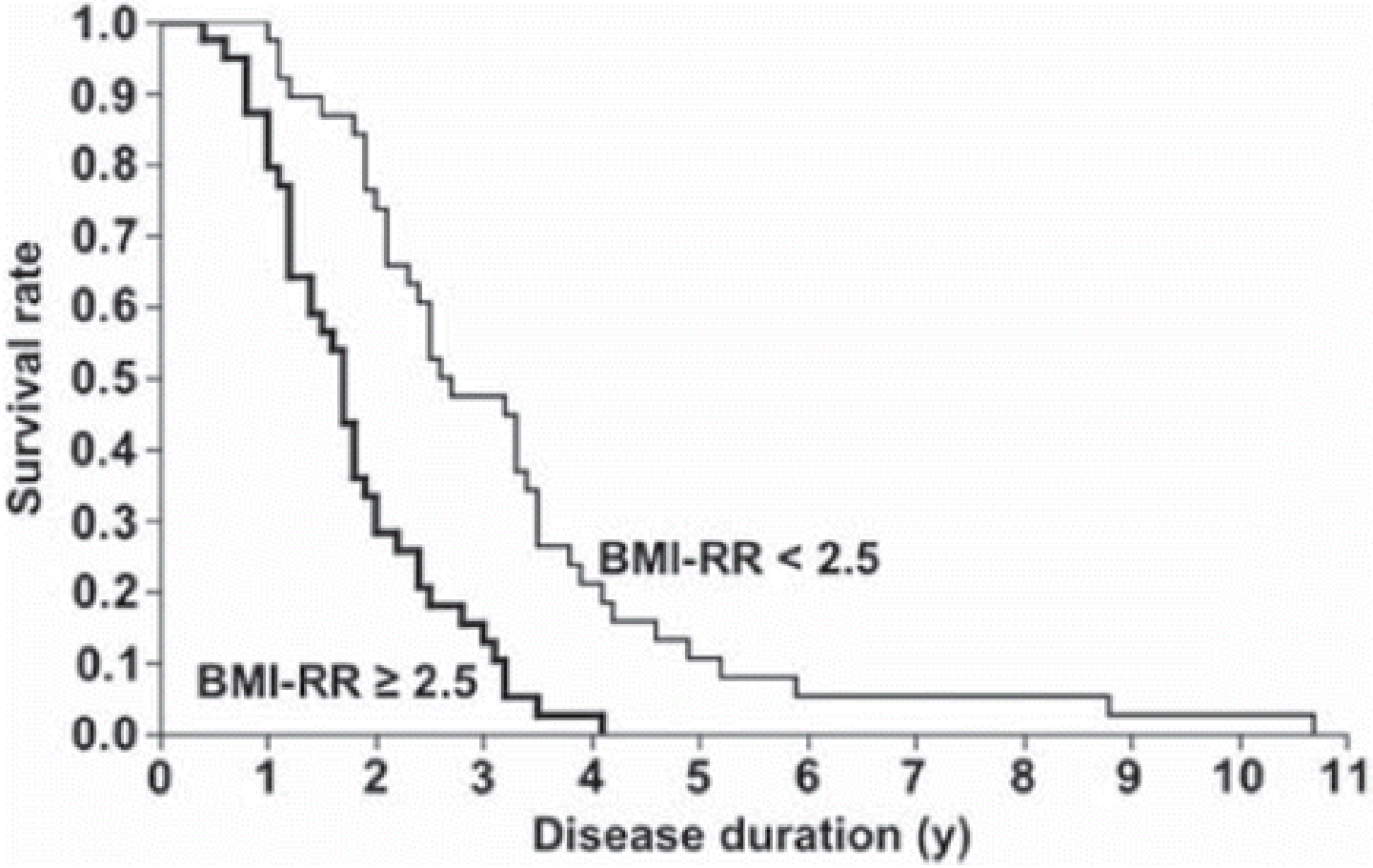
CARMEL ARMON[1] & LORENE M. NELSON[2]

[1]*Tufts University School of Medicine/Baystate Medical Center, Springfield, Massachusetts, and* [2]*Stanford University School of Medicine, Stanford, California, USA*

Abstract

Our objective was to evaluate the epidemiological literature regarding the association between trauma to the head and ALS, in order to determine if trauma to the head is a risk factor for ALS. A Medline literature search was conducted for the period between 1980 and October 2010 using the search terms: ('head trauma' OR 'head injury') AND (ALS OR 'amyotrophic lateral sclerosis' OR MND OR 'motor neuron disease'). The references of primary articles and reviews were checked to assure completeness of the search. Articles with primary data and reference groups were reviewed. The American Academy of Neurology evidence based method for classification of evidence for inferring causality and assigning level of conclusion was used. Twelve of 14 articles published since 1980 met the inclusion criteria. One class II article and three class III articles showed an association between a single instance of head trauma and ALS that did not exceed what might be seen due to chance alone. Eight class IV evidence articles could not inform conclusions. We concluded that evidence based analysis of the epidemiologic literature does not permit concluding that a single instance of head trauma is a risk factor for, or causes, ALS (Level U conclusion).

Key words: *Amyotrophic lateral sclerosis, analytic epidemiology, evidence based review, association, causation*



Toshio Shimizu et al. Reduction rate of body mass index predicts prognosis for survival in amyotrophic lateral sclerosis: A multicenter study in Japan
June 2012, Vol. 13, No. 4 , Pages 363-366

Amyotrophic Lateral Sclerosis, 2012; 13: 372–377

informa
healthcare

ORIGINAL ARTICLE

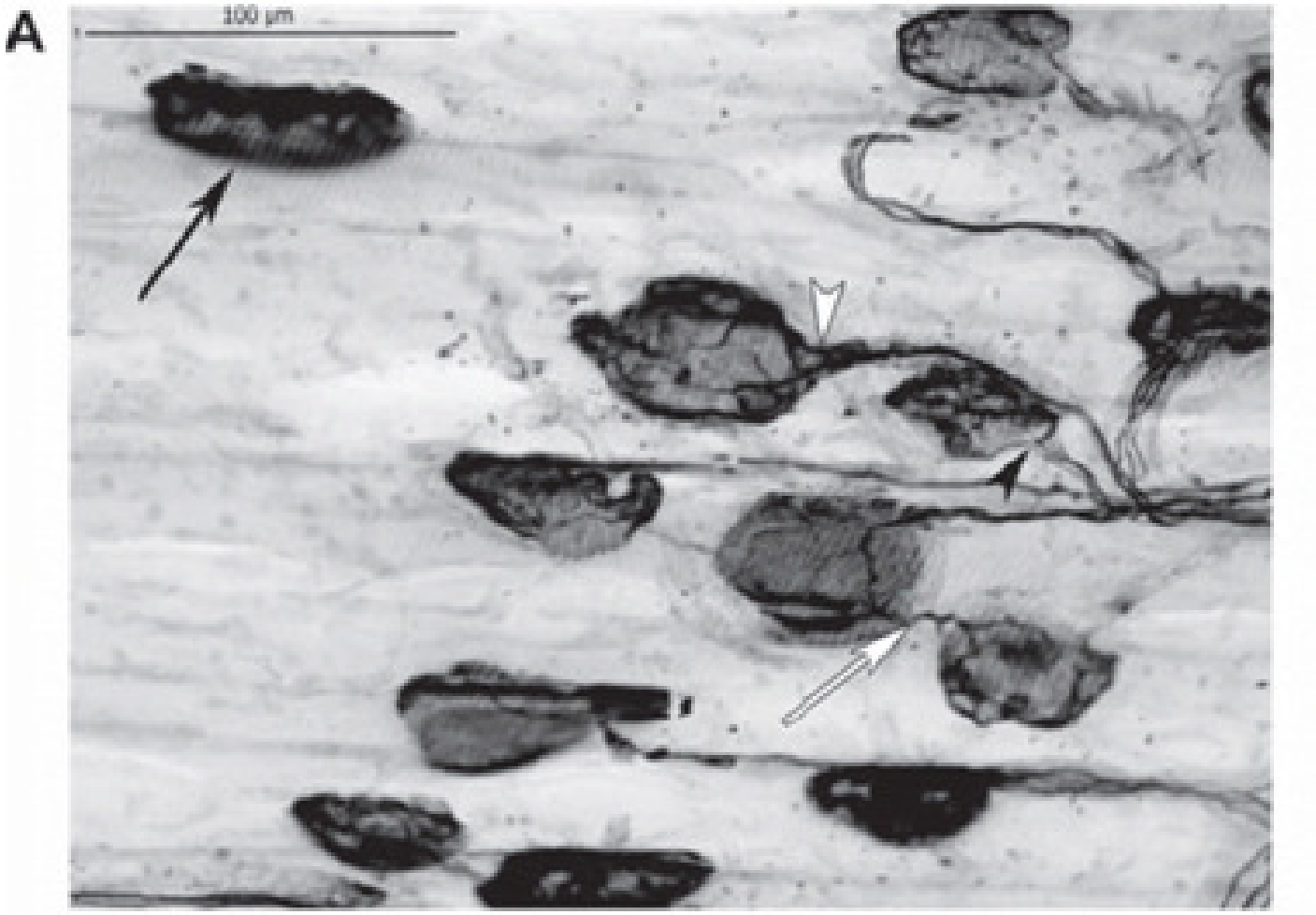
Reducing systemic hypermetabolism by inducing hypothyroidism does not prolong survival in the SOD1-G93A mouse

JIA LI, JILL M. PAULSON, FELIX D. YE, MINHEE SUNG, ANTHONY N. HOLLENBERG & SEWARD B. RUTKOVE

Department of Neurology and Department of Medicine, Division of Endocrinology, Beth Israel Deaconess Medical Center, Boston, Massachusetts, USA

Abstract

Bernadett Kalmar et al. Treatment with a coinducer of the heat shock response delays muscle denervation in the SOD1-G93A mouse model of amyotrophic lateral sclerosis
June 2012, Vol. 13, No. 4 , Pages 378-392



Verlaufsparameter zur Abschätzung von Therapieeffekten

Muscle Nerve. 2010 Sep;42(3):379-84.

Motor unit number index (MUNIX): a novel neurophysiological technique to follow disease progression in amyotrophic lateral sclerosis.

Neuwirth C, Nandedkar S, Stålberg E, Weber M.

Neuromuscular Diseases Unit and Kantonsspital St. Gallen, St. Gallen, Switzerland. Christoph.neuwirth@kssg.ch

Abstract

Motor unit number estimation techniques in amyotrophic lateral sclerosis (ALS) patients are technically challenging and time-consuming. The Motor Unit Number Index (MUNIX) is a novel technique based on surface-EMG recordings and requires only 3-5 minutes per muscle. The objective was to explore the feasibility of longitudinal MUNIX measurements in ALS patients. In seven patients enrolled in a clinical trial, eight muscles were studied every 2 months for up to 15 months in addition to the revised ALS-functional rating scale, slow vital capacity, and compound muscle action potentials. The method was well tolerated and easy to perform. Initial MUNIX measures were significantly reduced compared to controls (487 +/- 194 vs. 1459 +/- 113; $P < 0.001$). Relative drop from baseline paralleled the clinical course and was greater than the drop of other markers of disease progression. MUNIX measurements in multiple muscles are suitable for serial neurophysiologic investigations in ALS. Further longitudinal data are needed for reliability validation.

PMID: 20589888 [PubMed - indexed for MEDLINE]

ORIGINAL RESEARCH ARTICLE
published: 25 October 2012
doi: 10.3389/fpsyg.2012.00443

Attitudes toward assisted suicide and life-prolonging measures in Swiss ALS patients and their caregivers

Ralf Stutzki[1]*, Ursula Schneider[2], Stella Reiter-Theil[1] and Markus Weber[2]

[1] *Clinical Ethics Support and Accompanying Research, University Hospital Basel/Psychiatric University Hospitals Basel, Institut für Bio- und Medizin Ethik, University of Basel, Basel, Switzerland*
[2] *Muskelzentrum/ALS Clinic, Kantonsspital St. Gallen, St. Gallen, Switzerland*

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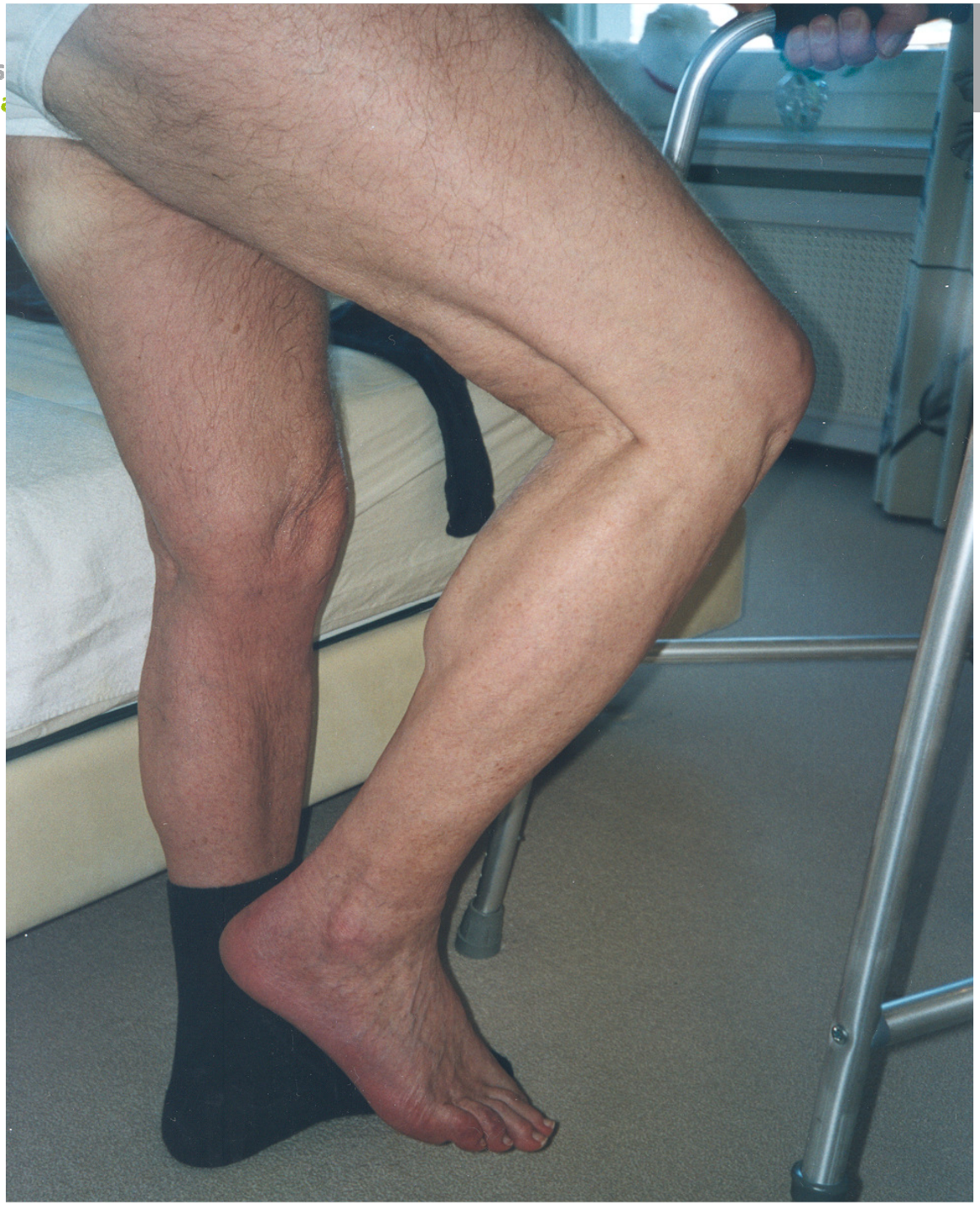
e-mail: ralf.stutzki@unibas.ch

Objectives: In Switzerland, assisted suicide (AS) is legal, provided that the person seeking assistance has decisional capacity and the person assisting is not motivated by reasons of self-interest. However, in this particular setting nothing is known about patients' and their caregivers' attitudes toward AS and life-prolonging measures. **Methods:** Data was retrieved through validated questionnaires and personal interviews in 33 patients and their caregivers covering the following domains: physical function according to the revised Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS-R), demographic data, quality of life, anxiety, depression, social situation, spirituality, burden of disease, life-prolonging, and life-shortening acts. **Results:** In patients the median time after diagnosis was 9 months (2–90) and the median Amyotrophic Lateral Sclerosis (ALS) FRS-R score was 37 (22–48). The majority of patients (94%; $n = 31$) had no desire to hasten death. Patients' and caregivers' attitudes toward Percutaneous Endoscopic Gastrostomy (PEG) and Non-Invasive Ventilation (NIV) differed. Significantly more patients than caregivers (21.2 versus 3.1%) stated that they were against NIV ($p = 0.049$) and against PEG (27.3 versus 3.1%; $p = 0.031$). Answers regarding tracheotomy were not significantly different ($p = 0.139$). Caregivers scored significantly higher levels of "suffering" ($p = 0.007$), "loneliness" ($p = 0.006$), and "emotional distress" answering the questionnaires ($p < 0.001$). Suffering ($p < 0.026$) and loneliness ($p < 0.016$) were related to the score of the Hospital Anxiety and Depression Scale (HADS) in patients. **Conclusion:** A liberal legal setting does not necessarily promote the wish for AS. However, the desire to discuss AS is prevalent in ALS patients. There is a higher level of suffering and loneliness on the caregivers' side. A longitudinal study is warranted.

Keywords: ALS, motor neuron disease, quality of life, depression, end of life




MARIJUANA
IS
MEDICINE

JNNP

Tetrahydrocannabinol (THC) for cramps in amyotrophic lateral sclerosis: a randomised, double-blind crossover trial

M Weber, B Goldman and S Truniger

J Neurol Neurosurg Psychiatry 2010 81: 1135-1140 originally published online May 24, 2010
doi: 10.1136/jnnp.2009.200642

Bilsland LG, Greensmith L. Curr Pharm Des. 2008;14(23):2306-16. Review

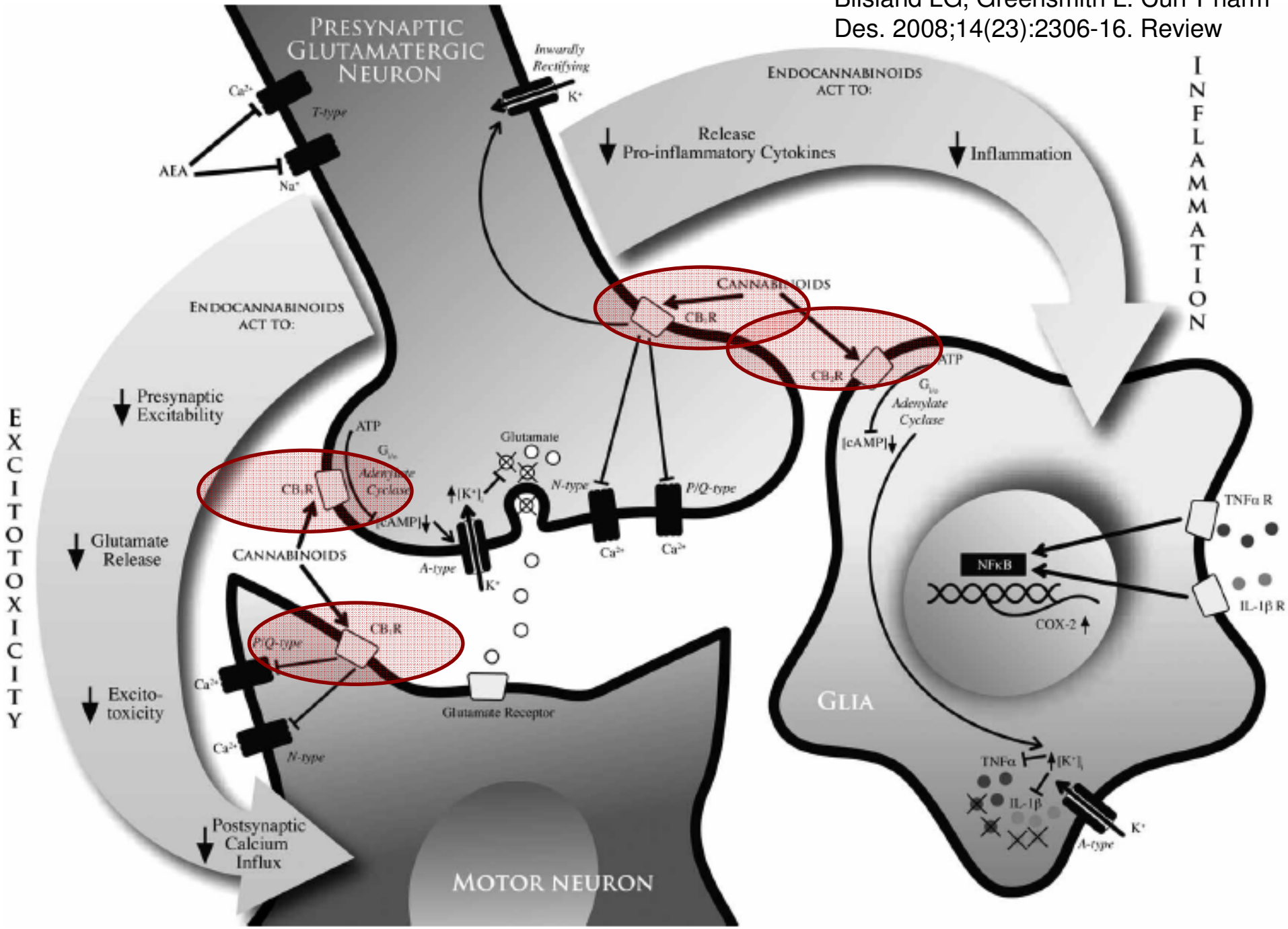


Table 1. Summary of Studies Manipulating the Endocannabinoid System in *In Vitro* and *In Vivo* Models of ALS

Manipulation of Endocannabinoid System	Dose and Onset of Treatment	Potential Mechanism of Action	Effects in ALS Models	Ref.
WIN-55,212-2	*In vivo*: 5mg/kg from symptom onset	Activation of CB_1 and CB_2 receptors.	Delayed disease progression in SOD1 mice 4% increase in lifespan of SOD1 mice	[87] [84]
AM-1241	*In vivo*: 3mg/kg 0.3mg/kg from symptom onset	Selective CB_2 receptor agonist	Extended lifespan of SOD1 mice by 11% Extended lifespan of SOD1 mice by 7%	[84]
AM-1241	*In vivo*: 1mg/kg presympto-matically	Selective CB_2 receptor agonist	Delayed disease progression in SOD1 mice	[38]
Δ^9-THC	*In vivo*: 20mg/kg from symptom onset	Activation of CB_1 and CB_2 receptors, also recep-tor independent anti-oxidative actions	Delayed disease progression in SOD1 mice and extended lifespan by 5%	[85]
Δ^9-THC	*In vitro*: 0.5μM	Activation of CB_1 and CB_2 receptors, also recep-tor independent anti-oxidative actions	Neuroprotective against kainate mediated toxicity in motor neurons *in vitro*	[53]
Cannabinol	*In vivo*: 5mg/kg presymptomatically	Non-psychoactive cannabinoid. Binds to CB_1 and CB_2 receptors but with lower affinity than Δ^9-THC	Delayed disease onset in SOD1 mice	[145]
Faah ablation	*In vivo*: From conception	Elevated AEA levels	Delayed disease progression in SOD1 mice	[87]
CB_1 receptor ablation	*In vivo* : From conception	Ablates potential neuroprotective contribution of CB_1 receptors	Extended lifespan in SOD1 mice by 13%	[87]

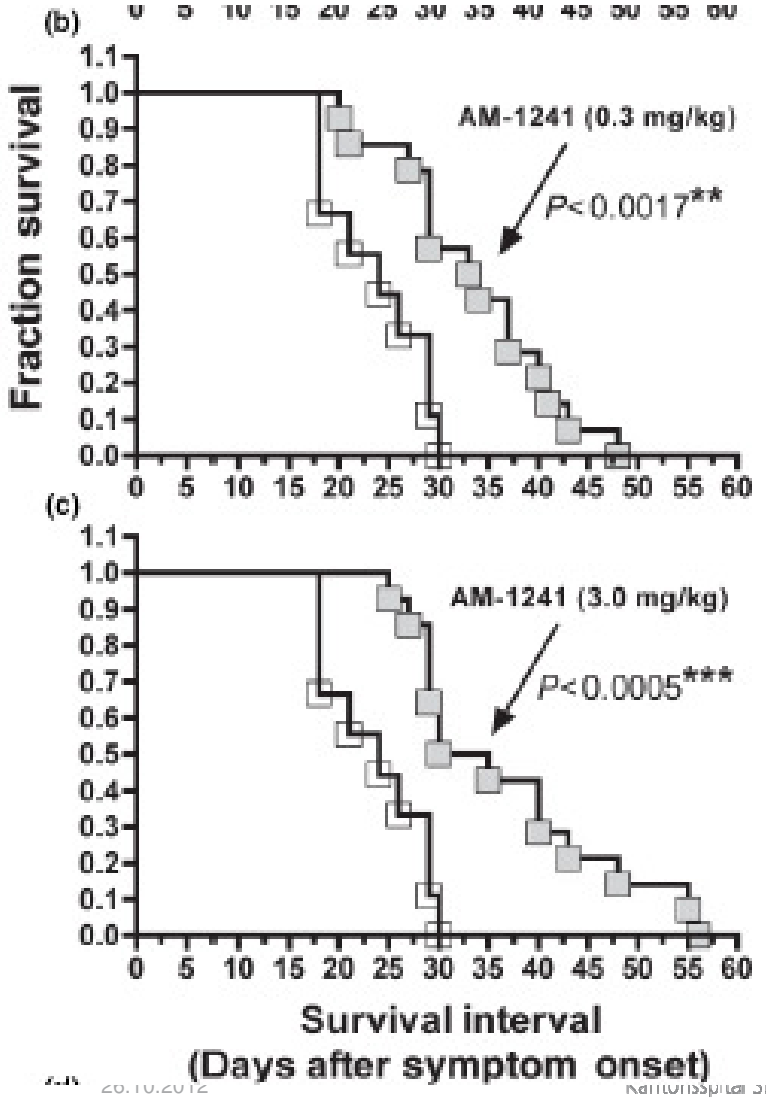
Several manipulations of the endocannabinoid system have been tested in models of ALS, with varying results. This table summarises the results of these studies to date.

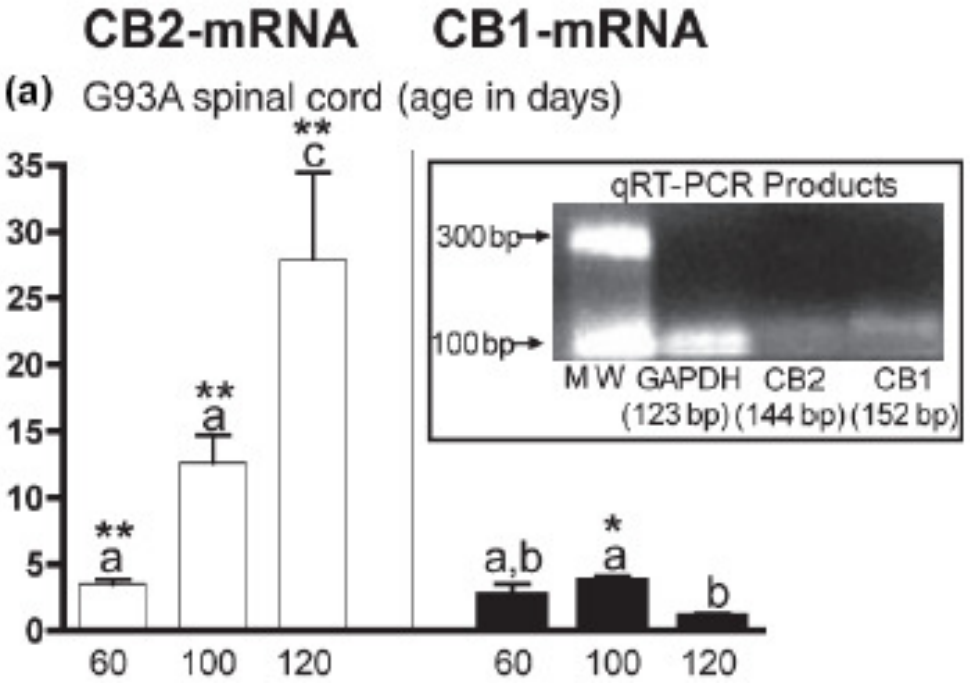
Bilsland LG, Greensmith L. Curr Pharm Des. 2008;14(23):2306-16. Review

J Neurochem. 2007 April ; 101(1): 87. doi:10.1111/j.1471-4159.2006.04346.x.

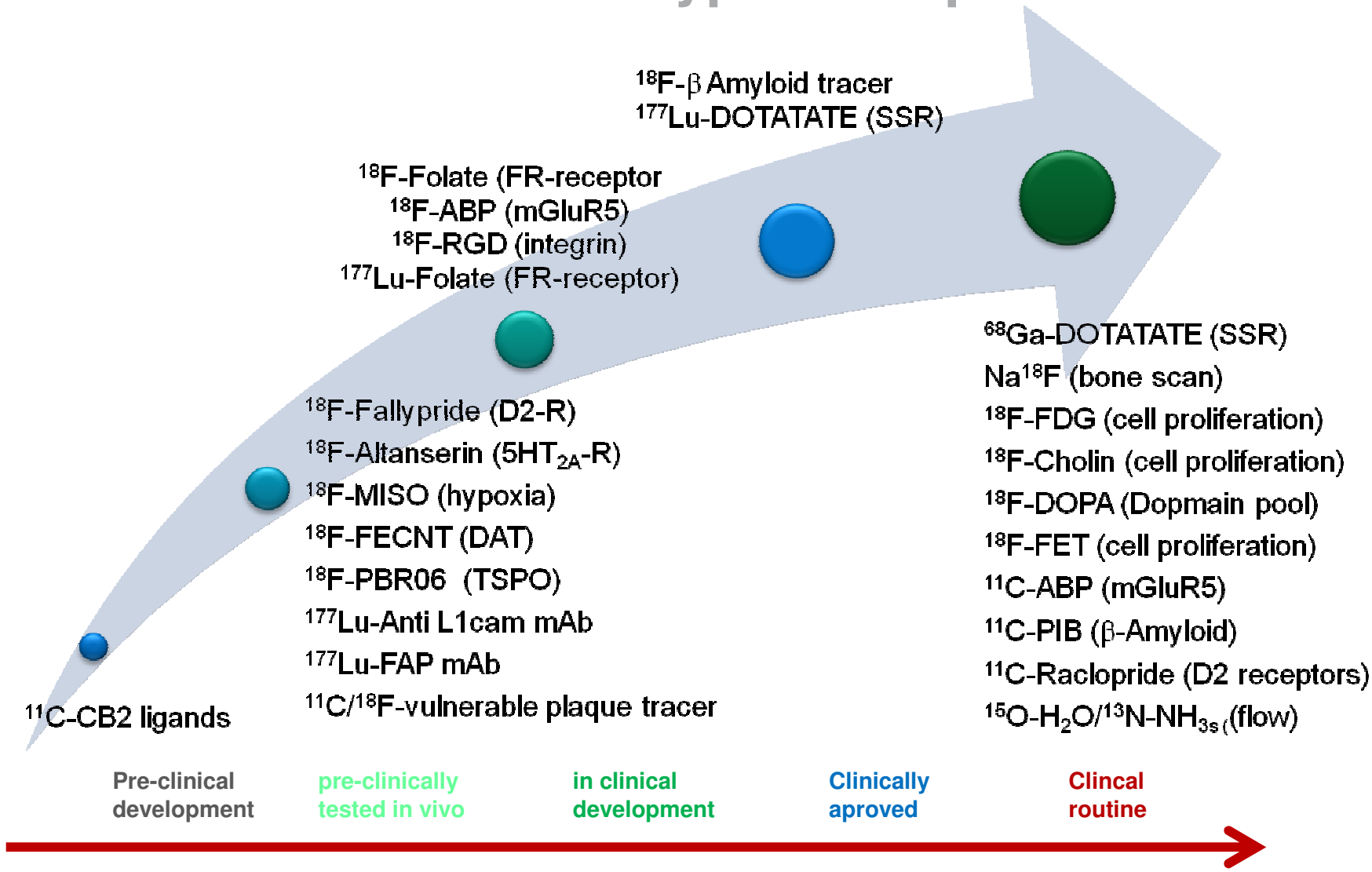
The CB2 cannabinoid agonist AM-1241 prolongs survival in a transgenic mouse model of amyotrophic lateral sclerosis when initiated at symptom onset

Jennifer L. Shoemaker, **Kathryn A. Seely**, **Ronald L. Reed**, **John P. Crow**, and **Paul L. Prather**
Department of Pharmacology and Toxicology, College of Medicine, University of Arkansas for Medical Sciences, Little Rock, Arkansas, USA





Marker für Cannabinoid Typ 2 Rezeptor



Neue Gene neue Hoffnung ?

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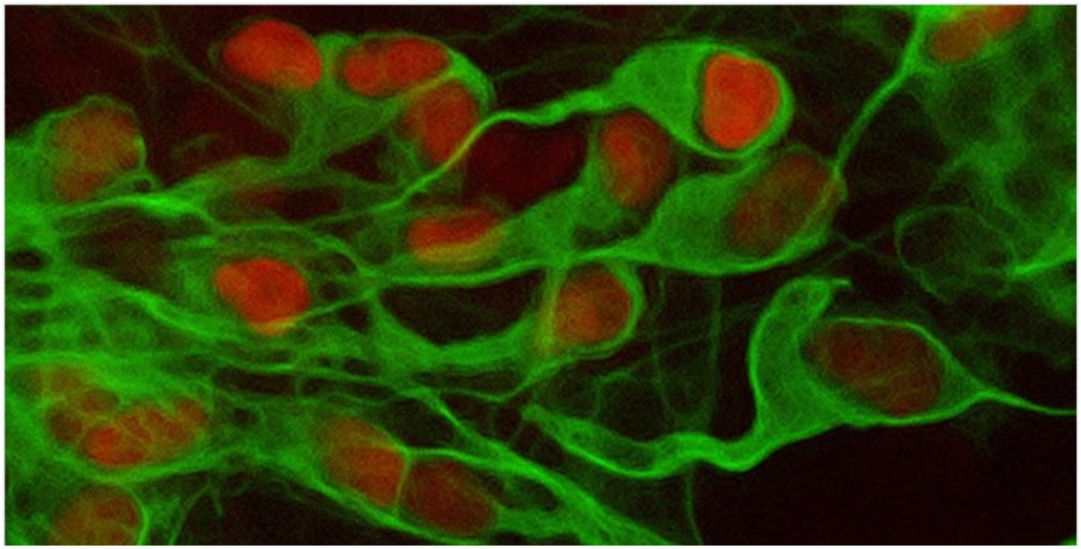
24. Okt. 2012, 17:23

Home > Wissen > Gesundheit > Ursache für Nervenerkrankung ALS gefunden

22.08.11 | **Neurologie**

Ursache für Nervenerkrankung ALS gefunden

Forscher wollen die Ursache für die amyotrophe Lateralsklerose gefunden haben. Das könnte zu wirksameren Medikamenten führen und der Krankheit den Schrecken nehmen.



ARTIKEL EMPFEHLEN

E-Mail

2 Twittern

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Kommentare (2) Drucken

ANZEIGE

Genetik

- Erstes Gen (1993) Superoxiddismutase SOD
- Weitere Gene: ALSIN (ALS2), VAPB, Dynactin, TDP-43, FUS, Optineurin, UBQLN2,C9ORF72, Profilin und andere.
- Bei sporadischer ALS Suche nach sogenannten Risikogenen (susceptibility genes)

Genetische Mutationen in der Schweiz

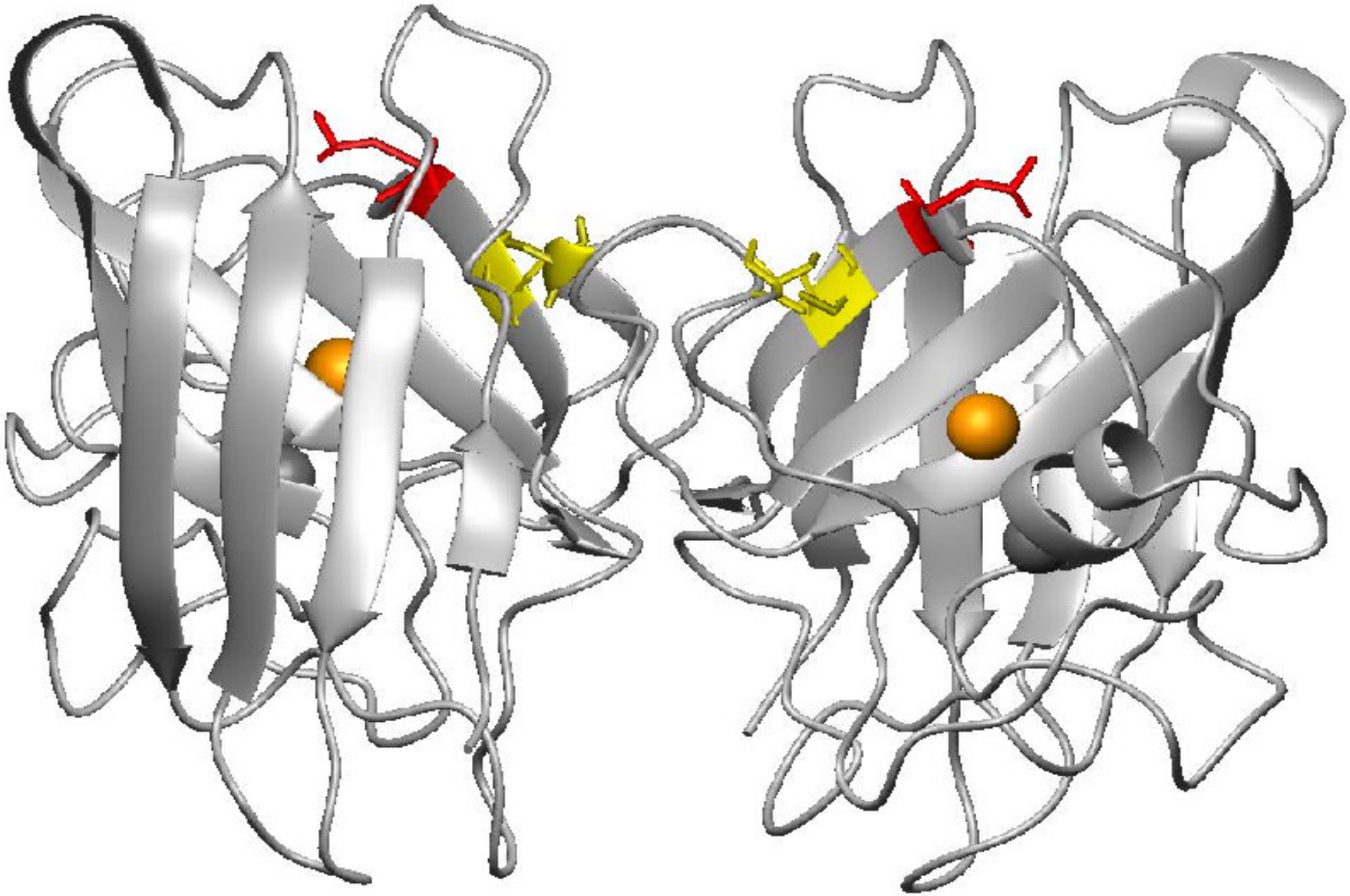
- SOD
- TDP 43
- Optineurin
- Ubiquinin 2
- C9ORF72

SUPEROXIDDISMUTASE (SOD)

- Enzym katalysiert die Umwandlung von giftigen Anionen zu Wasserstoffperoxid (H_2O_2)
- 156 unterschiedliche SOD Mutationen

Pathogenese der Motoneurondegeneration

- Fehlen der Superoxiddismutase (SOD) erzeugt keine ALS
- Wahrscheinlich “Giftung” des Enzyms



Muskelzentrum/ALS Clinic