Amyotrophic lateral sclerosis - a neurodegenerative disease

COGAIN Camp
2. june 2005

Ole Gredal
Department of Neurology
H:S Bispebjerg Hospital,
Copenhagen

Alternative names

- Amyotrophic lateral sclerosis (ALS)
- Lou Gehrig’s disease (in the USA)
- Maladie de Charcot (in France)
- Motor neuron disease (in the UK)

The purpose of the talk

- Which kind of disease is ALS/MND ?
- Which part of the nervous system is affected in ALS/MND ?
- What are the symptoms of ALS/MND ?
- How many people are suffering from ALS/MND in Denmark ?
- How to diagnose ALS/MND ?
- How to treat or cure ALS/MND ?

The purpose (2)

ALS-Care – how is it organized in Denmark ?

- What to do when the patient can’t feed ?
- What to do when the patient can’t breathe ?
- What to do when the patient can’t communicate ?
- How long time do the victims survive ?
- Psychological aspects of decision-making in ALS/MND ?

The human brain

- The weight of the human brain is 1.5 kilogram
- How many neurons are in the cortex ??
- 30 thousand millions or 30 billions neurons
- It will take you 1000 year to count them all, if you count one per second
- 1 cubic millimetre contain 120,000 neurons and they make up contact with 276 million synapses on other neurons

---

Epidemiology of ALS

- Average age of onset is 60 years (range: 21-93 years)
- ALS affects more men than women, by a ratio of 3:2
- The worldwide incidence of ALS is 1.5 cases per 100,000 people per year
- 75-100 new ALS/MND cases in Denmark per year

- The prevalence is 4–6 per 100,000 people
- There are approximately 300 patients with ALS in Denmark and worldwide 60,000

Signs and symptoms

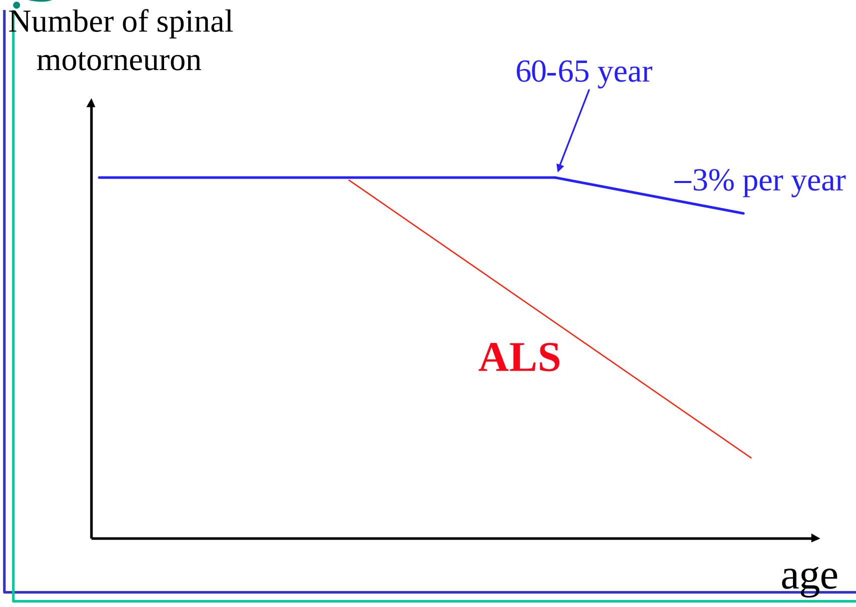
- **The initial signs of ALS are focal**

- **Signs and symptoms include:**
  - muscle wasting and weakness (key, smacking a foot, stairs)
  - fasciculation
  - difficulty in swallowing
  - slurred speech

- **Some functions remain intact throughout the disease**
  - Intellect
  - eye movement
  - bowel and bladder control
  - sense of touch and pinprick

Muscle wasting in ALS

Muscle wasting of the tongue



Limb-onset ALS

- 75% of patients have limb-onset ALS
- Weakness, atrophy and fasciculations in the limbs are prominent signs
- Initially limb(s) on one side of the body are affected,
  but the disease spreads to both sides of the body
- Bulbar (speech and swallowing) signs develop later

Bulbar-onset ALS

- Accounts for around 25% of ALS patients
- Affects the bulbar area of the brain first - speech and swallowing

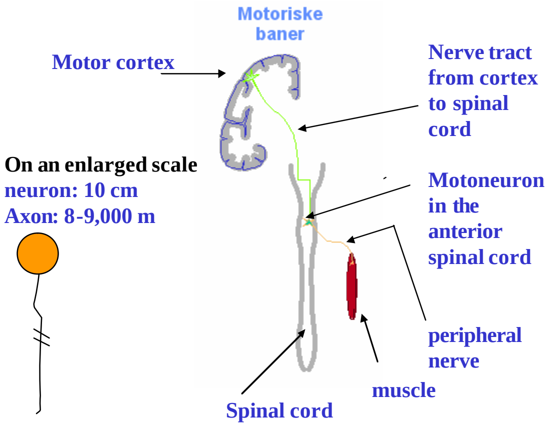
- Progresses more rapidly than limb-onset ALS
- Patients may show diminished control of emotions and a higher degree of dementia

Respiratory onset of ALS

- Only 1-2 percent
- The patient may need respiratory support (ex. invasiv ventilation) before the diagnosis is made

---

Neuronal tracts affected in ALS



Motor cortex

Nerve tract from cortex to spinal cord

On an enlarged scale
neuron: 10 cm
Axon: 8-9,000 m

Motoneuron in the anterior spinal cord

peripheral nerve

muscle

Spinal cord

pathology: loss of the motoneuron in the anterior part of spinal cord – but not in cortex.

ALS - diagnosis

- History
- Clinical neurological examination
- Neurophysiological assessment
- Radiological assessment
- Clinical laboratory assessment

The diagnosis of ALS (1)

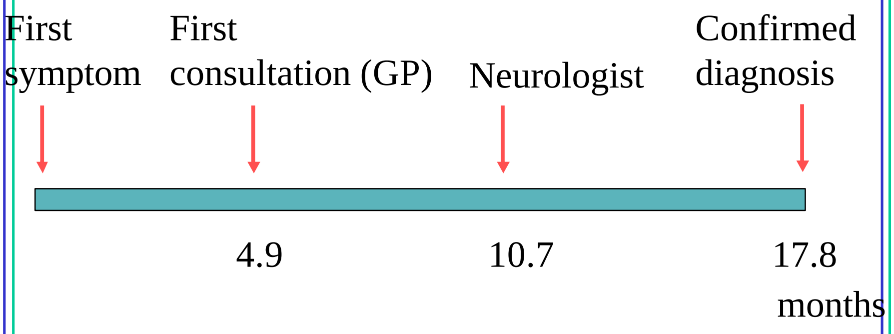
- The *presence* of:
  - Evidence of *lower motor neuron (LMN) degeneration* by clinical, electrophysiological or neuropathologic examination
  - Evidence of *upper motor neuron (UMN) degeneration* by clinical examination,
  - *Progressive spread of symptoms or signs* within a region or to other regions, as determined by history or examination

The diagnosis of ALS (2)

- The absence of:
  - *electrophysiological and pathological evidence of other disease processes* that might explain the signs of LMN and/or UMN degeneration, and
  - *neuroimaging evidence of other disease processes* that might explain the observed clinical and electrophysiological signs.

Time to diagnosis

91 patients in Europe (Germany, Italy, Spain) (R.Dengler 1999)



Sporadic ALS

- In about 90% of cases, the disease appears to occur spontaneously

- The causative factor(s) of sporadic ALS is not known

Familial ALS

- About 5 – 10% of the total number of patients with ALS have familial ALS (F-ALS)
- Genetic abnormalities have been identified in some cases of FALS
  - 20% of patients with FALS have a mutation in the gene for the enzyme Cu,Zn-Superoxide Dismutase (SOD-1)
  - > 100 different mutations in the SOD-1 gene

Pathogenesis of ALS

- Numerous hypotheses have been investigated for links with the pathogenesis of ALS
  - glutamate excitotoxicity
  - genetic factors (SOD-1 and other mutations)
  - injury due to free radicals
  - cytoskeletal changes
  - autoimmune mechanisms
  - failure of neurotrophic factors
  - unusual viral infections
  - environmental toxins

The FALS-SOD1 transgenic mouse

The best animal model to reproduce accurately ALS pathology

- Overexpress the mutated form of SOD-1 found in familial ALS
- Tremor and weakness from ~ 80 days
- Death at ~ 140 days
- Selective loss of motoneurones.

Treatment

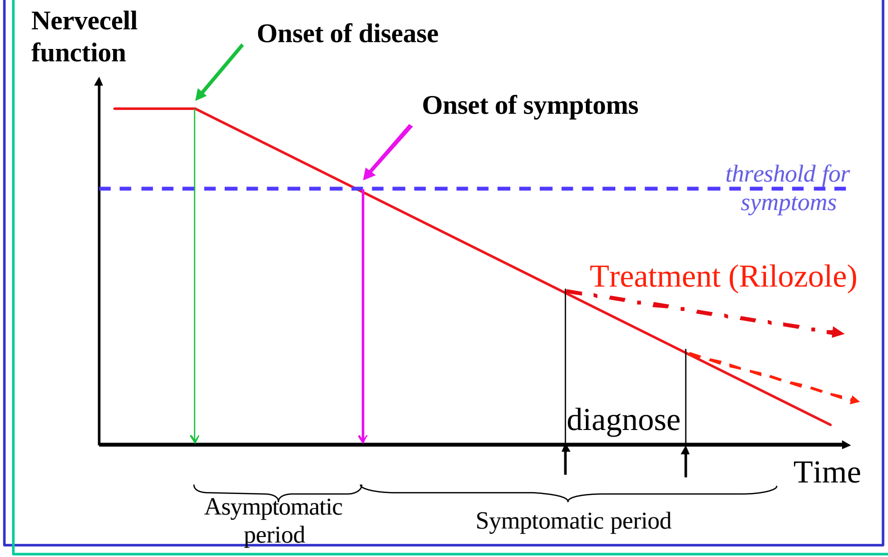
- There is currently no cure for ALS
- Until now, only symptomatic / palliative treatment has been available
- Riluzole is the first therapy to demonstrate efficacy in terms of survival in two clinical trials

---

Riluzole treatment

- Clinical trials: Number needed to treat = 11
  3-4 months longer survival after Rilozole
- Three clinical studies have shown > 12 months longer survival after Riluzole treatment compared to no treatment
- Treatment should be initiated as early as possible after the patient has been informed of the diagnosis.

Effect of Rilozole ?



Disease progression

- 50% of motor neurons may be lost before clinical symptoms develop
- The rate at which ALS progresses varies widely between patients
- Several prognostic factors have been identified
- The most common cause of death in patients with ALS is respiratory failure
- ALS is invariably fatal, usually leading to death within 3–5 years after onset of symptoms

Developing models of care

What is care?

- To care is showing solicitude
- To give care is to nurse and to protect

A model of care

- A care system, which takes care of all aspects of the disease, that afflicts a person
- A system where the dignity and the right of self-determination for the single individual is maintained

Care team in the ALS clinic

- The team should be able to take care of the patient in the hole course of the disease
- Cover all problems that can arise from maximizing function in the beginning to palliative care in the terminal phase

---

ALS – Organisation in Denmark

At hospital

- Neurologist
- Physiotherapist
- Trained nurse
- Psychologist
- Occuoational therapist
- Social worker
- Speech therapist
- Dietitian

ALS-Patient
and
his relatives

At home

- Physician (GP)
- Home care
- District nurse
- Social worker
- Physiotherapist
- Occuoational therapist

Institute of NMD
ALS-counselor

ALS counselor scheme

- A connection between the social services and the hospital
- Visits the patients regularly in their homes, support the patients and can press the social services to act quickly
- Act in collaboration with the local neurological department

The tasks are (1)

- To role out the diagnosis
- To break the news
- To inform about symptomatic treatment
- Make arrangement about next appointment

The tasks are (2)

- Rehabilitation
- Assisting aids
- Psychological help
- Social security when life conditions are changing
- Advice and aids from the speechtherapist

Tasks later on (1)

- To monitor weight loss
- Refer to dietician
- Refer to percutaneous endoscopic gastrostomi (PEG) = feeding tube

Tasks later on (2)

- To monitor respiratory capacity
- Ask for symptoms of nocturnal hypoxia
- Refer to the respiratory center

- The respiratory aids should be discussed with each patient well before the development of respiratory insufficiency

---

The terminal phase

- At home
- At a hospice
- At the hospital
- At a nursinghome

- Advanced directives

Care in Denmark is free of charge and the same for all patients ?

- ALS-Patients have to pay 500 euro for medication per year
- Disability aids and equipment is free of charge
- Personal helper is free of charge

ALS - symptomatic interventions

- Reduced strength and muscular atrophy
- Spasticity, spasms, muscles cramps and pain
- Depression, anxiety, emotional lability and insomnia
- Bulbar symptoms
  - Sialorrhea
  - Loss of weight and dysphagia
  - communication
- Respiratory problems
  - Bronchial secretions
  - Insufficient ventilation
- The terminal stage

Nutrition and dysphagia

- High calorie, soft diet
- Smaller, more frequent meals
- Weekly monitoring of weight (by patient)
- Use of nutritional supplements
- Flexing head forward when swallowing/turning head
- Thickening liquids
- Education on PEG (verbal/printed/patient meeting, upcoming video)

Feeding tube - Percutaneous Endoscopic Gastrostomy

- Literature suggests its beneficial effect in ALS
  - >50% patients experience dysphagia at some time
  - No randomized trials of PEG vs no PEG

Denmark

1974 - 1986	1993 - 1998
2% PEG	46% PEG
Survival 23 months	Survival 33 months

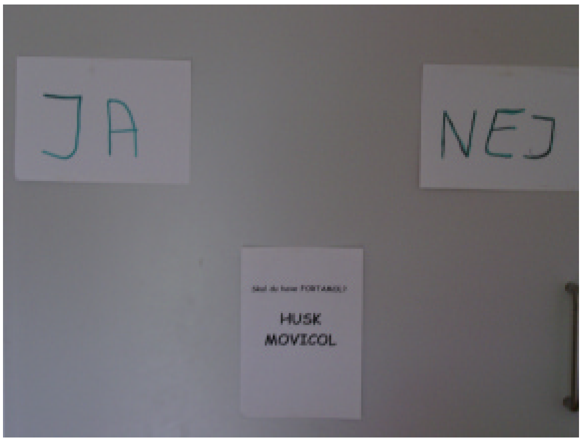
Communication in ALS patients

- Regular assessment (i.e., every 3-6 months) of communication by a trained S&LT is recommended.
- The use of appropriate communication support systems should be provided as required

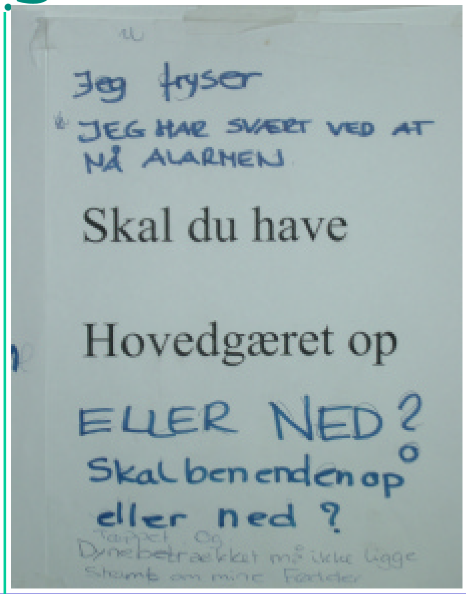
---

Communication

Yes or No



The written instructions on the walls were used by a 39 years old ALS-victims in 2004. He was 2½ year in a nursing home before he died. The last 6 months he was laying in the bed.



Jeg fryser

JEG HAR SVÆRT VED AT NÅ ALARMEN

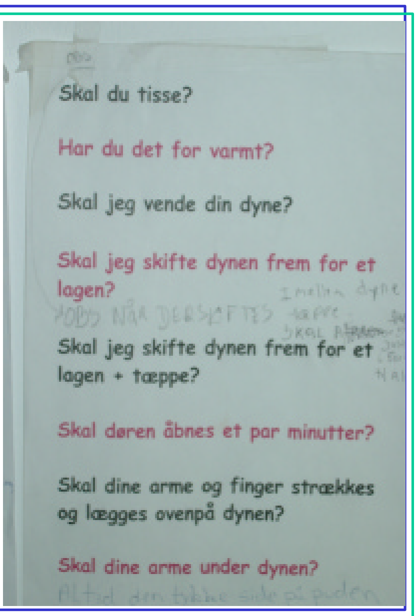
Skal du have

Hovedgæret op

ELLER NED?

Skal benenden op eller ned?

Tæppet og Dynebetrækket må ikke ligge Stramt om mine Fødder



Skal du tisse?

Har du det for varmt?

Skal jeg vende din dyne?

Skal jeg skifte dynen frem for et lagen?

Imellem dyne

OBS NÅR DER SKIFTES

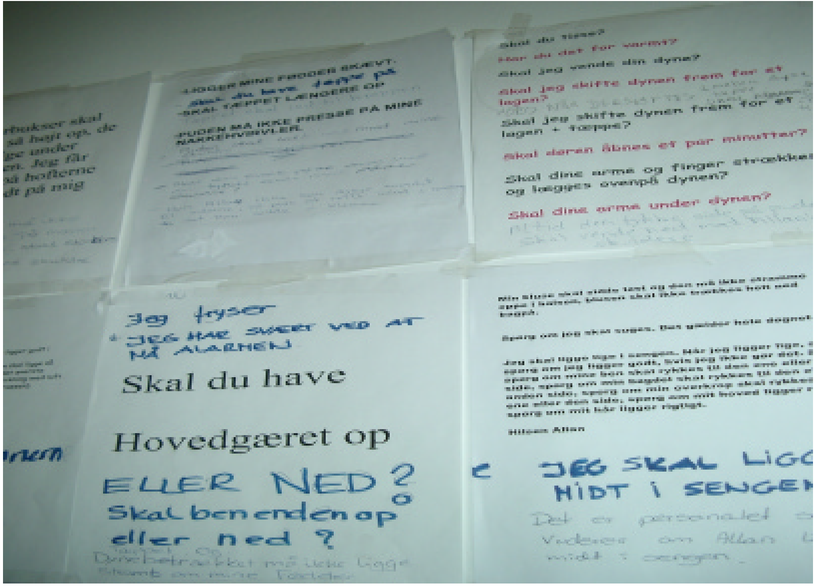
Skal jeg skifte dynen frem for et lagen + tæppe?

Skal døren åbnes et par minutter?

Skal dine arme og finger strækkes og lægges ovenpå dynen?

Skal dine arme under dynen?

Altid den tykke side på puden



Skal du tisse?

Har du det for varmt?

Skal jeg vende din dyne?

Skal jeg skifte dynen frem for et lagen?

Skal jeg skifte dynen frem for et lagen + tæppe?

Skal døren åbnes et par minutter?

Skal dine arme og finger strækkes og lægges ovenpå dynen?

Skal dine arme under dynen?

Jeg fryser

JEG HAR SVÆRT VED AT NÅ ALARMEN

Skal du have

Hovedgæret op

ELLER NED?

Skal benenden op eller ned?

JEG SKAL LIGG

MIDT I SENGEN

Pulmonary Care

- Symptoms or signs of respiratory insufficiency should be checked at each visit. (including symptoms of nocturnal hypoventilation)

- Forced vital capacity (FVC) reduces 3.5% per month
- Insufficiency of coughing: peak-flow < 150 l/min
- Hypoventilation during sleep can occur when FVC < 50 %
  - Symptoms: exhaustion during daytime, awake in a sweat, wake-up-headache in the morning
  - Treatment NIPPV = BiPAP

Measurement of Forced Vital Capacity

FVC can be much lower in lying position due to paresis of the diaphragma muscle

---

BiPAP-equipment

To be used during sleep to improve quality of life.

The patient should be informed about the temporary nature of NIV/ BiPAP. The maximum use is 12-16 hours per day.

Invasive ventilation ?
(tracheostomy and respirator)

- Very individualized
  - Not until signs/symptoms evident
- Inflluenced by physician attitudes and recommendations
- High functioning patient more likely to choose tracheostomy
- Quality of life can be preserved
- When survival is a must for the patient and the relatives
- Advance directives put in place for most tracheostomy patients

---

Final month of Life

- Most common difficulties:
  - difficulty communicating 62%
  - dyspnea 56%
  - insomnia 42%
  - discomfort/pain 48%

Better when hospice was in place.

(Ganzini L et al.: 2002)

What Affects Survival?

- Baseline health and genetics
- Site of onset and rate of progression
- Referral time to treatment
- Quality of care available to patient
- Choices of care made by the patient and the relatives
  - Medication/nutrition/exercise/pulmonary support

Psychological problems

- Fear of total dependence
- Accept or denial of the disease
- Accept of technical aids
- Depression
- Death
- The wish to decide for oneself the time of death - euthanasia
- Change of rôles
  - in the family
  - the parent rôle

Psychological Intervention

How the individual copes with his situation depends on the following conditions:

- Personality
- Gender
- Age
- Intellectual and emotional development
- Social and cultural relations
- Religion

Accept of technical aids

- accept crutches or elbow sticks, wheelchair, neck collar, speaking computer etc,
- but often not PEG - being kept artificially alive ?
- NIV or BiPAP ?
- Invasive ventilation ?
  - 5 % ?
  - 20 patients in Denmark in 2004

Conclusion

ALS - field of problems

- A rapidly progressive disease
- Unknown etiology
- No causal treatment or cure
- Expected survival about 3 years
- A relatively rare disease - unknown by local health care professionals
- A complex disease requesting many specialists within a short time

---

---

1. Fear of dependence

- the fear of losing the existential freedom
- the painful feeling of having lost control over one's own life

- put the dread into words and try to change the dread into fear, despair and anger, thereby turning the dread into feelings that can be released and expressed
- look at the present functions and not to focus on the final situation
- open his eyes to things and activities still within reach

2. Accept of the disease

- it is often possible to learn to live with the disease
- patients who relate to their disease will still appreciate life in spite of their severe handicaps

- difficult to cope with denial because the resistance can be very massive
- The denial is often based on the belief that the disease will go away if you just keep up your daily training and refuse to become dependent on technical aids.

---

4. Depression

- Minor depressions are common

- Beck's depression questionnaire

5. Death

- At the beginning, the talks may be philosophical
- Existentialistic questions: "What is the purpose of my life now?" or "Why me?"

---

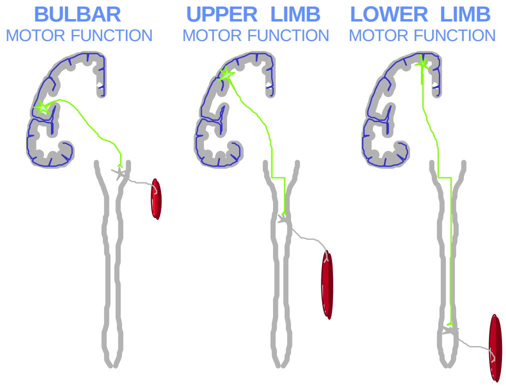
6. The wish to decide the time of death - euthanasia

- the wish for euthanasia is increasing ?

7. Change of rôles

- In the family
  - division of labour
  - the relative is often alone with his or her feelings and frustrations
- To be parents
  - Do we have to tell the child about the disease?
  - When do we tell the child what the disease implies?
  - the child will no longer take orders from the patient

Upper motor neuron signs



- Loss of pyramidal tract

- Spasticity (increased tone)
- Extensor plantar response
- Clonus
- Pathologic hyperreflexia

Lower motor neuron signs

- Selective loss of ventral horn cells in brainstem and spinal motor neurons
- Relative sparing of oculomotor neurons

- Weakness, paresis and paralysis
- Muscle wasting
- Areflexia
- Fasciculations

The El Escorial Criteria in the diagnosis of ALS

- **Clinically definite ALS**
  - UMN + LMN signs in 3 regions
- **Clinically probable ALS**
  - UMN + LMN signs in 2 regions
  - UMN signs rostral to LMN
- **Clinically probable - laboratory supported ALS**
  - UMN + LMN signs in1region, positive EMG for LMN in 2 limbs
  - UMN signs in 1 region, positive EMG for LMN in 2 limbs
- **Clinically possible ALS**
  - UMN + LMN signs in 1 region
  - or UMN signs in 2 or more regions and UMN signs rostral to LMN signs
- **(Clinically suspected ALS)**
  - only LMN signs in 2 or more regions

ALS Therapeutics 2005

- **What have been tried**
- **New Approaches**

Sixteen unique therapeutic approaches have been tried in ALS in past 12 years.

- **Anti-glutamate**
  - Riluzole
  - Talampanal
  - Topiramate
  - Neurontin
  - Dextromethorphan
- **Growth Factors**
  - BDNF-IT and SC
  - CNTF
  - IGF-1
  - Xaliproden
- **Antioxidants/Bioenergetics**
  - Creatine
  - Vitamin E
- **Anti-inflammatory**
  - Celebrex
- **Anti-apoptotic**
  - TCH386
  - Pentoxyfilline
  - Tamoxifen

New approaches to therapy in ALS

- Symptomatic

- Improved pulmonary therapy
- Early nutritional intervention

- Brain activated assistive technology (brain computer interfaces)

New Approaches to Therapy in ALS.

Neuroprotective / Restorative:

- Drugs → Phase II or III

- Genes and protein delivery

- Inactivation of toxic gene products

- Neural stem cells

Candidate drugs – already in trials or about to start in USA

Anti-apoptotic
- Minocycline

Anti-glutamate
- ONO-2506
- Ceftriaxone

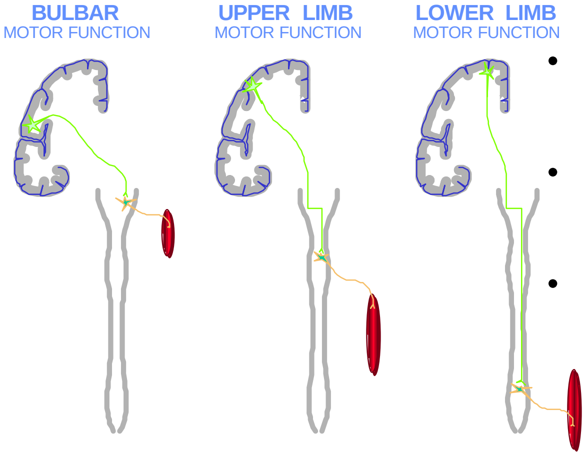
Antioxidant/Bioenergetics
- Coenzyme Q10
- AEOL10150

Neurotrophic factor
- IGF-1

Histone deacetylase inhibitors
- Sodium phenylbutyrate

HSP enhancer
- Arimoclomol

Diagnosis of ALS
Motor neuron involvement



- Upper motor neuron signs
- Lower motor neuron signs
- Progression

Pathogenesis of ALS

- The disease process of ALS could be initiated and predated by months or years by a trigger likely to be multifactorial and cumulative.
- As an initial trigger(s), environmental factors may be important as well as aging may play a crucial role with multiple defective or degraded gene products accumulating during progressing years. (Eisen 1995)

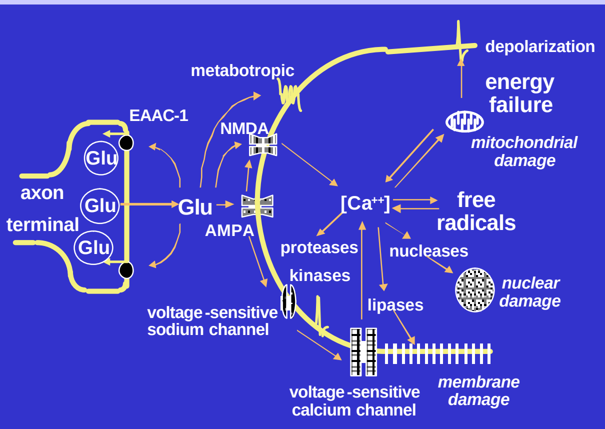
THEORETICAL MECHANISMS UNDERLYING EXCITOTOXICITY

- Excess glutamate release
- Abnormal glutamate leakage
- Impaired glutamate re-uptake
- Altered receptor sensitivity

EXCITOTOXICITY AND MOTOR NEURONE DISEASE

- Glutamate levels in CSF (and plasma)
- Glutamate levels in post-mortem CNS tissue
- Abnormalities of glutamate re-uptake
- Alteration in the density of glutamate receptors in the motor system in MND
- Exogenous excitotoxins
- Experimental and animal models
- Therapeutic trials of anti-glutamate drugs

Glutamate Excitotoxicity



Mechanisms of excitotoxicity and cellular events

Excitotoxicity and disease

- Neurolathyrism and Guam-type ALS with Parkinson’s disease have some symptoms similar to those seen in ALS
- These diseases are known to be related to high levels of excitatory amino acids in the diet, which lead to excitotoxicity and neuronal death

---

ALS/MND Genetic

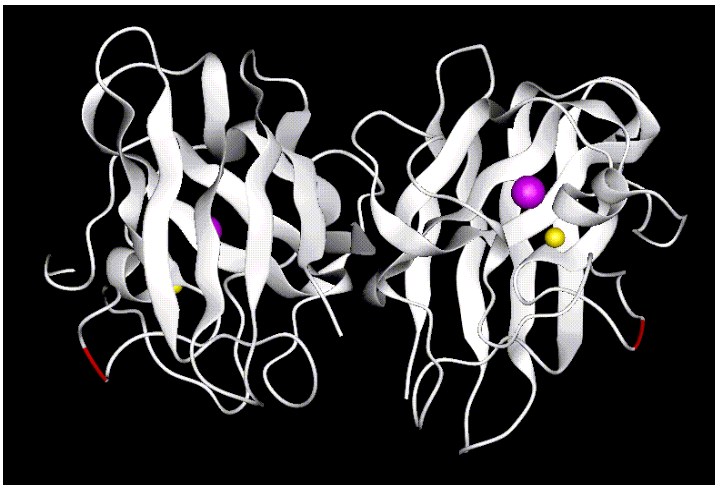
Disease	Inheritance	Gene
S-ALS	none	unknown
F-ALS:	dominant or recessive	SOD1,ALS1

Cu,Zn Superoxide Dismutase or SOD-1 mutations

- The enzyme Cu,Zn superoxide dismutase (SOD-1) is responsible for detoxifying reactive oxygen species within the cell
- Mutations found in familial ALS may endow the SOD-1 enzyme with a new function that is deleterious for motoneurones - a toxic gain of function

---

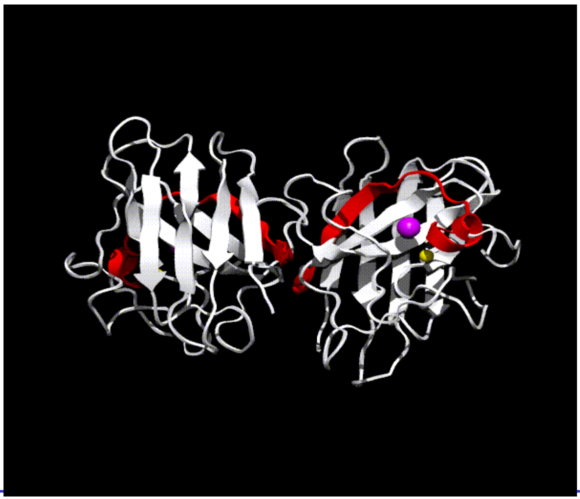
SOD1-mutation (D76Y)



SOD-1 mutation (127ins)

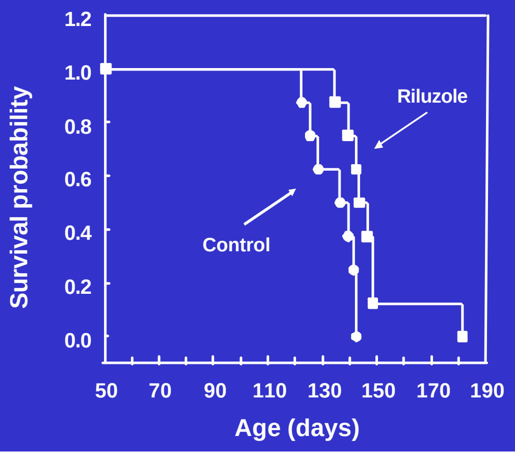
Wild-type	Leu 126	Gly 127	Lys 128	Gly 129	Gly 130	Asn 131	Glu 132	Glu 133
	TTG	GGC	AAA	GGT	GGA	AAT	GAA	GAA
Mut	Leu 126	Gly 127	***Gly 128***	***Gln 129***	***Arg 130***	***Trp 131***	***Lys 132***	*STOP*
	TTG	GG**T**	**GGG**	CAA	AGG	TGG	AAA	TGA

SOD-1-mutation 127ins – 132 stop



The FALS-SOD transgenic mouse

Effect of riluzole on survival in FALS-SOD transgenic mice



MOTOR NEURONE NEUROTROPHIC FACTORS

- Ciliary neurotrophic factor (CNTF)
- Brain derived neurotrophic factor (BDNF)
- Insulin-like growth factor (IGF-1)
- Glial-derived neurotrophic factor (GDNF)
- Neurotrophin-3
- Neurotrophin-4/5

RECENT THERAPEUTIC TRIALS IN MOTOR NEURONE DISEASE

- Anti-glutamate

– Riluzole	+
– Gabapentin	+ trend

- Neurotrophic factors

– CNTF	-
– BDNF	-
– IGF-1	+/-

- Anti-oxidants

– N-acetyl cysteine	+ trend
– Vitamin E	+ in SOD1 mouse

Therapies that have not demonstrated efficacy in ALS (1)

- Most of the treatments investigated for ALS have been unsuccessful
- Treatments that have not demonstrated efficacy include:
  - Subcutaneously administered CTNF
  - Subcutaneously administered BDNF
  - Thyrotropin releasing hormone and its analogues
  - Immunosuppressive therapy
  - Calcium channel blockers
  - Lamotrigine

Therapies that have not demonstrated efficacy in ALS (2)

- Gangliosides
- Antiviral agents
- Testosterone
- Chelation therapy
- Antiglutamate agents, such as branched-chain amino acids and dextromethorphan
- Anti-oxidants

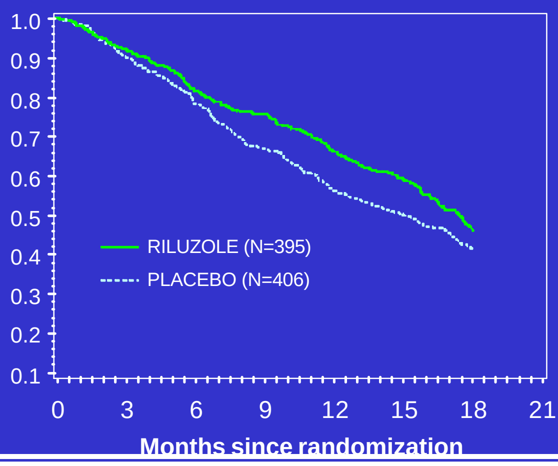
KEY ISSUES IN ALS/MND RESEARCH

- 1. What molecular pathways lead to cell death of motor neurones?
- 2. What factors are responsible for selective vulnerability of certain motor neurone groups?
- Are the pathways of cell death amenable to therapeutic intervention to the benefit of patients?

MOTOR NEURONE GROUPS SPARED IN MND

- III, IV, VI nuclei in brainstem - eye movements
- Onuf's nucleus sacral spinal cord - pelvic floor muscles

Meta-analysis - Results



WILCOXON: p = 0.016

LOGRANK: p = 0.043

HOMOGENEITY: p = 0.208

Guidelines for the treatment of ALS in Denmark

- Made by the Danish Society for Research in ALS
- The standards are normative
- Most neurological departments have now uniform principles for interventions

---

Goals for outcome and process in ALS- guidelines

- Goals for outcome
  - Optimal symptomatic interventions
  - Competent professional counselling

- Goals for the process
  - Satisfactory information
  - Continuity in the course of interventions
  - The patient is involved in all decisions
  - Well planned and properly timed interventions

ALS/MND

- Models of care has been developed in several countries within the last 10-15 years
- They depend on the local structure of the health- and social services
- Due to the low frequency of ALS the care model must be anchored in the hospital service

---

When is a model of care needed?

- When the disease is chronic severe, perhaps lifethreatening and multisymptomatic
- often the case in neurological disorders

Regular examinations

- The patient is seen in the ALS clinic every 2 or 3 month or when necessary
- The neurologist, the nurse and the physiotherapist are present
- Other team members can be send for
- Clinical examination, treatment and referrals are registered on data sheets

Functional scales

- A variety of scales and tests are available to assess the functional capacity of patients with ALS
  - Muscle strength testing (MRC scale, TNQE, MVIC)
  - Composite functional scales (Norris scale, Appel scale)
  - Respiratory function tests (FVC, peak-flow)
  - ALS Functional rating scale

Symptomatic treatments

- A number of palliative therapies are available for relieving the symptoms of ALS
  - physiotherapy
  - speech therapy
  - pharmacological intervention to treat symptoms
  - tracheostomy
  - gastrostomy

ALS clinic

For out-patients

- Day hospital with easy access to all team members
- Meals and bed available, when more than one examination

For in-patients

- ALS ward
- Educated staff
- Team members are wellknown from the dayhospital
- Open admission

First contact after diagnosis

- Peace and quiet
- No haste
- Relative or caregiver present
- Explain possible treatment
- What kind of help is available?
- Present team members and dayhospital
- Open admission

Expanding the care to the primary sector

- Information to the patients general practitioner
- Direct contact and collaboration between team members and their collegues in the social services concerning:
  - aids and alterations in the house
  - home care or physiotherapy

Telephone hours

- Daily telephone hour to the physiotherapist
- Direct line to the headnurse

Contact book

- The book follows the patient
- Contains:
  - Information concerning the disease, medication, appointments etc.
  - contact numbers to team members
  - advanced directives

Written information

- Leaflets about different symptoms and signs
- Books, free of charge for patients

Mutual conferences

- The team meets once a month
- The individual patient is discussed and measures taken to avoid delays
- The ALS counselor from the Institute of Neuromuscular Diseases participate

Patient support alliance

- Local groups
- Meetings for patients, their relatives and caregivers are arranged with
  - informal talks
  - instructions or demonstrations
  - visits

Quality control

- To maintain the standards in the treatment, the ALS team meets to evaluate the development

- To develop and keep evidens-based clinical guidelines

ALS-case

November 1996

61 year old male

No family history of ALS

First appearance of bulbar symptoms in august 96, progression.

Control of the tongue, cleaning the mouth, mild speech impairment and mild difficulties to swallow especially water, drooling and fatigue in the jaw muscles.

Loss of weight (122 kg to 98 kg in 2 years) after stopping alchohol.

Sensory symptoms on the left side of the face and in both feets

Frontal headache during 2 months, pain in the back, hips and knees. No complains from arms and legs.

Retired with a pension, divorced, 2 children (19 and 20 years)

Small apartment at 2.th floor, no lift (elevator)

Which others complains will you ask for if ALS ?

Neurological examination

Dysartria, do not have to repeat

Paresis of the muscles in the face, tongue (atophy, faciculations)

Increased jaw reflex

Increased reflexes and mild spasticity in the right arm and leg

Which investigations do you order and what to tell to the patient ?

CT-scan: Frontal cortical atrophy
X-ray of thorax: normal
Vital Capacity: 4 litre (98 %)
Bloodsamples: normal
EMG: neuropathy

Interventions or treatments ?

Speech therapy (15 lessons)
Dietitian ?

January 1997

Aggravation of the speech difficulties, ligthwriter (dyslexia)

Information to the patient, what to tell ?
Other treatment or interventions ?

February 1997

Lose the faculty of speech, increasing swallowing problems, increasing spasticity in the right side

Interventions ?

March 1997

Clinical examination and EMG in the face: bulbar ALS

No EMG alterations in the arms or legs

MRI: frontal cortical atrophy, protusion of the discus VI/VII

Body weight: 95 kg

Increasing problems with drooling

Mild depression

Vital capacity 1.5 litre

Interventions ?

May 1997

Fall, pain in the ribs (costal muscles). Emergency ward.

ALS-counselors: can’t use the lightwriter with the telephone (PC)

Using 1½ hour 2 times the days for feeding

Do not have a liquidizer (blender),

Interventions ?

Fall again, stayed overnight at hospital

June 1997

PEG at the hospital. Who pay for the diet ?

Restructuring of debts by the social worker.

Paresis in the right arm.

July 1997

ALS-counselors:

Increasing problems due to paresis in the right side (bath, turn in bed, get up erect, feed, make food)

Aids from the occupational therapist (nødkald)(telephone answering machine ??). Start to provide another housing.

Physiotherapist 2 times the week (pain and spasticity)

Local mobil care 2 time the week, distrect nurse x 1/week.

August 1997

ALS-counselors: and out-patient clinic:

Gait disturbances and falls, need a walker, wheelchair and transport (not a public bus)

Can’t contact anybody (only when he fall)

Start treatment with anti-spasticty drug

Starting CPAP (10 cm water x 3 daily)

Recommended for rehabilitation in Spain

September 1997

Approval to “nursing home” 1. October

License for a electric wheelchair

Out-patient clinic:

Dropfoot, body weight 84 kg, ½ litre increasing to 1½ litre. Can’t hold the head erect (neck collar).

I see the daughter for the first time

ALS-counselors and the local mobil care:

Needs more assistance

October 1997

Rehabilitaion in Spain !, but return because of falls, can’t contact anybody.

Die suddenly due to failure of respiration (oxygen ?)

Percutaneous Endoscopic Gastrostomy

- Literature suggests its beneficial effect in ALS
  - >50% patients experience dysphagia at some time
  - No randomized trials of PEG vs no PEG
  - 2001 Albert et al- biggest predictor of PEG use was patients baseline preference. Recommended early education.
  - 1999 Kasarski et al- (retrospective review)increased mortality with PEG insertion if FVC<50%.
  - 2002 Gregory et al- PEG <50% no effect on survival if used with NPPV, conscious sedation and oxygen.
  - 2003 ALS Care group- (retrospective review) late insertion of PEG no effect on survival. Recommended aggressive, proactive nutritional management.

- Nutrition management
  - Evaluating dysphagia
- Respiratory management
  - Early indicators of respiratory insufficiency
  - NPPV effects and use
  - Withdrawal of pulmonary support
- Palliative care
  - Managing Pain and dyspnea of ALS
  - Hospice and advance directives

- Monitor weight/FVC at each visit
- Begin education at first sign of dysphagia or FVC < 75%. (MD, Nurse, Speech Therapist)
- Interventional Radiology for Insertion
  - Anesthesiologist, conscious sedation, NPPV
- 2 day admission
- Begin feedings and education on care of PEG
- Discharge to Visiting Nurse Care for follow-up

ALS - PEG

1974 - 1986	1993 - 1998
• 2% PEG	• 46% PEG
• Survival 23 months	• Survival 33 months

Enteral nutrition in ALS Patients

- Bulbar dysfunction and nutritional status, including at least ***weight, should be checked at each visit***.
- 2. The patient and spouse should be referred to a dietician as soon as dysphagia appears. A speech and language therapist can give valuable advice on swallowing techniques.
- 3. The timing of PEG/PRG is based on an individual approach taking into account bulbar symptoms, malnutrition (weight loss > 10 %), respiratory function and the patient’s general condition. ***Thus, early operation is highly recommended.***
- 4. When PEG is indicated, patient and carers should be informed: a) of the benefits and risks of the procedure; b) that it is possible to continue to take food orally as long as it is possible; c) that deferring PEG to a late disease stage may increase the risk of the procedure.
- 5. Percutaneous Radiologic Gastrostomy (PRG; RIG) is a suitable alternative to PEG. This procedure can be used as the procedure of choice or when the PEG is deemed hazardous
- 6. Tubes with large diameter should be recommended for both PEG and PRG in order to prevent tube obstruction.
- 7. Prophylactic medication with antibiotics on the day of the operation may reduce the risk of infections.

Pulmonary Care

- PFT’s each visit (FVC and MIP)
- Breathing exercises
- Early introduction to NPPV
- Meet RT, see and try equipment
  - BIPAP and cough assist (In-exsufflator)
  - Success highly dependent on first approach and home care follow-up.

Issues Regarding Tracheostomy

- What - very individualized
  - Not until signs/symptoms evident
- Present all options, provide resource material (printed, video, patient meeting)
- Inflluenced by physician attitudes and recommendations
- Resources (finances and caregivers) are a big influence
- High functioning patient more likely to choose tracheostomy
- Advance directives put in place for most tracheostomy patients

BiPaP-behandling

- Ca. 1 års længere overlevelse,
- men mere væsentligt er livskvaliteten

Non-invasive and invasive ventilation

- 1. Symptoms or signs of respiratory insufficiency (including symptoms of nocturnal hypoventilation) should be checked at each visit.
- 2. VC is the most available and practical test for the monitoring of respiratory function on a regular basis. If possible, VC should be measured both standing/sitting and lying.
- 4. Nocturnal oxymetry, available at home, is recommended in patients with symptoms of nocturnal hypoventilation.
- 5. Symptoms or signs of respiratory insufficiency should initiate discussions with the patient and the caregivers about all treatment options such as NIV, TV and the terminal phase. Early discussions are needed to allow advance planning and directives. **The patient should be informed about the temporary nature of NIV** (which is primarily directed towards improving quality of life rather than prolonging it (as opposed to TV)).
- 7. TV can prolong survival for many months and can improve patient's quality of life, but it has major impact upon carers, and be undertaken only after full discussion of the pro's and con's with the patient and carers.
- 8. Oxygen therapy alone should be avoided as it may exacerbate CO_2 retention and mouth dryness.

ABSTRACT

- People affected with possible ALS should be examined as soon as possible by an experienced neurologists.
- **Early diagnosis should be pursued and a number of investigations should be performed with high priority.**
- The patient should be informed of the diagnosis by a consultant with a good knowledge of the patient and the disease.
- **Following diagnosis, the patient and relatives should receive regular support from a multi-diciplinary care team.**
- Medication with riluzole should be initiated as early as possible.
- **PEG is associated with improved nutrition and should be inserted early. The operation is hazardous in patients with VC < 50%. RIG may be a better alternative.**
- Non-invasive positive pressure ventilation improves survival and quality of life but is unfortunately underused. Maintaining the patients ability to communicate is essential.
- **During the entire course of the disease, every effort should be made to maintain patient autonomy.**
- Advance directives for palliative end of life care are important and should be fully discussed early with the patient and relatives *respecting the patients social, religious and cultural background*.