

ALS, Amyotrophe Lateralsklerose, amyotrophic lateral sclerosis, Myatrophische Lateralsklerose, Lou-Gehring Syndrom, Motor neuron disease, Charcot Krankheit.

Die **Amyotrophe Lateralsklerose (ALS)** ist eine degenerative Erkrankung des motorischen Nervensystems. **Ursachen der ALS** <http://www.als-charite.de/home/ursachen/>

Bildgebende Verfahren: Elektromyografie (EMG, Messung der elektrischen Muskelaktivität) und die Messung der **Nervenleitgeschwindigkeit** (ENG, Elektroneurografie).

Zum Ausschluss anderer neurologischer Erkrankungen: **Magnet-Resonanztomografie** (MRT), **Blut-Untersuchungen, Hirnwasser-Untersuchung** (Liquorpunktion).

Verde F et al. (2018) **Neurofilament light chain in serum for the diagnosis of amyotrophic lateral sclerosis**. J Neurol Neurosurg Psychiatry; DOI: 10.1136/jnnp-2018-318704 <https://jnnp.bmj.com/content/early/2018/10/11/jnnp-2018-318704>

Für die Therapie: Abgrenzung z.B.: zu **Parkinson (Schüttellähmung), Multipler Sklerose (MS)**, zu **Unterformen der ALS** (sporadisch, familiär, endemisch), **progressive spinale muskuläre Atrophie** oder der **Neuro-Borreliose**.

Amyotrophic lateral sclerosis (ALS) is a degenerative disease of the motor nervous system. **Causes of the ALS** <http://www.als-charite.de/home/ursachen/>

Electromyography (EMG, measurement of electrical muscle activity) and the measurement of **nervous conduction velocity** (ENG, Electoneurography).
To the exclusion of other neurological diseases: **magnetic resonance tomography** (MRT), **blood tests, brain water examination** (cerebrospinal fluid).

For the therapy: delimitation, eg: **Parkinson's disease, multiple sclerosis (MS), subforms of ALS** (sporadic, familial, endemic), progressive spinal cord muscular atrophy or **neuro-borreliosis**.

Immunology

Cruts M (1993), Cashman NR (1985), Jeong SY (2009), Mitchell J (2010), Deng HX (2011), DeJesus-Hernandez M (2011), Renton AE (2011), Herdewyn S (2012), Friedland RP (2012), Boeve BF (2012)

Bacteria

Waisbren BA (1987), Fredrikson S (1988), ElAalaoui F (1990), Halperin JJ (1990), Hänsel Y (1946, 1995), Miller AI (2017)

Mycoses, fungi

Alonso R (2017)

Toxins

Watts DL (1988), Dextro DT (1991), Yasui M (1993), Zecca L (2004), Mastroberardino PG (2009), Wang Q (2011), Rouault TA (2013), Veyrat-Durebex C (2014)

Charcot, J. M. (1874) De la sclérose latérale amyotrophique. Le Progrès médical, series 1, 2 : 325-327, 341-342, 453-455.

Gawel M, Zaiwalla Z, Rose FC. (1983) Antecedent events in motor neuron disease. J Neurol Neurosurg Psychiatry. 46(11), 1041-3.

[Salazar AM](#), [Masters CL](#), [Gajdusek DC](#), [Gibbs CJ Jr](#) (1983) **Syndromes of amyotrophic lateral sclerosis and dementia: relation to transmissible Creutzfeldt-Jakob disease.** *Ann Neurol.* 14(1), 17-26. <https://www.ncbi.nlm.nih.gov/pubmed/6351721>

« **The findings suggest that most cases of dementia associated with early amyotrophy are more closely related to classic amyotrophic lateral sclerosis than to transmissible Creutzfeldt-Jakob disease and do not deserve the label of "amyotrophic Creutzfeldt-Jakob disease** »

Cashman NR, Gurney ME, Antel JP. (1985) Immunology of amyotrophic lateral sclerosis. Springer Semin Immunopathol. 8(1-2), 141-52. Review.

Waisbren BA, Cashman N, Schell RF, Johnson R. (1987) **Borrelia burgdorferi antibodies and amyotrophic lateral sclerosis.** Lancet. 2(8554), 332-3.

Fredrikson S, Link H. (1988) **CNS-borreliosis selectively affecting central motor neurons.** Acta Neurol Scand 78, 181-184 [Medline].

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EIAlaoui F, Medejel A, AlZemmouri K, Yahyaoui M, Chkili T. (1990) **Syphilitic lateral amyotrophic sclerosis.** A study of 5 cases. Rev Neurol 146, 41-44 [Medline].

[Halperin JJ](#), [Kaplan GP](#), [Brazinsky S](#), [Tsai TF](#), [Cheng T](#), [Ironsides A](#), [Wu P](#), [Delfiner J](#), [Golightly M](#), [Brown RH](#), et al. (1990) **Immunologic reactivity against Borrelia burgdorferi in patients with motor neuron disease.** *Arch Neurol.* 47(5), 586-94. <http://www.ncbi.nlm.nih.gov/pubmed/2334308>
„**There appears to be a statistically significant association between ALS and immunoreactivity to B burgdorferi, at least among men living in hyperendemic areas.**“

[Yasui M](#), [Ota K](#), [Garruto RM](#) et al. (1993) **Concentrations of zinc and iron in the brains of Guamanian patients with amyotrophic lateral sclerosis and parkinsonism-dementia.** *Neurotoxicology.* 14(4), 445-50. <http://www.ncbi.nlm.nih.gov/pubmed/8164889>

Oba H, Araki T, Ohtomo K, Monzawa S, Uchiyama G, Koizumi K, Nogata Y, Kachi K, Shiozawa Z, Kobayashi M. (1993) **Amyotrophic lateral sclerosis: T2 shortening in motor cortex at MR imaging.** *Radiology.* 189(3), 843-6. *PubMed.* <https://www.ncbi.nlm.nih.gov/pubmed/8234713>

Cruts M, Engelborghs S, van der Zee J, Van Broeckhoven C (1993) **C9orf72-Related Amyotrophic Lateral Sclerosis and Frontotemporal Dementia.** In Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJ, Stephens K, Amemiya A. *GeneReviews.* Seattle (WA): University of Washington, Seattle. [PMID 25577942](https://pubmed.ncbi.nlm.nih.gov/25577942/).

Carelli V, Liguori R, Cordivari C, Bianchedi G, Montagna P. (1994) **Ceftriaxone is ineffective in ALS.** *Ital J Neurol Sci.* 15(1), 66.

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Halperin J, Logigian E, Finkel M, Pearl R. (1996) Practice parameters for the diagnosis of patients with nervous system Lyme borreliosis (Lyme disease). *Neurology.* 46, 619_27.

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„Here we report that minocycline delays disease onset and extends survival in ALS mice. Given the broad efficacy of minocycline, understanding its mechanisms of action is of great importance. We find that minocycline inhibits mitochondrial permeability-transition-mediated cytochrome c release. Minocycline-mediated inhibition of cytochrome c release is demonstrated in vivo, in cells, and in isolated mitochondria. Understanding the mechanism of action of minocycline will assist in the development and testing of more powerful and effective analogues. Because of the safety record of minocycline, and its ability to penetrate the blood-brain barrier, this drug may be a novel therapy for ALS.“

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“By studying the accumulation and cellular distribution of iron during ageing, we should be able to increase our understanding of these neurodegenerative disorders and develop new therapeutic strategies.”

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[Qureshi M](#), [Bedlack RS](#), [Cudkowicz ME](#). (2009) **Lyme disease serology in amyotrophic lateral sclerosis.** Muscle Nerve. 40(4), 626-8. doi: 10.1002/mus.21438. [Abstract URL](#), [DOI BibTeX](#) <http://www.ncbi.nlm.nih.gov/pubmed/19697382>
„Lyme disease was rare in 414 patients with ALS and is not likely to be causative.“

Williams AH et al. (2009) MicroRNA-206 Delays ALS Progression and Promotes Regeneration of Neuromuscular Synapses in Mice. *Science*, 326, 1549-1554.

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<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2867752/>
„DAO [mutation in the D-amino acid oxidase gene (R199W DAO)] controls the level of D-serine, which accumulates in the spinal cord in cases of sporadic ALS and in a mouse model of ALS, indicating that this abnormality may represent a fundamental component of ALS pathogenesis.“

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CONCLUSIONS: These results provide evidence that iron is involved in the pathogenesis of ALS and iron chelation therapy may have the potential for the prevention and treatment of ALS.

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Renton AE, Majounie E, Waite A et al. (2011) **A hexanucleotide repeat expansion in C9ORF72 is the cause of chromosome 9p21-linked ALS-FTD**. *Neuron*. 72 (2), 257–68. doi:10.1016/j.neuron.2011.09.010. PMC 3200438. PMID 21944779.

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[Rouault](#) TA (2013) **Iron metabolism in the CNS: implications for neurodegenerative diseases**. *Nature Reviews Neuroscience* 14, 551–564 doi:10.1038/nrn3453 <https://www.nature.com/articles/nrn3453>

Deng HX, Chen W et al. (2011) **Mutations in UBQLN2 cause dominant X-linked juvenile and adult-onset ALS and ALS/dementia**. In: *Nature*. doi:10.1038/nature10353
„Here we show that mutations in UBQLN2, which encodes the ubiquitin-like protein ubiquilin \square 2, cause dominantly inherited, chromosome-X-linked ALS and ALS/dementia. We describe novel ubiquilin \square 2 pathology in the spinal cords of ALS cases and in the brains of ALS/dementia cases with or without UBQLN2 mutations. Ubiquilin \square 2 is a member of the ubiquilin family, which regulates the degradation of ubiquitinated proteins. Functional analysis showed that mutations in UBQLN2 lead to an impairment of protein degradation. Therefore, our findings link abnormalities in ubiquilin \square 2 to defects in the protein

degradation pathway, abnormal protein aggregation and neurodegeneration, indicating a common pathogenic mechanism that can be exploited for therapeutic intervention.“

Dr David Martz - 2011 IDA Research Award <https://www.youtube.com/watch?v=UY9FdULDV6M>

MacDonald A (2012) [TREATMENT TO REVERSE MOTOR NEURON DISEASE](#)

Veyrat-Durebex C, Corcia P, Mucha A (2014) Research Article. **Iron Metabolism Disturbance in a French Cohort of ALS Patients.** BioMed Research International. Volume 2014 (2014), Article ID 485723, 6 pages. <http://dx.doi.org/10.1155/2014/485723> <http://www.hindawi.com/journals/bmri/2014/485723/>
„**Conclusion. This is the first study showing a higher concentration of serum iron in ALS patients, strengthening the involvement of a deregulation of iron metabolism in ALS“.**

Ahmet Z Burakgazi AZ (2014) **Lyme Disease -Induced Polyradiculopathy Mimicking Amyotrophic Lateral Sclerosis..** The International journal of neuroscience. [Abstract URL](#), [DOI](#) [BibTeX](#)

NIH **Amyotrophic Lateral Sclerosis (ALS) Publications** (2014)
http://www.ninds.nih.gov/disorders/amyotrophiclateralsclerosis/pubs_ALS.htm

MMWR (2014) Prevalence of Amyotrophic Lateral Sclerosis — United States, 2010–2011. Surveillance Summaries / Vol. 63 / No. 7 ISSN: 1546-0738
<http://www.cdc.gov/mmwr/pdf/ss/ss6307.pdf>

[Chio A](#), [Calvo A](#), [Dossena M](#), [Ghiglione P](#), [Mutani R](#), [Mora G](#) (2009) **ALS in Italian professional soccer players: the risk is still present and could be soccer-specific.** [Amyotroph Lateral Scler.](#) 10(4):205-9. doi: 10.1080/17482960902721634.
<https://www.ncbi.nlm.nih.gov/pubmed/19267274>
« **The absence of ALS cases in professional road cyclists and basketball players indicates that ALS is not related to physical activity per se.** »

[Alonso R](#), [Pisa D](#), [Fernández-Fernández AM](#) (2017) **Fungal infection in neural tissue of patients with amyotrophic lateral sclerosis.** [Neurobiol Dis.](#) 108, 249-260. doi: 10.1016/j.nbd.2017.09.001. Epub 2017 Sep 6. <https://www.ncbi.nlm.nih.gov/pubmed/28888971>
„**Overall, our present observations provide strong evidence for mixed fungal infections in ALS patients. The exact mixed infection varies from patient to patient consistent with the different evolution and severity of symptoms in each ALS patient.**“

- ➔ **Elektrolyte und Spurenelemente** http://www.xerlebnishaft.de/elektro_spur_ph.pdf
- ➔ **Wasserstoffionenkonzentration, PH-Wert** <http://www.kabilahsystems.de/ph.pdf>
- ➔ **Mitochondrien Dysfunktion etc.** <http://www.xerlebnishaft.de/mitochondrien.pdf>,
Mitochondrien Therapie http://www.kabilahsystems.de/q10_und_l.pdf
- ➔ **Zytoskelett-Krankheiten** <http://www.xerlebnishaft.de/zytoskelett.pdf>
- ➔ **Fettsäuren (Zellmembran)** <http://www.kabilahsystems.de/ungesaettfetts.pdf>
- ➔ **Biogene Amine und Peptide** <http://www.kabilahsystems.de/biogeneamineundpeptide.pdf>
- ➔ **Zytokine, zelluläre Abwehr** http://www.xerlebnishaft.de/kommentinhalt_zell.pdf

- ➔ **Antimikrobiotikose** <http://www.kabilahsystems.de/antibiosetherapieplan.pdf>
- ➔ **Begleit-Therapien** <http://www.kabilahsystems.de/kommentmedbegleittherapie.pdf>
- ➔ **Antibiotikatherapie Spektrum** www.kabilahsystems.de/therap_01_basis.pdf

- ➔ **C9orf72** <https://en.wikipedia.org/wiki/C9orf72>

Vaulont S, Lou DQ, Viatte L, Kahn A (2005) **Of mice and men: the iron age.** J. Clin. Invest. 115(8), 2079–2082, doi:10.1172/JCI25642, PMID 16075054, PMC 1180554
<https://www.ncbi.nlm.nih.gov/pubmed/16075054>
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1180554/>

**Eisen-Toxizität sei bei ca. 30% der ALS – Patienten nachweisbar;
Iron toxicity is seen at about 30% of ALS – patients;**

**Diagnostik: Klinik, Ferritin, Transferrin, Serumeisen.
Diagnose: Clinic, Ferritin, Transferrin, Serum iron.**

**Therapie: Aderlass, Chelattherapie mit Deferasirox (oral, einmal täglich)
Therapy: Bloodletting, chelation with deferasirox (orally once daily) oder/or
Deferipron (cave Neutropenie oder Agranulozytose), oder Deferoxamin als Infusion**

„Sehr aufwändig für die Erkrankten: So müssen diese in der Regel an fünf bis sieben Tagen pro Woche eine acht- bis zwölfstündige Infusion in das Unterhautfettgewebe erhalten. Da die Eisenchelate-Therapie über viele Jahre verläuft, war die Therapietreue in der Vergangenheit häufig entsprechend schlecht - zum Teil mit ernsthaften gesundheitlichen Folgen“.

"Very consuming for the patients: these must usually five to seven days per week an eight- to twelve-hour infusion received in the subcutaneous fatty tissue. Since the iron chelate Therapy extends over many years, treatment adherence was often in the past correspondingly poor - some with serious health consequences."

Dexter DT, Carayon A, Javoy-Agid F et al. (1991) **Alterations in the levels of iron, ferritin and other trace metals in Parkinson's disease and other neurodegenerative diseases affecting the basal ganglia.** Brain 114, 1935-75

Mastroberardino PG, Hoffman EK, Horowitz MP et al. (2009) **A novel transferrin/TfR2-mediated mitochondrial iron transport system is disrupted in Parkinson's disease.** Neurobiol. Dis. 34(3), 417–431, [doi:10.1016/j.nbd.2009.02.009](https://doi.org/10.1016/j.nbd.2009.02.009), [PMID 19250966](https://pubmed.ncbi.nlm.nih.gov/19250966/), [PMC 2784936](https://pubmed.ncbi.nlm.nih.gov/2784936/)
<https://www.ncbi.nlm.nih.gov/pubmed/19250966>

➔ **Parkinson, Alzheimer** <http://www.erlebnishaft.de/alzheimerspirochaetosis.pdf>

➔ **Miller AI (2017) Lyme Disease.** <https://www.youtube.com/watch?v=Fr61GV8JCYQ>

[Bernt - Dieter Huismans](http://www.Huismans.click) Letzte Revision Januar 2019 www.Huismans.click 
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