Supplementary Table 1: ALS Reversals- Diagnostic Information

ID	Regions with upper motor neuron signs on exam	Regions with lower motor neuron signs on exam	Regions with EMG denervation (D) and reinnervation (R)	Lab tests to exclude mimics
2	lumbosacral	cervical, lumbosacral	D: cervical, thoracic, lumbosacral R: cervical, lumbosacral	PTH, RF, SPEP, TSH, Free T4, CBCd, BMP, CK, CRP, HIV 1/2, Syphilis Treponemal IgG, HTLV1/2, AChR Binding Ab, Lyme ELISA, CSF Glucose, CSF Cells, CSF OCBs, CSF Lyme ELISA
4	lumbosacral	bulbar, cervical, thoracic, lumbosacral	D: cervical	'Lyme IgG IgM Ab', CMP, CBCd, TSH, B12, Magnesium; Free T4 (1.9 ng/dL)
5	cervical, lumbosacral	cervical, thoracic	D: cervical, lumbosacral R: cervical, lumbosacral	TSH, PSA

6	bulbar, cervical, lumbosacral	cervical, lumbosacral	D: cervical, lumbosacral	GM1, SPEP, ESR
8 (1)	cervical, lumbosacral	cervical, lumbosacral	D: cervical, lumbosacral	CBCd, CK, ESR, SPEP, 'TFTs', B12, ANA, Ca, Lead, Mercury, Arsenic, 'CSF'
9 (1)	lumbosacral	cervical, thoracic, lumbosacral	D: bulbar, cervical R: cervical, lumbosacral	CBCd, CK, ESR, SPEP, 'TFTs', B12, ANA, Ca, Lead, Mercury, Arsenic
10 (1)	cervical, lumbosacral	cervical, thoracic, lumbosacral	D: lumbosacral R: lumbosacral	CBCd, CK, ESR, SPEP, 'TFTs', B12, ANA, Ca, Lead, Mercury, Arsenic, 'CSF'
11 (1)	none	cervical, thoracic, lumbosacral	D: cervical, thoracic, lumbosacral R: cervical, thoracic, lumbosacral	CBCd, CK, ESR, SPEP, 'TFTs', B12, ANA, Ca, Lead, Mercury, Arsenic, 'CSF'

12 (2)	bulbar, cervical, lumbosacral	bulbar, cervical, lumbosacral	D: bulbar, cervical, thoracic, lumbosacral R: bulbar, cervical, thoracic, lumbosacral	CK, 'Ganglioside Abs', 'Paraneoplastic Abs'
13 (3)	cervical, lumbosacral	bulbar, cervical, lumbosacral	D: bulbar, cervical, thoracic, lumbosacral R: bulbar, cervical, thoracic, lumbosacral	Electrolytes, CK, 'TFTs', SPEP, 'Complement and Vitamin levels', HTLV 1/2, VDRL, 'HIV', RF, ANA, Anticardiolipin, Lupus Anticoagulant, SSA, SSB, Anti-DNA, Anti-RNP, Anti-Sm, Lead, Mercury, Arsenic, PSA, CEA, AFP, 'CSF'
14	bulbar, cervical	bulbar, cervical, lumbosacral	D: cervical, lumbosacral R: cervical, lumbosacral	CK, TSH, SPEP
22 (4)	lumbosacral	bulbar, cervical, lumbosacral	D: cervical, thoracic, lumbosacral R: cervical, thoracic, lumbosacral	CBCd, Ca, BMP, 'TFTs', SPEP, GM1, GD1a, GT1b, CSF Cells, CSF Protein

23 (5)	cervical, lumbosacral	bulbar, cervical, lumbosacral	D: bulbar, cervical, lumbosacral R: bulbar, cervical, lumbosacral	Anti-RNP, P-ANCA, C-ANCA, HTLV-1, 'low-titer IgM anti-GM1', 'CSF'
24	cervical, lumbosacral	bulbar, cervical, lumbosacral	D: cervical, lumbosacral	CK, CBC, TSH, RF, RPR, 'HIV', 'HTLV', SPEP, B12, 'C3b/Raji Cell', 'C1q Binding Ab', GM1, CSF Cells, CSF Protein, CSF Glucose, CSF OCBs, CSF VDRL
25 (6)	cervical, lumbosacral	cervical, lumbosacral	D: cervical, lumbosacral R: cervical, lumbosacral	CBC, ESR, SPEP, Ca
26 (7)	none	bulbar, cervical, lumbosacral	'diffuse denervation in the form of fibrillation, giant potentials, positive spikes, and reduced interference pattern'	Lead, Arsenic, Mercury, 'TFTs', CSF 'including CSF protein'; CK 'minimally elevated'
27 (8)	none	cervical, lumbosacral	D: cervical R: cervical	'Laboratory data were normal except for CSF protein of 76 mg/dL'

28	bulbar, 'brisk reflexes throughout'	cervical, lumbosacral	D: cervical, lumbosacral R: cervical, lumbosacral	ANA, ANCA, 'ENA', 'tTG'
31 (9)	cervical, lumbosacral	cervical, lumbosacral	D: cervical, lumbosacral R: cervical, lumbosacral	None
32 (10)	bulbar, cervical, lumbosacral	cervical, lumbosacral	D: cervical R: cervical, lumbosacral	ESR, TSH, RPR, CSF Cells, CSF Protein
33 (11)	bulbar, cervical, lumbosacral	cervical, lumbosacral	D: cervical, lumbosacral R: cervical, lumbosacral	'Paraneoplastic panels', 'Ganglioside panels', and 'CSF'
34 (12)	cervical, lumbosacral	cervical, lumbosacral	D: cervical, lumbosacral R: cervical, lumbosacral	CSF Cells; AChR Binding Ab (9.47 nmol/L), Striational Ab ('15,360'), AChR Modulating Ab ('100% loss'), 'positive thyroglobulin ab', 'positive ANA', CSF Protein ('50 mg%')

35 (13)	none	bulbar, cervical, lumbosacral	D: cervical R: cervical	MuSK Ab RIA, Cu
37	bulbar, cervical, lumbosacral	cervical, lumbosacral	D: bulbar, cervical, thoracic, lumbosacral R: bulbar, cervical, thoracic, lumbosacral	RF, 'Citrullinated peptic ab', SSA, SSB, Anti JO-1, CBC, CMP, Ca, MMA, RPR, ANNA Type 1-3, AGNA-1, PCA Type 1, 2, Tr, Amphiphysin Ab, CRMP-5-IgG, Striational Ab, P/Q-, N-Type Ca Channel Binding Ab, AChR Binding Ab, AChR Ganglionic Neuronal Ab, VGKC Ab, HTLV1/2, HIV1/2, B12, TSH, Free T4; Cu (2.09 mcg/mL), CK (373 U/L), ESR (58 mm/hr), ANA (1:160 speckled, 1:40 nucleolar)
38	bulbar, cervical, lumbosacral	bulbar, cervical, lumbosacral	D: bulbar, cervical, thoracic, lumbosacral R: bulbar, cervical, thoracic, lumbosacral	HIV 1, Folate, B12, TSH, ESR, Lyme ELISA, SSA, SSB, BMP, CBC, CSF Cells, CSF VDRL; positive RPR/FTA-ABS, Thiamine (11.7 ng/mL), ANA (1:160 speckled)
42	cervical, lumbosacral	bulbar, cervical	D: cervical R: cervical, lumbosacral	None

50	bulbar, lumbosacral	bulbar, cervical, lumbosacral	D: cervical, lumbosacral R: bulbar, cervical, lumbosacral	CBCd, B12, CK, SPEP, TSH, Lyme ELISA, 'serologic testing for myasthenia'
54	none	cervical, lumbosacral	D: cervical, lumbosacral R: cervical, lumbosacral	HIV 1, CBC, Electrolytes, TSH, ESR, RPR, IgG, IgA, IgM, ANA, Lyme Fluorescent EIA, Cryoglobulins, GM-1
60	none	bulbar, cervical, lumbosacral	D: cervical, lumbosacral R: cervical, lumbosacral	ANA, IgG, IgA, IgM, Urine Arsenic, Urine Lead, Urine Mercury
67	bulbar, cervical, lumbosacral	cervical, lumbosacral	D: cervical, thoracic, lumbosacral R: cervical, lumbosacral	FTA-ABS, RF, ANA, 'TFTs', CBCd, 'PEP', Ca, GM1, GD1b; CK (1562 IU/L)
76	none	cervical, lumbosacral	R: cervical, thoracic, lumbosacral D: lumbosacral	'Negative serology for syphilis, Lyme, and HIV', 'CBC, renal function, thyroid'; CK (271 U/L), IgG Kappa Paraprotein ('could not be quantified')

77	bulbar, thoracic	cervical, thoracic, lumbosacral	D: cervical, thoracic, lumbosacral R: cervical, thoracic, lumbosacral	'Negative serology for syphilis, Lyme, HIV', CK; TSH (6.8 mIU/L), B12 (148 pmol/L), Homocysteine ('27.5')
84	bulbar, cervical, lumbosacral	bulbar, cervical, lumbosacral	D: cervical, lumbosacral R: cervical, lumbosacral	ANCA, Immunofixation, 'complement', CRP, SPEP, Lead, Mercury, Arsenic, B12, GM1, GM2, GM3, GD1a, GD1b, GT1b, GQ1b, ESR, Anti-dsDNA, SSA, SSB, Anti-Centromere, Anti-Histone, Anti-Smooth Muscle, Anti-RNP, Anti-Ribosomal, AMA-M2, Anti-PCNA, Anti-Topoisomerase 1, 'kappa/lambda light chains', Beta-hexosaminidase, HBsAg, TSH, PTH, CBC, LDH, CSF Cells, CSF Protein; CK ('789'), ANA (1:160 speckled)
92	lumbosacral	bulbar, cervical, lumbosacral	D: cervical, thoracic, lumbosacral R: cervical, lumbosacral	CBCd, CK, HIV1/2, Syphilis Treponemal IgG, CRP, Free T4, TSH, B12, RF, SPEP, Lyme ELISA, HTLV 1/2, AchR Binding Ab, CSF Protein, CSF Cells; ANA (1:80 speckled), PTH (90 pg/mL)
97	bulbar, cervical, lumbosacral	bulbar, cervical, lumbosacral	D: cervical, thoracic, lumbosacral R: bulbar,	tTG IgA, Cu, CBC, Free T4, B12, ANA, ANNA type 1-3, AGNA-1, PCA Type 1, 2, Tr, Amphiphysin Ab, CRMP-5-IgG, Striational Ab, P/Q-, N-Type Ca Channel Binding Ab, AchR Binding Ab, AchR

			cervical, thoracic, lumbosacral	Ganglionic Neuronal Ab, VGKC Ab, SPEP, CRP, ESR, Cryoglobulins, MPO ELISA, PR3 ELISA; p-ANCA ('positive'), CK (251-5393 U/L), TSH (0.66-87.3 mIU/L)
99	bulbar, cervical, lumbosacral	bulbar, lumbosacral	D: lumbosacral R: lumbosacral	Unknown

PTH= parathyroid hormone; RF= rheumatoid factor; (S)PEP= (serum) protein electrophoresis; TSH= thyroid stimulating hormone; T4= thyroxine; CBC(d)= complete blood counts (with differential); BMP= basic metabolic panel; CK= creatine kinase; CRP= C-reactive protein; HIV= human immunodeficiency virus; Ig= immunoglobulin; HTLV= human t-lymphotrophic virus; AchR= acetylcholine receptor; Ab= antibody; CSF= cerebrospinal fluid; OCBs= oligoclonal bands; CMP= comprehensive metabolic panel, PSA= prostate specific antigen; ESR= erythrocyte sedimentation rate; TFTs= thyroid function tests; ANA= anti-nuclear antibody; Ca= calcium; VDRL= venereal disease research laboratory test; SS(A/B)= Sjögren's-syndrome related antigen (A/B); RNP= ribonucleoprotein, Sm= smith; CEA= carcinoembryonic antigen; AFP=alpha-fetoprotein; (P/C)-ANCA= (perineuclear/cytoplasmic) anti-neutrophil cytoplasmic antibody; RPR= rapid plasma 9ollap; ENA= extractable nuclear antigen; tTG= tissue transglutaminase; AchR= acetylcholine receptor; MuSK= muscle-specific kinase; RIA= radioimmunoassay; Cu= copper; MMA= methylmalonic acid; ANNA= antineuronal nuclear antibody; AGNA= anti-glial/neuronal nuclear antibody; PCA= Purkinje cell cytoplasmic antibody;

CRMP= collapsin response-mediator protein; VGKC= voltage-gated potassium channel; FTA-ABS= fluorescent treponemal antibody absorption test; EIA= enzyme immunoassay; dsDNA= double stranded DNA; AMA= antimitochondrial antibody; PCNA= proliferating cell nuclear antigen; HBsAg= hepatitis B serum antigen; LDH= lactate dehydrogenase; MPO= myeloperoxidase; PR3= proteinase 3

This table includes information used to confirm the diagnoses of cases. Uncited cases were identified through chart review. All cases had a history of progressive weakness involving more than one body region. All cases had exclusion of mimics by electrophysiological testing, except participant 33, for whom nerve conduction study data was not available. There were 4 cases (participants 8, 9, 25, and 26) who did not have neuroimaging and 3 additional cases (participants 4, 60, and 75) in whom presence or absence of neuroimaging could not be confirmed. Only abnormal values are specified in the list of lab tests.

Supplementary Table 2: ALS Reversals- Reversal Information

ID	Months between symptom onset and nadir	Key measures at nadir	Key measures at maximum improvement	Months between nadir and maximum improvement
2	5	Exam: D 5/4, B 4/4, T 4+/4+, WE 3/4, HF 5/4, KE 5/4+	Exam: D 5-/5, B 5-/5, T 5/5, WE 3/5, HF 5-/5-, KE 5/5	9
4	144	'on a ventilator and in a wheelchair… almost totally paralyzed'	Exam: frontalis 5/4, neck flexion/extension 2/2, T 0/3, B 0/1, Grip 3/0, APF 3/3 Respiratory: 10 min off ventilator with no dyspnea	206
5	5	ALSFRS-R: 39 Exam: D 3/5, B 4/4, T 4/5, WE 4/4, FE 3/5, FDI 3/4, APB 5/3	ALSFRS-R: 43 Exam: normal strength	3

6	48	*Exam: 'slight weakness of quads and hamstrings', 'dramatic weakness in right LE ADF, APF, inversion, eversion', left ADF 4+	*Exam: decreased strength in distal right LE with atrophy and foot drop, otherwise 5/5 throughout	32
8	1	*Exam: 'mild weakness of anterior neck, shoulder, and upper arm muscles, mild weakness of the intrinsic muscles of one hand, marked weakness of psoas muscles, and mild weakness of the distal leg muscles'	*Exam: barely perceptible weakness in the upper arms	5
9	3	*Exam: cervical and lumbosacral weakness	*Exam: normal strength	12
10	4	*Exam: cervical and lumbosacral weakness	*Exam: normal motor exam	8
11	4	*Exam: lumbosacral weakness EMG: abundant positive waves and moderate numbers of fibrillation potentials in all four limbs	*Exam: normal strength EMG: no positive waves or fibrillation potentials	12
12	48	ALSFRS-R: 31	ALSFRS-R: 47	43
13	16	Exam: 3/3 UE strength, 2/2 LE strength	*Exam: normal strength EMG: normal	26

		EMG: acute and chronic denervation involving bulbar, axial, and appendicular myotomes		
14	60	*Exam: weakness in neck flexion/extension, T 4+/3+, APF 3+/4, ADF 3+/3	Exam: SCM/trapezius 5/5, T 5/5, APF 4/4, ADF 4/4 Respiratory: improved FVC	40
22	12	*Exam: bilateral UE and LE weakness	*Exam: mild weakness in right limbs EMG: reinnervation, but no denervation in limb muscles	18
23	12	Exam: neck 2.5, UE 2.5/2.5, proximal LE 3/3 EMG: diffuse denervation and reinnervation in the extremities	Exam: neck 4, UE 4/4, proximal LE 4/4 EMG: denervation in tongue and left ECR but not other limb muscles	12
24	96	ALSFRS-R: 29	ALSFRS-R: 41	Unknown
25	7	*Exam: minimal weakness in left UE and LE; moderate weakness in left hamstrings; more pronounced weakness in left biceps, iliopsoas, and gastroc	*Exam: minimal left wrist extensor weakness, otherwise normal exam EMG: no definite evidence of denervation	7

26	28	unable to walk, feed himself, turn over in bed, move the blanket, or hold head up when propped in a sitting position	could make certain movements which he had previously lost, independent in taking care of himself and traveling for business	Unknown
27	14	*Exam: D 3/3, parascapular muscles 4/4, B 4/4, T 4/4, slightly less weakness of hand muscles, HF 4+/4+	*Exam: normal	7
28	9	Exam: FE 3/3, shoulder flexion/extension 4/4, HF 4/4, HE 4/4, '4-4+/5' throughout	*Exam: 'generally does not present in any way now with features of MND', 'has good strength and this was demonstrated by no weakness on proximal testing when he went down on his haunches'	11
31	135	ALSFRS-R: 37	ALSFRS-R: 47	69
32	8	*Exam: quadriplegic with breathing dysfunction	*Exam: return to baseline of bulbar and cervical function, ability to walk, not run	17
33	18	ALSFRS-R: 27 HHD: upper 90%, lower 100%	ALSFRS-R: 46 HHD: upper 125%, lower 116%	9
34	8	ALSFRS-R: 30	ALSFRS-R: 43	1

		Respiratory: FVC 1.37	*Exam: 'muscle power improved', 'foot drop resolved partially' Respiratory: FVC 1.63	
35	36	ALSFRS-R: 21 Exam: WF 0/0, WE 0/0, HF 2-/2-, KE 2-/2-, ADF 2-/2-	ALSFRS-R: 29 Exam: WF 2-/2-, WE 2-/2-, HF 3-/3-, KE 4/4, ADF 5/5	12
37	8	Exam: proximal UE 4+/4+, intrinsic hand muscles 4+/4+, proximal LE 3/3, distal LE 4+/4+ EMG: denervation and reinnervation in bulbar, cervical, thoracic, and lumbosacral regions	Exam: UE 5/5, LE 4+/4+ EMG: normal in cervical, thoracic, and lumbosacral regions (bulbar not tested)	7
38	19	EMG: denervation and reinnervation of bulbar, cervical, thoracic, and lumbosacral regions ALSFRS: 28	EMG: no evidence of active denervation or reinnervation (bulbar not tested) ALSFRS-R: 42	23
42	8	ALSFRS-R 41 Exam: FA 0/0, FE 0/3	ALSFRS-R 47 Exam: FA 5/4, FE 5/5	18

50	24	*Exam: weakness of tongue and neck flexion, hand weakness L>R, proximal LE 4/4, distal LE 4+/4+	Exam: cranial nerves intact, normal strength	3
54	5	*Exam: D 4.2/5, T 4.2/5, WE 4.8/5, WF and bilateral intrinsic hand muscle weakness, ADF 4.8/4.2, EHL 4.2/4.2, FDL 5/4.5, PL 5/4, PT 5/4.8	*Exam: weakness in left ADF/APF, otherwise 5/5 strength throughout EMG: reinnervation, but no active denervation in bilateral LE	2
60	8	'unable to walk or stand, respiratory difficulty with apneic spells, speech changes and dysphasia'	'able to walk three miles, had no speech, swallowing, or breathing difficulties, and exercised 3x per week'	60
67	24	Exam: D 5-/5-, B 5-/5, T 4/5, WE 4/4, hand intrinsics 4/4, HF 3/3, ADF 4+/4+	Exam: 4/4 FE, 4/4 FF, 4/4 HF, otherwise 5/5 EMG: resolution of fascics and sustained PSWs in all muscles tested; some unsustained PSWs +/- fibs remain	70
76	18	*Exam: distal weakness of the legs left > right, trouble walking, climbing stairs, unable to jog	*Exam: very mild foot drop, no limitations in daily life	24

77	20	Respiratory: FVC 63% predicted *Exam: weakness of bilateral biceps and deltoids	Respiratory: FVC >80% predicted *Exam: full strength of biceps and deltoids	5
84	32	ALSFRS-R 22	ALSFRS-R 26	1
92	12	EMG: acute and chronic denervation of right arm and bilateral legs; acute denervation of thoracic paraspinals	EMG: fasciculations of left FDI; otherwise normal	21
97	48	ALFRS-R 21 Used gastrostomy tube for medications	ALSFRS-R 29 Gastrostomy tube removed	12
99	132	ALSFRS-R 25 Exam: D 4/4, B 4+/4-, T 4+/4-, WF 4+/3, FE 4+/4+, FF 5/4, FA 4+/4+, ADM 5/3, HAd 4+/4+, KE 4+/4, KF 4+/4+, ADF 5/3 Respiratory: FVC 79% predicted	ALSFRS-R 32 *Exam: full strength Respiratory: FVC 90% predicted	13

SCM= sternocleidomastoid; D= deltoid; B= biceps; T= triceps; WF= wrist flexion; WE= wrist extension; ECR= extensor carpi radialis; FE= finger extension; FF= finger flexion; FDI= first dorsal interosseous; APB= abductor pollicis brevis; FA= finger abduction; ADM= abductor digiti minimi; HF= hip flexion; HE= hip extension; HAd= hip adduction; KF= knee flexion; KE= knee

extension; ADF= ankle dorsiflexion; APF= ankle plantarflexion; PL= peroneus longus; PT= peroneus tertius; EHL= extensor hallucis longus; FDL= flexor digitorum longus; UE= upper extremity; LE= lower extremity; ALSFRS(-R)= ALS Function Rating Scale(-Revised); EMG= electromyogram; HHD: handheld dynamometry; FVC= forced vital capacity; PSW= positive sharp waves

This table includes information on magnitude and duration of improvements made by cases. Strength is noted as 'right/left' unless otherwise specified.

*On exams marked with asterisks, some or all strength measurements were not made using the medical research council scale.

Supplementary Table 3: Treatments used by ALS Reversals

Treatments	Dose Range (units/day)	Odds Ratio	CI	Statistical Test	Result
Curcumin	N/A	348	66.5-1,820	X^2= 48.1	p< .0001
Luteolin	300-2,000 mg	333	44.9-2,460	X^2= 32.3	p< .0001
Cannabidiol	N/A	261	55.1-1,230	X^2= 49.2	p< .0001
Azathioprine	125-150 mg	133	24.5-721	X^2= 32.2	p< .0001
Copper	0.7-2 mg	24.6	5.52-109	X^2= 17.7	p= .0041
Glutathione	>1300 mg	18.9	4.30-83.4	X^2= 15.1	p= .0155
Vitamin D	200-5000 IU	6.99	2.77-17.6	X^2= 16.99	p= .0057
Fish Oil	1600 mg	6.44	2.40-17.3	X^2= 13.68	p= .0331

Abbreviations: ALS= amyotrophic lateral sclerosis; N/A= not available

There were 153 independent medications and supplements used by cases at the time of their maximum improvement including 36 treatments used by more than one reversal. For 8 of these 36 treatments, the odds they were being taken by a participant were greater for cases than controls. Dosages used by participants are included as available. Information on duration of treatment was unavailable. p-values shown are post-Bonferroni correction.

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