ALS motor phenotypes – classification according to the onset region, propagation of motor neuron symptoms, and the degree of upper and/or lower motor neuron dysfunction ("ALS-OPM Phenotype Classification"): guidance and commentary for the use in clinical practice and research

ALS-OPM
Version 3.3

Patient-ID

Date of visit

(O) Onset region	*Commentary*
☐ O1) **Head onset:** Onset with dysarthria, dysphonia or dysphagia.	*Synonymous to bulbar or pseudo-bulbar onset; for hypophonia see O3r.* *Dysphonia should only be classified as O1 when O3r is excluded.*
☐ O2d) **Arm onset, distal:** Onset with weakness or slowed, poorly coordinated voluntary movements of the distal arm (hand and forearm).	*History of fasciculations or muscle atrophy in the arm is not classified as onset.*
☐ O2p) **Arm onset, proximal:** Onset with weakness or slowed, poorly coordinated voluntary movements of the proximal arm (shoulder and upper arm).	*History of fasciculations or muscle atrophy in the arm is not classified as onset.*
☐ O2x) **Arm onset, not otherwise classifiable:** Onset with weakness or slowed, poorly coordinated voluntary movement of the arm; however, the distinction between distal or proximal onset cannot be made.	*History of fasciculations or muscle atrophy in the arm is not classified as onset.*
☐ O3r) **Trunk respiratory onset:** Onset with weakness of the respiratory trunk muscles presenting as dyspnea or hypophonia.	*Hypophonia should only be classified as O3r when O1 is excluded.*
☐ O3a) **Trunk axial onset:** Onset with weakness of the axial trunk muscles presenting as dropped head syndrome, camptocormia, or truncal postural instability due to axial muscle weakness.	*In the presence of dyspnea or hypophonia, O3a should be classified as O3r. Axial instability should only be classified as O3a when O4 is excluded.*
☐ O4d) **Leg onset, distal:** Onset with weakness or slowed, poorly coordinated voluntary movements of the distal leg (foot and calf).	*History of fasciculations or muscle atrophy in the leg is not classified as onset.*
☐ O4p) **Leg onset, proximal:** Onset with weakness or slowed, poorly coordinated voluntary movements of the proximal leg (hip and thigh).	
☐ O4x) **Leg onset, not otherwise classifiable:** Onset with weakness or slowed, poorly coordinated voluntary movements of the leg; however, the distinction between distal or proximal onset cannot be made.	*History of fasciculations or muscle atrophy in the arm is not classified as onset.*

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(P) Propagation (“vertical spreading”)	*Commentary*
☐ P0(n) **No propagation (number of months):** Absence of propagation of motor neuron symptoms from the region of onset to another, vertically distant body region: Neurological examination or history taking shows no evidence of weakness or slowed, poorly coordinated voluntary movements in the muscles of the head, arm, trunk, or leg, including dysarthria, dysphagia, dysphonia, dyspnea, dropped head syndrome, axial instability, or camptocormia. The temporal qualifier of the absence of propagation denotes the number of months (n) from symptom onset to the date of assessment.	*Horizontal spreading from one arm or leg to the other is not classified as propagation.* *Motor neuron signs such as fasciculations, muscle atrophy, increased or pathological reflexes are not classified as propagation.*
☐ P1(n) **Propagation (number of months):** Propagation of motor neuron symptoms from the region of onset to another, vertically distant body region has occurred: Neurological examination or history taking provides evidence of weakness or slowed, poorly coordinated voluntary movements in the muscles of the head, arm, trunk, or leg, including dysarthria, dysphagia, dysphonia, dyspnea, dropped head syndrome, axial instability, or camptocormia. The temporal qualifier denotes the time between symptom onset and the involvement of the next vertically distant body region. It is expressed as the number of months (n) from symptom onset to the date of assessment or to the date in the patient’s history when propagation occurred.	*Motor neuron signs such as fasciculations, muscle atrophy, increased or pathological reflexes are not classified as propagation.*
☐ P1(x) **Propagation (uncertain number of months):** Propagation of motor neuron symptoms from the region of onset to another, vertically distant body region has occurred: Neurological examination or history taking provides evidence of weakness or slowed, poorly coordinated voluntary movements in the muscles of the head, arm, trunk, or leg, including dysarthria, dysphagia, dysphonia, dyspnea, dropped head syndrome, axial instability, or camptocormia. The temporal qualifier denotes the time between symptom onset and the involvement of the next vertically distant body region. However, there is no date (x) in the patient’s history when propagation occurred. Also, the date of assessment is more than 12 months from onset or from the last neurological examination.	*Motor neuron signs such as fasciculations, muscle atrophy, increased or pathological reflexes are not classified as propagation.*

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(M) Degree of upper and/or lower motor neuron dysfunction (UMN/LMN)		*Commentary*
☐	M0 **Balanced upper and lower motor neuron dysfunction:** Balanced combined UMN (slowed, poorly coordinated voluntary movements, increased deep tendon reflexes and/or spastic muscle tone, pseudobulbar affect) and LMN dysfunction (weakness and associated atrophy).	*Synonymous to "classic ALS", "Charcot ALS" or "typical ALS".*
☐	M1d **Dominant upper motor neuron (UMN) dysfunction:** Dominant UMN dysfunction (slowed, poorly coordinated voluntary movements, increased deep tendon reflexes and/or spastic muscle tone, pseudobulbar affect) with only discrete LMN dysfunction (weakness and associated atrophy) relative to the UMN dysfunction.	*During disease, weakness may also progress; however, it must be associated with increased spastic muscle tone and remain substantially less pronounced than slowed, poorly coordinated voluntary movements; otherwise, classify M0.*
☐	M1p **Pure UMN dysfunction:** Pure UMN dysfunction (slowed, poorly coordinated voluntary movements, increased deep tendon reflexes and/or spastic muscle tone, pseudobulbar affect) and no presence of LMN dysfunction (weakness and associated atrophy).	*Weakness related to LMN dysfunction must not fall below MRC grade 5 in any body region; otherwise, classify as M1d or M0. Weakness clearly associated with increased spastic muscle tone does not preclude classification as M1p. This phenotype, when persisting for 48 months, is also known as "primary lateral sclerosis (PLS)".*
☐	M2d **Dominant lower motor neuron (LMN) dysfunction:** Dominant LMN dysfunction (weakness and associated atrophy) with only discrete UMN dysfunction (preserved deep tendon reflexes) relative to LMN dysfunction.	*UMN dysfunction must be discrete and exclude slowed, poorly coordinated voluntary movements, increased reflexes and/or spastic muscle tone in any of the body regions; otherwise, classify as M0.*
☐	M2p **Pure LMN dysfunction:** Pure LMN dysfunction (weakness and associated atrophy) and no presence of UMN dysfunction (slowed, poorly coordinated voluntary movements, preserved or increased deep tendon reflexes and/or spastic muscle tone).	*This phenotype, when persisting for 48 months, is also known as "progressive muscle atrophy (PMA)".*
☐	M3 **Dissociated upper and lower motor neuron dysfunction:** Dominant LMN dysfunction (weakness and associated atrophy) with only discrete UMN dysfunction (preserved deep tendon reflexes) relative to LMN dysfunction in the arms, and dominant UMN dysfunction (slowed, poorly coordinated voluntary movements, increased deep tendon reflexes and/or spastic muscle tone) with only discrete LMN dysfunction (weakness and associated atrophy) relative to the UMN dysfunction in the legs.	*Synonymous to "brachial atrophic paraspastic variant" of ALS.*

Region	Upper motor neuron (UMN)	Lower motor neuron (LMN)
Head	*Clinical symptoms* • slowed, poorly coordinated voluntary movements of the tongue leading to dysarthria, dysphonia and/or dysphagia *Clinical signs* • hyperreflexia of mandibular reflex • pseudobulbar affect • snout reflex • exaggerated gag reflex	*Clinical symptoms* • weakness with associated muscle atrophy of the tongue leading to dysarthria, dysphonia and/or dysphagia *Clinical signs* • muscle atrophy of the tongue • fasciculations of the tongue
Arm	*Clinical symptoms* • slowed, poorly coordinated voluntary movements in hand, arm or shoulder *Clinical signs* • preserved reflexes in wasted or weak muscles • increased reflexes • hyperreflexia • Hoffman sign • increased velocity-dependent tone (spasticity) in hand and arm	*Clinical symptoms* • weakness with associated muscle atrophy of hand, arm or shoulder muscles *Clinical signs* • muscle atrophy of hand, arm or shoulder muscles • persistent fasciculations in muscles with weakness and/or atrophy • absent reflexes
Trunk	*Clinical symptoms* • slowed, poorly coordinated voluntary movements of paraspinal, costal and abdominal muscles *Clinical signs* • pathological abdominal reflexes	*Clinical symptoms* • weakness with associated muscle atrophy of paraspinal, costal and abdominal muscles *Clinical signs* • muscle atrophy of paraspinal, costal and abdominal muscles • persistent fasciculations in muscles with weakness and/or atrophy
Leg	*Clinical symptoms* • slowed, poorly coordinated voluntary movements of foot, leg or hip *Clinical signs* • preserved reflexes in wasted or weak muscles • increased reflexes • hyperreflexia • increased velocity-dependent tone (spasticity) in foot, leg or hip • Babinski sign • crossed adductor reflex	*Clinical symptoms* • weakness with associated muscle atrophy of foot, leg or hip muscles *Clinical signs* • muscle atrophy of foot, leg or hip muscles • persistent fasciculations in muscles with weakness and/or atrophy • absent reflexes