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 use in clinical practice and research

ALS-OPM
Version 3.3

Patient-ID

Date of assessment (dd/mm/yyyy)

(O) Onset region

Date of symptom onset (mm/yyyy)

			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 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 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 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, axial instability, or camptocormia.	*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 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).	*History of fasciculations or muscle atrophy is not classified as onset.*
☐	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 is not classified as onset.*

(P) Propagation ("vertical spreading")

Commentary

☐ P0(n) **No propagation**

(number of months since symptom onset)

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 co-ordinated 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 neurological examination, in which propagation was excluded.

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**

Date of propagation:

(mm/yyyy)

Captured by:

☐ History
☐ Neurological examination

(number of months since symptom onset)

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 neurological examination, in which propagation was found, 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 neurological examination, in which propagation was found, 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.

(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.*

Terms	Definitions
Body region	The body is classified into four anatomical regions: head, arm, trunk and leg.
Increased deep tendon reflex	Exaggerated or brisk reflex response.
Hyperreflexia	Abnormally exaggerated deep tendon reflex, often associated with increased reflex spread beyond the stimulated territory.
Lower motor neuron signs	Muscle atrophy of the muscles in the head, arm, trunk, and/or leg; absent reflexes; fasciculations of the tongue; persistent fasciculations in muscles with atrophy and/or weakness.
Lower motor neuron symptoms	Weakness with associated muscle atrophy of the muscles in the head, arm, trunk, and/or leg.
Motor neuron dysfunction	Clinical signs and symptoms of upper and/or lower motor neuron involvement.
Onset region	Body region presenting with first motor neuron symptoms. The body is differentiated in four regions: head, arm, trunk and leg.
Onset criteria	Motor neuron symptoms of weakness and/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. Motor neuron signs such as fasciculations, muscle atrophy, increased or pathological reflexes are not classified as onset.
Preserved deep tendon reflex	Minimal yet clearly elicitable reflex response in a muscle group that is weak and atrophic.
Propagation	Spreading of motor neuron symptoms from the onset region to another, verticaly located body region. Horizontal spreading from one arm or leg to the other is not considered as propagation.
Propagation criteria	Motor neuron symptoms 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. Motor neuron signs such as fasciculations, muscle atrophy, increased or pathological reflexes are not classified as propagation.
Upper motor neuron signs	Emotional lability; preserved reflexes in wasted or weak muscles, increased reflexes, hyperreflexia, and increased velocity-dependent tone (spasticity); pathological abdominal reflexes; Babinski sign; Hoffman sign.
Upper motor neuron symptoms	Slowed, poorly coordinated voluntary movements of the muscles in the head, arm, trunk, and/or leg.
Weakness	Reduction in the ability of a muscle or muscle group to generate voluntary force.