

The MLD initiative

Standard operating procedure

NERVE CONDUCTION STUDIES (ELECTRONEUROGRAPHY – ENG)

Version	1.0
Status	Definitive version
Date	06/03/2024
Purpose of this document	Describe the standard operating procedure for conducting nerve conduction studies in patients with metachromatic leukodystrophy to enable cross-center comparison and analysis.

Version control

Version number	Revision date	Summary of major changes

A) Baseline parameters

1) Patient information

- Recorded patient information must include: sex, age, body weight, and height

2) Procedural information (please keep constant across measurements)

- Recorded procedural information must include: measurement side, limbs temperature, and exact location of stimulation and recording sites, and use of anesthesia, and type and size of electrode.

3) Source data

- Provide result tables, preferably also curves, graphical views and used normative values

B) Laboratory Procedures

1) Measurement side

- Measurements are always taken on the right side of the body. The left side is optional and is preferably additionally measured in patients with previous investigations on the left side.

2) Type of electrode

- Surface electrodes

3) Parameter Settings according to local lab (please keep constant across measurements)

3.1) Motor Nerve Conduction Studies

Filters: Low Frequency according to local lab
High Frequency according to local lab
Gain: 0.5 mV – 5 mV/div

3.2) Sensory Nerve Conduction Studies

Filters: Low Frequency according to local lab
High Frequency according to local lab
Gain: 1 – 50 μ V/div

Filtersettings according to local lab (add lab)	Low-freq	High-freq
Motor		
AMC	20 Hz	2 kHz
Tubingen/Milan	20 Hz	5 kHz

Sensory		
AMC	20 Hz	3 kHz
Tubingen/Milano?	20 Hz	2 kHz

3.3) Antidromic

- All sensory studies should be measured in an antidromic direction, except for the medial plantar nerve (only performed in children younger than 12 months of age if sural nerve is not recordable)

4) Temperature Measurements

- The limb temperature will be measured at the beginning and end of each nerve conduction study. The temperature at start and end must be recorded on each nerve tracing.
- For the peroneal, tibial and sural nerve conduction studies, temperature is measured in the lower calf of the side tested. The limbs temperature should be $\geq 32^{\circ}\text{C}$.

5) Nerve Stimulation

- Surface electrical stimulation will be used. In children under 2 years, we will use a pediatric stimulator with an inter-electrode distance of 15 mm;
- The duration of stimulus current is 0.1 to 0.2 ms, or can be enlarged if necessary (please note)
- Depending on circumstances: often non-recurrent is easier to bare; if recurrent than the stimulation rate is 1/sec.
- The intensity of stimulation should be increased in steps until a supramaximal evoked response is obtained.

6) Averaging

- Sensory responses may be averaged to improve the signal to noise ratio and to facilitate accurate measurement of the onset latency and amplitude.
- The number of averaged responses, up to 10, must be electronically printed out on the tracings

7) Amplitude Measurements

7.1) Motor amplitude

- The CMAP amplitude is measured from the baseline to the negative peak to the nearest 0.1 mV.
- The markers are placed at $500 \mu\text{V}/\text{div}$; afterwards motor responses may be displayed over 2 divisions for readability.
- Please also provide the area of the negative peak of the CMAP

7.2) Sensory Amplitude

MLD harmonized NCS protocol based on OSR-MLD protocol

- The SNAP amplitude is measured from the baseline to the negative peak to the nearest $0.1 \mu V$. Please record the measurement used.
- The markers are placed at $10 \mu V/div$.

8) Latency Measurements

- Latencies should be rounded to the nearest 0.1 ms.

8.1) Motor Latency

- The latency is measured at the onset of the negative peak of the CMAP obtained after supramaximal stimulation, or at the onset of the initial positive component if this precedes to negative peak.
- The markers are placed at $500 \mu V/div$.

8.2) Sensory Latency

- The latency is measured at the onset of the negative peak.
- The markers are placed at $10 \mu V/div$.

Optional: Add some figures of electrode placements and marker placements

C) Nerve Conduction Studies in Infants and Children

1) MOTOR STUDY

- The preferred sequence of motor nerve testing is 1) ulnar nerve, 2) peroneal nerve, and 3) tibial nerve (optional).

1.1)

ULNAR MOTOR STUDY

Recording site: Abductor digiti minimi (ADM) muscle (medial hypothenar eminence):
G1 placed over the muscle belly
G2 placed over the fifth proximal interphalangeal joint

Stimulation sites: 1. Wrist: medial wrist, adjacent to the flexor carpi ulnaris tendon
2. Elbow: distal to the medial epicondyle

1.2)

PERONEAL MOTOR STUDY

Recording sites: Extensor digitorum brevis (EDB) and tibial anterior (TA) muscle:

EDB: G1 placed over the muscle belly
G2 placed distally over the metatarsal-phalangeal joint of the little toe

TA: G1 placed over the muscle belly (1/3 distance fibular head-lateral malleolus)
G2 placed 4-6 cm distal at tibia

Stimulation sites:

1. Ankle: anterior ankle, slightly lateral to tibialis anterior tendon
2. Distal to fibular head
3. Proximal to fibular head (optional)

Optional:

1.3)

TIBIAL MOTOR STUDY

Recording site: Abductor hallucis brevis (AHB) muscle:
G1 placed over the muscle belly
G2 placed over the metatarsal-phalangeal joint of the great toe

Stimulation sites: 1. Medial ankle: proximal and posterior to the medial malleolus
2. Popliteal fossa: mid-posterior knee over the popliteal pulse

2) SENSORY STUDY

- The preferred sequence of sensory nerve testing is, 1) sural nerve, and 2) median nerve 3) ulnar nerve (optional), 4) medial plantar nerve (only in children younger than 12 months of age if sural nerve is not recordable).

2.1) ULNAR SENSORY STUDY (ANTIDROMIC)

Recording site: Vth finger (digit 2):
Ring electrodes with G1 placed over the metacarpal-phalangeal joint
G2 placed 2-3 cm distally over the distal interphalangeal joint

Stimulation sites: 1. Wrist: medial wrist, adjacent to the flexor carpi ulnaris tendon
2. Elbow: at the medial epicondyle

2.2) SURAL SENSORY STUDY (ANTIDROMIC)

Recording site: posterior to the lateral malleolus
G1 placed posterior to the lateral malleolus
G2 placed 2 cm distally
Average up to 10 responses

Stimulation site: Over the sural nerve (4-10 cm proximal to the ankle)

Optional:

2.3) MEDIAN SENSORY STUDY (ANTIDROMIC)

Recording site: Index finger (digit 2):
Ring electrodes with G1 placed over the metacarpal-phalangeal joint
G2 placed 2-3 cm distally over the distal interphalangeal joint

Stimulation sites: Wrist: middle of the wrist between the tendons to the flexor carpi radialis and palmaris longus
Antecubital fossa: medial to the brachial artery pulse

2.4) MEDIAL PLANTAR (ORTHODROMIC) only in children younger than 12 months of age

Recording Site: Medial ankle:
G1 placed slightly proximal and posterior to the medial malleolus
G2 placed 3–4 cm proximally

Stimulation Sites: Great toe (medial plantar sensory):
Ring electrodes, with cathode placed proximally near the metatarsal-phalangeal joint of the great toe; anode placed 1-1.5 cm distally

Optional: Add some figures of electrode placements and marker placements