# Influence of IVIG on nerve excitability in multifocal motor neuropathy (MMN)

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Peripheral neuropathies |
| **Study type** | Observational non invasive |

## Summary

### ID

NL-OMON42955

**Source**
ToetsingOnline

**Brief title**
IVIG and excitability in MMN

### Condition

- Peripheral neuropathies

**Synonym**
Multifocal motor neuropathy (MMN). This term is familiar to all MMN patients.

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Universitair Medisch Centrum Utrecht
**Source(s) of monetary or material Support:** Prinses Beatrix Spierfonds

## Intervention

**Keyword:** excitability-tests., intravenous immunoglobilin, ion-channel, Multifocal motor neuropathy

## Outcome measures

### Primary outcome

To assess the change in excitability parameters induced by IVIG infusion. This will be achieved by comparing excitability-parameters between the time of maximal weakness (just before the next IVIG infusion) and the time of maximal clinical improvement. .

### Secondary outcome

To analyse the correlation between the degree of excitability changes after IVIG infusion, the presence of anti-GM1-antibodies and the degree of clinical improvement.

# Study description

### Background summary

MMN is a progressive disorder of peripheral nerves in adults which leads to muscle weakness in arms and legs without sensory deficits. Nerve conduction studies in MMN show localized sites in peripheral nerves where impulse conduction is blocked in motor axons but normal in sensory axons. Half of MMN patients exhibit high-titer serum antibodies against a peripheral nerve ganglioside. MMN is treated by immunoglobulin courses which result in temporary improvement in about 80% of the patients. Several immunological mechanisms of action were hypothesized to be beneficial, including those which stimulate remyelination and axonal regeneration. Still none of those is consistent with a rapid clinical improvement seen after IVIG infusion. Thus it was proposed that IVIG could normalize axonal membrane properties and nerve excitability, still without preventing permanent muscle weakness and muscle atrophy due to loss of affected motor axons. Prevention of this unfortunate course of events first requires more knowledge of pathogenesis in MMN. This is largely unknown because there is no animal model and because state-of-the-art nerve pathology studies

are lacking in MMN.

## Study objective

To assess the change in excitability parameters induced by IVIG infusion. This will be achieved by comparing excitability-parameters between the time of maximal weakness (just before the next IVIG infusion) and the time of maximal clinical improvement.

## Study design

We will investigate 45 MMN patients on the IVIG treatment, included from the UMC Utrecht database together with newly diagnosed MMN patients. IVIG is not a study procedure, but a standard treatment for MMN patients, so the schedule of infusions will not be influenced by that research. Three groups, each consisting of 15 MMN patients, will be investigated: one with motor nerve conduction abnormalities without loss of motor axons, one with loss of motor axons without conduction abnormalities, and one group without abnormalities. In each group the forearm segment of the median nerve will be investigated. Pre- and post- IVIG infusion excitability variables will be compared within MMN patients, as well as with healthy controls excitability data. 15 healthy controls will be selected from a larger cohort of healthy subjects with similar age and sex distribution who already have been investigated, using completely identical measurement procedures as those of the MMN patients.

Per patient, two sets of excitability-tests will be performed on the median nerve at the wrist: one just before next IVIG infusion (as close as possible to the next infusion when the patients are at the maximal of their muscle weakness) and one on the peak of the clinical improvement, which is individual and will differ between subjects. For newly diagnosed patients the first excitability measurement will be done prior to their very first IVIG infusion, on the same day; for the second visit they will be asked to contact the coordinating investigator when they start to feel motor improvement after their first IVIG infusion to agree on the appointment. After each set of recordings clinical testing will be performed. The whole investigation during the first visit takes 1 hour and 30 minutes and consists of the following procedures: 1. Motor nerve conduction study of the median nerve in the forearm in order to verify the EMG-abnormalities still occur; this entails delivering electrical stimuli at the wrist and elbow. Duratiion 5-10 min. 2. Sensory conduction of the median nerve of the third and fourth finger to exclude carpal tunnel syndrome; this is important since carpal tunnel syndrome affects excitability-variables. Duration: 10-15 minutes. 3. Warming the forearm and hand to 37°C by wrapping them into a plastic blanket through which water at 37°C flows. Duration: 30 minutes. 4. Excitability-test of median nerve motor axons at the wrist. Duration: 30 minutes. 5. Clinical assessment of the median nerve by MRC grading of the abductor pollicis brevis muscle. Duration: 15 min.

The examination on the second visit includes points 3-5 and will last around 1 hour.

### Study burden and risks

Slight physical discomfort due to electrical stimulation and brief local skin reddening due to skin electrode adhesive gel may occur. There are no known risks for the study procedure based on the literature and on our experience in previous excitability and nerve conduction studies (excitability protocol *Sensory axons in MMN* NL53422.041.15). Patients will benefit indirectly from the study because more will be known about pathogenetic mechanisms in MMN which, in turn, may lead to development of treatment strategies aimed at axonal protection.

## Contacts

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## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

1. Diagnosis of MMN according to internationally accepted criteria of the European Federation of Neurological Societies and Peripheral Nerve Society (EFNS/PNS criteria).
2. One median nerve (left or right) with any of the following findings in the forearm segment:
(a) conduction block, defined as segmental reduction of compound muscle action potential (CMAP) area of at least 30% or signs of demyelination: conduction velocity decrease up to 38 m/s or less and/or DML 5.3 ms or more and/or increased CMAP duration prolongation in the forearm of at least 30%;
(b) motor axon loss defined as decreased CMAP amplitude of 3 mV or less;
(c) normal conduction studies.
3. Treatment with IVIG.
4. Age range will be considered between 18 and 99 years.

## Exclusion criteria

1. Other causes for neuropathy than MMN, including carpal tunnel syndrome (CTS).
2. Use of medication affecting peripheral nerve ion-channel currents.

# Study design

## Design

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| Study type: | Observational non invasive |
| Intervention model: | Other |
| Allocation: | Non-randomized controlled trial |
| Masking: | Open (masking not used) |

**Primary purpose:** Basic science

## Recruitment

NL

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| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 17-11-2016 |
| Enrollment: | 45 |
| Type: | Actual |

# Ethics review

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| Approved WMO Date: | 05-10-2016 |
| Application type: | First submission |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
|---|---|
| CCMO | NL58940.041.16 |