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Measurement of cortical, nerve, and muscle excitability in early phase clinical drug development

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Stellingen behorende bij het proefschrift

MEASUREMENT OF CORTICAL, NERVE, AND MUSCLE EXCITABILITY IN EARLY PHASE CLINICAL DRUG DEVELOPMENT

1 TMS-EMG can be a useful tool for proof-of-pharmacology of drugs targeting cortical excitability. (*this thesis*)

2 Measurement of peripheral nerve excitability using NETT should be considered as proof-of-pharmacology in clinical development of novel sodium channel blockers, although its sensitivity to effects of subtype selective sodium channel blockers should be investigated further. (*this thesis*)

3 MVRC proved useful to confirm target engagement of ClC-1 inhibition in healthy subjects. (*this thesis*)

4 Pharmacological ClC-1 inhibition is promising as symptomatic treatment for muscle weakness in myasthenia gravis. (*this thesis*)

5 For drug candidates with a novel mechanism of action careful selection of a pharmacological biomarker to be used in early phase clinical studies can create significant additional value.

6 A tool to evaluate the individual response in drug-naïve patients with epilepsy would improve targeted anti-epileptic therapy. Whether TMS-EMG/EEG could be such a tool remains to be determined.

7 Early phase drug studies in myasthenia gravis should not solely rely on clinical rating scales, because of the variability of the disease. Specific biomarkers, such as electrophysiological measurements, are essential to increase the chance of finding a relevant signal.

8 Consumption of a puffer fish can be paradoxical: both deadly exciting and resulting in a complete loss of excitability.

9 We should practice science with the boundless curiosity of a child.

10 'Energy cannot be created or destroyed; it can only be changed from one form to another'. (*Albert Einstein*)
As excitability represents the transmission of energy, all our sensations, thoughts and actions may be regarded as a continuation of universal energy.

11 Creating something with your hands can revive creativity when writing a thesis.