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Letter to the Editor

Normal Values for Magnetic Resonance Neurography should only be Established in Individuals with Ruled-Out Nerve Pathology

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Letter to the Editor

We read with interest the article by Keküllüoglu *et al*. on a retrospective study characterizing the demographic and morphological variations of quantitative magnetic resonance neurography (MRN) parameters of the peroneal nerve and evaluating the methodological implications of including the epineurium on signal intensity-based measurements [1]. The cross-sectional area (CSA) of the peroneal nerve increased with age, and the signal intensity (SI) measured with and without the epineurium showed excellent agreement with no evidence of clinically relevant systematic bias [1]. The study is interesting, but some ambiguities remain to be clarified.

The first point relates to the retrospective design of the study [1]. Retrospective designs have several disadvantages, such as poor data quality, missing data, the inability to prove causality (only association), susceptibility to memory bias and selection bias, difficulties in controlling for confounding variables, and a generally lower level of evidence compared to prospective studies [2].

The second point is that not all factors that determine the CSA of a peripheral nerve were included in the analysis [1]. The CSA of a nerve depends not only on age, gender, and body mass index (BMI), but also on height, ethnicity, physical activity, axon thickness, endoneurium and perineurium thickness, and laterality. Taller people tend to have a larger nerve CSA than shorter people. Studies have shown that nerve sizes in Asian populations are smaller than in Caucasian populations [3]. People who exercise regularly have a larger CSA of the nerves supplying the trained muscles than people who do not exercise regularly. Since everyone has a preferred leg (e.g., soccer players), it is important to include laterality in the analysis. Were all MRI examinations performed on the preferred leg or not?

The third point relates to the definition of "healthy" [1]. Why was a 3T knee MRI performed on the subjects included in the study? The indication for an MRI suggests that the 114 individuals included had at least one knee problem. Since knee pathology can secondarily affect nerve course, structure, morphology, and function [4], the study should only include patients without knee pathology. Knee conditions that can affect adjacent nerves include valgus or varus deformities, osteoarthritis, ganglia, synovial cysts, dislocations or subluxations, a history of casts or splints, or a Baker's cyst. One limitation in this regard is that the patients included were not systematically subjected to nerve conduction studies prior to inclusion in the study. Since neuropathies, especially knee neuropathies, can be subclinical, it would have been imperative to rule out large fiber neuropathy before including an individual in the study.

The fourth point is that the measurements were not precisely defined [1]. Since branching of the tibial nerve and peroneal nerve is highly variable, different measurements may have contributed to differences between subjects, even though none exist.

The fifth point relates to the measurement of the outer epineurium diameter. Since the epineurium appears hypointense in 3T MRI and since the tissues surrounding the epineurium are also hypointense, it is often difficult to clearly distinguish the boundary of the epineurium from the surrounding tissues. This can lead to incorrect measurements and thus to unreliable results.

Overall, healthy individuals who are examined for normative MRI data must be screened for nerve pathologies using nerve conduction studies before being included in a study. In addition, normative data should be collected prospectively rather than retrospectively.

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