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PNS PERIPHERAL NERVE SOCIETY

Characterization of a Peripheral Nerve Injury–Induced Symptomatic Neuroma Model in Göttingen Minipigs (GMP)

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Introduction:

Preclinical research on peripheral nerve injury and repair has primarily focused on rodent models, with limited studies in larger animals. However, a suitable large-animal model is crucial for the translational evaluation of new technologies. Göttingen Minipigs (GMP) were selected due to their physiological similarity to humans in terms of peripheral nerve structure, function, and repair, their acceptability in toxicological studies, and their suitability for long-term follow-up due to slower growth rates.

Methods:

Male and female GMPs underwent peroneal nerve dissection (>2 cm; Figure 1) and were followed for one year. Some female animals received Integra tube implants for nerve repair. Functional and sensory assessments included computerized gait analysis, tactile and heat sensitivity tests, electrophysiology (cMAP and DSNAP), locomotor activity (open field), leg functional scoring, and behavioral assessments. At study termination, neuromas, skin, lumbar DRGs, and spinal cords were collected for histological analysis.

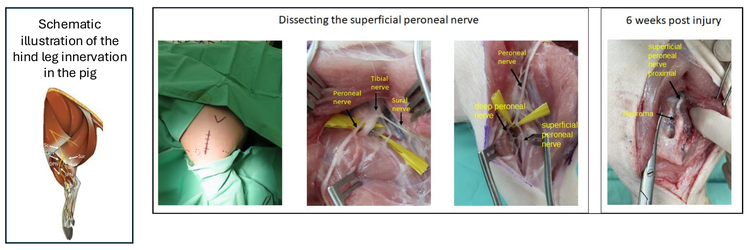

Figure 1: Left: Schematic illustration of hind leg innervation. Middle: Postmortem images of GMP hind leg innervation. Right: Neuroma developed at the dissected peroneal nerve site.

Conclusions:

- The pig neuroma model closely resembles the human condition, particularly in that not all animals develop pain—mirroring the variability observed in humans. The anatomical size of pigs allows for the creation of critical nerve gaps ranging from 4–7 cm, and even exceeding 7 cm.
- Behavioral assessments, including both spontaneous (non-evoked) and stimulus-evoked responses, indicate persistent thermal hyperalgesia in the subset of animals that do develop pain. Despite this, the animals retain functional mobility, making them suitable for evaluation through locomotor behavior assays.
- While rabbits remain the most widely used large-animal model for peripheral nerve injury, the pig model supports a broader range of assessments for both data collection and functional analysis.

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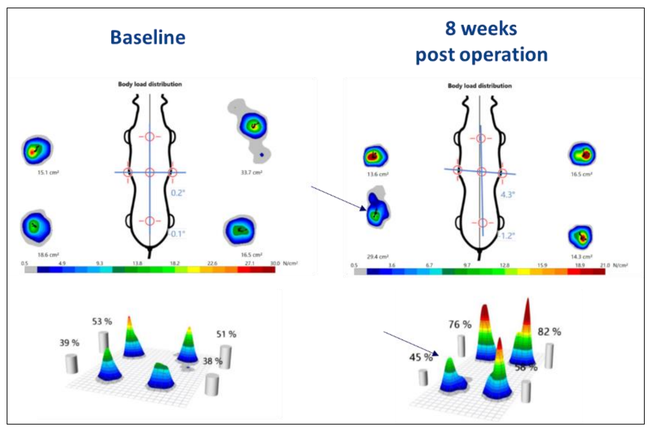
Results

Non-Evoked Outcome Measure

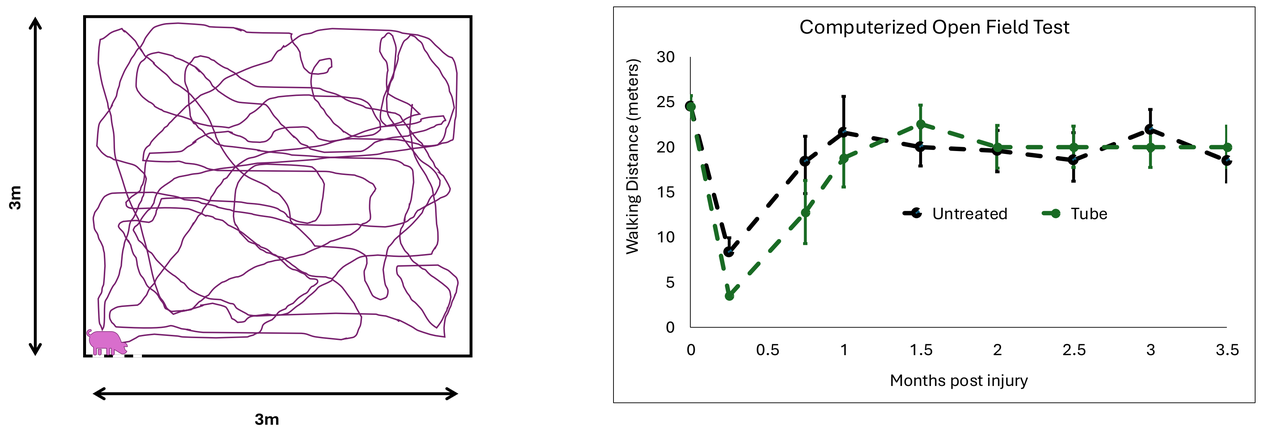


Left: Schematic illustration of computerized gait analysis using the Zebris Medical apparatus.

Right: Representation of the vertical force applied by the hind legs of non-symptomatic and symptomatic animals.

Symptomatic animals showed a clear difference between the force applied by the operated leg (blue column) and the force applied by the intact leg (orange column). The difference, indicated by black arrows, suggests that the animals carried their body weight on the intact, healthy leg and avoided carrying weight on the injured, operated leg.

Mobility Assay

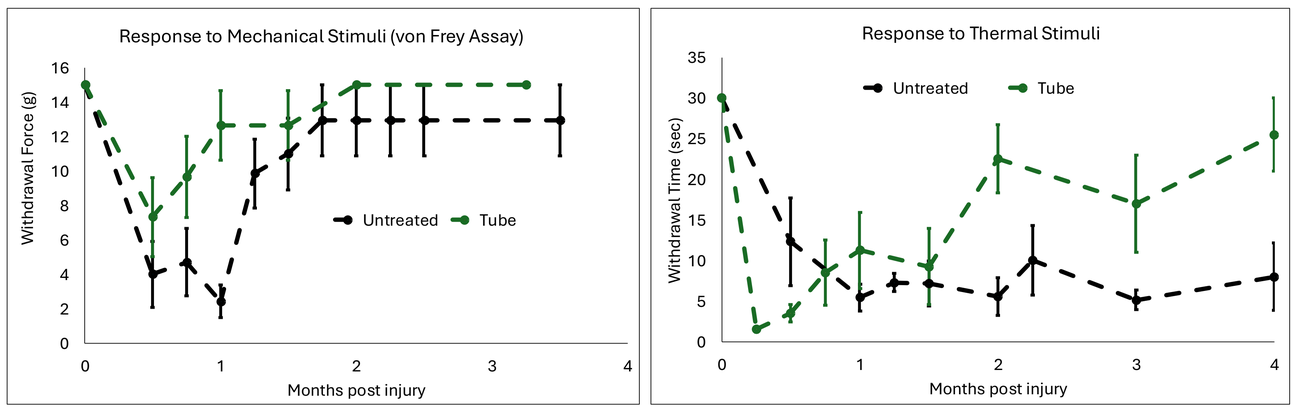


Left: Schematic illustration of a typical walking pattern in pigs without no pain or dysfunction. The animals move throughout arena without preference.

Right: Total walking distance recorded over a 5-minute period.

The data shows that the animals regained functionality 3 to 4 weeks post-injury.

Response to Evoked Stimulation

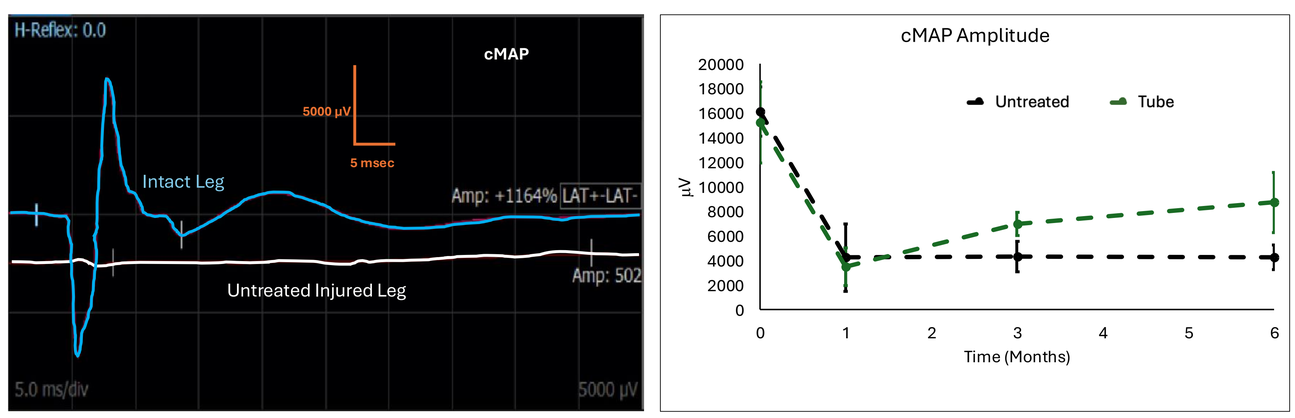


Left: Response to mechanical stimuli. The data suggests transient tactile allodynia, with full recovery observed after 1.5 to 2 months.

Right: Response to thermal stimuli. Following the injury, untreated animals exhibited persistent heat hyperalgesia, indicated by a low withdrawal time (black line).

Implementation of the tube reduced thermal hyperalgesia starting at 2 months post-injury and implementation (green line).

Compound Muscle Action Potential (cMAP)



Left: Schematic illustration of the electrical cMAP wave in pigs. The blue line represents cMAP recorded from the intact leg; the white line represents cMAP recorded one month post-injury. As expected, following the injury, there is no signal transmission, and therefore no cMAP wave is observed.

Right: Mean group amplitude of cMAP. One month post-injury, a substantial reduction in amplitude is evident. This low amplitude persisted throughout the study period (black line). Following tube implantation (green line), a moderate yet consistent improvement in cMAP amplitude was observed.