# Burst Spinal Cord Stimulation in a Rat Model of Chronic Neuropathic pain

## Valorization

### Chapter 2

The burst waveform has many parameters that can be explored and optimized, one such parameter being amplitude. Our research found that while both waveforms are equally effective, their optimal effects are achieved at different amplitude settings. To our surprise, the study received a number of critical comments; dr. De Ridder and dr. Vanneste criticized our study based on the shape of the waveform we used. Instead of a rebuttal, we would like to take this opportunity to underline the importance of objective and unbiased research, especially when it comes to assessing the various parameter variations of (burst) SCS. When objectivity is lost firm beliefs that lack substantial scientific foundation will prevail, causing further polarization, which will inevitably bring the progression of the field to a halt.

### Chapter 3

Our investigation of the analgesic effect of burst and tonic SCS, over time, led to the observation that burst SCS requires significantly more time for its analgesic effect to fully wash in. The delayed wash-in, and subsequently delayed wash-out, had important consequences for the application of burst SCS in the clinical setting. For example, it is now corroborated by clinical observations that the burst waveform is not optimal for patients that require immediate pain relief. However, burst SCS simultaneously delivered with a waveform that does not exhibit a delayed wash-in (if the technology permits) could still yield successful outcomes in the aforementioned patient group.

### Chapter 4

We demonstrated that GABA plays a key role in the analgesic mechanisms underlying burst SCS. In the past, similar experimental findings were successfully translated to the clinical setting; neuropathic pain patients with a deficient tonic SCS effect showed improved pain relief following intrathecal administration of subeffective doses of baclofen. Interestingly, our results were not in line with a study that investigated the GABAergic mechanisms underlying burst SCS in 2015. Taking into account the important role GABA plays in the mechanisms underlying tonic SCS we encourage further investigation of the GABAergic mechanisms underlying SCS waveforms.

**Chapter 5**

We investigated a novel operant testing method able to assess motivational and cognitive aspects of pain processing. The pain field, especially the neuromodulation niche, is currently undergoing a shift of focus towards supraspinal processing. With the introduction of novel SCS-paradigms, that are hypothesized to have strong supraspinal effects, the preclinical field is in need of assessment methods able to address such hypotheses. In this chapter, we have paved the way for preclinical pain assessment able to address both the sensory and emotional aspects of pain. We believe that implementation of operant testing methods such as these can significantly improve the translation to the clinic.

**Chapter 6**

In the last chapter, by means of fMRI, we assessed the supraspinal mechanisms of tonic and burst SCS in a chronic pain model. We found that burst SCS and tonic SCS both activate brain areas associated with the medial and lateral pain pathways. Additionally, we found that burst SCS might have additional analgesic properties over tonic SCS by the activation of brain areas associated with the reward-system and the raphe nuclei. In light of these new findings, we believe that more research is still required before we can advocate the use of specific waveforms for specific patient populations.