Specific aims

The purpose of this protocol is to investigate a possible novel treatment for intractable visceral pain in patients with chronic pancreatitis. Pain is a major contributor to the poor quality of life in patients with chronic pancreatitis. The refractory nature of this condition to medical and surgical procedures prompted us to hypothesize that one mechanism leading to pain in these patients is the dysfunction of brain cortical regulation of visceral sensation. This notion is particularly supported by findings that patients with chronic pancreatitis can continue to experience disabling pain even after total pancreatectomy, suggesting that symptoms are sustained by a pancreas-independent, neural-based mechanism.

Visceral sensation is particularly processed in the secondary somatosensory area - SII. Therefore, chronic pancreatitis pain may be sustained by a dysfunction of SII rather than by pancreatic inflammation alone. We hypothesize further, that the dysfunction of SII is one of hyper-excitability. According to this hypothesis, suppression of SII activity may help control the pain in patients with chronic pancreatitis. Temporary inhibition of SII activity can be obtained by a novel tool, namely transcranial magnetic stimulation (TMS), which can suppress brain excitability non-invasively beyond the duration of the TMS if appropriate stimulation parameters are employed. In our initial sham controlled, double blind pilot trial of 5 subjects with idiopathic chronic pancreatitis, TMS applied to SII resulted in significant pain improvement in 3 of the subjects.

We will rigorously test our hypothesis that chronic pancreatitis pain is sustained by a dysfunction of SII characterized by hyperexcitability through two specific aims:

1. The first aim of this study is to examine whether slow repetitive TMS (rTMS) applied to SII in patients with pain and chronic pancreatitis has an analgesic effect as measured by changes in the Visual Analogue Scale (VAS) for pain and a decrease in analgesic intake, as well as an overall improvement in quality of life. In addition, if this study finds a significant effect of rTMS on pain reduction, the duration of this effect will be further assessed. TMS will be applied at parameters of stimulation known to decrease excitability.

2. The second aim of the study is to assess the safety of rTMS in this patient population. In our pilot study none of the patients experienced any adverse effects of a single session of rTMS. However, the extension of the study protocol to a 15-day course of daily rTMS requires careful safety assessment. Fifteen-day courses of rTMS have been used for treatment of various neuropsychiatric diseases without any complications if safety guidelines are carefully followed. We will adhere to the current safety recommendations for rTMS endorsed by the International Society for Transcranial Stimulation and the International Federation for Clinical Neurophysiology. Therefore, we hypothesize that the proposed rTMS protocol will be safe for our patient population.