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PERCUTANEOUS PNS RELIEVES PERSISTENT POSTOPERATIVE PAIN AND IMPROVES FUNCTION AFTER TKA: RESULTS FROM A PLACEBO-CONTROLLED RCT

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Introduction

Total knee arthroplasty (TKA) is an effective surgery used to treat end-stage knee osteoarthritis. Despite positive results for many patients, approximately 10-20% of patients continue to experience persistent postoperative pain following TKA (i.e., pain >3 months after surgery or past the time of normal tissue healing), which is associated with functional limitations and poor quality of life and has limited treatment options [1]. Opioids are often used to treat postoperative pain but can lead to increased risk of dependence, misuse, gastrointestinal symptoms, and cardiorespiratory side-effects [2]. 60-day percutaneous peripheral nerve stimulation (PNS) is a minimally invasive, non-opioid treatment option that has demonstrated efficacy for controlling and treating postoperative pain [3]. The objective of the present study was to evaluate 60-day percutaneous PNS in a multicenter, randomized, double-blind, placebo-controlled trial for the treatment of persistent postoperative pain after knee replacement surgery. Additional goals included determining if 60-day percutaneous PNS improves function and walking ability for patients with postoperative pain. Outcomes presented here are for the end of treatment as long-term follow-up is ongoing.

Materials and Methods

Patients with postoperative pain following knee arthroplasty were screened for participation in this post-market, institutional review board (IRB)-approved, prospectively registered (NCT04341948), multicenter, double-blind, placebo-controlled, randomized trial conducted across a variety of clinical care settings. Written informed consent was obtained prior to participation in the study. Subjects were randomized into either the active PNS group or the placebo stimulation (sham control) group. Subjects and a designated evaluator were blinded to group assignments. Key inclusion criteria included age ≥21 and persistent moderate to severe baseline pain (average daily pain score ≥5 out of 10 across 7 days and stable for 2-weeks; brief pain inventory short form [BPI-SF] question #5) following knee replacement. Key exclusion criteria included body mass index (BMI) >40 kg/m2, a change in prescribed medication affecting knee pain within the past 4-weeks or current high opioid use (≥90 mg morphine equivalent dose), diagnosis of diabetes, and conditions contraindicated by the PNS system's instructions for use. During the trial, patients were

asked not to exceed baseline medication use other than approved over-the-counter (OTC) medications.

Subjects underwent ultrasound-guided placement of percutaneous fine-wire coiled PNS leads (SPRINT PNS system; SPR Therapeutics Inc., Cleveland, OH, USA) to target the femoral and sciatic nerves on the leg with postoperative pain [4]. Treatment lasted for 8-weeks, and blinded evaluators collected outcome data during the treatment period and at 1-month after end of treatment (i.e., 3 months after start of treatment). After the 1-month follow-up visit, subjects were unblinded and placebo (sham) stimulation subjects were given the opportunity to crossover and receive active stimulation. The study was designed to follow active stimulation subjects (both from initial randomization and crossover) for 12-months following the start of treatment, and long-term follow-up is still ongoing for this study. Thus, only end of treatment outcomes are presented here.

Efficacy of 60-day percutaneous PNS was assessed based on prospectively defined endpoints for pain relief, function, and quality of life. The primary efficacy outcome for the study was the proportion of subjects with clinically significant (≥50%) pain relief during weeks 5-8 compared to baseline assessed with daily pain diaries (BPI-SF #5), which were also used to assess average pain relief. Functional endpoints included improvements relative to baseline on the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and the Six-Minute Walk Test (6MWT, distance walked over 6 minutes). Quality of life was assessed using the Patient Global Impression of Change (PGIC).

Results/Case Report

Fifty-two subjects were randomized and received treatment for postoperative pain following TKA, and 41 subjects (n=20 and n=21 for the active PNS and placebo [sham] groups, respectively) reported data during the primary endpoint period (weeks 5-8). Across subjects, the median time since surgery was 2.5 years (range: 0.6 to 18.7 years). Additional outcomes from follow-up (up to 12-months after treatment) and crossover are still being collected. A significantly greater proportion of subjects in the active PNS group (60%; 12/20) compared to the placebo (sham) group (24%; 5/21) responded with ≥50% pain relief relative to baseline ($p<0.05$) during weeks 5-8 of treatment. The average reduction in pain scores across weeks 5-8 relative to baseline was also significant (54% vs. 28% reduction for active PNS versus placebo [sham] stimulation subjects, respectively; $p <0.05$). Subjects with active PNS also reported statistically significant improvements in function. Active PNS subjects reported a 62% improvement in total WOMAC score compared to a 35% improvement in the placebo (sham) group ($p<0.05$). Additionally, subjects in the active PNS group demonstrated a significant increase in distance walked compared to the placebo (sham) group (6MWT; 47% vs. -9% change from baseline, $p<0.05$) among subjects that completed a test (n=18 and n=20 for active PNS and placebo [sham], respectively). Finally, a larger proportion of subjects in the active PNS group (90%; 18/20) had clinically meaningful improvements in quality of life (PGIC ≥ 1) compared to the placebo (sham) group (55%; 11/20, $p<0.05$). All study-related adverse events were non-serious and required only minor treatment (e.g., skin irritation, pruritus, and bruising).

Discussion

This multicenter, randomized, double-blind, placebo-controlled trial evaluated the effectiveness of 60-day percutaneous PNS as a minimally invasive, non-opioid, safe, reversible treatment for persistent postoperative pain to enhance pain relief, functional outcomes, and quality of life following TKA. While prior studies have demonstrated that percutaneous PNS may be effective for treating acute postoperative pain [3-5], most subjects in the present study (34 out of 52) enrolled > 2 years after TKA, highlighting the chronicity of the subjects' postoperative pain from their knee surgery and/or preoperative pain that remained untreated by knee surgery and other pain treatments. Despite the chronicity of the subjects' pain, the 60-day percutaneous PNS treatment provided significant pain relief, improvements in function, and improved quality of life compared to placebo (sham) stimulation during

treatment, suggesting that 60-day percutaneous PNS is a viable option for persistent postoperative pain. 60-day percutaneous PNS also promoted increased mobility during treatment, which may be beneficial for promoting increased activity and functional recovery for TKA patients with decreased postoperative mobility.

References

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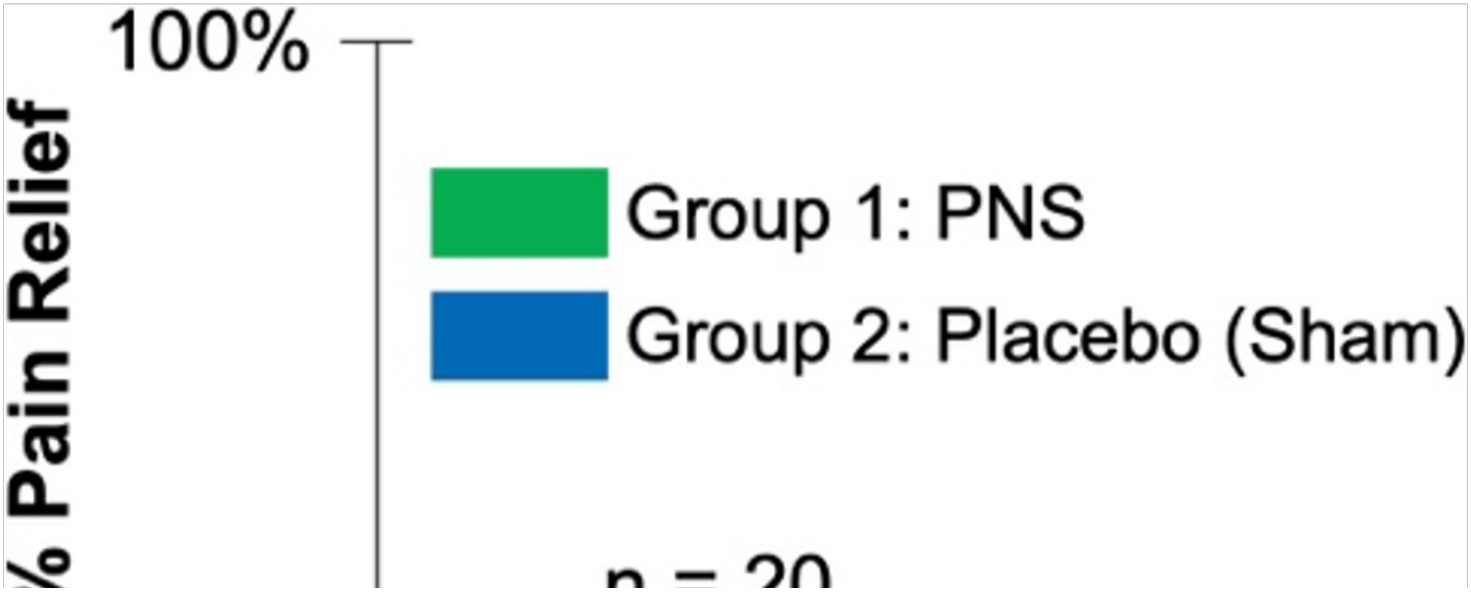
Disclosures

Yes

Tables / Images



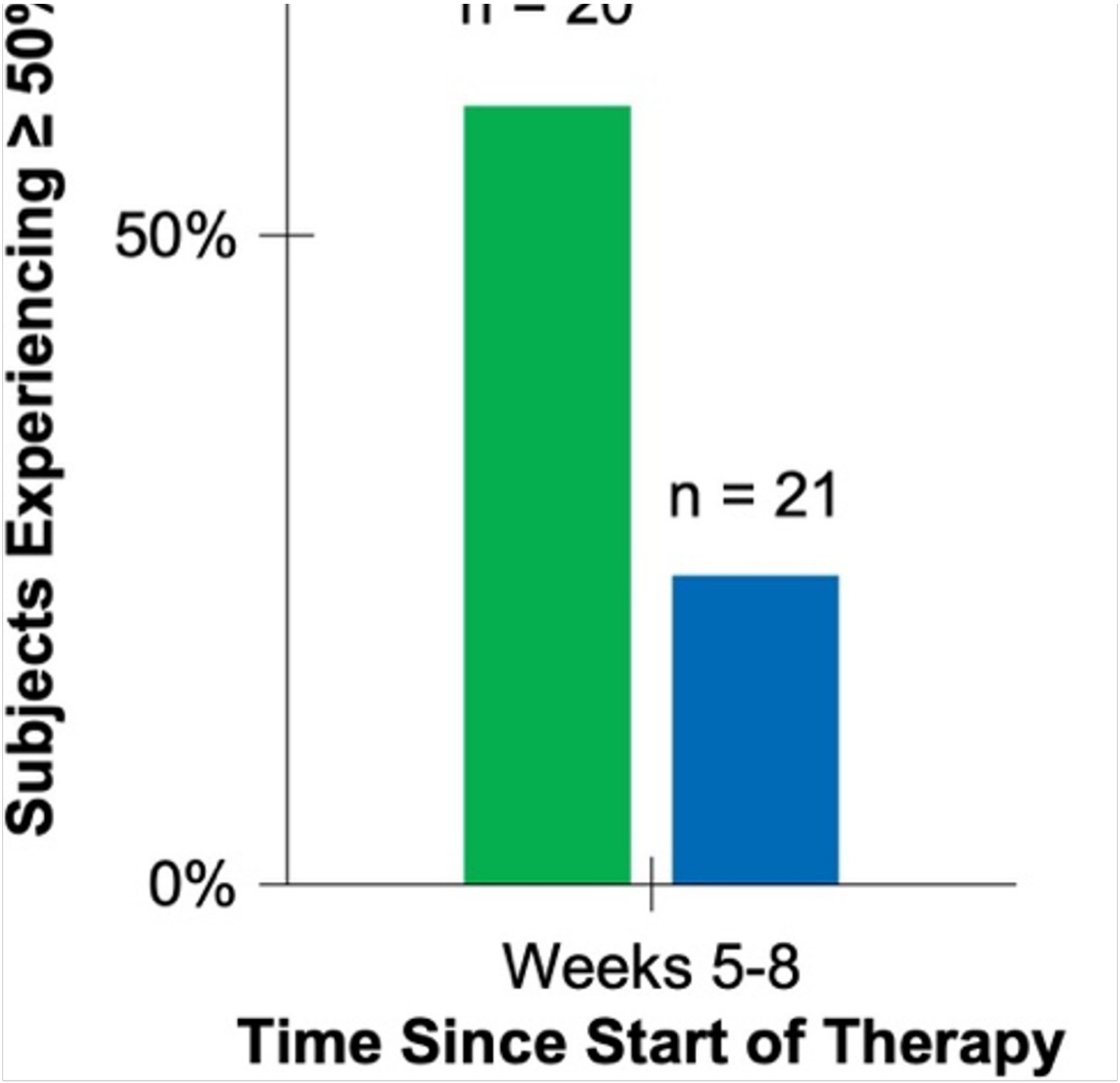


Figure 1: Proportion of subjects that achieved clinically significant pain relief calculated by comparing average daily pain scores during 1-week baseline period to the average pain scores during weeks 5-8 of the 8-week treatment period (60% active PNS

vs. 24% placebo [sham], p<0.05).

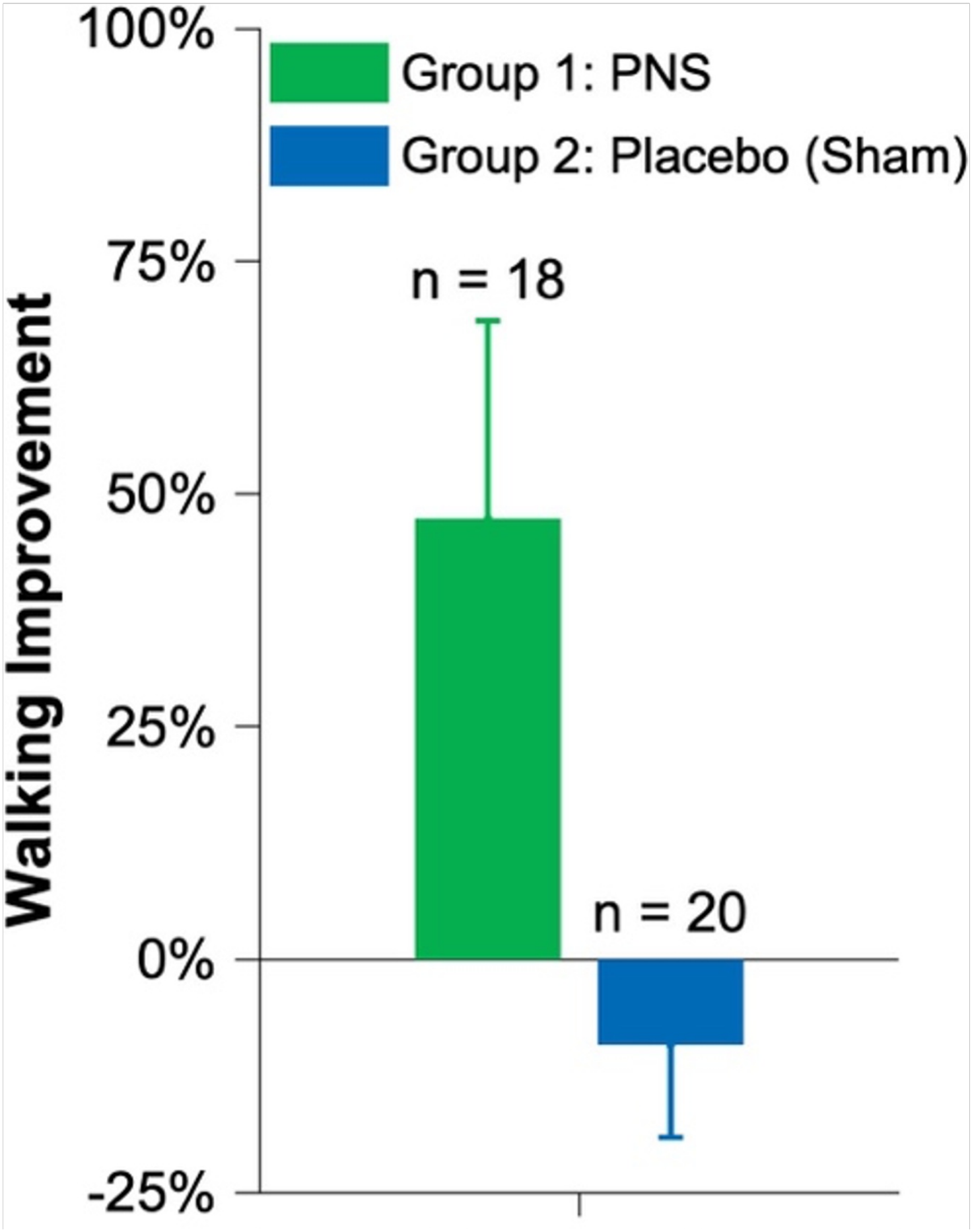


Figure 2: Mean functional improvement from baseline to end of treatment in walking ability quantified through a six-minute walk test that records the distance participants walk in a six-minute interval. Error bars show the standard error (47% active PNS vs. -9% placebo [sham], $p<0.05$).