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Original Article

Evaluation of acupuncture on pain intensity and sleep quality in patients with neuropathic pain following spinal cord injury

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Abstract: Objective: To assess the efficacy of incorporating acupuncture into standard pharmacotherapy for neuropathic pain following spinal cord injury (SCI-NP) and investigate the potential influence of age and disease duration on this effect. Methods: We conducted a retrospective review of 312 patients with SCI-NP who were treated at Northwest University First Hospital from March 2022 to August 2024. According to the hospital information system, patients either received standard pharmacotherapy alone (control) or pharmacotherapy in conjunction with acupuncture (study). The duration of both regimens was four weeks. The main outcomes were changes in the Pain Rating Index (PRI), the Visual Analogue Scale (VAS), and the Present Pain Intensity (PPI). Secondary outcomes included sleep quality (Pittsburgh Sleep Quality Index, PSQI), inflammatory markers (Interleukin-1 beta, Interleukin-6, Tumor Necrosis Factor-alpha), immune indices (Immunoglobulin A, Immunoglobulin G), and adverse events. Results: The combination resulted in more significant decreases in PRI, VAS, and PPI, as well as more notable enhancements in PSQI, inflammatory markers, and immunoglobulin levels (all $P<0.0001$), compared to pharmacotherapy alone. The rates of adverse events were comparable between groups ($P>0.05$). Age-by-duration analysis revealed that in patients aged 40-50 years, an extended disease duration correlated with a diminished probability of pain improvement ($P=0.018$); conversely, no definitive association was found in individuals over 50 years ($P=0.694$). Conclusion: Adding acupuncture to conventional pharmacotherapy reduced pain, improved sleep quality, and shifted inflammatory and immune indices in a favorable direction, without an increase in adverse events. Treatment response varied by patient profile: among those aged 40 to 50 years, longer disease duration was linked to a lower likelihood of pain improvement, while no clear duration effect was seen in older patients.

Keywords: Spinal cord injury, neuropathic pain, acupuncture, pharmacotherapy, effect modification

Introduction

Spinal cord injury (SCI) is a major central nervous system injury that impairs movement, sensation, and autonomic control [1]. The global incidence is about 40-80 per million, and new cases in China have been rising, most often in young adults after traffic accidents, falls, or other trauma [2]. Neuropathic pain (NP) is a common and disabling complication of SCI, affecting about 40%-70% of patients [3]. People describe burning, stabbing, or electric shock-like pain, often with allodynia and hyperalgesia; furthermore, sleep and mood are frequently disturbed [4].

SCI-related NP reflects disrupted neural pathways together with persistent neuroinflammation and immune changes [5]. Activated microglia and astrocytes release Interleukin-1 beta (IL-1β), Interleukin-6 (IL-6), and Tumor Necrosis Factor-alpha (TNF-α), which amplify nociception and lower pain thresholds. Immune imbalance, including changes in immunoglobulins, may help sustain pain [6]. These processes interact with sleep problems and can form a cycle that hinders rehabilitation. Current care relies on drugs such as pregabalin, gabapentin, certain antidepressants, and, in selected cases, opioids [7]. Many patients respond poorly or cannot tolerate adverse effects (for exam-

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ple, somnolence, dizziness, or gastrointestinal symptoms). Drug therapy also tends to target pain relief alone and does not consistently address inflammation, immune dysfunction, and sleep problems at the same time.

Acupuncture is widely used for chronic pain in clinical practice [8]. Experimental and clinical studies suggest it modulates nociceptive pathways and engages endogenous analgesic systems; it can reduce pro-inflammatory cytokines and influence autonomic and hypothalamic-pituitary-adrenal (HPA) axis activity. Evidence also points to immune modulation (for example, changes in immunoglobulins) [9] and better sleep [10, 11]. These features make acupuncture a plausible adjunct for SCI-related NP. However, many prior studies have focused mainly on pain scores and have not evaluated sleep quality, inflammatory markers, and immune indices together [12]. Clinicians also observe variation in response by age and disease duration, but potential interactions between these factors and treatment outcomes are rarely examined.

We therefore reviewed 312 patients with SCI-related NP to test whether adding acupuncture to standard pharmacotherapy can alleviate pain, improve sleep quality, reduce levels of inflammatory markers (IL-1β, IL-6, TNF-α), and increase immune indices (Immunoglobulin A [IgA], Immunoglobulin G [IgG]). We also examined whether age group and disease duration interact to influence pain improvement.

Methods and materials

Sample size calculation and collection

Although the present study was retrospective in nature, a theoretical sample size estimation was performed to ensure adequate statistical power. Referring to the randomized controlled trial by Ge et al. [13] on acupuncture for SCI-NP, a moderate effect size (Cohen's $d \approx 0.5$) based on improvements in Visual Analogue Scale (VAS) scores was used. With a two-sided significance level of $\alpha=0.05$ ($Z=1.96$), statistical power ($1-\beta$) $=0.80$ ($Z=0.84$), and expected effect size $\delta=0.5$, the calculated minimum required sample size was 63 patients per group. Allowing for a 10% attrition rate, approximately 70 cases per group were needed, totaling 140 patients. In the present retrospective study, medical records of 312 patients with SCI-NP who had received treatment at Northwest University First Hospital between March 2022 and August 2024 were reviewed. Based on the treatment regimens they had actually undergone, patients were classified into two groups: a control group, consisting of 144 patients who had received conventional Western medicine alone, and a study group, consisting of 168 patients who had received acupuncture in addition to conventional Western medicine. All included patients met the predefined inclusion and exclusion criteria, and the final sample size met the statistical requirements for data analysis. This study has been approved by the Ethics Committee of Northwest University First Hospital.

Inclusion and exclusion criteria

Inclusion criteria: 1) Conformity to diagnostic criteria for SCI-NP; 2) Age 18-70 years; 3) Time since injury ≥1 month with complete clinical records.

Exclusion criteria: 1) Concurrent severe cardiac, hepatic, or renal dysfunction or malignant tumors; 2) Coexisting chronic pain from other etiologies (e.g., osteoarthritis, postherpetic neuralgia); 3) Acupuncture hypersensitivity, hemorrhagic disorders, or pregnant/lactating women; 4) Incomplete treatment protocol adherence or missing data.

Intervention protocols

Control group (conventional Western medicine): Oral pregabalin (Qilu Pharmaceutical Co., Ltd., 75 mg/capsule, batch numbers: 20201218, 20211009, 20220813, 20230603, 20240208) was prescribed at a dosage of one capsule, twice daily; oral mecobalamin tablets (Eisai Co., Ltd., Japan, 4 units/tablet, batch numbers: 20201124, 20210903, 20220712, 20230510, 20240424) was prescribed at a dosage of two tablets, twice daily. The treatment was continued for 4 weeks.

Study group (conventional Western medicine combined with acupuncture [electroacupuncture] and massage): Acupuncture therapy was provided in addition to the conventional regimen used in the control group. The main points were Zusanli (ST36), Sanyinjiao (SP6), Yanglingquan (GB34), Quchi (LI11), Hegu (LI4),

Taichong (LR3), and Fengfu (GV16). According to the patient's condition, additional points were chosen when appropriate - for example, Weishu (BL21) and Neiguan (PC6) were used for gastrointestinal weakness, Qiduan (EX-UE12) and Shixuan (EX-UE11) for sensory disturbances in the limbs, and Fenglong (ST40) for excess phlegm and dampness.

The point prescription followed traditional Chinese medicine principles aimed at regulating Qi and blood, activating the meridian circulation, exerting analgesic effect, and calming the mind. The protocol drew on earlier clinical studies of SCI-related NP. ST36 and SP6 served as the core points. GB34, LI11, and LI4 addressed pain and circulation. LR3 was selected to regulate liver Qi. GV16 targeted the Governing Vessel and produced a calming effect. Points were individualized according to each patient's symptoms, with adjustments made as priorities changed. Patients with diminished appetite, abdominal distension, or diarrhea also received stimulation at the BL21 and PC6. Those with limb numbness or abnormal sensations were treated with acupuncture at the Qiduan and Shixuan. For patients showing heavy, greasy tongue coating or sputum retention, ST40 was selected and treated to transform phlegm and dispel dampness.

To ensure procedural consistency and reproducibility, all acupuncture treatments were performed in accordance with the *World Health Organization Standard Acupuncture Point Locations in the Western Pacific Region (WHO, 2008)*. Before study participation, all rehabilitation physicians completed unified training and competency assessment of acupoint localization, needling manipulation, and electroacupuncture operation. A standardized operation manual specified acupoint positioning, insertion depth, manipulation technique, electrical parameters, and safety monitoring. Disposable stainless-steel filiform needles (0.25 mm × 40 mm, Suzhou Tianyi Acupuncture Instruments Co., Ltd.) were inserted perpendicularly until the *de-qi* sensation (soreness, numbness, or distension) was elicited, with a standardized insertion depth of approximately 10-25 mm, depending on acupoint location and patient body type. Electroacupuncture (Yingdi KWD-808I) was applied using alternating dense-sparse waves of 2/100 Hz for 20 minutes, and the current intensity was gradually increased to the patient's maximum tolerance (typically 1.0-2.0 mA). Acupuncture and massage were performed on alternate days, three times per week, for four consecutive weeks, each session lasting approximately 30 minutes. Senior physicians periodically audited procedures to ensure adherence and minimize inter-operator variability.

Each session also included massage of local regions such as Fengchi (GB20), Fengfu (GV16), the cervical and shoulder areas, and grasping at Jianjing (GB21), combined with digital pressure at Baihui (GV20) and Sishencong (EX-HN1) to relax muscles, enhance circulation, and potentiate analgesia.

To enhance practical feasibility and clinical promotion, an individualized yet standardized adjustment framework was adopted. ST36 and SP6 were regarded as the core points for all patients to ensure baseline analgesic and regulatory effects. For younger patients (<40 years) or those with shorter disease duration (<6 months), treatment emphasized activating Qi and blood through GB34, LI11, LI4, and LR3 to achieve rapid pain relief. In patients aged 40-50 years with short disease duration, GV16 and GB20 were added to enhance calming and anti-inflammatory actions. For those of the same age group but with longer disease duration (≥6 months), ST40, BL21, and PC6 were incorporated to improve gastrointestinal and immune regulation. In older patients (>50 years), therapy focused on tonification and sleep improvement, using GV20, EX-HN1, and PC6 to calm the mind and promote restorative sleep. For cases with significant insomnia, additional needling at GV20, EX-HN1, and PC6 was applied, while gastrointestinal weakness prompted the inclusion of BL21 and PC6.

This structured yet flexible framework enables clinicians to tailor treatment according to patient characteristics while maintaining procedural uniformity and reproducibility, thereby enhancing the feasibility of clinical implementation in both tertiary and community rehabilitation settings. Treatment efficacy was assessed at the end of the fourth week.

Clinical data collection

We retrieved data from the hospital information system and cross-checked entries with labora-

tory and nursing records to verify key variables. Baseline covariates were: age (<40, 40-50, >50 years), sex, body mass index (BMI) (<25 vs ≥25 kg/m^2), disease duration (<6 vs ≥6 months), education (< high school vs ≥ high school), occupation (employed vs other), smoking and alcohol history (yes/no), diabetes and hypertension (yes/no), injury cause (traffic accident, fall, other), and injury level (C1-C7, T1-T11, T12-L1). Outcomes were defined a priori. Pain measures included the Pain Rating Index (PRI), VAS, and Present Pain Intensity (PPI). Sleep was assessed with the Pittsburgh Sleep Quality Index (PSQI). Inflammatory markers were serum IL-1β, IL-6, and TNF-α; immune indices were serum IgA and IgG. Safety was monitored as adverse events (nausea/vomiting, fatigue, dizziness/headache, orthostatic hypotension). All assessments were performed by trained staff using standard procedures at baseline and after treatment.

Functional assessments

Trained assessors collected pain outcomes at baseline and 3 months after treatment. We used the Short-Form McGill Pain Questionnaire (SF-MPQ) PRI (0-45, with higher scores indicating more severe pain) [14, 15], a 10 cm VAS (0= no pain, 10= worst imaginable pain) [16], and the McGill PPI (scored 0-5, where 5 represents 'excruciating' pain) [17]. Sleep was measured with the PSQI, which sums seven components (subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, use of sleep medication, daytime dysfunction), each scored 0-3, for a total of 0-21; higher scores indicate poorer sleep, and a total score >5 suggests poor sleep quality [18].

Laboratory parameter testing

Laboratory markers were measured at baseline and the morning after completion of the 4-week treatment period. Fasting venous blood (3 mL) was collected and centrifuged (3,000 rpm, 10 min) to obtain serum. Serum IL-1β, IL-6, and TNF-α were quantified with Enzyme-Linked Immunosorbent Assay kits from Shanghai Enzyme-linked Biotechnology Co., Ltd. (China), and optical density was read on a Multiskan FC microplate reader (Thermo Fisher Scientific, USA). Serum IgA and IgG were measured by immunoturbidimetry on an ADVIA 2400 analyzer (Siemens, Germany) with matched reagents. Assays followed manufacturer instructions; instruments were calibrated and routine quality control was performed by laboratory staff.

Pain improvement assessment criteria

We prespecified pain-improvement thresholds in line with International Association for the Study of Pain and Food and Drug Administration guidance and with cutoffs commonly used in prior studies. For the PRI, a decrease of ≥5 points or ≥30% from baseline was considered clinically meaningful; for the VAS, a decrease of ≥2 points or a post-treatment score ≤3 indicated pain relief; for the PPI, a decrease of ≥1 category or a post-treatment score ≤1 indicated none or only mild pain. Only when patients simultaneously met improvement criteria for all three indicators was pain improvement determined; failure to meet all criteria simultaneously was defined as unimproved pain [19].

Outcome measures

This study designated pain-related scores as primary outcome measures, including pre- and post-treatment changes in PRI, VAS, and PPI scores. Secondary outcome measures included: 1) sleep quality; 2) inflammatory marker levels; 3) immune function indicators; 4) treatment safety indicators, specifically adverse event incidence including nausea/vomiting, fatigue, dizziness/headache, and orthostatic hypotension.

Statistical analysis

Data were analyzed in R (4.3.3) and SPSS (26.0). Normality of continuous variables was checked with the Kolmogorov-Smirnov test. Normally distributed data are reported as mean ± standard deviation; between-group differences were tested with independent samples t tests and within-group pre-post changes with paired t tests. Non-normal data were analyzed with nonparametric tests. Categorical variables are summarized as n (%) and compared with chi-square tests or Fisher's exact test when expected counts were small. Pearson correlation assessed associations among pain scores, sleep quality, inflammatory markers, and immune indices. Interaction analyses used multivariable logistic regression to examine age, disease duration, and their interaction in relation to treatment response. All tests were two-sided with alpha =0.05.

Table 1. Baseline characteristics comparison analysis

Variable	Total	Control Group (n=144)	Study Group (n=168)	Statistical Value	*P* Value
Age				0.267	0.875
<40 years	104 (33.33%)	50 (34.72%)	54 (32.14%)		
40-50 years	143 (45.83%)	64 (44.44%)	79 (47.02%)		
>50 years	65 (20.83%)	30 (20.83%)	35 (20.83%)		
Sex				0.419	0.517
Male	147 (47.12%)	65 (45.14%)	82 (48.81%)		
Female	165 (52.88%)	79 (54.86%)	86 (51.19%)		
BMI				0.901	0.343
≥25 kg/m^2	95 (30.45%)	40 (27.78%)	55 (32.74%)		
<25 kg/m^2	217 (69.55%)	104 (72.22%)	113 (67.26%)		
Disease Duration				0.505	0.477
≥6 months	184 (58.97%)	88 (61.11%)	96 (57.14%)		
<6 months	128 (41.03%)	56 (38.89%)	72 (42.86%)		
Educational Level				1.137	0.286
≥ High school	151 (48.40%)	65 (45.14%)	86 (51.19%)		
< High school	161 (51.60%)	79 (54.86%)	82 (48.81%)		
Occupation				1.873	0.171
Employed	263 (84.29%)	117 (81.25%)	146 (86.90%)		
Other	49 (15.71%)	27 (18.75%)	22 (13.10%)		
Smoking History				0.275	0.600
Yes	164 (52.56%)	78 (54.17%)	86 (51.19%)		
No	148 (47.44%)	66 (45.83%)	82 (48.81%)		
Alcohol Consumption History				0.985	0.321
Yes	48 (15.38%)	19 (13.19%)	29 (17.26%)		
No	264 (84.62%)	125 (86.81%)	139 (82.74%)		
Diabetes History				1.074	0.300
Yes	32 (10.26%)	12 (8.33%)	20 (11.90%)		
No	280 (89.74%)	132 (91.67%)	148 (88.10%)		
Hypertension History				0.418	0.518
Yes	41 (13.14%)	17 (11.81%)	24 (14.29%)		
No	271 (86.86%)	127 (88.19%)	144 (85.71%)		
Injury Etiology				0.521	0.771
Traffic accident	144 (46.15%)	65 (45.14%)	79 (47.02%)		
Fall injury	115 (36.86%)	56 (38.89%)	59 (35.12%)		
Other	53 (16.99%)	23 (15.97%)	30 (17.86%)		
Injury Location				1.498	0.473
C1-C7	127 (40.71%)	57 (39.58%)	70 (41.67%)		
T1-T11	157 (50.32%)	71 (49.31%)	86 (51.19%)		
T12-L1	28 (8.97%)	16 (11.11%)	12 (7.14%)		

Note: BMI, Body Mass Index.

Results

Baseline characteristics comparison

Baseline characteristics were similar between groups. Distributions of age, sex, BMI, disease duration, education, occupation, smoking, alcohol use, diabetes, hypertension, injury etiology, and injury location did not differ (age P=0.875; sex P=0.517; BMI P=0.343; disease duration P=0.477; education P=0.286; occupation P=0.171; smoking P=0.600; alcohol use

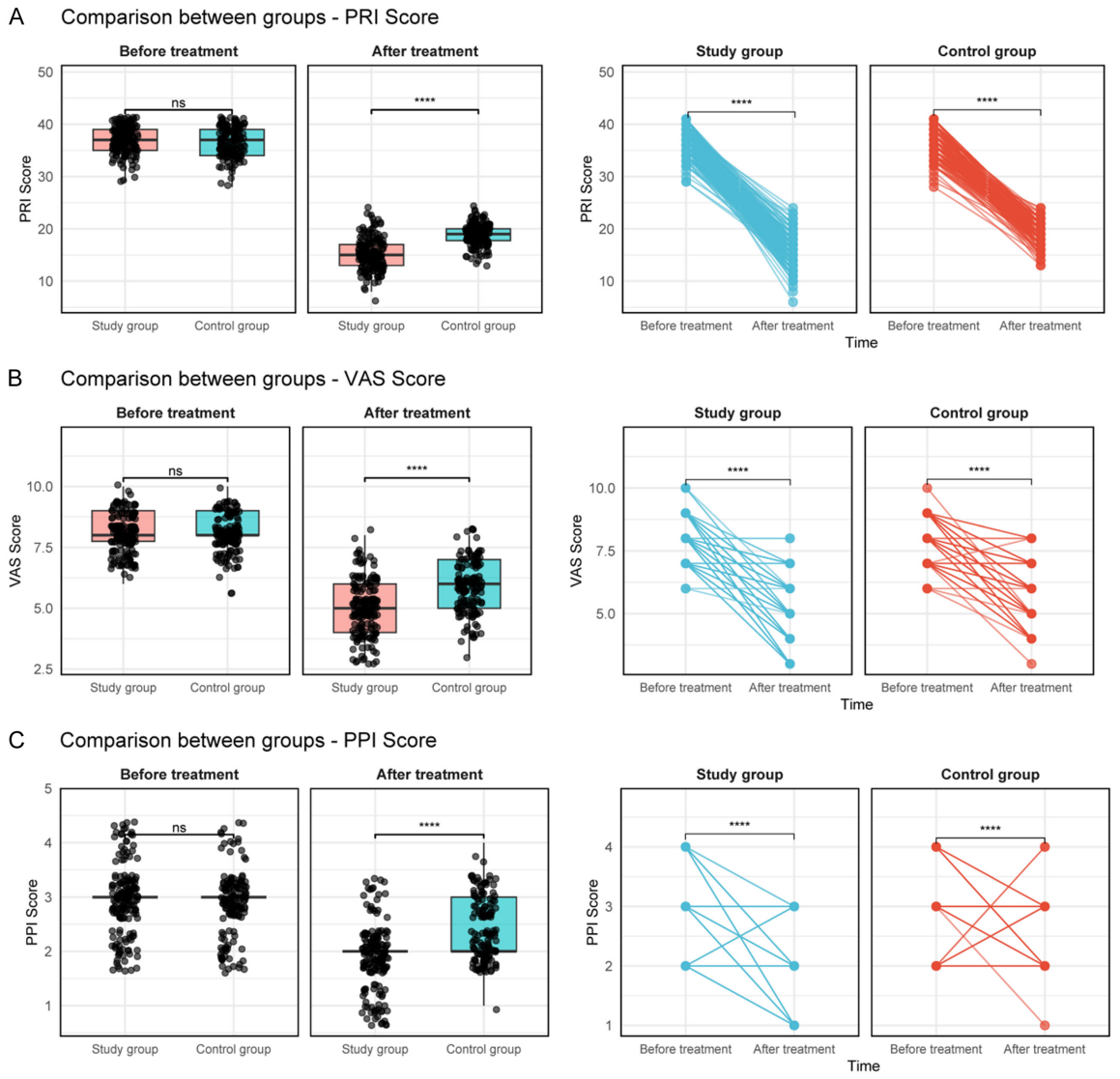

Figure 1. Effects of acupuncture treatment on SF-MPQ scores in patients with neuropathic pain following spinal cord injury. A. Changes in PRI scores. B. Changes in VAS scores. C. Changes in PPI scores. Note: SF-MPQ: Short-Form McGill Pain Questionnaire, PRI: Pain Rating Index, VAS: Visual Analogue Scale, PPI: Present Pain Intensity, ****P<0.0001, ns: no significance.

P=0.321; diabetes P=0.300; hypertension P=0.518; injury etiology P=0.771; injury location P=0.473; **Table 1**).

Changes in SF-MPQ scores pre- and post-treatment

Analysis conducted before and after treatment demonstrated notable disparities in the changes of SF-MPQ scores between the study and control groups. PRI scores (**Figure 1A**) indicated no significant pre-treatment differences between groups (P>0.05). After treatment, PRI scores decreased significantly in both groups (both P<0.0001), with a markedly greater reduction in the study group than in the control group. VAS scores (**Figure 1B**) also showed no significant baseline differences (P>0.05). Post-treatment VAS scores declined substantially in the study group (P<0.0001), whereas the control group showed only a modest reduction (P<0.0001). Similarly, PPI scores (**Figure 1C**) did not differ significantly before treatment (P>0.05), but decreased more in the study group than in the control group after treatment (both P<0.0001). Overall, the study group

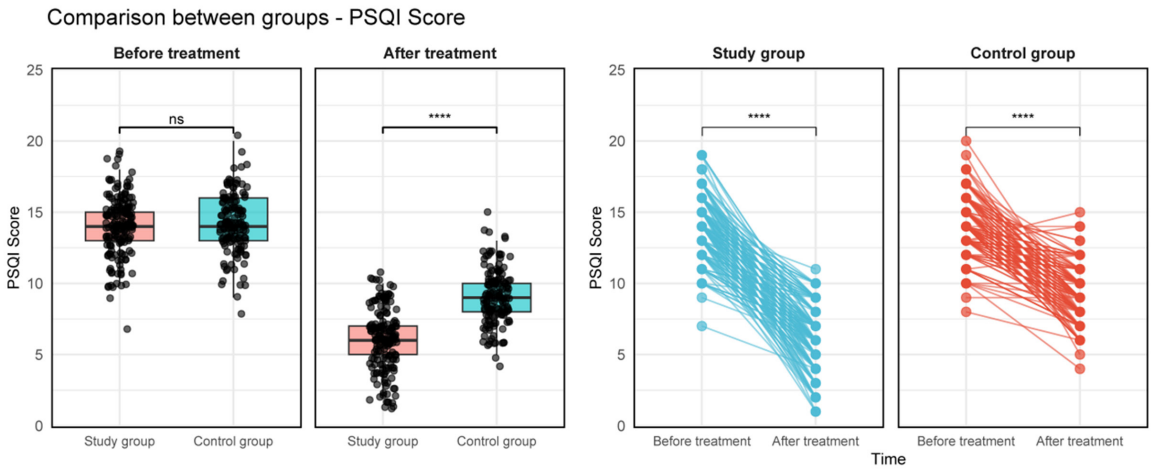

Figure 2. Effects of acupuncture treatment on sleep quality in patients with neuropathic pain following spinal cord injury. Note: PSQI: Pittsburgh Sleep Quality Index, ****P<0.0001, ns: no significance.

exhibited greater reductions across all three pain measures, indicating that acupuncture provided additional analgesic benefit for SCI-NP compared with pharmacotherapy alone.

Changes in sleep function scores pre- and post-treatment

Baseline PSQI did not differ between groups (P>0.05). After treatment, PSQI declined in the study group (P<0.0001), while the control group demonstrated smaller reduction (P<0.0001). The study group showed more significant change in PSQI than the control group, indicating an added sleep benefit of acupuncture in SCI-related NP (**Figure 2**).

Comparison of inflammatory marker levels Pre- and Post-treatment

At baseline, IL-1β, IL-6, and TNF-α did not differ between the study and control groups (all P>0.05). After treatment, concentrations declined in the study group (IL-1β **Figure 3A**; IL-6 **Figure 3B**; TNF-α **Figure 3C**; all P<0.0001). The control group also showed decreases (all P<0.0001), but the magnitude was smaller. Between-group comparisons favored the study group, indicating an added anti-inflammatory effect of acupuncture in SCI-related NP (**Figure 3**).

Comparison of immunoglobulin levels Pre- and Post-treatment

The assessment of immunoglobulin levels indicated no significant pre-treatment disparity in IgA levels (**Figure 4A**) between the study and control groups (P>0.05). However, the study group had a much bigger increase in IgA levels after treatment (P<0.0001) than the control group (P<0.0001). For IgG (**Figure 4B**), pre-treatment levels exhibited no significant differences (P>0.05); however, post-treatment IgG levels increased significantly in both groups (both P<0.0001), with the study group showing a significantly greater elevation than the control group. This indicates that acupuncture significantly enhances immune function in SCI-NP patients.

Comparison of adverse events in acupuncture treatment

In the comparison of adverse events (see **Table 2**), there were no significant differences between the groups in the number of nausea/vomiting, fatigue, dizziness/headache, or orthostatic hypotension. The study group had a nausea/vomiting rate of 3.57%, while the control group had a rate of 3.47%, which was not statistically significant (P=0.962). The study group had a fatigue rate of 4.17%, while the control group had a rate of 4.86%, which was also not statistically significant (P=0.768). The study group had a dizziness/headache rate of 4.76%, while the control group had a rate of 6.94%, which was also not statistically significant (P=0.410). The study group had an orthostatic hypotension rate of 2.98%, while the control group had a rate of 4.86%, which was also not statistically significant (P=0.388). Overall, acupuncture treatment did not significantly increase the number of adverse events.

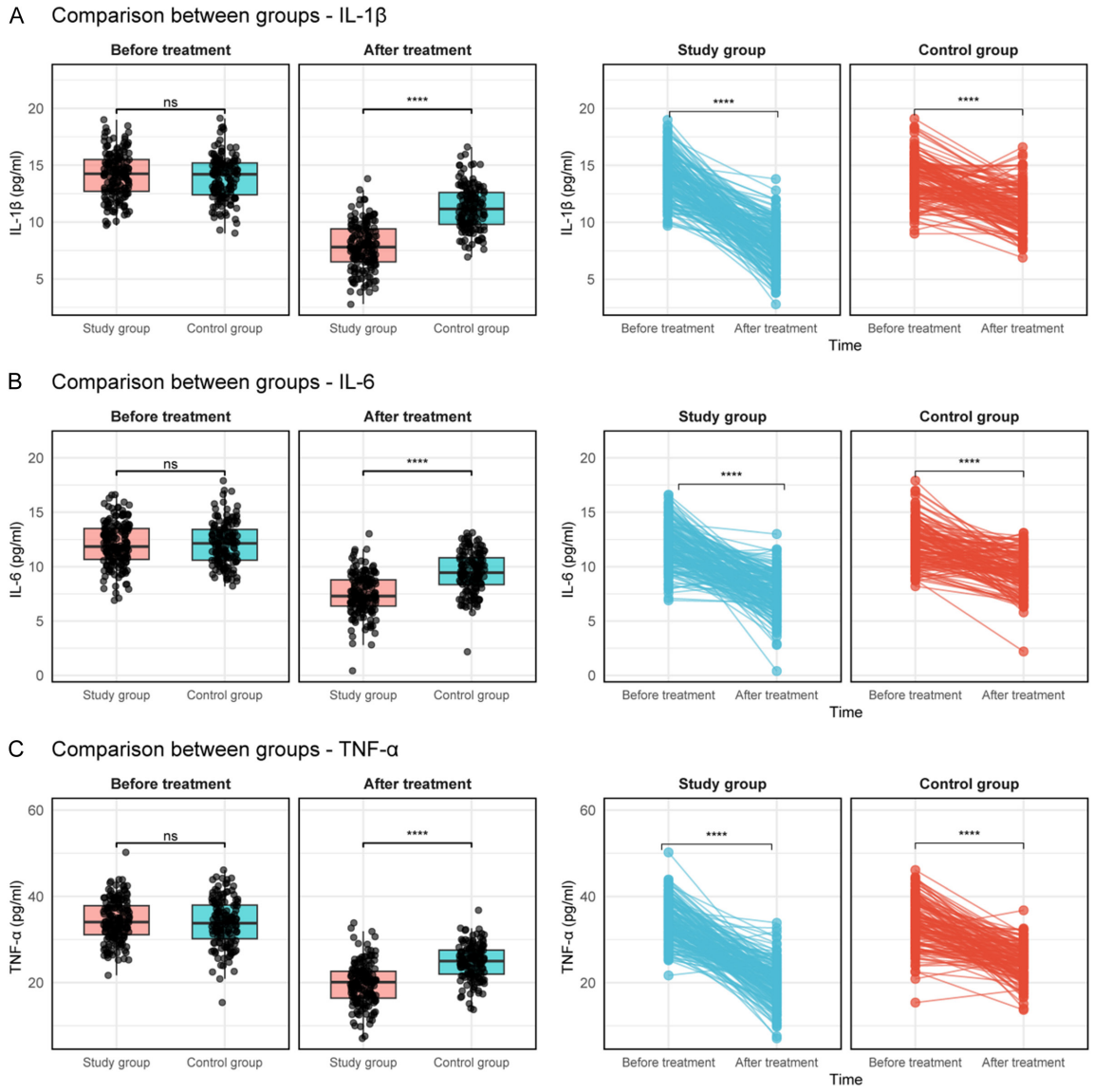

Figure 3. Effects of acupuncture treatment on inflammatory marker levels in patients with neuropathic pain following spinal cord injury. A. Changes in IL-1β levels. B. Changes in IL-6 levels. C. Changes in TNF-α levels. Note: IL-1β: Interleukin-1 Beta, IL-6: Interleukin-6, TNF-α: Tumor Necrosis Factor-alpha, ****P<0.0001, ns: no significance.

Correlation analysis between functional scores and inflammatory and immune markers

Pre-treatment correlation analysis (**Figure 5**) showed that PPI and PRI (P<0.0001), VAS (P< 0.0001), IL-6 (P<0.0001), TNF-α (P<0.0001), and IL-1β (P<0.0001) were all strongly related to each other. Following treatment (**Figure 6**), PPI continued to exhibit a significant positive correlation with PRI (P<0.0001), VAS (P< 0.0001), IL-6 (P<0.0001), TNF-α (P<0.0001), and IL-1β (P<0.0001). Furthermore, post-treatment PPI exhibited significant negative correlations with IgA (P<0.0001) and IgG (P<0.0001). PRI exhibited significant positive correlations with PSQI (P<0.0001), IL-6 (P<0.0001), TNF-α (P<0.0001), and VAS (P<0.0001). PSQI displayed negative correlations with IgA (P< 0.0001) and IgG (P<0.0001). These results demonstrate that post-acupuncture treatment, the associations between functional scores and inflammatory and immune markers were enhanced, especially for PSQI, PPI, and VAS indicators, with correlations among inflammatory and immune markers being further reinforced.

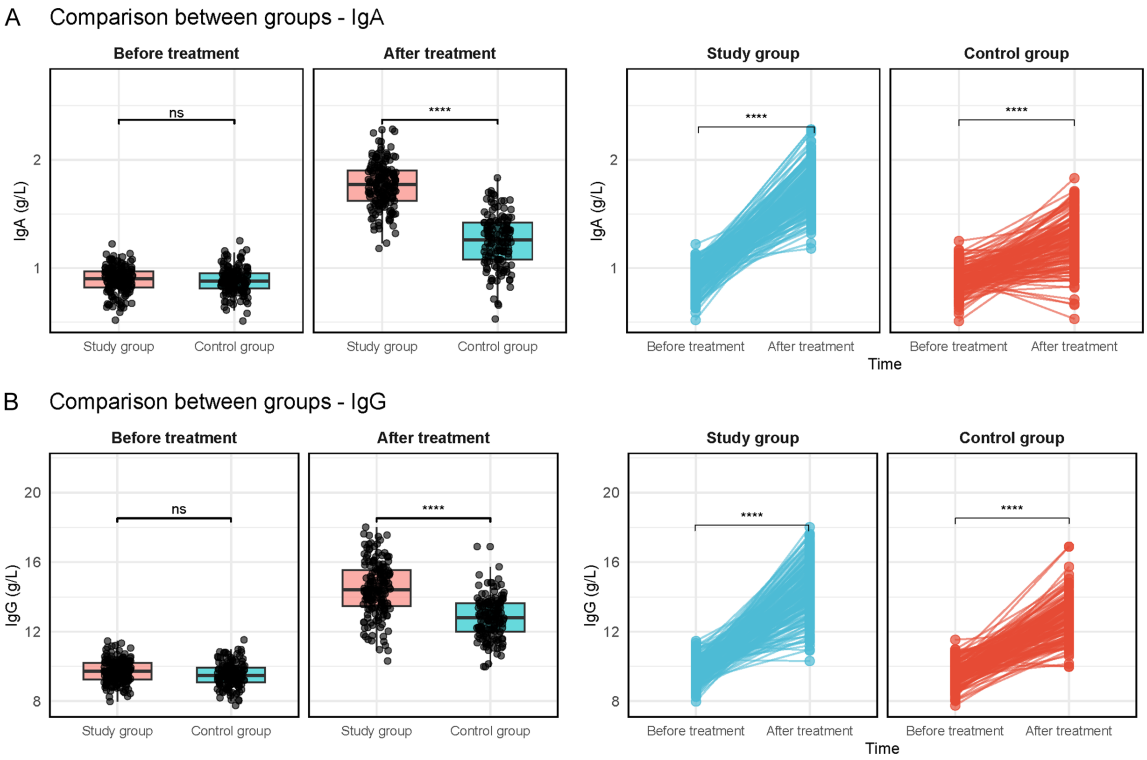

Figure 4. Effects of acupuncture treatment on immunoglobulin levels in patients with neuropathic pain following spinal cord injury. A. Changes in IgA levels. B. Changes in IgG levels. Note: IgA: Immunoglobulin A, IgG: Immunoglobulin G, ****P<0.0001, ns: no significance.

Table 2. Adverse event statistics

Variable	Nausea/Vomiting	Fatigue	Dizziness/Headache	Orthostatic Hypotension
Control Group (n=144)	5 (3.47%)	7 (4.86%)	10 (6.94%)	7 (4.86%)
Study Group (n=168)	6 (3.57%)	7 (4.17%)	8 (4.76%)	5 (2.98%)
χ^2 Value	0.002	0.087	0.679	0.745
P Value	0.962	0.768	0.41	0.388

Patient distribution by improvement status in pain intensity

Figure 7 shows how patients are spread out across varying degrees of improvement in pain scores (PRI, VAS, PPI). Based on established threshold criteria, an improvement in PRI score of at least 5 points or a reduction rate of at least 30% showed that most patients had significant pain improvement after treatment. A total of 173 patients met improvement criteria for all three scores (PRI, VAS, PPI) at the same time. A VAS score improvement of at least 2 points or at most 3 points is in line with efficacy standards in most pain intervention trials and shows trends in pain relief. An improvement in the PPI score (at least a 1-point or a 1-grade drop) also showed that most patients had a significant decrease in pain intensity after treatment. The upper panel of the Venn diagram shows that 173 patients fall into the intersection of PRI, VAS, and PPI improvements. This means that this group saw significant improvements in all pain score dimensions, meeting clinically significant relief standards.

Clinical characteristic comparison between pain improvement and non-improvement groups

Baseline characteristics showed that the groups that improved their pain and those that didn't were very different in terms of age and length of illness. Group comparisons

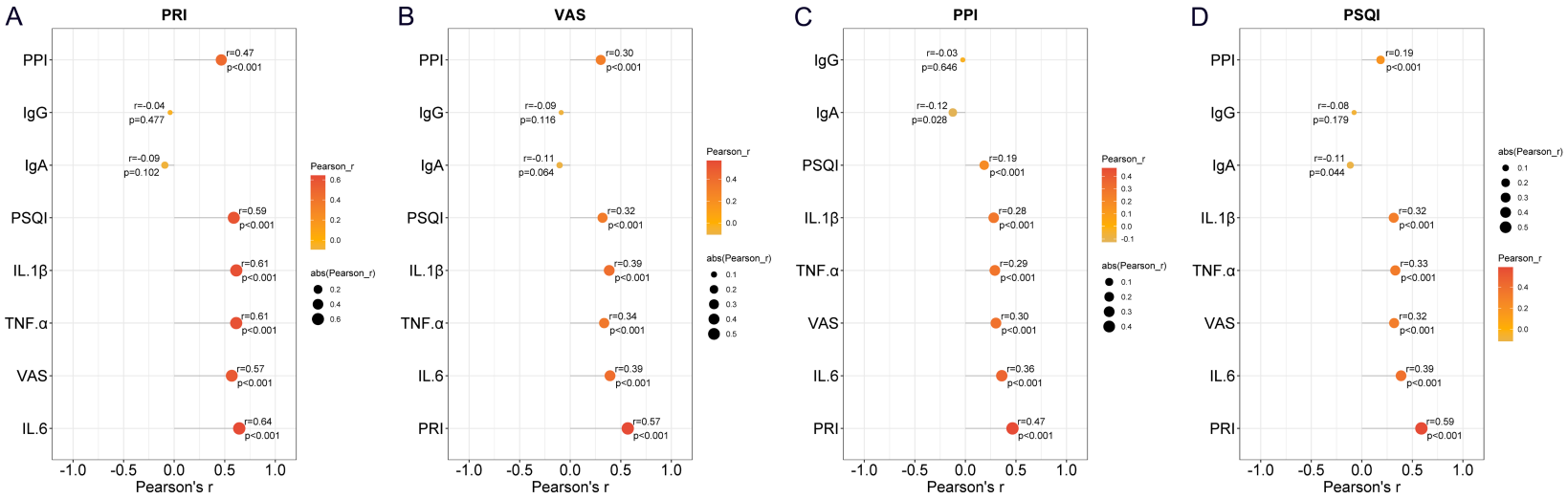

Figure 5. Correlation analysis between functional scores and inflammatory and immune markers at pre-treatment. A. Correlations between PRI scores and other variables. B. Correlations between VAS scores and other variables. C. Correlations between PPI scores and other variables. D. Correlations between PSQI scores and other variables. Note: PRI: Pain Rating Index, VAS: Visual Analog Scale, PPI: Pain Pressure Intensity, PSQI: Pittsburgh Sleep Quality Index, IL-1β: Interleukin-1 Beta, IL-6: Interleukin-6, TNF-α: Tumor Necrosis Factor-alpha, IgA: Immunoglobulin A, IgG: Immunoglobulin G.

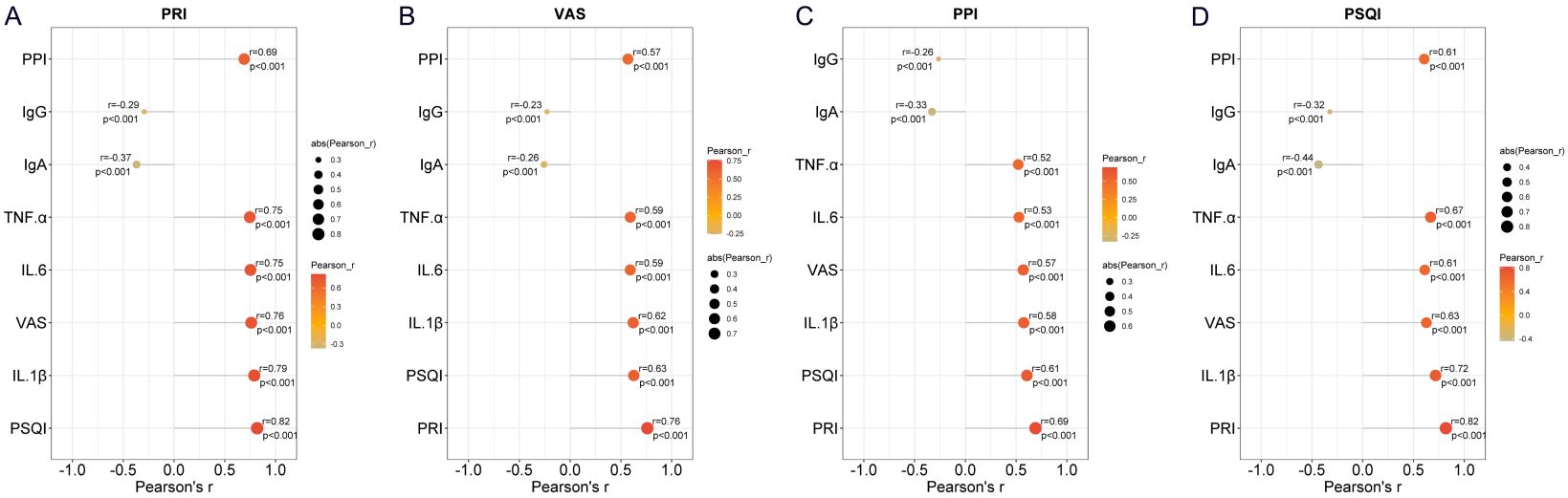

Figure 6. Correlation analysis between functional scores and inflammatory and immune markers at post-treatment. A. Correlations between PRI scores and other variables. B. Correlations between VAS scores and other variables. C. Correlations between PPI scores and other variables. D. Correlations between PSQI scores and other variables. Note: PRI: Pain Rating Index, VAS: Visual Analog Scale, PPI: Pain Pressure Intensity, PSQI: Pittsburgh Sleep Quality Index, IL-1β: Interleukin-1 Beta, IL-6: Interleukin-6, TNF-α: Tumor Necrosis Factor-alpha, IgA: Immunoglobulin A, IgG: Immunoglobulin G.

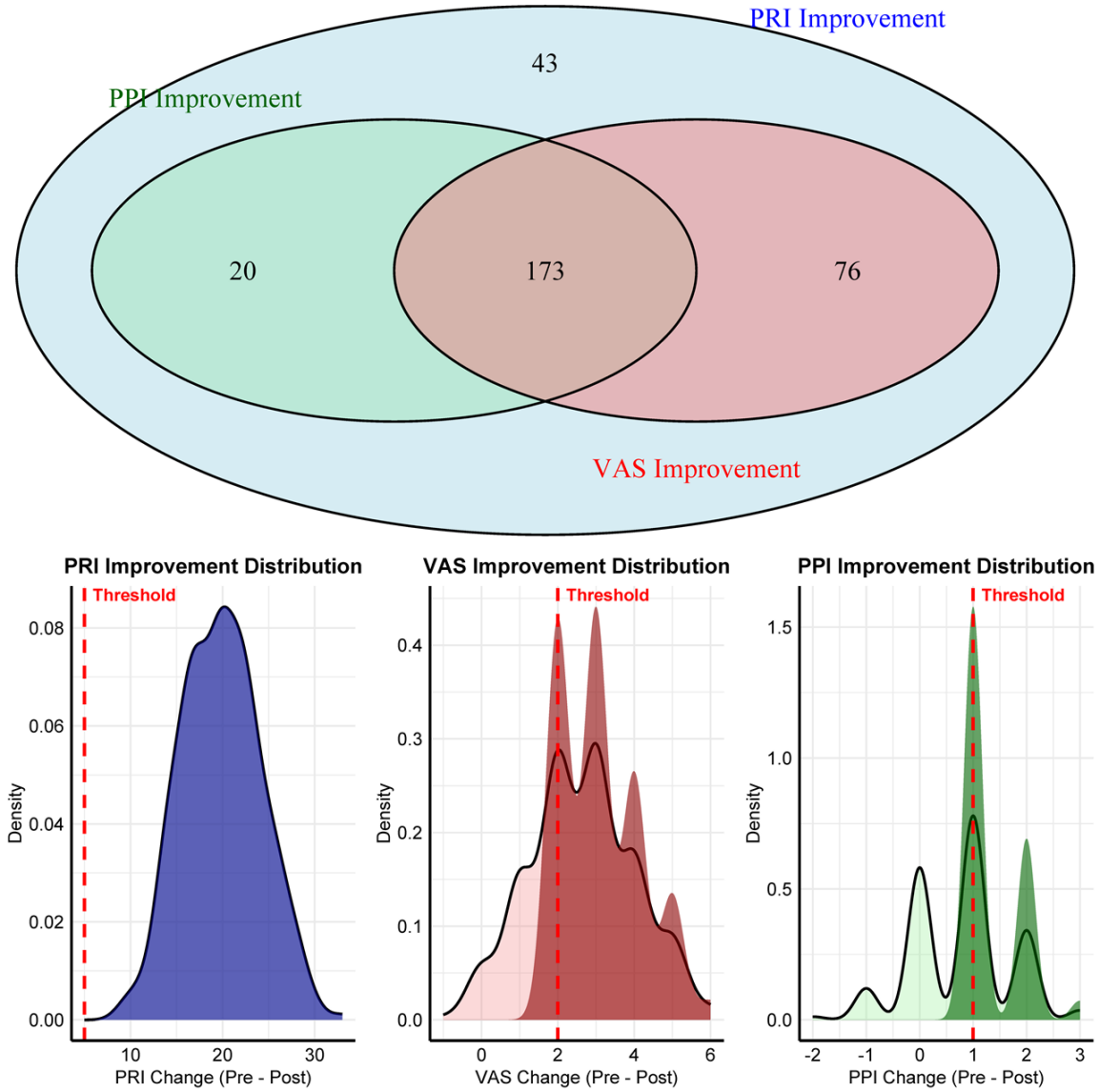

Figure 7. Patient distribution by improvement status in pain intensity. Note: PRI: Pain Rating Index, VAS: Visual Analog Scale, PPI: Pain Pressure Intensity.

showed imbalances in age and disease duration. Patients aged 40-50 years were more common in the improvement group, while those younger than 40 years were more common in the non-improvement group (P=0.002). Shorter disease duration (<6 months) was enhanced in the improvement group (P=0.005). There were no significant differences between groups for other variables, such as sex (P=0.734), BMI (P=0.160), educational level (P=0.604), occupation (P=0.795), smoking history (P=0.503), alcohol consumption history (P=0.903), diabetes history (P=0.160), hypertension history (P=0.929), injury etiology (P=0.330), and injury location (P=0.288) (**Table 3**).

Table 3. Clinical characteristics comparison between patients with and without pain improvement

Variable	Total	Pain Unimproved (n=139)	Pain Improved (n=173)	Statistical Value	*P* Value
Age				12.273	0.002
<40 years	104 (33.33%)	48 (34.53%)	56 (32.37%)		
40-50 years	143 (45.83%)	51 (36.69%)	92 (53.18%)		
>50 years	65 (20.83%)	40 (28.78%)	25 (14.45%)		
Sex				0.116	0.734
Male	147 (47.12%)	64 (46.04%)	83 (47.98%)		
Female	165 (52.88%)	75 (53.96%)	90 (52.02%)		
BMI				1.974	0.160
≥25 kg/m^2	95 (30.45%)	48 (34.53%)	47 (27.17%)		
<25 kg/m^2	217 (69.55%)	91 (65.47%)	126 (72.83%)		
Disease Duration				7.755	0.005
≥6 months	184 (58.97%)	94 (67.63%)	90 (52.02%)		
<6 months	128 (41.03%)	45 (32.37%)	83 (47.98%)		
Educational Level				0.268	0.604
≥ High school	151 (48.40%)	65 (46.76%)	86 (49.71%)		
< High school	161 (51.60%)	74 (53.24%)	87 (50.29%)		
Occupation				0.068	0.795
Employed	263 (84.29%)	118 (84.89%)	145 (83.82%)		
Other	49 (15.71%)	21 (15.11%)	28 (16.18%)		
Smoking History				0.449	0.503
Yes	164 (52.56%)	76 (54.68%)	88 (50.87%)		
No	148 (47.44%)	63 (45.32%)	85 (49.13%)		
Alcohol Consumption History				0.015	0.903
Yes	48 (15.38%)	21 (15.11%)	27 (15.61%)		
No	264 (84.62%)	118 (84.89%)	146 (84.39%)		
Diabetes History				1.975	0.160
Yes	32 (10.26%)	18 (12.95%)	14 (8.09%)		
No	280 (89.74%)	121 (87.05%)	159 (91.91%)		
Hypertension History				0.008	0.929
Yes	41 (13.14%)	18 (12.95%)	23 (13.29%)		
No	271 (86.86%)	121 (87.05%)	150 (86.71%)		
Injury Etiology				2.219	0.330
Traffic accident	144 (46.15%)	68 (48.92%)	76 (43.93%)		
Fall injury	115 (36.86%)	45 (32.37%)	70 (40.46%)		
Other	53 (16.99%)	26 (18.71%)	27 (15.61%)		
Injury Location				2.492	0.288
C1-C7	127 (40.71%)	58 (41.73%)	69 (39.88%)		
T1-T11	157 (50.32%)	65 (46.76%)	92 (53.18%)		
T12-L1	28 (8.97%)	16 (11.51%)	12 (6.94%)		

Note: BMI, Body Mass Index.

Interactive relationship between age, disease duration, and improvement status in pain intensity

Figure 8 illustrates the joint association of age group and disease duration with pain improvement. As shown in the interaction analysis (**Table 4**), the effect of disease duration on pain improvement differed significantly across age groups. The interaction term for patients aged 40-50 years was statistically significant (P=0.018): within this age group, longer dis-

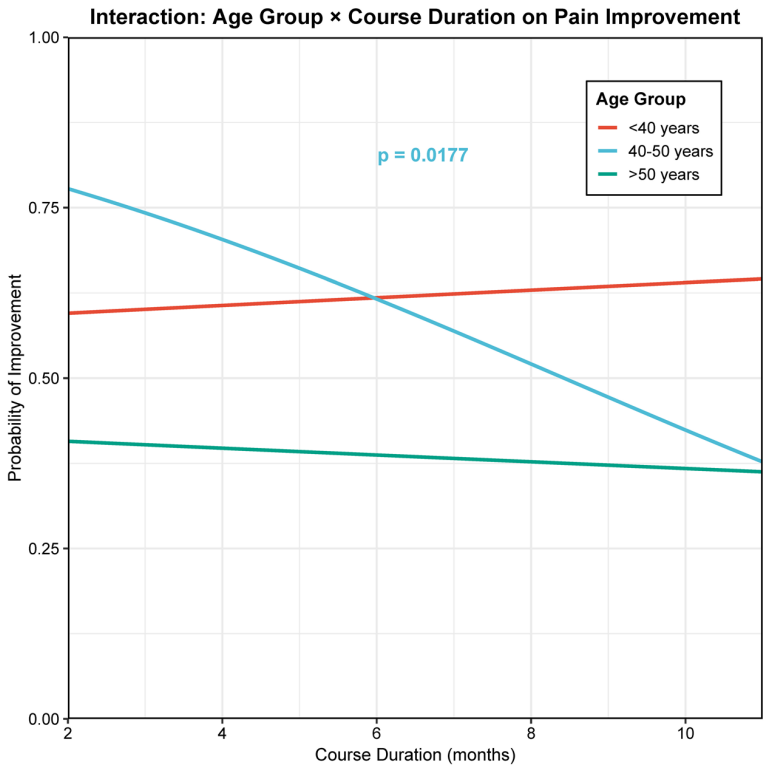

Figure 8. Interactive relationship between age group and disease duration on pain improvement. Note: Pain Improvement Group (0= No Improvement, 1= Improvement), Age Group (<40 years, 40-50 years, >50 years), Course of Disease (Months).

Table 4. Interaction analysis results of age group and disease duration on pain improvement

Variable	Estimate	Std Error	Z value	*P* value
(Intercept)	0.338	0.470	0.720	0.472
Age Group 40-50	1.304	0.671	1.944	0.052
Age Group >50	-0.671	0.805	-0.834	0.404
Course_of_disease	0.024	0.067	0.357	0.721
Age Group 40-50:Course_of_disease	-0.219	0.092	-2.372	0.018
Age Group >50:Course_of_disease	-0.045	0.114	-0.393	0.694

ease duration was associated with a lower probability of pain improvement (slope P= 0.017). In contrast, the interaction terms for patients younger than 40 years (P=0.472) and those older than 50 years (P=0.694) were not significant, indicating no clear evidence that disease duration materially affected the likelihood of pain improvement in these age groups. Overall, these patterns suggest that the impact of disease duration on pain improvement is age dependent and is most pronounced among patients aged 40-50 years.

Discussion

Compared with pharmacotherapy alone, adding acupuncture produced larger reductions in PRI, VAS, and PPI, indicating an adjunctive analgesic effect. Prior work reports benefits across multiple pain scales [20]. In SCI-related NP, Yang et al. observed a significant analgesic effect of acupuncture [21], and Eller et al. emphasized the safety and adaptability of nonpharmacologic strategies, including acupuncture for SCI pain management [22]. Sleep quality also improved in the acupuncture group, as shown by lower PSQI scores. Parallel gains in pain and sleep have been described in NP cohorts treated with acupuncture and likely reflect shared neurobiological pathways. Taken together, our data and the literature support integrating acupuncture with standard pharmacotherapy for SCI-NP, especially for patients seeking better pain control and sleep quality without additional adverse events.

Patients who received acupuncture plus pharmacotherapy showed larger declines in IL-1β, IL-6, and TNF-α and greater increases in IgA and IgG than controls. Acupuncture has been reported to modulate immune responses after SCI, such as by reducing inflammatory activity and improving immune indices [8]. After SCI, activated microglia and astrocytes release pro-inflammatory cytokines that facilitate nociceptive transmission and lower pain thresholds [24]. Experimental studies also show that electroacupuncture shifts macrophage polarization from an M1 to an M2 phenotype, which dampens neuroinflammation and pain [25]. Other work notes concurrent suppression of pro-inflammatory cytokines and enhancement of anti-inflammatory signaling with acupuncture

[26], a change that can interrupt feedback between inflammation and pain. Additional mechanisms include reduced neuronal hyperexcitability and recruitment of descending inhibitory pathways [23]. These mechanisms provide a biologic context for the biomarker and clinical improvements observed in this cohort.

In this cohort, pro-inflammatory cytokines (IL-1β, IL-6, TNF-α) declined while IgA/IgG increased. Pain tracked positively with cytokines, whereas both pain and PSQI tracked negatively with IgA/IgG. These data support a compact working model: acupuncture engages neuroimmune control, lowers inflammatory drive, shifts humoral immunity toward balance, and - through these biological changes - improves pain and sleep. This finding is coherent with psychoneuroimmunology evidence linking sleep, immune function, and inflammatory tone [27] and with preclinical data, which showed that electroacupuncture suppresses microglial/NF-κB-NLRP3 signaling relevant to IL-1β and TNF-α [28]. Because IL-1β is a canonical product of inflammasome activation, its reduction is compatible with lower inflammasome/glial signaling. Although we did not assay NLRP3, caspase-1, or glial markers, the observed cytokine pattern aligns with that pathway and warrants direct measurement in future studies [28].

Acupuncture likely acts beyond segmental analgesia in SCI-related NP. Stimulation engages central circuits that influence recovery and nociception, including dorsal horn interneuron networks and descending modulatory pathways from midbrain and medullary centers to the spinal cord [26]. Restoring balance in these systems reduces central sensitization, stabilizes sensory gain, and strengthens endogenous inhibition, which lowers spontaneous pain and tactile hyperalgesia. Thalamocortical and limbic regions involved in salience, affect, and arousal are also implicated, linking pain control with sleep regulation. By reducing hyperarousal and nociceptive drive, acupuncture appears to facilitate sleep onset and continuity while alleviating daytime pain. Larger declines in PRI, VAS, and PPI, together with lower PSQI scores, in the acupuncture group are consistent with a central-modulation account.

Stress-arousal physiology likely helps connect the biomarker and PSQI changes. Sleep and immune function influence each other bidirectionally, and altered inflammatory tone can sustain hyperarousal. Acupuncture has been reported to modulate this interconnected system of sleep, immunity, and inflammation. In our data, improvement in sleep quality (as measured by a reduction in PSQI score) accompanied cytokine reductions and higher IgA/IgG, consistent with tighter sleep-immune coupling. Prospective work should add multi-timepoint cortisol/adrenocorticotropic hormone (ACTH) with cytokines and immunoglobulins to test mediation [27, 29].

Beyond earlier studies in diabetic neuropathy and in pain associated with cancer, we focused on SCI-NP and evaluated several domains at once, including pain ratings, sleep quality, circulating cytokines such as IL-6 and TNF-α, and immunoglobulins. The data are consistent with a neuroimmune mechanism in which acupuncture improves central inhibitory control and restores HPA axis feedback. In turn, pro-inflammatory output falls, glial drive lessens, and sleep improves. The observed biomarker shifts align with clinical improvement seen with stable medication. To test this mechanism, future work should collect corticotropin-releasing hormone, ACTH, and cortisol at repeated time points, follow cytokines and immunoglobulins longitudinally, and relate their changes to pain and sleep using mediation analysis. Findings from such studies may support more targeted care, for instance, selecting acupuncture for patients who present with high inflammatory markers or marked sleep disturbance.

This study shows that adding acupuncture to conventional pharmacotherapy relived pain, improved sleep, reduced levels of inflammatory cytokines, and increased immunoglobulins in patients with NP after SCI, without increasing adverse events. Prior reports, including Eller et al. [22], note that opioids, anticonvulsants, and antidepressants often provide limited relief and can cause side effects. Acupuncture offers a nonpharmacologic alternative for patients with poor medication tolerance or drug allergies. We also found an interaction between age and disease duration. Among patients aged 40-50 years, longer duration was associated with a lower probability of pain improvement. These results support integrating acupuncture

into care and tailoring protocols for patient age and disease duration.

Acupuncture may relieve NP and sleep disturbance through coordinated neuroimmune and inflammatory mechanisms. Dysregulation of the HPA axis links pain, stress, and insomnia. Improved feedback regulation of the corticotropin-releasing hormone, ACTH, and cortisol pathway could reduce stress-related inflammation and ease symptoms [30]. In our cohort, lower IL-1β, IL-6, and TNF-α together with better PSQI scores fit with partial normalization of HPA-axis activity. Acupuncture may also reduce neuronal hyperexcitability and inhibit glial activation, which would lessen pro-inflammatory cytokine release and central sensitization [31]. This pattern is consistent with the observed increases in IgA and IgG and suggests movement toward immune homeostasis. At a molecular level, electroacupuncture has been reported to inhibit NLRP3 inflammasome activation and to limit microglial pyroptosis, interrupting inflammatory cascades relevant to NP [32]. Taken together, these mechanisms agree with our biomarker profile and help explain the parallel improvements in pain and sleep when acupuncture is added to medication.

This single-center retrospective study suggests that adding acupuncture to conventional pharmacotherapy benefits patients with SCI-related NP. But the study remains limited because the sample came from one hospital and the observation window was four weeks, which leaves durability and longer-term safety unresolved. Specifically, laboratory biomarkers were measured at baseline and after the 4-week treatment period, whereas pain and sleep scores were assessed at baseline and 3 months after treatment to evaluate short-term maintenance of effect. The retrospective design means that the associations between cytokines or immunoglobulins and clinical improvement are correlational. A prospective, multicenter design with longitudinal sampling would test whether cytokines mediate treatment effects on pain and sleep and should include repeated measures of the HPA axis. Longer follow-up is needed to evaluate maintenance of benefit and adverse events. Most outcomes were patient-reported (pain scores and PSQI), so reporting bias is possible. We also relied solely on subjective questionnaires without objective sleep monitoring (e.g., polysomnography) or pain physiological assessment (e.g., quantitative sensory testing), which limits our ability to detect treatment-related changes in sleep architecture or sensory thresholds. Adding objective measures such as actigraphy, quantitative sensory testing, heart-rate variability, or neuroimaging would strengthen inference. Future work should also tailor acupuncture protocols to age, disease duration, and immune status.

Conclusion

This study supports the conclusion that adding acupuncture to conventional Western medicine alleviated SCI-related NP, improved sleep, reduced inflammatory markers, and increased immunoglobulins, with no increase in adverse events over the study period. Pain improvement varied by age and disease duration: among patients aged 40-50 years, longer duration was associated with a lower probability of improvement. These results justify the integration of acupuncture into standard care for SCI-NP and identify patient age and disease duration as key factors for personalizing treatment and guiding future research.

Disclosure of conflict of interest

None.

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References

[1] Anjum A, Yazid MD, Fauzi Daud M, Idris J, Ng AMH, Selvi Naicker A, Ismail OHR, Athi Kumar RK and Lokanathan Y. Spinal cord injury: pathophysiology, multimolecular interactions, and underlying recovery mechanisms. Int J Mol Sci 2020; 21: 7533.

[2] Eli I, Lerner DP and Ghogawala Z. Acute traumatic spinal cord injury. Neurol Clin 2021; 39: 471-488.

[3] Widerström-Noga E. Neuropathic pain and spinal cord injury: management, phenotypes, and biomarkers. Drugs 2023; 83: 1001-1025.

[4] Sun L, Peng C, Joosten E, Cheung CW, Tan F, Jiang W and Shen X. Spinal cord stimulation and treatment of peripheral or central neuro-

pathic pain: mechanisms and clinical application. Neural Plast 2021; 2021: 5607898.
[5] Kohno K, Shirasaka R, Yoshihara K, Mikuriya S, Tanaka K, Takanami K, Inoue K, Sakamoto H, Ohkawa Y, Masuda T and Tsuda M. A spinal microglia population involved in remitting and relapsing neuropathic pain. Science 2022; 376: 86-90.
[6] Ye Y, Su X, Tang J and Zhu C. Neuropathic pain induced by spinal cord injury from the glia perspective and its treatment. Cell Mol Neurobiol 2024; 44: 81.
[7] Tong C, Zhengyao Z, Mei L, Dongpo S, Qian H and Fengqun M. Pregabalin and gabapentin in patients with spinal cord injury-related neuropathic pain: a network meta-analysis. Pain Ther 2021; 10: 1497-1509.
[8] He K, Hu R, Huang Y, Qiu B, Chen Q and Ma R. Effects of acupuncture on neuropathic pain induced by spinal cord injury: a systematic review and meta-analysis. Evid Based Complement Alternat Med 2022; 2022: 6297484.
[9] Wang N, Zhao L, Zhang D and Kong F. Research progress on the immunomodulatory mechanism of acupuncture in tumor immune microenvironment. Front Immunol 2023; 14: 1092402.
[10] Wu J and Zhao Z. Acupuncture in circadian rhythm sleep-wake disorders and its potential neurochemical mechanisms. Front Neurosci 2024; 18: 1346635.
[11] Khosravaninezhad Y, Moshfeghinia R, Liaghat L, Ghazipoor H, Kaheni Y, Javidan A, Mirzaee Y, Azadmehr A, Hashemi Y and Pasalar M. Effect of acupressure and acupuncture on sleep quality in cancer patients with insomnia: a systematic review and meta-analysis. Explore (NY) 2025; 21: 103192.
[12] Norrbrink C and Lundeberg T. Acupuncture and massage therapy for neuropathic pain following spinal cord injury: an exploratory study. Acupunct Med 2011; 29: 108-115.
[13] Ge SY, Hu MM, Li KP, Wu CQ, Xu GH and Dong L. Comparative efficacy of common rehabilitation treatments for patients with neuropathic pain after spinal cord injury: a systematic review and network meta-analysis. Neurol Sci 2025; 46: 3547-3557.
[14] Liu LY, Su Y, Wang RR, Lai YY, Huang L, Li YT, Tao XY, Su MH, Zheng XY, Huang SC, Wu YN, Yu SY, Liang FR and Yang J. Transcutaneous electrical acupoint stimulation benefits postoperative pain relief of oocyte retrieval: a randomized controlled trial. J Integr Med 2024; 22: 32-38.
[15] Zhao H, Wang C, Wang X, Ju J, Yan C and Shi B. Efficacy and safety of acupuncture in the treatment of radicular cervical spondylosis: a systematic review and meta-analysis. Comb Chem High Throughput Screen 2024; 27: 2951-2962.
[16] Iordache SD, Frenkel Rutenberg T, Pizem Y, Ravid A and Firsteter O. Traditional physiotherapy vs. fascial manipulation for the treatment of trigger finger: a randomized pilot study. Isr Med Assoc J 2023; 25: 286-291.
[17] Wu W, Meng T, Jin F, Li J, Huang J, Guo Z, Yu M and Zhou Y. Effects of resveratrol on postmenopausal women: a systematic review and meta-analysis. Front Pharmacol 2025; 16: 1588284.
[18] Zitser J, Allen IE, Falgàs N, Le MM, Neylan TC, Kramer JH and Walsh CM. Pittsburgh Sleep Quality Index (PSQI) responses are modulated by total sleep time and wake after sleep onset in healthy older adults. PLoS One 2022; 17: e0270095.
[19] Dworkin RH, Turk DC, Farrar JT, Haythornthwaite JA, Jensen MP, Katz NP, Kerns RD, Stucki G, Allen RR, Bellamy N, Carr DB, Chandler J, Cowan P, Dionne R, Galer BS, Hertz S, Jadad AR, Kramer LD, Manning DC, Martin S, McCormick CG, McDermott MP, McGrath P, Quessy S, Rappaport BA, Robbins W, Robinson JP, Rothman M, Royal MA, Simon L, Stauffer JW, Stein W, Tollett J, Wernicke J and Witter J; IMMPACT. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. Pain 2005; 113: 9-19.
[20] Kannan P, Bello UM and Winser SJ. Physiotherapy interventions may relieve pain in individuals with central neuropathic pain: a systematic review and meta-analysis of randomised controlled trials. Ther Adv Chronic Dis 2022; 13: 20406223221078672.
[21] Yang Y, Tang Y, Qin H and Xu J. Efficacy of transcutaneous electrical nerve stimulation in people with pain after spinal cord injury: a meta-analysis. Spinal Cord 2022; 60: 375-381.
[22] Eller OC, Willits AB, Young EE and Baumbauer KM. Pharmacological and non-pharmacological therapeutic interventions for the treatment of spinal cord injury-induced pain. Front Pain Res (Lausanne) 2022; 3: 991736.
[23] Ma X, Chen W, Yang NN, Wang L, Hao XW, Tan CX, Li HP and Liu CZ. Potential mechanisms of acupuncture for neuropathic pain based on somatosensory system. Front Neurosci 2022; 16: 940343.
[24] Li X, Huang Y and Bai J. Spinal astrocytes involved in the pathogenesis and treatment of neuropathic pain. Front Cell Neurosci 2025; 19: 1547524.
[25] Shi G, Hao X, Tu JF, Chen W, Fu Y, Ma X, Liu C and Li H. Electroacupuncture regulates macrophage polarization to alleviate the neuropathic pain induced by spared nerve injury. J Pain Res 2025; 18: 663-671.

[26] Feng Z, Cui S, Yang H, Wang Y, Zhou X, Wong J, Lai L, Yang Z, Huang B, Zheng H and Xu M. Acupuncture for neuropathic pain: a meta-analysis of randomized control trials. Front Neurol 2022; 13: 1076993.
[27] Irwin MR. Why sleep is important for health: a psychoneuroimmunology perspective. Annu Rev Psychol 2015; 66: 143-172.
[28] Yuan M, Wang D, Yang J and Lan H. The NLR family pyrin domain containing 3 inflammasome in the mechanism of electroacupuncture: current status and future perspectives. Front Aging Neurosci 2022; 14: 913881.
[29] Liu C, Zheng S, Wu W, Wang X, Qin S, Zhao Y, Xi H and Wan Q. Effects of acupuncture on the hypothalamus-pituitary-adrenal axis in chronic insomnia patients: a study protocol for a randomized controlled trial. Trials 2019; 20: 810.
[30] Zheng JY, Zhu J, Wang Y and Tian ZZ. Effects of acupuncture on hypothalamic-pituitary-adrenal axis: current status and future perspectives. J Integr Med 2024; 22: 445-458.
[31] Chen Y, Li D, Li N, Loh P, Guo Y, Hu X, Zhang J, Dou B, Wang L, Yang C, Guo T, Chen S, Liu Z, Chen B and Chen Z. Role of nerve signal transduction and neuroimmune crosstalk in mediating the analgesic effects of acupuncture for neuropathic pain. Front Neurol 2023; 14: 1093849.
[32] Kui W, Li Y, Gu Z, Xie L, Huang A, Kong S, Song L, Li L, Yu J, Xue CC and Wang K. Electroacupuncture inhibits NLRP3-mediated microglial pyroptosis to ameliorate chronic neuropathic pain in rats. J Pain Res 2025; 18: 1115-1129.