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Effect of Acupuncture Treatment on Post-stroke Depression by Using Diamond-Like Ultra-Thin Nano-Coating Technology

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ABSTRACT

This study aimed to explore the effect of acupuncture on account of composite diamond-like nano-membrane sensors (DLNF) sensors on post-stroke depression. Titanium/antigen-diamond-like carbon (Ti/Ag-DLC) composite DLNF sensors were prepared by coating Ti and Ag composites on the surface of DLC by radio frequency magnetron sputtering technology. The scanning electron microscope (SEM), X-ray photoelectron spectrometer (XPS), Raman spectrometer, nanoindenter, and sliding friction tester were adopted to analyze the characterization of Ti/Ag-DLC composite membrane, the chemical state of the main constituent elements on the surface, structural characteristics, membrane hardness, and tribological properties, respectively. 132 patients with post-stroke depression in our hospital were selected as the research objects, they were divided into the control group (receiving conventional treatment) and the acupuncture group (receiving acupuncture based on conventional treatment) according to different treatment methods, with 66 cases in each group. The depression of the two groups of patients before the treatment and 4 and 8 weeks after the treatment were compared. The psychological resilience scale and Herth scale were used to evaluate the mental toughness and hope level of patients. The results showed that when the Ag content was less than 0.55%, the Ti/Ag-DLC composite surface was smooth and showed no obvious particles, the membranes with different content had obvious absorption peaks at 1560 cm^{-1} and the friction life in a high vacuum environment was extended to around 900 revolutions. After 4 and 8 weeks of treatment, the scores of the hammer depression scale (HDS) in the two groups were significantly lower than before treatment (P<0.01) and the scores of the acupuncture group were much lower after 4 and 8 weeks of treatment in contrast to the control group (P<0.01). The optimism, self-strength, and tenacity in the psychological resilience scale of the acupuncture group patients rose higher than those in the control group (P<0.05) after 8 weeks of treatment. The Herth scale score of the acupuncture group was greatly higher compared with that of the control group after 8 weeks of treatment (P<0.01). It showed that the Ti/Ag-DLC composite DLNF sensor with good hardness and friction performance was prepared in this study. Acupuncture therapy could improve the negative emotions of patients with post-stroke depression, enhance mental resilience, and help raise the level of hope. Therefore, it was proved to be a potentially effective treatment.

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Introduction

Stroke is a common disease in neurology, especially in the elderly, and it brings great life pressure to patients and their families (1). Depression is a common complication of stroke. It belongs to a kind of emotional and mental disorder caused by stroke. Patients suffer from sleep disorders, depression, lack of interest in anything, and physical discomfort for a long time. In severe cases, it can even be life-threatening (2,3). According to relevant research statistics, post-stroke depression has a high incidence (about 25%-75%), disability rate, and fatality rate (up to 70%-90%), which has a great impact on the quality of life of patients (4,5). At present, the pathogenesis of the disease is not clear. Most experts believe that the incidence of post-stroke depression is closely related to the low central nervous system function (6,7). In terms of treatment, studies have found that timely detection and advanced interventional treatment could effectively reduce the mortality of patients (8) In the past, the treatment of depression was mainly treated with western medicine. However, most patients had a strong dependence on such drugs and the disease was easy to relapse once the drugs were stopped (9). Therefore, acupuncture therapy in traditional Chinese medicine has been well developed in the treatment of post-stroke depression through people's continuous exploration and

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researches. Studies have found that the acupuncture therapy has a good effect on the treatment of this disease, with fewer side effects and no symptoms such as drug dependence (10). The acupuncture treatment is to stimulate the corresponding acupoints of the brain as the main treatment method. Thus, the intensity of stimulation will have a certain effect on the therapeutic effect.

In order to make acupuncture stimulation on acupoints more effective, further enhance the needle feeling of acupuncture points, and improve the therapeutic effect by conducting external stimulation, someone proposed a kind of diamond-like membrane sensor (11). Diamond-like (12) is an amorphous carbon material with high hardness, high elasticity, low friction coefficient, high wear resistance, stable chemical structure, and good biocompatibility (13). Therefore, the diamond-like membrane has been widely applied in various fields as a coating, such as aerospace, optoelectronics, biomedicine, and mechanical engineering (14). In addition, studies have found that the introduction of nano-structure into diamond-like membranes can greatly improve the macroscopic properties of the membranes, and achieve excellent mechanical and tribological properties of the membranes (15).

Therefore, diamond-like membrane sensors on account of Ti/Ag composite nanoscale were used to enhance the stimulation intensity of acupuncture in this study. In the future, it will be used for the treatment of patients with post-stroke depression and evaluate its therapeutic effect to provide safer and more effective treatment for patients with post-stroke depression.

Materials and methods

Study objects

In this study, 132 patients with stroke complicated with depression who visited our hospital from January 2020 to January 2021 were randomly selected as the study objects. Among them, there were 75 male patients and 57 female patients, ranging in ages from 40 to 78 years old, with an average age of 55.89 ± 15.91 years old. The course of the disease ranged from 18 months to 24 months, with an average course of 21.35 ± 5.41 months. There were 70 patients with cerebral infarction and 62 patients with cerebral hemorrhage. According to different treatment methods, 132 patients were divided into the control group (routine treatment) and the acupuncture group (acupuncture in addition to routine treatment), with 66 patients in each group. The depression of the two groups was compared by *Hamilton Depression Scale* (HAMD) (16) before the treatment and 4 and 8 weeks after the treatment. The mental resilience scale (17) and the Herth hope scale (18) were used to evaluate the mental resilience and hope levels of the two groups before the treatment and 8 weeks after the treatment. This study had been approved by the relevant medical ethics committee.

There were five requirements in the inclusion criteria. First, all patients were diagnosed according to *the Third Edition of Chinese Classification and Diagnostic Criteria for Mental Disorders* (19). Second, cerebral infarction or cerebral hemorrhage was diagnosed by MRI or CT on account of *the Diagnostic Criteria Formulated by the Fourth National Academic Conference on Cerebrovascular Diseases* (20). Third, the condition of all patients was relatively stable, conscious, and able to better cooperate with the doctor's treatment. Fourth, informed consent was obtained from patients and their families. Fifth, none of the patients had a history of depression, and the disease developed about 3 weeks after stroke.

There were three requirements in the exclusion criteria. First, patients who received antidepressant medication within 3 weeks or less of onset. Second, patients with serious liver, kidney, other organ diseases, and a history of depression or depression with endogenous depression, addictive substances caused by depression patients. Third, the patients' consciousness was blurred and didn't cooperate with the doctors' examination and treatment.

Therapeutic methods

The control group: It was suggested to conduct routine treatment, reduce intracranial pressure, adjust electrolytes, etc. Patients took sertraline hydrochloride tablets orally. The dosage was 50 mg once a day for 8 weeks.

The acupuncture group: Acupuncture and moxibustion were performed based on routine treatment in the control group. Specific operation: Patients were required to keep position supine and acupunctured in shuxue, Si Shencong, Zhi Sanzhen,

Danzhong, Neiguan, Taichong and so on. Attention should be paid to routine disinfection of acupuncture points and acupoints before acupuncture. Acupuncture should be carried out with the technique of smoothing, reinforcing, and reducing, which was suitable for patients to have acid distension at the acupuncture site. The retention time of acupuncture and moxibustion should be controlled at about 30 minutes, once a day, six times a week, for 8 weeks.

Preparation of composite diamond-like nano-membrane sensors

In this study, magnetron sputtering technology was used to coat nano-Ti and nano-Ag on the diamond-like surface to prepare Ti/Ag-DLC composite diamond-like nano-membrane sensors. Diamond-like membranes could be prepared by many methods, which could be divided into two categories: Physical vapor deposition (PVD) and chemical vapor deposition (CVD) technologies (21). Magnetron sputtering technology was a kind of physical vapor deposition technology, which was widely used in the preparation of decorative coatings, protective coatings, optical coatings, and wear-resistant coatings (22). Magnetron sputtering technology has the advantages of simple equipment, low pollution, and deposition of ions in a wide energy range. At present, it is one of the commonly used methods to prepare diamond-like membranes in the industry.

Magnetron sputtering is a diamond-like membrane prepared by argon ion sputtering graphite target by argon ion sputtering. In this study, magnetron sputtering vacuum coating equipment was applied to prepare composite diamond-like nano-membrane. Substrate materials included SUS304 stainless steel sheet (1Cr18Mn8Ni5N, thickness of 0.8mm, Shanghai Chen Chong Industry & Trade Co., LTD.), silicon sheet (P-type (111) crystal face, thickness of 0.6mm, Suzhou Silicon Electronics Technology Co., LTD.), silver (Purity 99.9%, Dongyang Baitan Guoqing Gold and Silver Silk Factory), titanium target materials, graphite target, methane, argon gas, 3.5% sodium chloride electrolyte, ultrasonic cleaner, electrochemical workstation (PMC-2000, USA), acetone, natural diamond wafer knives, anhydrous ethanol, deionized water, and so on.

Before the coating: First of all, it was advised to remove oil stains from the substrate surface of substrate materials (Stainless Steel Sheets, silicon wafer). The specific method was to use acetone, anhydrous ethanol, and deionized water respectively for ultrasonic cleaning of substrate materials for about 15 minutes. After that, the substrate material was put into the deposition chamber and the substrate material was cleaned by argon plasma bombardment using the Kaufman ion source (23) for 15 minutes to remove the oxide on the substrate surface, and then the membrane was prepared.

The following is the whole process of preparing Ti/Ag-DLC composite diamond-like nano-membrane: A. Preparation of titanium transition layer (200nm): Sputtering target was high purity titanium target. The sputtering gas was 80 sccm high purity argon (99.99%) and the gas flow of argon was adjusted to maintain the chamber pressure at about 0.7 Pa. It was suggested to turn on the medium-frequency pulse direct current (DC) power supply (duty ratio is about 81%), set the sputtering power to 80 watts, and set the deposition time to 40 mins. B. Ti/Ag-DLC membranes were deposited on the Ti transition layer: It was advised to set the power of the carbon-silver composite target to 150 watts, the power of the titanium target to 80 watts, and the dc voltage to 110V. Under the gas flow ratio of 20 sccm of high purity methane (CH_4) (99.99%) / 40 sccm of high purity anatomical record (Ar) (99.99%), the working pressure was 0.7 Pa. Carbon target sputtering power was 150 W (RF power supply). The silver content in the thin membrane was controlled by the rotation speed of the substrate, which was 5 r/min (the power of the carbon-silver composite target was 0W), 5 r/min, 3 r/min, and 1 r/min. The corresponding samples were named T1, T2, T3, and T4, respectively. The silver content in the thin membrane was controlled by the rotation speed of the substrate, which was 5 r/min (the power of the carbon-silver composite target was 0W), 5 r/min, 3 r/min, and 1 r/min, and the corresponding samples were named T1, T2, T3, and T4, respectively. The deposition time was set to 1 hour, and the membrane thickness was 1.5 ± 0.1 μm. Afterward, the Ti/Ag-DLC composite nanodiamond film coating was combined with the acupuncture surface to improve the conduction of needle sensation.

Detection methods

A scanning electron microscope (SEM) (24) was used to observe the morphology and diameter of nanomaterials.

X-ray photoelectron spectroscopy (XPS) (25) was used to detect the surface substances of nanomaterials.

Raman Spectrometer, also known as Raman Spectrometer (26), was used to analyze structures and bonding bonds in nanomaterials.

Nano-indentation apparatus was used to test the hardness and young modulus of micro-and nano-scale thin membranes. The test results were calculated according to the force and injection curve. During the test, the depth of pressing should be kept below (10%) of the membrane thickness to avoid the influence of substrate hardness on the measurement results.

The sliding friction test machine was mainly applied to test the tribological properties of thin membranes. The dual part was a GCr15 steel ball with a diameter of 5 mm. The test parameters were set as the following: Vibration frequency was 2 Hz, sliding range was 5 mm, sliding time was 30 min, all tests were carried out at room temperature 25 ± 2 °C, relative humidity 35~50%, and the overall environment was a high vacuum.

Statistical methods

SPSS21.0 software was used to process data. The counting data were expressed as % and the measurement data were expressed as mean ± standard deviation. $P<0.05$ indicated that the difference was statistically significant.

Results and discussion

Test results of Ti/Ag-DLC composite membrane

Figure 1 showed the surface signs of Ti/Ag-DLC composite membranes of T1, T2, T3, and T4 samples detected by SEM at different rotational speeds. When the rotation speed was 3 r/min and 1 r/min, the thin surface of the Ti/Ag-DLC composite was smooth without obvious particles. At this point, the content of Ag was below (0.55%) by XPS detection.

Figure 2 showed the Raman spectra of T1, T2, T3, and T4 at the wavelength of 1000cm-1-1800cm-1. The Ti/Ag-DLC composite membranes had obvious absorption peaks at the wavelength of 1560 cm-1 at different rotational speeds (with different Ag content).

Figure 3A showed the hardness test results of four groups of samples by a nano-indentation instrument. T1 was 2.43 ± 0.24 GPa, T2 was 2.21 ±0.22 GPa, T3 was 2.50 ±0.25 GPa, and T4 was 2.51 ± 0.25 GPa, showing no significant difference ($P>0.05$). However, under the test of the sliding friction tester, when the thin membrane had a lot of friction marks, T1 was 2110 ±211 rpm, T2 was 2105 ±210 rpm, T3 was 2211±221 rpm, and T4 was 2119 ±211 rpm, which were all increased by about 900 rpm compared with the 1200 rpm of conventional DLC membrane, as shown in Figure 3B.

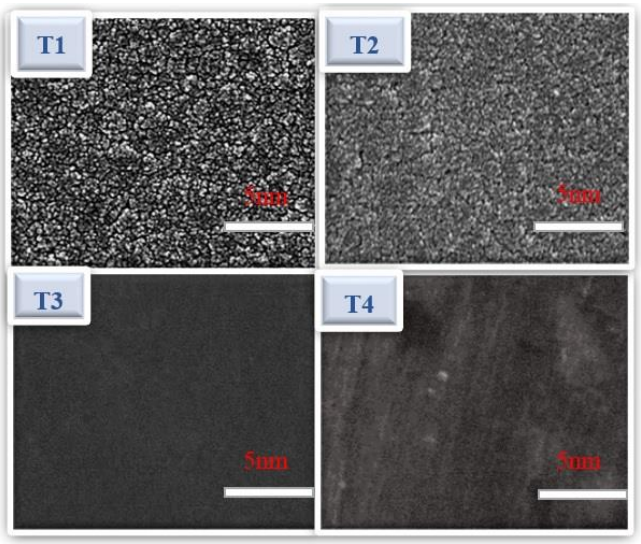

Figure 1. SEM detection results at different speeds (×20nm).

Table 1. Element content at different rotational speeds

Elements (%) \ Groups	T1	T2	T3	T4
Ti	0	9.12	15.23	19.65
Ag	5.67	1.22	0.54	0.34
C	94.33	89.66	84.23	80.01

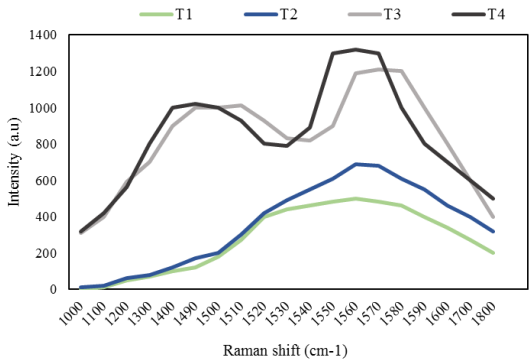

Figure 2. Raman spectrum Gaussian decomposition diagram.

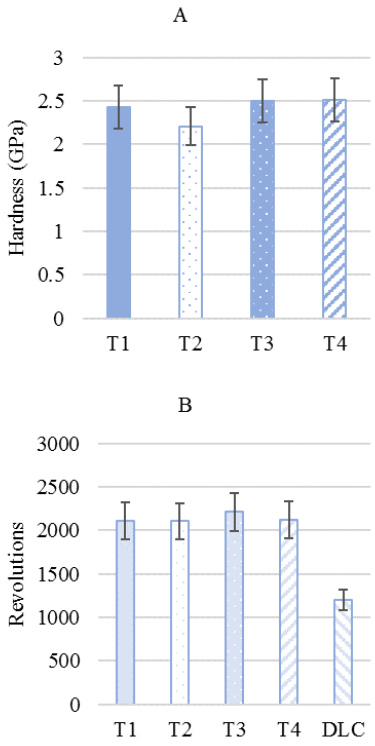

Figure 3. Hardness and friction performance test results (A was hardness test results. B was the test results of friction performance).

Comparison of general data between the two groups

The general clinical data of the two groups were compared as follows. In terms of gender distribution, there were 36 male patients (48.00%) and 30 female patients (52.63%) in the control group. In the acupuncture group, 39 cases (52.00%) were male and 27 cases (47.37%) were female. There was no significant difference in male and female distribution within the two groups (P>0.05). In terms of age, the average age of the control group was 56.19 ± 6.01 years old, and that of the acupuncture group was 55.76 ± 4.98 years old, with no significant difference (P>0.05), as shown in Figure 4A. In terms of the course of the disease, the average course of disease in the control group was 22.33 ± 5.51 months, and the average age in the acupuncture group was 23.67 ± 4.71 months, with no significant difference (P>0.05), as shown in Figure 4B. In terms of the distribution of stroke types, there were 36 cases of cerebral infarction (51.43%) and 32 cases of cerebral hemorrhage (51.61%) in the control group. In the acupuncture group, there were 34 patients with cerebral infarction (48.57%) and 30 patients with cerebral hemorrhage (48.39%), with no significant difference (P>0.05), as illustrated in Figure 4C. The comparison of general data between the two groups suggested that the study was comparable.

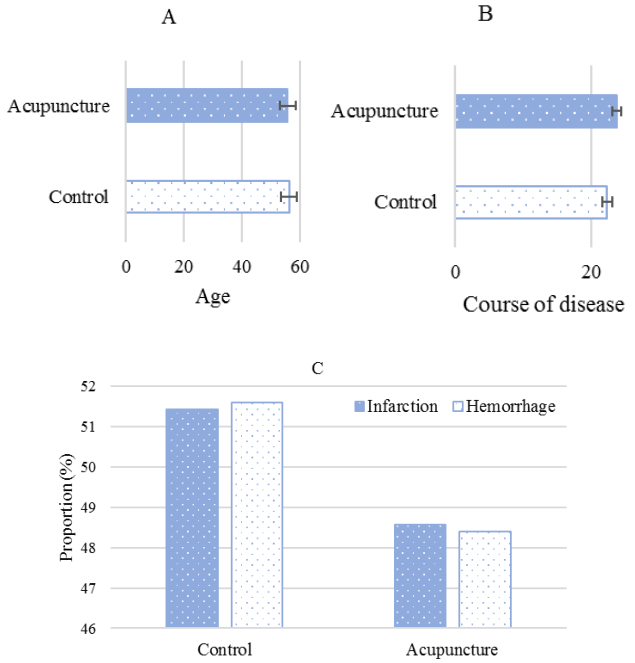

Figure 4. Comparison of general data between the two groups (A: Average age. B: Average course of the disease. C: Type of stroke.).

Depression scores

Figure 2 showed the Hamilton depression scale scores of the two groups before the treatment and at the 4th and 8th week after the treatment. After comparison, the scores of the Hamilton depression scale in the two groups after 4 and 8 weeks of treatment were significantly lower than those before treatment (P<0.01), and the scores of the Hamilton depression scale in the acupuncture group were significantly lower than those in the control group after 4 and 8 weeks of treatment (P<0.01).

Table 2. Comparison of Hamilton depression scale scores

Groups	Hamilton depression scale score		
	Before the treatment	Four weeks after the treatment	Eight weeks after the treatment
Control group	27.33 ± 1.51	20.11 ± 1.21*#	16.24 ± 1.03*#
Acupuncture group	27.43 ± 1.55	18.02 ± 1.10*#	10.04 ± 1.01*#

Note: "*" indicated that the scores of the Hamilton depression scale before and after the treatment in the two groups were statistically significant (P<0.01). "#" indicated that the comparison of Hamilton depression scale scores between the two groups after treatment was statistically significant (P<0.01).

Mental resilience scale scores

Before the treatment and 8 weeks after the treatment, the mental resilience scale scores of the two groups included three dimensions optimism, self-reliance, and tenacity. The total optimistic scores before and after the treatment were 70.23 ± 5.67 points and 93.48 ± 4.90 points in the control group, 71.25 ± 5.66 points and 110.38 ± 4.99 points in the acupuncture group, respectively, as shown in Figure 5A. The total self-improvement scores were 68.12 ± 3.66 and 90.38 ± 5.99 in the control group, 70.89 ± 4.16 and 109.38 ± 4.59 in the acupuncture group, as shown in Figure 5B. The total tenacity scores were 69.45 ± 5.66 points and 90.38 ± 4.19 points in the control group, 71.33 ± 5.71 points and 114.11 ± 6.09 points in the acupuncture group, respectively, as shown in Figure 5C.

The scores of optimism, self-reliance, and tenacity in the two groups increased after the treatment. And by comparing the rising trend of the scores of the two groups before and after the treatment, the optimism of the acupuncture group, the scores of self-strengthening, tenacity increased by 39.13 ± 3.78 points, 38.49 ± 5.32 points, and 42.78 ± 4.89 points, respectively, which were higher than those of the control group 23.25 ± 2.78 points, 22.26 ± 2.72 points, and 20.38 ± 2.99 points, respectively, as shown in Figure 6.

Herth hopes scale scores

Table 3 showed the scores of the Herth hope scale in the two groups before and after the treatment for 8 weeks: 15.73 ± 2.67 points and 25.33 ± 4.89 points in the control group, 16.22 ± 2.66 points and 36.98 ± 5.78 points in the acupuncture group. After comparison, the scores on the Herth hope scale were improved in both groups after 8 weeks of the treatment. The scores on the Herth hope scale in the acupuncture group were significantly higher than those in the control group after 8 weeks of treatment (P<0.01).

Table 3. Comparison of Herth hope scale score results

Groups	Herth hope scale score results	
	Before the treatment	8 weeks after the treatment
Control group	15.73 ± 2.67	25.33 ± 4.89*
Acupuncture group	16.22 ± 2.66	36.98 ± 5.78*

Note: "*" means the comparison was statistically significant (P<0.05).

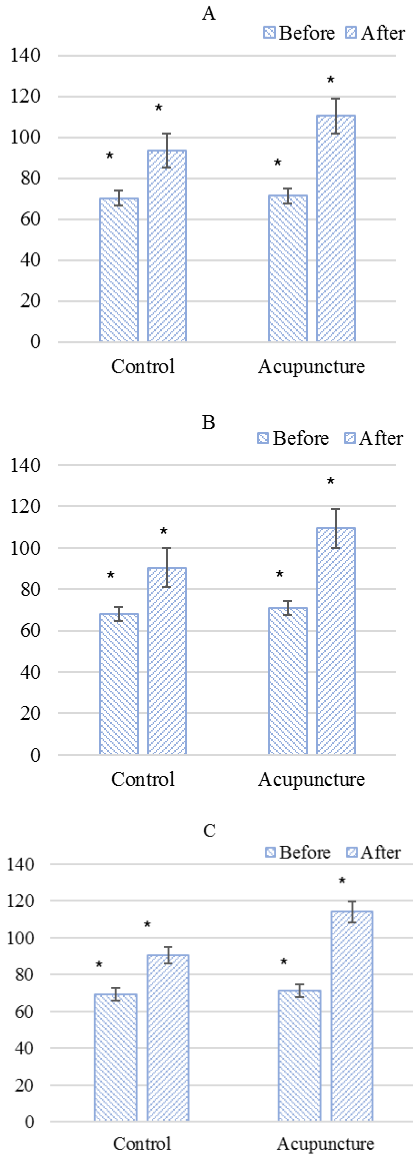

Figure 5. Comparison of mental resilience scale scores between the two groups (A: Optimism B: Self-strengthening C: Tenacity). Note**:** "*" means the comparison is statistically significant (P<0.05).

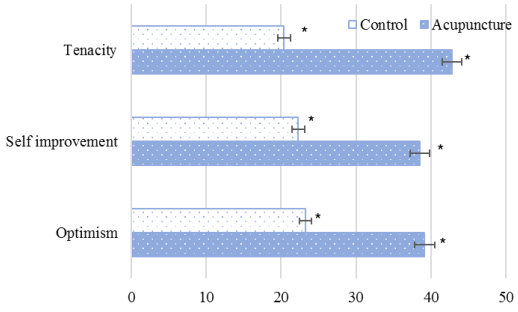

Figure 6. Comparison of the trend of mental resilience scale score before and after the treatment. Note: "*" means the comparison was statistically significant (P<0.05).

In this study, in order to further improve the therapeutic effect of acupuncture therapy in depression after stroke, acupuncture therapy on account of Ti/Ag-DLC nanocomposite membrane sensor was used to improve the hardness, durability, and stimulation conductivity of acupuncture. Ti/Ag-DLC nanocomposite membranes were improved on account of DLC membranes. After test analysis, when the Ag content was less than (0.55%), the thin surface of the Ti/Ag-DLC composite was smooth without obvious particles. The membranes with different Ag contents had obvious absorption peaks at 1560 cm^{-1}, and the friction life was extended to about 900 revolutions in a high vacuum environment. It was suggested that the effect of Ti/Ag-DLC nanocomposite membranes was better than conventional DLC membranes. Subramanian et al. (2018) (27) also doped elements such as Ti and Si into DLC membranes. The results showed that the DLC membranes doped with Ti and Si had higher charge transfer resistance and higher biocompatibility. Kawaguchi et al. (2021) (28) combined titanium (Ti), aluminum (Al), and niobium (Nb) into DLC membranes to obtain composite DLC membranes with better application performance (high surface smoothness, excellent tribological properties, and high biocompatibility). Many other researchers had conducted similar studies and achieved good application effects (29-31).

After that, acupuncture therapy on account of Ti/Ag-DLC nanocomposite membrane sensors was combined with conventional treatment for post-stroke depression, the application effect was compared with that of conventional treatment. By observing and comparing the scores of the Hamilton depression scale, mental resilience scale, and Herth hopes scale between the two groups, the scores of the acupuncture group were better than those of the control group after the treatment (P<0.05). It suggested that acupuncture combined with the treatment of post-stroke depression could not only improve the treatment effect but also indirectly showed the good application prospect of acupuncture in clinical treatment. The results of this study were consistent with a large number of related studies. Related studies by Lu et al. (2017) (32) suggested that post-stroke depression could be significantly improved with the assistance of acupuncture therapy. Cai et al. (2018) (33) pointed out that compared with antidepressants, acupuncture had relatively stable efficacy in the treatment of post-stroke depression and could reduce side effects, which was consistent with the results of Li et al. (2018) (34). Tseng et al. (2017) (35) used acupuncture therapy in the preventive treatment of post-stroke depression, and the results showed that acupuncture could reduce the risk of post-stroke depression. All the above studies showed that acupuncture therapy had its unique advantages in the treatment of post-stroke depression. Therefore, in addition to other medical applications of nanomaterials (36-39), this study exhibited the effect of acupuncture treatment on post-stroke depression by diamond-Like ultra-thin nano-coating technology.

Conclusions

In this study, acupuncture on account of Ti/Ag composite diamond-like nano-membrane sensors was used to treat patients with post-stroke depression, and the effect of acupuncture therapy on patients' depression was evaluated. The results showed that Ti/Ag-DLC composite membrane sensors with better hardness and friction performance were prepared on account of a diamond-like diamond. Acupuncture therapy could improve the negative emotions of patients with post-stroke depression, enhance psychological resilience, help improve the level of hope and be a potentially effective treatment method. However, this study did not compare the side effects of conventional therapy and acupuncture therapy, which made the research indicators inadequate and needs to be paid attention to in future studies. However, through this study, it was acknowledged that acupuncture therapy has good potential advantages in the clinical treatment of depression after stroke. Its future development can be expected.

Acknowledgments

Not applicable.

Conflict interest

The authors declare that they have no conflict of interest.

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