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Clinical Observation of Wound Healing in Burn Patients with Depression Based on Serum Neurotrophic Factor Levels

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Abstract: *Objective:* To explore the relationship between serum levels of brain-derived neurotrophic factor (BDNF), nerve growth factor (NGF), and neurotrophin-3 (NT-3) in burn patients and their depressive status and wound healing outcomes, providing clinical evidence for early identification and intervention of post-burn depression. *Methods:* A total of 120 burn patients were enrolled and divided into a depression group (n = 58) and a non-depression group (n = 62) based on scores from the Self-Rating Depression Scale (SDS) and Hamilton Depression Rating Scale (HAMD) upon admission. Serum BDNF, NGF, and NT-3 levels were measured on days 1, 7, and 14 after admission, and compared with indicators including wound healing time, infection rate, secondary grafting rate, and hospitalization duration. Pearson correlation analysis and multivariate logistic regression analysis were used to identify factors influencing delayed wound healing. *Results:* Serum BDNF and NGF levels were significantly lower in the depression group than in the non-depression group at all time points ($p < 0.05$), while NT-3 levels showed no significant difference between groups. The depression group had significantly longer wound healing times and hospital stays, as well as higher rates of wound infection and secondary grafting ($p < 0.05$). On day 7, serum BDNF and NGF levels were negatively correlated with wound healing time, whereas HAMD scores were positively correlated. Low BDNF levels, high HAMD scores, and larger total burn surface area were independent risk factors for delayed wound healing. *Conclusion:* Reduced serum neurotrophic factor levels in post-burn depression are closely associated with delayed wound healing. Serum BDNF may serve as a potential biomarker for predicting wound recovery. Early screening for depression and timely intervention in burn patients can improve wound healing outcomes.

Keywords: Burns; depression; Brain-derived neurotrophic factor; Wound healing; Serum neurotrophic factors

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1. Introduction

The rehabilitation process for burn patients often extends beyond the skin wound itself, and secondary

damage to the central nervous system has recently attracted increasing attention. Systemic inflammatory responses triggered by burns can alter blood-brain barrier permeability, affecting the expression of neurotransmitters and neurotrophic factors in the brain, thereby contributing to emotional disorders [1]. This mechanism has been confirmed in both animal models and autopsy studies, where infiltration of inflammatory factors leads to neuronal apoptosis in brain regions and impairments in cognitive and emotional functions [2]. Consequently, depression following burns is no longer simply viewed as a psychological stress response to trauma but may involve shared physiological pathways. Domestic scholars have observed that the psychological state of burn patients during rehabilitation is closely related to their level of post-traumatic growth, and psychological interventions can significantly improve patients' recovery experience, suggesting that emotional status may exert a reverse influence on the physical healing process [3].

One of the core pathological mechanisms of depression is the functional imbalance in the neurotrophic hypothesis, with downregulated BDNF expression in the hippocampus and prefrontal cortex considered a key factor in the development of mood disorders [4]. Multiple systematic reviews have also confirmed that serum BDNF levels can sensitively reflect the severity of depression and predict treatment response [5]. Meanwhile, depression does not exist in isolation within the nervous system; its negative impact on peripheral tissue repair has been well supported by evidence-based research. A systematic review and meta-analysis incorporating over fifty studies showed that depressive states significantly increase the risk of delayed wound healing, wound complications, and infections, with consistent associations observed across burn injuries, surgical wounds, and chronic ulcers [6]. Psychological stress suppresses local immune responses through persistent activation of the hypothalamic-pituitary-adrenal (HPA) axis, reducing neutrophil migration and cytokine secretion, thereby delaying the resolution of inflammation and re-epithelialization in wounds [7,8]. Under stress, the body also exhibits measurable changes in various biological markers across neuroendocrine, immune, and metabolic systems, providing potential for quantifying the effects of psychological stress on the body from a serological perspective [9]. Persistent release of pro-inflammatory cytokines has also been shown to disrupt normal processes at each stage of wound healing, delaying granulation tissue formation and angiogenesis [10]. In burn patients, pain and psychological stress often exacerbate each other; targeted analgesia and emotional management have been proven to improve overall recovery outcomes [11].

Previous domestic studies have also found that exogenous growth factors such as recombinant human basic fibroblast growth factor can elevate serum VEGF and EGF levels in burn patients and promote wound healing, indirectly indicating a close relationship between local and systemic growth factor levels and wound outcomes. However, most existing research focuses on single growth factors or individual psychological indicators [12]. Clinical data systematically exploring the interplay among serum neurotrophic factors—molecules with dual roles in neural regulation and tissue repair—and post-burn depression and wound healing remain limited. This study aims to provide quantifiable biological evidence for early identification of post-burn depression and assessment of wound prognosis by measuring serum BDNF, NGF, and NT-3 levels at different time points in burn patients, comparing differences in wound recovery between depressed and non-depressed groups, and analyzing the correlation between neurotrophic factor levels and delayed wound healing, as well as identifying independent risk factors.

2. Materials and methods

2.1. General information

A total of 120 burn patients were enrolled in this study. Upon admission, patients were assessed using the Self-Rating Depression Scale (SDS) combined with the Hamilton Depression Rating Scale (HAMD), and classified into a depression group (n = 58) and a non-depression group (n = 62) based on assessment results. No statistically significant differences were found between the two groups regarding gender, age, total body surface area (TBSA) affected by burns, depth classification of burns, or cause of injury ($p > 0.05$), indicating comparability. See **Table 1**.

Table 1. Comparison of general characteristics between the two groups

Item	Depression group (n = 58)	Non-depression group **(n = 62)**	**t/χ^2**	***p*-value**
Age (years, $\bar{x}\pm s$)	42.3 ± 11.6	40.8 ± 10.9	0.735	0.464
Gender (male/female, n)	34/24	38/24	0.089	0.766
TBSA（%，$\bar{x}\pm s$）	28.4 ± 9.7	26.9 ± 9.2	0.877	0.382
Proportion of deep second-degree burns (%)	62.1	59.7	0.070	0.792
HAMD score (points, $\bar{x}\pm s$)	22.6 ± 4.3	6.1 ± 2.5	25.412	< 0.001

2.2. Detection methods and observation indicators

Serum levels of BDNF, NGF, and NT-3 were measured on day 1, day 7, and day 14 after hospital admission. Wound healing time, wound infection rate, secondary skin grafting rate, and length of hospital stay were recorded. The correlation between serum neurotrophic factor levels and HAMD scores on day 7 with wound healing time was analyzed. Delayed wound healing (healing time exceeding the median of the entire group) was used as the dependent variable in a multivariate logistic regression analysis, incorporating HAMD score, BDNF level, NGF level, TBSA, and burn depth.

3. Results

3.1. Comparison of serum neurotrophic factor levels between the two groups

At all-time points, serum BDNF and NGF levels in the depression group were significantly lower than those in the non-depression group ($p < 0.05$). In the depression group, BDNF and NGF levels reached their lowest point on day 7 and showed slight recovery by day 14, but still did not reach the levels observed in the non-depression group. There was no statistically significant difference in NT-3 levels between the two groups ($p > 0.05$), suggesting that NT-3 is less sensitive to depressive status compared to BDNF and NGF. See **Table 2**.

Table 2. Comparison of serum neurotrophic factor levels between the two groups ($\bar{x}\pm s$)

Indicator	**Time Point**	**Depression group (n = 58)**	**Non-depression group (n = 62)**	***t* Value**	***p* Value**
BDNF (ng/mL)	Day 1	12.4 ± 3.1	15.8 ± 3.4	5.618	< 0.001
	Day 7	10.9 ± 2.8	16.7 ± 3.6	9.845	< 0.001
	Day 14	11.6 ± 3.0	18.2 ± 3.9	10.401	< 0.001
NGF (pg/mL)	Day 1	85.3 ± 18.6	102.7 ± 20.1	4.912	< 0.001
	Day 7	79.8 ± 16.4	108.5 ± 19.8	8.729	< 0.001
	Day 14	83.2 ± 17.9	115.6 ± 21.3	8.887	< 0.001

Indicator	Time Point	Depression group (n = 58)	Non-depression group (n = 62)	*t* Value	*p* Value
NT-3 (ng/mL)	Day 1	4.2 ± 1.1	4.4 ± 1.0	1.028	0.306
	Day 7	4.0 ± 1.0	4.3 ± 1.2	1.462	0.146
	Day 14	4.1 ± 1.1	4.5 ± 1.1	1.977	0.051

3.2. Comparison of wound healing outcomes between the two groups

The depression group had significantly longer wound healing time and hospitalization duration compared to the non-depression group. Additionally, the rates of wound infection and secondary skin grafting were higher in the depression group, with all differences being statistically significant ($p < 0.05$), indicating a concurrent relationship between depressive state and poor wound outcomes. See **Table 3**.

Table 3. Comparison of Wound Healing-Related Indicators between the Two Groups

Indicator	Depression group (n = 58)	Non-depression group (n = 62)	Statistical value	*p* value
Wound healing time（d，$\bar{x} \pm s$）	24.6 ± 6.8	18.3 ± 5.4	$t = 5.712$	< 0.001
Incidence of wound infection (%)	27.6 (16/58)	11.3 (7/62)	$\chi^2 = 5.324$	0.021
Secondary skin grafting rate (%)	19.0 (11/58)	6.5 (4/62)	$\chi^2 = 4.412$	0.036
Hospitalization duration (d, $\bar{x} \pm s$)	31.5 ± 8.2	24.7 ± 7.1	$t = 4.883$	< 0.001

3.3. Correlation between serum neurotrophic factor levels and wound healing time

Pearson correlation analysis showed that serum BDNF and NGF levels on day 7 were negatively correlated with wound healing time (r = -0.512, $P < 0.001$; r = -0.468, $p < 0.001$), indicating that lower levels of neurotrophic factors were associated with longer healing times. HAMD scores were positively correlated with wound healing time (r = 0.487, $p < 0.001$). No significant correlation was found between NT-3 levels and wound healing time. See **Table 4**.

Table 4. Correlation between serum neurotrophic factor levels and wound healing time

Parameter	*r* value	*p* value
BDNF (day 7)	-0.512	< 0.001
NGF (day 7)	-0.468	< 0.001
NT-3 (day 7)	-0.114	0.187
HAMD score	0.487	< 0.001

3.4. Multivariate logistic regression analysis of factors influencing delayed wound healing

Using delayed wound healing as the dependent variable and including HAMD score, BDNF level, NGF level, TBSA, and burn depth as independent variables in a multivariate logistic regression analysis, results indicated that low BDNF levels, high HAMD scores, larger TBSA, and burns deeper than deep second-degree were independent risk factors for delayed wound healing ($p < 0.05$). See **Table 5**.

Table 5. Multivariate logistic regression analysis of factors influencing delayed wound healing

Variable	β	SE	Wald χ^2	OR（95%CI）	*p* value
HAMD score	0.186	0.052	12.78	1.204 (1.087–1.334)	< 0.001
BDNF (day 7)	-0.243	0.079	9.46	0.784 (0.672–0.916)	0.002

Variable	β	SE	Wald χ^2	OR (95%CI)	*p* value
TBSA	0.071	0.031	5.25	1.074 (1.010–1.142)	0.022
Burn depth (deep second-degree or deeper)	0.412	0.198	4.33	1.510 (1.025–2.225)	0.037

4. Discussion

The results of this study show that serum levels of BDNF and NGF in patients with depression were consistently lower than those in non-depressed patients at all time points after admission, while no significant difference was observed in NT-3 levels between the two groups. BDNF plays a role in maintaining emotional homeostasis by modulating synaptic plasticity in hippocampal and prefrontal neurons. Its downregulated expression is not only a biomarker of depression but may also serve as a key molecular hub mediating the interaction between physical stress and emotional disorders [1]. Burns themselves act as a potent source of physical stress; the resulting systemic inflammatory response can disrupt the blood-brain barrier, allowing peripheral inflammatory factors to enter the central nervous system, thereby suppressing BDNF synthesis and release [2]. This mechanism may explain the persistently low serum BDNF levels observed in depressed patients in our study.

Regarding wound healing, patients in the depressive group exhibited significantly prolonged healing times and hospital stays, along with higher rates of infection and secondary skin grafting, indicating that depression indeed adversely affects burn wound outcomes. This finding aligns with international systematic reviews on various types of wounds, which consistently demonstrate a stable association between depression and delayed wound healing and increased risk of complications, although the independent impact of anxiety on wound healing remains unclear [6]. Mechanistically, chronic psychological stress may continuously activate the hypothalamic-pituitary-adrenal (HPA) axis, suppress local immune cell function, and reduce secretion of pro-repair cytokines, thereby delaying the transition from the inflammatory phase to the proliferative phase of wound healing [7,8]. There is also a bidirectional amplification effect between pain and psychological stress: wound-related pain serves as a source of stress, and stress exacerbation further impairs inflammatory regulation and healing processes. Excessive expression of pro-inflammatory cytokines has been shown to disrupt the normal rhythm of granulation tissue formation and angiogenesis, a mechanism indirectly supported by the elevated infection and secondary grafting rates observed in the depressive group in this study [10].

Correlation analysis further revealed that serum BDNF and NGF levels on day 7 were significantly negatively correlated with wound healing time, whereas HAMD scores showed a positive correlation with healing duration. These findings suggest that emotional state and neurotrophic factor levels may influence wound outcomes through a shared neuroendocrine pathway rather than independently. Multivariate logistic regression analysis indicated that low BDNF levels, high HAMD scores, larger TBSA, and deeper burn depth were all independent risk factors for delayed wound healing. Among these, BDNF—being a quantifiable serum marker—deserves particular attention for its predictive value. Previous studies have demonstrated that exogenous growth factor interventions can elevate serum VEGF and EGF levels in burn patients and accelerate wound repair [12]. In light of our findings, improving the depressive state of burn patients—thereby indirectly upregulating BDNF and other neurotrophic factors—may represent a feasible therapeutic strategy within comprehensive burn wound management.

It should be noted that this study is a single-center cross-sectional observation with a limited sample size, which prevents us from establishing a clear causal relationship between decreased BDNF levels and delayed wound healing. The lack of significant differences in NT-3 levels may also relate to its expression characteristics in peripheral blood and the timing of detection. Future research could consider expanding the sample size and extending follow-up periods, incorporating anti-depressant interventions to dynamically assess changes in BDNF levels and wound healing outcomes, thereby further validating the specific mechanisms of neuroendocrine pathways in burn wound repair.

5. Conclusion

This study demonstrates that post-burn depression is closely linked to attenuated serum BDNF and NGF levels, while NT-3 appears less responsive to depressive status. Depressed burn patients experienced prolonged wound healing time, longer hospital stays, and higher rates of infection and secondary skin grafting compared with their non-depressed counterparts. Serum BDNF levels on day 7 were independently associated with delayed wound healing, alongside HAMD score, total burn surface area, and burn depth, suggesting that neurotrophic factor depletion and depressive severity jointly contribute to impaired tissue repair through shared neuroendocrine and inflammatory pathways. These findings support the clinical value of early psychological screening (e.g., SDS/HAMD) combined with serum BDNF monitoring as a practical strategy for identifying burn patients at risk of delayed wound healing, and highlight the potential benefit of integrating psychological intervention into standard burn wound management to improve recovery outcomes. Given the single-center, cross-sectional design of this study, these conclusions should be validated in larger, multicenter, longitudinal cohorts that incorporate antidepressant or psychological interventions to clarify causality.

Disclosure statement

The authors declare no conflict of interest.

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