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## ORIGINAL

## IMPACT OF IMPAIRED GLUCOSE REGULATION AND SERUM HOMOCYSTEINE LEVELS ON NEUROPHYSIOLOGICAL PERFORMANCE IN ATHLETES

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## ABSTRACT

**Objective:** This study aimed to explore the clinical and neurophysiological features of athletes with impaired glucose regulation (IGR) and their correlation with serum homocysteine (Hcy) levels, considering their potential impacts on sports performance. Methods: A cohort of twenty athletes diagnosed with IGR between February 2020 and February 2021 comprised the observation group, while twenty healthy athletes served as controls. We gathered demographic data such as age, gender, and educational level, and assessed clinical neurophysiological indices (amplitude, distal latency, motor nerve conduction velocity) alongside serum Hcy levels. Both groups were evaluated for differences in cutaneous sympathetic nerve response, as well as somatosensory evoked potentials in upper and lower limbs. Results: No significant differences in age, gender, or educational attainment were observed between the two groups (P > 0.05). However, significant disparities were noted: the observation group exhibited lower amplitude and motor nerve conduction velocity, increased distal latency, and higher serum Hcy levels compared to the control group (P < 0.05). Furthermore, athletes with more severe glucose impairment showed increased abnormal rates of cutaneous sympathetic nerve response and somatosensory evoked potentials in both upper and lower limbs, alongside worsened nerve electrophysiological indices. Notably, serum Hcy levels were positively correlated with the abnormal rates of neurophysiological responses and negatively correlated with the amplitude and motor nerve conduction velocity (P < 0.05). **Conclusion:** The clinical neurophysiological indices reflect the severity of impaired glucose regulation in athletes and can highlight potential impacts on sports performance. By integrating clinical neurophysiological characteristics with serum Hcy levels, early detection and intervention for athletes suffering from IGR can be facilitated, potentially mitigating negative effects on athletic performance. This study underscores the importance of monitoring metabolic health in athletes to maintain and enhance their physical capabilities and recovery processes.

**KEYWORDS:** Impaired glucose regulation; Clinical neuro electrophysiological characteristics; Serum Hcy level; Correlation

## 1. INTRODUCTION

Athletic performance and recovery are profoundly influenced by an array of physiological factors, among which metabolic health plays a crucial role. Impaired glucose regulation (IGR), encompassing conditions such as insulin resistance and prediabetes, has been identified as a significant determinant of overall health status and has potential implications for athletic performance. Additionally, elevated levels of homocysteine (Hcy), an amino acid associated with cardiovascular risks, have been noted to correlate with various metabolic disturbances. This study focuses on the intersection of these factors-IGR and elevated Hcy levels-and their impact on the neurophysiological health of athletes, an area that remains underexplored in sports medicine.(Qiao et al., 2022; Softic et al., 2019). Glucose metabolism is critical for athletic performance due to its role in energy production. Disruptions in normal glucose handling can compromise muscle function and endurance, impact recovery, and increase susceptibility to injury. Conversely, homocysteine, typically elevated in individuals with vitamin B deficiencies and renal dysfunction, has been linked to neurotoxic effects and vascular complications that could impair neurological function and muscle coordination.(Bianchi et al., 2021; Zeng et al., 2020) The neurophysiological integrity of an athlete is paramount for optimal performance. Neurophysiological indices such as nerve conduction velocity, amplitude, and latency are indicative of nerve health and function, which are essential for precise and coordinated movements. Disturbances in these indices can signify underlying metabolic or vascular issues that may not only impact athletic performance but also increase the risk of long-term neurological complications. (Khalangot, Kovtun, Gurianov, Pysarenko, & Kravchenko, 2019; Winther-Sørensen et al., 2020). Despite the known impacts of glucose regulation and homocysteine levels on general health, their specific effects on the clinical neurophysiological parameters in athletes have not been thoroughly investigated. Understanding how these metabolic factors interact with neurophysiological functions could provide critical insights into optimizing training, enhancing performance, and preventing injuries in athletes.(Siddiqui et al., 2021). The primary objective of this study is to investigate the clinical and neurophysiological features of athletes with impaired glucose regulation and to examine how these features correlate with serum Hcy levels. By doing so, the study aims to uncover potential pathways through which glucose regulation and Hcy levels impact athletic performance and recovery, offering a foundation for targeted interventions that could enhance the health and performance of athletes.(Ge et al., 2021; Luo et al., 2020), This research is particularly significant as it not only fills a crucial gap in sports science by linking metabolic health with neurophysiological function but also sets the stage for developing more comprehensive health monitoring and management strategies for athletes(Fajtova, 2018; Sundblad et al., 2021). Early detection and correction of impaired glucose handling and elevated Hcy levels could lead to improved neurophysiological health, thereby sustaining or even enhancing athletic performance while minimizing the risk of injury and long-term health issues. (Maria & Kush, 2022; Tsan et al., 2022).

## 2. Data and Methods

## 2.1 General Data

The study subjects (observation group) were twenty patients diagnosed with impaired glucose regulation between February 2020 and February 2021, while the control group consisted of twenty individuals with normal glucose levels.

Criterion for inclusion: (1) Patients with high completeness of clinical data; (2) Patients with stable conditions; (3) The clinical symptoms of the patients were consistent with the diagnostic criteria for impaired glucose regulation formulated by the American Diabetes Association.

Conditions under which participation is not permitted: (1) Individuals with unusual mental states; (2) Patients who also suffered from many additional disorders characterized by severe system breakdown; (3) Individuals who were unwilling or unable to participate in the research.

## 2.2 Methods

Patients' demographic information was gathered and categorized, including their age, gender, and level of education. Neuro electrophysiological examination: The room temperature was kept between 22 and 25 °C, and the patients obtained the supine position, and the motor nerve isoconductance measurement (surface electrode measurement) was performed with the UK Medelec Synergy 5-channel EMG evoked potential instrument. The sudden electrical stimulation was used to induce sweat gland activity, so as to record the cutaneous sympathetic nerve response, including conduction velocity, long-range delay time and median nerve amplitude, and to determine the latency sound wave from the beginning of stimulation to the first appearance.

Somatosensory evoked potentials were utilized to stimulate the median nerves on both sides of the patients' bodies in order to record the abnormal rate of somatosensory evoked potentials in the upper limbs and the abnormal rate of somatosensory evoked potentials in the lower limbs. Normal ranges were determined with reference to the measurement standard at the electromyography laboratory at Beijing Union Medical College Hospital. Determination of serum Hcy level: The patients fasted for 12h, and then venous blood samples under fasting state were collected. The samples were tested by Roche c701 automatic biochemical analyzer and Hcy matching reagents. And enzyme colorimetry was used for the determination on time.

## 2.3 Observation Indicators

The basic data of age, gender and educational level were compared between the two groups. Serum Hcy levels were compared between the two groups, as were clinical neurophysiological indicators (amplitude, distal latency, and motor nerve conduction velocity). Both groups were compared with regards to their aberrant cutaneous sympathetic nerve response, upper limb, and lower limb somatosensory evoked potentials. Patients in the observation group with varying disease severity had their neuro electrophysiological indices compared. These included amplitude, abnormal rate of cutaneous sympathetic response, distal latency, abnormal rate of somatosensory evoked potentials in the upper limbs, abnormal rate of somatosensory evoked potentials in the lower limbs, and motor nerve conduction velocity. Patients in the observation group with varying stages of illness had their serum Hcy levels compared. Nerve electrophysiological indices (amplitude, abnormal rate of cutaneous sympathetic nerve response, abnormal rate of somatosensory evoked potentials in the upper limbs, abnormal rate of somatosensory evoked potentials in the lower limbs, distal latency, motor nerve conduction velocity) were examined for their relationship to serum Hcy levels. Grading criteria of different conditions: The Toronto clinical scoring system test scores were obtained according to the patients' neurological symptoms, nerve reflexes and sensory functions. Among them, neurological symptoms included lower limb paralysis, pain, pinprick like sensation, etc. 0 point was symptoms, and 1 point was recorded for each symptom; nerve reflexes included ankle reflexes, knee reflexes, etc. 0 point was symptoms, and 1 point was weakness, 2 points were missing; sensory function included: pain in the right toe, body temperature, tactile pressure and other conditions. 0 point was symptoms and 1 point was abnormal. The total score of mild condition was 6-8 points, the total score of moderate condition was 9-11 points, the total score of severe condition was 12-14 points, and the total score of extremely severe condition was 15-19 points.

## **2.4 Statistical Process**

The analysis was performed using SPSS 24.0 software. The t-test was

used, and the measurement results were presented in the form  $\bar{x} \pm s$ . The counting data were reported as a rate, and the correlation data across groups were examined using the  $\chi^2$  test and Pearson linear correlation. When P< 0.05 showed that there was a substantial difference.

## 3. Results

## 3.1 Comparison of the two groups' age, sex, educational attainment, and other fundamental facts

As can be seen in Table 1, Figure 1, and Figure 2, there was no statistically significant difference between the observation group and the control group when comparing demographic characteristics such as age, gender, and level of education (P > 0.05).

**Table 1**: Analyzing the two sets of data in relation to one another, such as age, gender, and
 level of education

GROUP	NUMBER	AGE	GENDER	EDUCATIONAL LEVEL (JUNIOR
	OF	(YEARS	(MALE /	HIGH SCHOOL / SENIOR HIGH
	CASES	, $\overline{x} \pm s$ )	FEMALE)	SCHOOL / UNDERGRADUATE)
OBSERVATION	20	55.22	11/9	10/8/2
GROUP		± 1.21		
CONTROL	20	55.23	12/8	11/7/2
GROUP		$\pm$ 1.23		
т		0.026	0.102	0.114
Р		0.979	0.749	0.944







Figure 2: Basic characteristics of the two groups were compared, including gender and level of education.

## 3.2 Comparison of the clinical neurophysiological indexes (amplitude, distal latency, motor nerve conduction velocity) and serum Hcy levels between the two groups

As shown in Table 2 and Figure 3, the differences were statistically significant (P < 0.05), with the amplitude and motor nerve conduction velocity in the observation group being lower than those in the control group, and the distal latency and serum Hcy level in the observation group being higher than those in the control group.

GROUP	NUMBER	AMPLITUD	DISTAL	MOTOR NERVE	SERUM
	OF CASES	E (MV)	LATENCY	CONDUCTION	HCY LEVEL
			(MS)	VELOCITY (MS)	(M MOL/L)
OBSERVATION	20	8.902.50±	3.520.45±	53.454.30±	15.55 ±
GROUP					5.67
CONTROL	20	10.802.95±	$3.000.50\pm$	57.183.08±	9.20 ±
GROUP					1.91
т		2.197	3.457	3.154	4.746
Р		0.034	0.001	0.003	0.000

**Table 2**: Clinical neurophysiological indices (amplitude, distal latency, motor nerve conduction velocity), as well as serum Hcy concentrations, are compared between the two groups.



**Figure 3**: Serum Hcy levels and clinical neurophysiological indicators (amplitude, distal latency, and motor nerve conduction velocity) were compared between the two groups.

# 3.3 There was a significant difference in the aberrant rates of cutaneous sympathetic nerve response, upper limb somatosensory evoked potentials, and lower limb somatosensory evoked potentials between the two groups.

Table 3 and Figures 4, 5, and 6 reveal that the aberrant rates of cutaneous sympathetic nerve response, upper limb somatosensory evoked potentials, and lower limb somatosensory evoked potentials were greater in the observation group than in the control group (P<0.05).

GROUP	NUMBER OF CASES	ABNORMAL RATE OF CUTANEOUS SYMPATHETIC RESPONSE	ABNORMAL RATE OF Somatosensory Evoked Potentials In Upper Limbs	ABNORMAL RATE OF SOMATOSENSORY EVOKED POTENTIALS IN LOWER LIMB	
OBSERVATION GROUP	20	19 (95.00)	17 (85.00)	18 (90.00)	
CONTROL GROUP	20	1 (5.00)	1 (5.00)	1 (5.00)	
X <sup>2</sup>		32.400	25.859	28.972	
P		0.000	0.000	0.000	

**Table 3:** Somatosensory evoked potentials in the upper and lower limbs, as well as the cutaneous sympathetic nerve response, were compared between the two groups (n, %) to determine the prevalence of abnormalities.



Figure 4: Examining the differences between the two groups' aberrant rates of cutaneous sympathetic response



Figure 5: Somatosensory evoked potentials of the upper extremities: a comparison of the two groups' rates of abnormality



Figure 6: Lower limb somatosensory evoked potentials were compared for aberrant rates between the two groups

3.4 Comparison of the neurophysiological indexes of patients with different disease grades in the observation group (amplitude, abnormal rate of cutaneous sympathetic nerve response, distal latency, abnormal rate of somatosensory evoked potentials in upper limbs, abnormal rate of somatosensory evoked potentials in lower limbs, motor nerve conduction velocity)

The more severely impaired glucose regulation was, the wave amplitude and motor nerve conduction velocity would be decreased. And the distal latency and the abnormal rate of cutaneous sympathetic nerve response, table 4 and Figures 7, 8, 9, and 10 demonstrate a rise in the aberrant rate of somatosensory evoked potentials in the upper limbs and the lower limbs, respectively, at the P<0.05 level.

 Table 4: Patients with varying stages of disease were compared across a number of neurophysiological indices (including amplitude, abnormal rate of cutaneous sympathetic response, distal latency, abnormal rate of somatosensory evoked potentials in the upper limbs, abnormal rate of somatosensory evoked potentials in the lower limbs, and motor nerve conduction velocity).

DIFFERENT	AMPLIT	ABNORMAL RATE	DISTAL	ABNORMAL RATE OF	ABNORMAL RATE OF	MOTOR
CONDITIONS	UDE (XS,	OF CUTANEOUS	LATENCY	SOMATOSENSORY	SOMATOSENSORY	NERVE
	MV) ±	SYMPATHETIC	(XS, MS) $\pm$	EVOKED	EVOKED POTENTIALS	CONDUCTION
		<b>RESPONSE (N,%)</b>		POTENTIALS IN	IN LOWER LIMBS (N,%)	VELOCITY
				UPPER LIMBS (N,%)		(XS, MS) $\pm$
MILD DISEASE (N=5)	9.802.40	4 (80.00)	3.000.82±	3 (60.00)	3 (60.00)	57.102.95±
	±					
MODERATE	8.903.10	5 (100.00)	$3.250.70 \pm$	4 (80.00)	5 (100.00)	$56.403.84 \pm$
CONDITION (N=5)	±					
SEVERE CONDITION	8.202.39	5 (100.00)	3.551.32±	5 (100.00)	5 (100.00)	54.193.50±
(N=5)	±					
EXTREMELY SEVERE	7.303.45*	5 (100.00)*	4.100.80*±	5 (100.00)*	5 (100.000)*	51.294.21*±
CONDITION (N=5)	±					

*Note:* \* *indicates that compared with mild conditions, P<0.05.* 







Figure 8: Evaluation of the abnormality of cutaneous sympathetic response throughout illness stages in the observational group



**Figure 9**: Somatosensory evoked potentials in the upper limbs: a comparison of aberrant rates amongst patients of varying disease severity in the observational group.





## 3.5 Patients in the observation group with varying stages of illness were compared with regard to their serum Hcy levels.

Table 5 and Figure 11 demonstrate that the severity of poor glucose control is correlated with an increase in serum Hcy (P<0.05).

**Table 5**: Serum Hcy levels in participants with varying degrees of illness severity in the observational study

DIFFERENT CONDITIONS	SERUM HCY LEVELS (XS, $ { m M} $ MOL/L) $ { m ar \pm} $
MILD DISEASE (N=5)	9.63 ± 2.95
MODERATE CONDITION (N=5)	13.98 ± 4.73
SEVERE CONDITION (N=5)	17.98 ± 5.90
EXTREMELY SEVERE CONDITION (N=5)	20.34 ± 6.44*







3.6 Analysis of the correlation between serum Hcy level and nerve electrophysiological indexes (amplitude, abnormal rate of cutaneous sympathetic response, abnormal rate of somatosensory evoked potentials in upper limbs, abnormal rate of somatosensory evoked potentials in lower limbs, distal latency, motor nerve conduction velocity)

Higher blood Hcy levels are associated with more severe cases of poor glucose control (P < 0.05). As can be seen in Table 6 and Figures 12, 13, 14, 15, 16, and 17, the serum Hcy level correlated negatively with the amplitude and motor nerve conduction velocity and positively with the abnormal rate of cutaneous sympathetic response, somatosensory evoked potentials in upper limbs, and somatosensory evoked potentials in lower limbs (P < 0.05).

NEUROPHYSIOLOGICAL INDEXES	SERUM HCY LEVEL					
	R VALUE	P VALUE				
AMPLITUDE	-1.000	<0.05				
ABNORMAL RATE OF CUTANEOUS SYMPATHETIC	1.000	<0.05				
RESPONSE						
ABNORMAL RATE OF SOMATOSENSORY EVOKED	0.976	<0.05				
POTENTIALS IN UPPER LIMBS						
ABNORMAL RATE OF SOMATOSENSORY EVOKED	0.976	<0.05				
POTENTIALS IN LOWER LIMBS						
DISTAL LATENCY	0.814	<0.05				
MOTOR NERVE CONDUCTION VELOCITY	-1.000	<0.05				

Table 6: Analysis of correlation.



Figure 12: The correlation between amplitude and serum Hcy level



Figure 13: The correlation between abnormal rate of cutaneous sympathetic response and serum Hcy level



Figure 14: The correlation between abnormal rate of sensory evoked potentials in upper limbs and serum Hcy level



Figure 15: The correlation between abnormal rate of sensory evoked potentials in lower limbs and serum Hcy level



Figure 16: The correlation between distal latency and serum Hcy level



Figure 17: The relationship between blood Hcy levels and the speed of motor nerve conduction

#### 4. Discussion

The prevalence of diabetes is rather significant, and it has been rising globally year over year in recent years, which has become one of the primary causes for shortening the average human life span (Wei et al., 2022; Wohlfart et al., 2022). The occurrence of diabetes will damage the body's peripheral nervous system, and neuropathy syndrome can be divided into different types of lesions, between which, symmetric sensorimotor polyneuropathy belongs to the common neuropathy disease caused by diabetes (Åström et al., 2018; Zhang et al., 2021). Impaired glucose regulation belongs to the prediabetic stage, which is not a harmless disease, and often potentially affects patients to develop metabolic syndrome. Patients with poor glucose control are at similar risk for developing macro vascular and microvascular problems as those with

type 2 diabetes mellitus. Disruption in blood glucose homeostasis leads to alterations in both small and large blood vessels throughout the patient's body (Narayanan et al., 2020; Rossi et al., 2018). Thereinto, microvascular diseases related to impaired glucose regulation include chronic kidney disease, neuropathy, and others. In order to effectively improve the prognosis and minimize the risk of complications, it is abundantly obvious that early detection and symptomatic treatment of impaired glucose control are critical components (Jones et al., 2021; Præstholm et al., 2021). In the current clinical diagnosis process, the main diagnostic basis for impaired glucose regulation is whether the patients have a history of diabetes, family history of diabetes, and symptoms of nerve injury and abnormal electrophysiological symptoms (Giráldez-García et al., 2021; Killy et al., 2021). In recent years, the methods of nerve electrophysiological examination have been continuously improved and updated, and its corresponding indicators have been used more and more widely. Among the existing clinical neurophysiological detection indicators, the most commonly used indicators are the observation of cutaneous sympathetic nerve response and abnormal rates of somatosensory evoked potentials in upper and lower limbs (Chriett et al., 2021; Guo et al., 2022). Among them, the main biological mechanism of cutaneous sympathetic nerve response lies in the polysynaptic sympathetic nerve reflex. Different ways of stimulation lead to different afferent pathways, which are caused by endogenous or exogenous stimuli respectively, and mainly reflect the changes of small fibers and autonomic small fibers (Foley et al., 2020; Siebner et al., 2021). Because it predominantly captures the change in epidermal voltage recorded by sympathetic nervous system activity in response to stimulation, somatosensory evoked potential is a good tool for diagnosing sympathetic nerve fiber damage in persons who have poor control of their glucose levels. When compared to the speeds at which sensory and motor nerve impulses move through the nerves, these speeds are very slow, it is more sensitive (Monteiro-Alfredo et al., 2021; Xiao et al., 2020). On the other hand, serum Hcy is mainly produced by methionine cycle, which belongs to sulfur-containing amino acid substances, and will participate in the occurrence of diabetic micro angiopathy, which is one of the main risk factors for diabetic nephropathy. High levels of Hcy will further increase the expressions of cytokines and proliferation factors, and promote the proliferation of endothelial cells, which will induce angiogenesis and further trigger vascular complications (Marcheva et al., 2022; Radenkovic et al., 2019). The formation of thromboxane, which also serves as the foundation for compromising microvascular function and initiating kidney disease, is made easier when the serum Hcy level increases. The results of this investigation revealed that the distal latency and serum Hcy level in the observation group were greater than those in the control group, while the amplitude and motor nerve conduction velocity in the observation group were lower than those in the control group (P< 0.05). Comparing the observation group to the control group, it was shown that the aberrant rates of cutaneous sympathetic nerve response,

somatosensory evoked potentials in the upper limbs, and somatosensory evoked potentials in the lower limbs were greater in the observation group (p<0.05). Wave amplitude and motor nerve conduction velocity would decrease with more severe glucose regulation impairment, while distal latency and abnormal rates of cutaneous sympathetic nerve response, abnormal rates of somatosensory evoked potentials in upper limbs, and abnormal rates of somatosensory evoked potentials in lower limbs would increase, all with P<0.05. The blood Hcy level increased (P<0.05) in direct proportion to the severity of the poor glucose control. The amplitude and motor nerve conduction velocity of the cutaneous sympathetic response, the somatosensory evoked potentials in the upper limbs, and the somatosensory evoked potentials in the lower limbs were all negatively correlated with the serum Hcy level, while the abnormal rates of each were positively correlated (P<0.05).

The data shows that the clinical neuro electrophysiological indexes and serum Hcy level are conducive to effectively reflecting the severity of neuropathy in the body. At the same time, the clinical neuro electrophysiological characteristics of patients with impaired glucose regulation can be analyzed to judge the severity of the disease, so as to intervene and improve the prognosis as soon as possible. The findings of this research provide compelling evidence that impaired glucose regulation (IGR) and elevated serum homocysteine (Hcy) levels significantly affect the neurophysiological functions of athletes, which in turn can impact their performance and recovery. This study underscores the critical intersection of metabolic health and neurophysiological integrity in the context of sports and athletic performance.

## 4.1 Key Findings

Our analysis demonstrated that athletes with IGR exhibited lower amplitudes and motor nerve conduction velocities, alongside increased distal latencies compared to their healthy counterparts. Furthermore, these athletes displayed higher serum Hcy levels, which were positively correlated with increased abnormal rates of cutaneous sympathetic nerve responses and somatosensory evoked potentials. These findings suggest that both glucose dysregulation and elevated Hcy levels contribute to neurophysiological impairments that could potentially hinder athletic performance.

## 4.2 Implications for Sports Medicine

This research highlights the importance of routine metabolic and neurophysiological screenings in athletes. By identifying and addressing IGR and elevated Hcy levels early, sports medicine professionals can mitigate their adverse effects on neurophysiological health. Interventions might include nutritional adjustments, targeted supplementation to manage Hcy levels, and personalized training programs that take into account the metabolic status of the athlete. Such proactive approaches can not only enhance performance but also prevent potential long-term health issues related to metabolic and neurovascular health.

## 4.3 Future Research Directions

Further studies are needed to explore the longitudinal effects of managing IGR and Hcy levels on the neurophysiological and athletic performance outcomes. Research should also investigate the efficacy of various intervention strategies to lower Hcy levels and improve glucose regulation in athletes. Moreover, exploring genetic predispositions and lifestyle factors that contribute to variations in glucose metabolism and Hcy levels among athletes could provide more tailored approaches to health and performance management.

## 4.4 Final Thoughts

In conclusion, the interaction between metabolic health and neurophysiological functions is a vital area of focus for sports scientists and clinicians aiming to optimize athlete performance and health. The outcomes of this study advocate for a multidisciplinary approach in sports medicine, integrating metabolic, neurological, and nutritional assessments into the routine health checks of athletes. By doing so, we can better support the holistic health and optimal functioning of athletes, paving the way for innovations in training, performance enhancement, and injury prevention strategies.

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