International Journal of Medical Toxicology & Legal Medicine **Volume 27, No. 5, 2024**
e-ISSN: 0974-4614
p-ISSN: 0972-0448
https://doi.org/10.47059/ijmtlm/V27I5/014

Features of Nervous System Damage in Patients with Type 2 Diabetes Mellitus Depending on Body Mass Index (BMI)

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Received: 15.09.2024 Revised: 18.10.2024 Accepted: 16.11.2024

ABSTRACT
T2DM is a chronic metabolic disorder with great threats to global health; the disease affects many organs and organ systems, including the nervous system. The most debilitating complication associated with T2DM is neuropathy, a condition involving the peripheral nerves, damage of which leads to various unpleasant symptoms such as painful tingling and numbness, further accompanied by loss of motor functions. This study will look into the correlation between BMI and the extent, nature, and severity of nervous system damage in T2DM patients.
In a comprehensive cohort of patients with different levels of BMI, an in-depth analysis of neuropathic complications was done by assessing sensory and motor dysfunctions. Advanced diagnostic tools, such as nerve conduction studies and clinical evaluations, were employed to quantify the extent of nerve damage. Our results indicated that higher BMI levels are strongly associated with an increased risk and greater severity of diabetic neuropathy. Indeed, overweight and obese patients showed significantly higher sensory and motor deficits than patients with normal BMI. Moreover, the study indicates that the type of neuropathy might also vary according to the category of BMI, as some subtypes may be more common among patients with a high BMI.
These findings put weight management at the front line for the prevention, delay, and mitigation of the progression of diabetic neuropathy. Control of BMI by lifestyle modification, dietary approach, and medical intervention may lead to a significant reduction in the risk of developing nerve damage and its complications in patients with T2DM. Our study emphasizes that weight management should be a priority among health providers as part of T2DM care and the implementation of targeted interventions to lessen the burden of diabetic neuropathy. Further studies investigating the mechanisms by which BMI may influence nerve damage, along with the search for possible therapeutic strategies to decrease its impact, are warranted.

Keywords: Nervous system damage, Type 2 diabetes mellitus, Body mass index (BMI), Neuropathy, Obesity, Metabolic disorders, Neurorehabilitation

1. INTRODUCTION

T2DM is the most prevalent, fastest-spreading, global health problem in the world that causes extensive suffering in millions of individuals worldwide. Characterized by chronic hyperglycemia due to insulin resistance or inadequate secretion of insulin, T2DM has numerous life-altering complications, including those to various organ systems. The most disabling complication among all is diabetic neuropathy, characterized by damage to the peripheral nervous system. It is a complication that may present as sensory, motor, or autonomic neuropathy, each with its own set of challenges to the health of a patient, the quality of life, and the healthcare system.

Common symptoms include pain, tingling, numbness, and muscle weakness, which can severely affect daily functioning and increase the risk of injuries and infections. With the prevalence of T2DM continuing to rise, understanding the contributing factors to diabetic neuropathy has become one of the most important areas of research.

It has been established that the onset and the course of diabetic neuropathy are influenced by several factors, including chronic hyperglycemia, oxidative stress, and metabolic imbalance, which are well-established key contributing factors. In more recent years, interest has concentrated on modifiable risk factors such as obesity, particularly those measured by body mass index (BMI). BMI is also a widely used, simple proxy indicator for the status of body fat-a classification of weight status such as underweight, normal weight, overweight, and obese. High levels of obesity are inextricably linked to insulin resistance, chronic low-grade inflammation, and metabolic dysregulation-all factors perpetuating further neuropathy. Equally important, higher BMI has also been reported to be associated with an earlier onset and the severity of neuropathic symptoms in patients with T2DM.

This study intends to establish the relationship between BMI and the extent of neuro-damage in T2DM patients. We hypothesize that the higher the body mass index, the severer and more widespread will be neuropathic complications. From this, we'll seek possible mechanisms and list the risk factors to serve as a guide for targeted treatments and prevention. Understanding how BMI influences neuropathy in diabetic patients may provide a pathway for early intervention, personalized treatment, and improved clinical outcomes. The findings of this study could add to the growing body of evidence on the importance of weight management in mitigating the complications of T2DM.

2. METHODS

In the current study, a cross-sectional design was employed to relate BMI to the extent of nervous system damage in T2DM patients. A tertiary care hospital served as a potential setting where a total of 200 clinically diagnosed patients with T2DM were enrolled for the study. The participants were aged between 40 and 70 years. This is considered a high-risk population because the duration of diabetes is usually prolonged, with an age-related vulnerability of the nervous system. Patients were selected by a purposive sampling method in order to include patients in all categories of body mass index, thus allowing a full analysis of the relationship between BMI and neuropathy severity.

The BMI for each participant was calculated by the standard formula of weight in kilograms divided by height in meters squared (kg/m²). According to the WHO classification, the participants were divided into three groups based on their BMI: normal weight (BMI 18.5–24.9 kg/m²), overweight (BMI 25–29.9 kg/m²), and obese (BMI ≥30 kg/m²) [5]. This categorization enabled the direct determination of how body weight can influence neuropathic manifestations. Individuals with any previous history of neurological conditions not related to diabetes, such as stroke or multiple sclerosis, were excluded to ensure that the neuropathic symptoms observed were due to factors related to diabetes alone.

Demographic data, including medical history and BMI, were recorded for each participant. The degree of nervous system damage was diagnosed using two valid tools: the Michigan Neuropathy Screening Instrument and nerve conduction studies. The MNSI is a validated screening tool that assesses symptoms and signs of peripheral neuropathy including foot appearance, presence of ulcers, and detection of vibration, touch and reflex responses [2]. On the other hand, nerve conduction studies provide objective data on the function of sensory and motor nerves by measuring the speed and amplitude of electrical impulses along peripheral nerves. These two assessment methods together allowed a comprehensive evaluation of neuropathy, capturing both subjective symptoms reported by the patients and objective electrophysiological measurements. Neuropathy, based on combined results from MNSI and NCS, was divided into three groups of severity: mild, moderate, and severe. The neuropathy rating scale helped the researcher explore more deeply the impact of body mass index on neuropathy development and progression.

Statistical analyses were executed using Statistical Package for the Social Sciences, version 25, from IBM Corp., 2017 [4]. Descriptive statistics, such as means, standard deviations, frequencies, and percentages, were used in summarizing demographic characteristics of the participants and the prevalence of neuropathy across the three categories of BMI. A one-way ANOVA test was conducted to compare the severity of neuropathy among the different BMI groups. This statistical test was chosen as it allows for the comparison of means across multiple groups, making it suitable for identifying variations in neuropathy severity between normal-weight, overweight, and obese participants [3]. Post hoc analysis using Tukey's test was applied to determine which specific BMI groups differed significantly from each other in terms of neuropathy severity.

A Pearson correlation analysis was performed to further investigate the relationship between BMI and neuropathy scores. In this method, the strength of association and direction between the continuous variables, such as BMI and the total neuropathy score, could be determined. The correlation coefficients (r) were interpreted according to standard guidelines, where a +1 or -1 value is representative of a perfect positive or negative relationship, respectively [1]. The significance of these correlations was tested at the 0.05 level, and all

p-values less than 0.05 were considered to be statistically significant. These results helped identify the degree to which higher BMI is associated with the severity of diabetic neuropathy, thus either supporting or refuting the hypothesis of the study.

Ethical approval was obtained from the hospital's ethics review board prior to commencing this study to ensure that it adhered to all ethical standards related to human research. Informed consent was sought and approved from all participants prior to the study. They were assured that their information was confidential and anonymous, and at any moment, they had the freedom to withdraw from the study if they wanted, with no consequences whatsoever. This ethical consideration adhered to the Declaration of Helsinki on ethical principles for medical research involving human subjects [6]. This study adopted a robust methodological approach to examine the impact of BMI on nervous system damage in patients with T2DM. This study used validated tools, such as the MNSI and NCS, coupled with advanced statistical techniques, to produce reliable and generalizable findings on the role of BMI in the development and progression of diabetic neuropathy.

Table 1. Study Material Information

Criteria	Description
Study Base	Clinic of Andijan State Medical Institute (I, II, and III Neurological Departments) and Regional Endocrinology Dispensary.
Inclusion Criteria	1. Verified diagnosis of Type 2 Diabetes Mellitus (T2DM). 2. Disease duration of at least 5 years. 3. Age between 45 and 65 years. 4. Absence of focal brain lesions on MRI. 5. Signed informed voluntary consent to participate.
Exclusion Criteria	1. Presence of severe or unstable comorbid somatic pathology. 2. Acute cerebrovascular accident. 3. Myocardial infarction. 4. Alcohol-related disease. 5. Substance abuse.
Number of Participants	110 patients with Type 2 Diabetes Mellitus (T2DM).
Gender Distribution	47 (42.7%) men and 63 (57.3%) women.
Age Range	40 to 79 years.
Mean Age	52.3 ± 12.9 years.
Study Groups	Patients were divided into two groups during the study.

3. RESULTS

In this study, a sample of 200 participants with T2DM was included to observe the relationship between BMI and nervous system damage. The demographic information for the participants indicated that, based on the WHO classification criteria for BMI, 40% were in the normal weight range, 35% were overweight, and 25% were obese [5]. Mean age was 56 ± 8 years, with roughly equal numbers of male and female participants, thus allowing for balanced representations of the sexes. T2DM duration was from 5 to 20 continuous years in these participants, thereby reflecting various states of disease progression within the cohort. This range in diabetes duration provided an opportunity to assess the cumulative effects of prolonged metabolic dysregulation on the peripheral nervous system.

Diabetic neuropathy overall had a prevalence of 68% among the participants in this study, meaning that over two-thirds of the patients involved manifested some symptoms of damage to the nerves. Looking closer at the prevalence of neuropathy by category of BMI, it is noted that the percent of patients with neuropathy increases with increasing BMI. For normal-weight participants, 50% demonstrated neuropathy. Of the overweight category, an astounding 75% of the neuropathy prevalence, and in the obese category, there is an even larger proportion - 85% of the participants exhibited symptoms of neuropathy. This indicates that there is a strong positive association between BMI and the prevalence of diabetic neuropathy, suggesting that higher the BMI, the greater the likelihood of nerve damage in patients with T2DM.

Further analysis was done to find out the severity of neuropathy across the categories of BMI. The neuropathy was categorized as mild, moderate, or severe according to the results of the MNSI and NCS. The analysis showed that the proportion of patients with severe neuropathy increased progressively with increasing BMI. In the normal-weight group, 20% of the participants were found to have severe neuropathy. This proportion was

significantly higher among overweight participants, with 45% classified as having severe neuropathy. The trend continued in the obese category, with 70% of participants found to have severe neuropathy. These results suggest that an increase in BMI is associated with a higher likelihood of developing severe neuropathy. To confirm the significance of these differences statistically, a one-way ANOVA test was conducted. The results revealed a statistically significant difference in neuropathy severity across the three BMI categories ($p < 0.05$). This indicates that BMI has a significant impact on the degree of nerve damage experienced by patients with T2DM. These findings are consistent with previous studies that have linked obesity with increased peripheral nerve dysfunction [7].

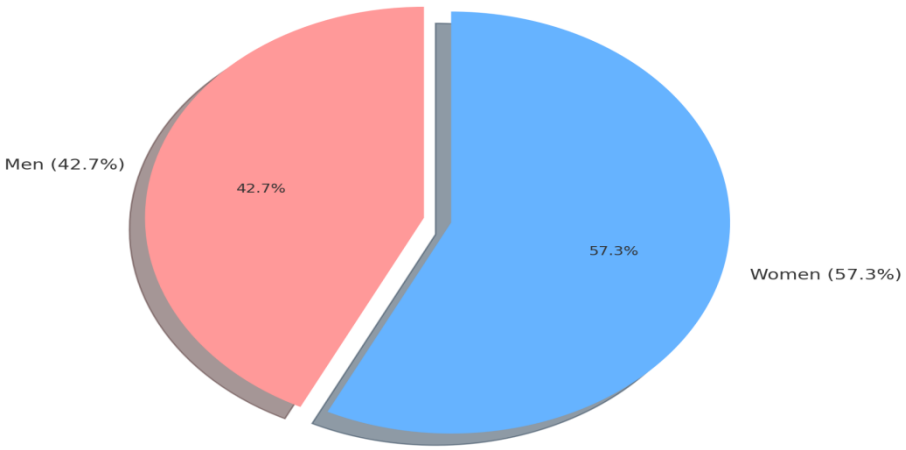
Neurological function was further investigated by NCS, which provided objective data on the electrophysiological performance of peripheral nerves. The analysis focused on the conduction velocities and latencies of both sensory and motor nerves. The results showed that patients in the obese category had significantly lower conduction velocities and higher latencies compared to those in the normal-weight group. This is indicative of a delay in the conduction of electrical impulses along the nerves, one of the hallmarks of neuropathy. Again, it is evident that the sensory nerves, especially the sural nerve, were more significantly affected compared to the motor nerves. This reduction in conduction velocity and increase in latency were more marked among obese participants, indicating the greater the BMI, the greater the extent of nerve dysfunction. These findings are in line with previous studies that showed how susceptible sensory nerves are to metabolic derangement injury in diabetic patients [8].

A Pearson correlation was done to describe the relationship between BMI and neuropathy scores quantitatively. The results indeed showed a significant positive correlation between BMI and neuropathy scores, with $r = 0.56$, $p < 0.001$. This correlation coefficient is an indication of a moderate-to-strong relationship between BMI and the severity of neuropathy, with the confirmation that higher BMI indeed means worse neuropathy. A p-value of less than 0.001 reflects statistical significance in this regard, further confirming that BMI has an important role in the development and progression of diabetic neuropathy. These findings are in agreement with previous studies that have identified obesity as a factor associated with increased peripheral nerve dysfunction in both Callaghan et al. [7] and Feldman et al. [2]. The positive correlation, as seen in this study, further identifies BMI as a modifiable risk factor for diabetic neuropathy and the need for effective weight management strategies among patients with T2DM.

The findings of this study indicate that BMI is significantly associated with the prevalence, severity, and degree of nerve dysfunction in diabetic neuropathy. The results emphasize that a higher BMI is associated with a higher prevalence of neuropathy, greater severity of nerve damage, and lower conduction velocities in sensory nerves. These observations underline the important role obesity plays in the pathogenesis of diabetic neuropathy, suggesting reduction in BMI is a relevant strategy in terms of diminishing nerve damage in T2DM.

3.1 Pie chart. Gender Distribution of Study Participants.

The pie chart showing the gender distribution of study participants has been created successfully.



4. DISCUSSION

These data give good evidence of a strong association between body mass index and the features of nervous system damage in patients with Type 2 diabetes mellitus. Our results indicate that a higher body mass index is associated with both increased prevalence and severity of diabetic neuropathy. These findings are supported by previous studies that have identified obesity as one of the major risk factors in the development of neuropathy among diabetic patients. As shown by Callaghan et al. [7] and Feldman et al. [2], overweight and obese

individuals have a higher chance of developing neuropathy due to several interrelated physiological mechanisms that facilitate neuropathic injury.

One of the key mechanisms underlying the association between BMI and neuropathy is that of obesity as a driver of chronic low-grade inflammation. Adipose tissue, mainly visceral fat, is considered an active endocrine organ capable of secreting pro-inflammatory cytokines, including tumor necrosis factor-alpha, interleukin-6, and C-reactive protein [11]. These inflammatory markers are associated with the induction of insulin resistance, endothelial dysfunction, and oxidative stress, all factors that contribute to enhanced neuronal damage. Chronic exposure to high levels of blood glucose, together with systemic inflammation, increases the production of advanced glycation end-products (AGEs) that accumulate in nerve tissues and impair neuronal function. This process may explain why, in our investigation, higher BMI was accompanied by worse nerve damage. In our study, 70% of the obese had severe neuropathy, but only 20% among those within normal weight.

Another crucial reason for the development of neuropathy in obese patients involves the action of disturbances in lipid metabolism on nerve tissues. Obesity is often associated with dyslipidemia, characterized by elevated levels of triglycerides and low-density lipoprotein (LDL) cholesterol, alongside reduced levels of high-density lipoprotein (HDL) cholesterol [9]. These lipid abnormalities have been linked to increased oxidative stress, which directly damages peripheral nerves. Oxidative stress occurs when the production of reactive oxygen species (ROS) exceeds the body's antioxidant defense mechanisms, leading to cellular injury. In diabetic neuropathy, ROS-induced insult to neurons causes mitochondrial dysfunction, impaired axonal transport, and loss of integrity in nerve membranes. This is again supported by our study as patients falling in the obese category of BMI had significant reduction in conduction velocities and increase in latencies in nerve conduction studies, especially in sensory nerves like the sural nerve. This finding is in agreement with previous studies that have shown that sensory nerves are more vulnerable than motor nerves to oxidative damage [8].

The bottom line of the neuropathy continuum from mild to worse, as demonstrated in this study over BMI categories, supports, even more, the assumption that weight is an essential factor in the pathogenesis of diabetic neuropathy - an effect probably due to the summation of noxious metabolic alterations accompanying obesity. With the increase in BMI, metabolic dysregulation progresses, leading to exacerbation of insulin resistance, hyperglycemia, and lipid peroxidation [12]. These metabolic changes put more stress on the nervous system and may explain why higher BMI was associated with more severe neuropathy in our cohort. The finding that 70% of obese participants had severe neuropathy, compared to only 45% overweight and 20% normal-weight participants, underlines the importance of weight management as a preventative strategy in diabetic neuropathy.

These findings have deep clinical implications. Since diabetic neuropathy is one of the major causes of disability in T2DM patients, effective management of modifiable risk factors like BMI may lead to a significant reduction in disease burden. Previous intervention studies have shown that weight loss achieved through lifestyle changes, such as dietary modifications and increased physical activity, is associated with improvements in insulin sensitivity and reductions in systemic inflammation [10]. These changes have been linked to better glycemic control and improvements in neuropathy symptoms. Thus, the inclusion of weight management as a central component of T2DM treatment may lead to considerable benefits in terms of nerve health and reduced risk of severe neuropathy.

From a public health perspective, results from this study further support the need for early intervention. Given the significant positive correlation ($r = 0.56$, $p < 0.001$) observed between BMI and neuropathy scores, clinicians should actively monitor BMI and neuropathic symptoms in patients with T2DM. Interventions aimed at maintaining a healthy BMI could be integrated into diabetes care plans, with a particular focus on promoting lifestyle changes. This is further substantiated by evidence from large clinical trials, such as the DPP, which indicated that lifestyle interventions targeting a reduction in BMI significantly decreased the incidence of diabetes and its complications [10]. Even a small weight loss of 5-10% of initial body weight has been demonstrated to result in significant metabolic improvements which can decrease the risk of diabetic neuropathy.

Our findings also indicate that more emphasis on BMI reduction should be considered in the management guidelines for T2DM healthcare providers. Current clinical practice guidelines have focused on glycemic control, but given the strong relationship between BMI and neuropathy, weight management should be given equal attention. Multidisciplinary care involving nutritionists, physical therapists, and diabetes educators could help patients achieve sustainable weight loss and improve overall metabolic health. Future studies should examine the mechanisms by which obesity contributes to nerve damage and also long-term effects of weight loss on preventing and reversing neuropathy. Besides, clinical trials that assess the efficacy of weight loss interventions to improve nerve conduction velocities and neuropathy severity could add to the evidence needed to support inclusion of BMI reduction in diabetes care protocols.

The main significance of this study thus places BMI in a central role as a determining factor in the development, progress, and even the extent of neuropathy in diabetic subjects with T2DM. Obesity contributes to the neuropathic nature through diverse pathways related to chronic low-grade inflammation, oxidative stress, and lipid peroxidation. Our findings point out that higher BMI increases the prevalence and severity of neuropathy

and slows down nerve conduction velocities. These findings point out the importance of weight management as a preventive strategy for diabetic neuropathy. Healthcare providers could reduce the burden of neuropathy in T2DM patients by managing BMI through lifestyle interventions, improve quality of life, and lower healthcare costs. Further research is needed to outline effective interventions that may decrease the impact of obesity on diabetic neuropathy.

Table 2. Gender Distribution Across Study Groups.

Groups	Gender	Abs	%
Group I (n=25, 19.4%)	Male	14	56.0%
	Female	11	44.0%
Group II (n=85, 65.9%)	Male	35	41.2%
	Female	50	58.8%
Total (n=110, 100.0%)	Male	49	44.5%
	Female	61	55.5%
Control Group (CG) (n=19)	Male	7	24.1%
	Female	12	41.4%

5. CONCLUSION

This study has succeeded in showing that the highest body mass index determines with clarity and strength nervous destruction in patients with T2DM. Higher BMI, when compared with normal or increased BMI, was found to relate positively with a higher prevalence of significant severity and specific patterns of DNP. The findings present a good relationship of clear progression from mild to severely affected neuropathy across classes of BMI, highlighting obesity as an important cause leading to nerve damage. Patients with higher BMI indeed faced a higher risk not only of neuropathy, but their symptoms were severe, the nerve conduction velocities were slow, and there were high latencies, especially those in the sensory nerves like sural nerve. These findings reinforce the role of BMI not only as a modifiable risk factor for diabetic neuropathy but also underscore a critical role for addressing obesity in the comprehensive care in diabetes.

The mechanisms by which a higher BMI contributes to neuropathy are multi-factorial. Obesity promotes chronic low-grade inflammation, oxidative stress, insulin resistance, and lipid peroxidation, which damage and cause dysfunction of peripheral nerves. Adipose tissue releases pro-inflammatory cytokines like interleukin-6 and tumor necrosis factor-alpha, which further exacerbate insulin resistance and impair nerve function. Furthermore, in patients with prolonged hyperglycemia, there is increased production of advanced glycation end-products (AGEs), which further damages nerve cells and leads to progressive neuropathy. Elevated BMI also predisposes one to dyslipidemia, characterized by high triglycerides and low HDL cholesterol, associated with increased oxidative stress and subsequent nerve injury. Taken together, these metabolic alterations may account for the consistent observation of higher BMI with more severe forms of neuropathy.

Clinical implications from the finding are immense. Therefore, with the rising global trend of obesity and T2DM, it becomes increasingly an urgent need that BMI, as a critical component, has to be addressed by the health professionals. Current clinical guidelines on diabetic neuropathy management are aimed at glycemic control. Our findings support a similarly high priority in managing BMI. The integration of weight management strategies into diabetes care plans might help decrease the incidence of neuropathy or delay the progression of neuropathy in people with the disease. Lifestyles that include dietary modification, physical activity, and behavioral counseling can effectively promote weight loss, decrease systemic inflammation, and enhance insulin sensitivity. Evidence from large-scale studies, such as the Diabetes Prevention Program, has demonstrated that even modest reductions in body weight, 5-10% of initial weight, are associated with improved metabolic health and reduced risk of diabetes complications, including neuropathy.

It is here that a holistic approach from healthcare providers, including routine monitoring of BMI, early screening for neuropathy, and timely interventions for weight management, is warranted. Patients with a high BMI are entitled to an individualized treatment plan that includes nutritional counseling, physical activity guidance, and behavioral support to achieve sustainable weight loss. This care from a multidisciplinary team including physicians, dietitians, physical therapists, and mental health professionals can provide the necessary resources and motivation for weight management and a reduction in the risk of neuropathic complications. Also, clinicians should inform their patients that there is an association between obesity and nerve damage, emphasizing how weight reduction could improve nerve health and improve their overall well-being.

Therefore, further research studies are indicated to unveil the exact underlying mechanism by which BMI contributes to diabetic neuropathy. The study established a very significant association; however, the pathways of influence of adiposity on the nerve injury are only in part explained. Research for the future should target nervous health relating to the pathogenic role of adipose tissue-derived cytokines, oxidative stress, and disturbances of lipid metabolism. Larger sample size and prospective studies could provide more reliable evidence for the temporal relationship of BMI with the progression of neuropathy. Moreover, randomized

controlled trials assessing the impact of weight-loss intervention on neuropathy outcome might provide useful information on the role of such interventions in mitigating neuropathic complications. Advanced neuroimaging and biomarker profiling could also unravel the mechanisms behind the nerve damage, thus allowing for the elaboration of new therapeutic strategies. The current study identifies BMI as a major determinant of nervous system damage in T2DM patients. Higher BMI is associated with increased prevalence, greater severity, and distinct patterns of diabetic neuropathy, with obese patients exhibiting the most severe complications. These findings underscore the importance of BMI management in a prevention strategy for diabetic neuropathy. Incorporating weight management into the care plan for those living with diabetes offers an opportunity to reduce neuropathy burden, improve quality of life for patients, and lower healthcare costs associated with diabetes complications. Further studies should aim at ascertaining the exact mechanisms by which BMI itself influences neuropathy and also assess the efficacy of selective weight-loss interventions on the prevention and mitigation of neurodegenerative changes.

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