NEUROPSYCHOLOGICAL DISORDERS IN WOMEN WITH METABOLIC SYNDROME: DYNAMICS AND A MULTIDISCIPLINARY APPROACH

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Abstract

Metabolic syndrome (MS) is one of the most important contemporary medical and social problems due to its increasing prevalence, multisystemic nature, and association with cardiovascular, cerebrovascular, endocrine, and neuropsychological complications. Although the metabolic and cardiovascular consequences of MS have been extensively studied, neuropsychological manifestations, particularly their dynamics in women, remain insufficiently investigated. Women with MS may develop cognitive impairment, anxiety, depressive symptoms, sleep disturbances, emotional instability, autonomic dysfunction, and reduced quality of life. These manifestations may negatively affect treatment adherence, social functioning, rehabilitation potential, and long-term prognosis.The aim of this study is to comprehensively evaluate the dynamics of neuropsychological disorders in women with metabolic syndrome and to develop an appropriate multidisciplinary approach for their early detection, correction, and rehabilitation. The planned study will include more than 100 women with metabolic syndrome receiving outpatient or inpatient medical care. A control group consisting of age-matched women without metabolic syndrome will also be examined. Clinical-neurological, biochemical, neuropsychological, genetic, and statistical methods will be applied. Cognitive functions will be assessed using the Montreal Cognitive Assessment (MoCA) and Addenbrooke's Cognitive Examination III (ACE-III). Anxiety and depressive symptoms will be evaluated using the Hospital Anxiety and Depression Scale (HADS) and the Depression Anxiety and Stress Scale (DASS-21). Health-related quality of life will be assessed using the EQ-5D questionnaire. Biochemical investigations will include glucose, glycated hemoglobin, lipid profile, insulin, homocysteine, and C-reactive protein. Genetic analysis will focus on the LDLR gene and its possible association with neuropsychological manifestations.

The expected results will contribute to the identification of clinical and biochemical risk factors associated with neuropsychological disorders in women with MS. The study may provide a scientific basis for early diagnosis and individualized multidisciplinary rehabilitation. The proposed multidisciplinary algorithm is expected to improve the quality of life of affected women and contribute to the prevention of disability and progression of neurological and metabolic complications.

Keywords: metabolic syndrome, women, neuropsychological disorders, cognitive impairment, anxiety, depression, sleep disturbances, LDLR gene, multidisciplinary approach, quality of life.

Introduction

Metabolic syndrome is a complex pathological condition characterized by a combination of abdominal obesity, insulin resistance, hyperglycemia, dyslipidemia, and arterial hypertension. It is frequently accompanied by chronic low-grade inflammation, endothelial dysfunction, hyperuricemia, abnormalities of hemostasis, and obstructive sleep apnea. The simultaneous presence of several

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metabolic and cardiovascular risk factors significantly increases the probability of cardiovascular and cerebrovascular disease and may negatively affect the functioning of the central nervous system.

The prevalence of metabolic syndrome has increased considerably worldwide during recent decades. Changes in lifestyle, insufficient physical activity, excessive caloric intake, obesity, chronic stress, and sleep disturbances are among the important factors contributing to its development. Women represent a particularly important population for investigation because metabolic and hormonal changes throughout the reproductive and post-reproductive periods may modify the clinical manifestations and progression of metabolic syndrome.

In recent years, increasing attention has been given to the relationship between metabolic disorders and brain function. Chronic hyperglycemia, insulin resistance, dyslipidemia, arterial hypertension, systemic inflammation, and endothelial dysfunction can adversely affect cerebral circulation and neuronal metabolism. These mechanisms may contribute to the development of cognitive and emotional disorders. Therefore, neuropsychological manifestations should not be considered isolated complications but rather an important component of the systemic effects of metabolic syndrome.

Cognitive impairment is one of the most clinically relevant neuropsychological manifestations associated with metabolic abnormalities. Patients may experience difficulties with attention, memory, executive functions, information processing, and cognitive flexibility. At the same time, anxiety, depressive symptoms, chronic fatigue, sleep disturbances, and stress may further aggravate cognitive performance. The interaction between these factors may create a vicious cycle in which metabolic abnormalities contribute to neuropsychological impairment, while psychological distress and poor sleep may adversely influence lifestyle, treatment adherence, and metabolic control.

Despite the growing number of studies concerning metabolic syndrome and cognitive impairment, several important questions remain unresolved. In particular, there is insufficient information concerning the dynamics of neuropsychological disorders specifically in women with metabolic syndrome, the relationship between neuropsychological manifestations and biochemical abnormalities, and the potential contribution of genetic factors. The correlation between cognitive, emotional, sleep-related, and autonomic disturbances also requires further investigation.

Aim of the Study

The aim of the study is to comprehensively assess the dynamics of neuropsychological disorders in women with metabolic syndrome, identify their clinical and biochemical determinants, investigate their possible association with LDLR gene characteristics, and develop a multidisciplinary approach algorithm for early diagnosis, treatment, and rehabilitation.

Materials and Methods

The planned study will be conducted at the Tashkent State Medical University, Termez Branch. More than 100 women with clinically diagnosed metabolic syndrome will be included in the study. The participants will be examined in outpatient and inpatient settings.

The study population will be divided into two principal groups:

1. **The main group** – women diagnosed with metabolic syndrome.
2. **The control group** – age-matched women without metabolic syndrome and without clinically significant metabolic disorders.

The clinical and neurological status of all participants will be evaluated using standardized clinical-neurological examination. Particular attention will be paid to complaints and manifestations related to cognitive function, emotional status, sleep quality, fatigue, autonomic symptoms, and quality of life.

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Biochemical assessment

A comprehensive biochemical evaluation will be performed to identify metabolic and inflammatory factors potentially associated with neuropsychological impairment. The planned laboratory parameters include fasting glucose, glycated hemoglobin (HbA1c), lipid profile, insulin, homocysteine, and C-reactive protein. These indicators will be analyzed in relation to the severity and dynamics of neuropsychological disorders.The assessment of glucose metabolism and HbA1c will allow evaluation of the degree of glycemic control. Lipid parameters will provide information regarding dyslipidemia, while insulin measurements may contribute to the assessment of insulin resistance. Homocysteine and C-reactive protein will be considered as potential markers associated with vascular and inflammatory mechanisms.

Neuropsychological assessment

A comprehensive neuropsychological evaluation will be performed using internationally recognized standardized instruments.

The **Montreal Cognitive Assessment (MoCA)** will be used for screening cognitive impairment, including difficulties in attention, executive functions, memory, language, visuospatial abilities, and orientation. The **Addenbrooke's Cognitive Examination III (ACE-III)** will provide a more detailed assessment of cognitive domains, including attention, memory, verbal fluency, language, and visuospatial functions. The emotional state of the participants will be assessed using the **Hospital Anxiety and Depression Scale (HADS)**. In addition, the **Depression Anxiety and Stress Scale (DASS-21)** will be used to evaluate symptoms of depression, anxiety, and psychological stress. Health-related quality of life will be assessed using the **EQ-5D questionnaire**, allowing the researchers to determine the relationship between neuropsychological impairment, functional limitations, and subjective quality of life.The repeated assessment of these parameters during the study will make it possible to evaluate the dynamics of neuropsychological disorders and determine whether changes in metabolic parameters are accompanied by corresponding changes in cognitive and emotional functioning.

Genetic investigation

A genetic component of the study will focus on the **low-density lipoprotein receptor (LDLR) gene**. The LDLR gene plays an important role in lipid metabolism and the regulation of circulating low-density lipoprotein cholesterol. Genetic variability affecting lipid metabolism may potentially contribute to individual differences in metabolic risk and associated neurological manifestations.

The study will investigate whether the characteristics of the LDLR gene are associated with neuropsychological disorders in women with metabolic syndrome. The results may help identify potential genetic markers associated with increased susceptibility to cognitive and emotional disturbances.

Statistical analysis

Statistical methods will be applied to determine differences between the main and control groups and to evaluate associations between neuropsychological scores and metabolic, biochemical, and genetic parameters. Correlation and regression analyses will be used to identify potential predictors of neuropsychological impairment. The dynamics of clinical and laboratory parameters will also be evaluated over the observation period.

Expected Results

It is expected that women with metabolic syndrome will demonstrate a higher frequency of neuropsychological abnormalities compared with women without metabolic syndrome. These abnormalities may include mild cognitive impairment, decreased attention and memory, reduced

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executive functioning, anxiety, depressive symptoms, increased psychological stress, sleep-related problems, and reduced quality of life.

The severity of neuropsychological impairment is expected to be associated with the degree of metabolic abnormalities. Higher levels of glucose and HbA1c, unfavorable lipid parameters, insulin resistance, increased inflammatory activity, and elevated homocysteine may demonstrate associations with poorer cognitive and emotional performance.

An important expected outcome of the study is the identification of clinically significant correlations between cognitive dysfunction and emotional disturbances. For example, anxiety, depression, and chronic stress may contribute to deterioration of attention and memory, while cognitive difficulties may, in turn, negatively affect emotional well-being and quality of life.

The study is also expected to clarify the potential relationship between LDLR gene characteristics and neuropsychological manifestations. Identification of such associations could contribute to a better understanding of individual susceptibility to neurological and cognitive complications in metabolic syndrome.

Discussion

The relationship between metabolic syndrome and neuropsychological dysfunction is likely to be multifactorial. Insulin resistance may influence neuronal energy metabolism and impair mechanisms involved in learning and memory. Chronic hyperglycemia can contribute to oxidative stress and vascular injury, while dyslipidemia and arterial hypertension may promote endothelial dysfunction and compromise cerebral perfusion.

Low-grade systemic inflammation may represent another important mechanism. Persistent inflammatory activation can affect neuronal function and may contribute to changes in mood and cognition. In addition, metabolic syndrome is frequently associated with obesity and obstructive sleep apnea, both of which can independently or synergistically affect cognitive performance and emotional stability.Sleep disturbances deserve particular attention because they may be both a consequence and a contributing factor of metabolic and neuropsychological dysfunction. Poor sleep can increase daytime fatigue, impair attention and memory, and intensify anxiety and depressive symptoms. Conversely, psychological stress and depressive symptoms may further reduce sleep quality and contribute to unhealthy lifestyle behaviors.

Therefore, neuropsychological disorders in women with metabolic syndrome should be evaluated from a multidimensional perspective rather than through isolated assessment of cognitive function. A comprehensive approach should include neurological, metabolic, psychological, behavioral, and genetic factors.The proposed multidisciplinary strategy may involve neurologists, endocrinologists, cardiologists, psychiatrists or clinical psychologists, nutrition specialists, rehabilitation professionals, and primary healthcare physicians. Such cooperation would facilitate early identification of high-risk patients and allow individualized intervention.

Multidisciplinary Approach

Based on the expected findings, a multidisciplinary algorithm for women with metabolic syndrome and neuropsychological disorders will be developed. The algorithm may include several consecutive stages.

The first stage will involve screening for metabolic and neuropsychological risk factors. The second stage will include detailed neurological, biochemical, cognitive, emotional, and quality-of-life assessment. The third stage will involve identification of patients requiring specialized interventions.

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The therapeutic and rehabilitation component will focus not only on metabolic control but also on neuropsychological rehabilitation. Individualized recommendations regarding nutrition, physical activity, sleep hygiene, psychological support, cognitive training, and adherence to pharmacological treatment may be incorporated into the algorithm.

Regular follow-up will be necessary to assess changes in metabolic and neuropsychological parameters. Repeated MoCA, ACE-III, HADS, DASS-21, and EQ-5D assessments may allow clinicians to evaluate treatment effectiveness and modify rehabilitation strategies.

Such a multidisciplinary model may improve early detection of neuropsychological disorders and prevent their progression. It may also improve treatment adherence, functional status, social adaptation, and quality of life.

Scientific Novelty

The scientific novelty of the planned research consists in the comprehensive investigation of neuropsychological disorders in women with metabolic syndrome in dynamics using clinical-neurological, biochemical, neuropsychological, and genetic approaches.

The study will attempt to establish relationships between neuropsychological manifestations and metabolic abnormalities, as well as to determine the potential contribution of LDLR gene characteristics to cognitive and emotional dysfunction.

Another important aspect of the study will be the development of a multidisciplinary algorithm for women with metabolic syndrome and neuropsychological disorders. This approach may provide a practical framework for individualized early intervention and rehabilitation.

Practical Significance

The practical significance of the study is related to the possibility of introducing an early screening and multidisciplinary management algorithm into clinical practice. Early identification of cognitive and emotional disorders may allow healthcare professionals to initiate appropriate preventive and rehabilitation measures before severe functional impairment develops.

The proposed approach may be particularly useful in primary healthcare, endocrinology, neurology, and rehabilitation services. Its implementation may contribute to improved quality of life, better treatment adherence, prevention of disability, and reduction of the long-term social and economic burden associated with metabolic syndrome.

Conclusion

Metabolic syndrome in women should be considered not only as a combination of metabolic and cardiovascular risk factors but also as a condition potentially associated with significant neuropsychological consequences. Cognitive impairment, anxiety, depression, stress, sleep disturbances, and reduced quality of life may substantially influence the clinical course of the disease and the effectiveness of treatment.

A comprehensive assessment of neuropsychological disorders in combination with metabolic, biochemical, and genetic parameters may provide a more complete understanding of the mechanisms underlying these complications. Investigation of the relationship between LDLR gene characteristics and neuropsychological manifestations may provide additional information regarding individual susceptibility to cognitive and emotional disorders.

The development of a multidisciplinary approach based on early screening, individualized assessment, metabolic correction, psychological support, cognitive rehabilitation, lifestyle modification, and continuous monitoring may improve the management of women with metabolic syndrome.

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The planned research is therefore expected to provide clinically relevant evidence for early detection and correction of neuropsychological disorders and to contribute to improving the quality of life and functional outcomes of women with metabolic syndrome.

Keywords: metabolic syndrome; women; neuropsychological disorders; cognitive impairment; MoCA; ACE-III; anxiety; depression; stress; sleep disorders; LDLR; insulin resistance; dyslipidemia; multidisciplinary rehabilitation; quality of life.

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