

Ministry of Education and Science of the Russian Federation
Federal Independent Educational Institution
«NATIONAL RESEARCH TOMSK POLYTECHNIC UNIVERSITY»

Research School of Chemical and Biomedical Technologies
Direction of training 12.04.04 «Biotechnical systems and technologies»
Department of Electronic Engineering

MASTER'S THESIS

Topic of the work
Detection of changes in brain structures on MRI for various diseases (Выявление изменений структур головного мозга на МРТ при различных заболеваниях)

UDC 004.42:616-009.2

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Planned program learning outcomes

Код результата	Результат обучения (выпускник должен быть готов)	Требования ФГОС, критериев и/или заинтересованных сторон
Профессиональные компетенции		
P1	Применять глубокие специальные естественнонаучные, математические, социально-экономические и профессиональные знания в инновационной инженерной деятельности при разработке, производстве, исследовании, эксплуатации, обслуживании и ремонте современной биомедицинской и экологической техники	Требования ФГОС (ОК-2, ОПК-2), Критерий 5 АИОР (п. 5.2.1), согласованный с требованиями международных стандартов <i>EUR-ACE</i> и <i>FEANI</i>
P2	Ставить и решать инновационные задачи инженерного анализа и синтеза с использованием специальных знаний, современных аналитических методов и моделей	Требования ФГОС (ОПК-1, 3; ПК- 1 – 4), Критерий 5 АИОР (п. 5.2.2), согласованный с требованиями международных стандартов <i>EUR-ACE</i> и <i>FEANI</i>
P3	Выбирать и использовать необходимое оборудование, инструменты и технологии для ведения инновационной практической инженерной деятельности с учетом экономических, экологических, социальных и иных ограничений	Требования ФГОС (ОК-9, ПК-10, 14, 18). Критерий 5 АИОР (пп. 5.2.3, 5.2.5), согласованный с требованиями международных стандартов <i>EUR-ACE</i> и <i>FEANI</i>
P4	Выполнять комплексные инженерные проекты по разработке высокоэффективной биомедицинской и экологической техники конкурентоспособной на мировом рынке	Требования ФГОС (ОК-2, 3; ПК-5 – 11, 14), Критерий 5 АИОР (пп. 5.2.3, 5.2.5), согласованный с требованиями международных стандартов <i>EUR-ACE</i> и <i>FEANI</i>
P5	Проводить комплексные инженерные исследования, включая поиск необходимой информации, эксперимент, анализ и интерпретацию данных с применением глубоких специальных знаний и современных методов для достижения требуемых результатов в сложных и неопределенных условиях	Требования ФГОС (ОК-2, 3; ОПК-5, ПК-1 – 4). Критерий 5 АИОР (пп. 5.2.2, 5.2.4), согласованный с требованиями международных стандартов <i>EUR-ACE</i> и <i>FEANI</i>
P6	Внедрять, эксплуатировать и обслуживать современное высокотехнологичное оборудование в предметной сфере биотехнических систем и технологий, обеспечивать его высокую эффективность, соблюдать правила охраны здоровья и безопасности труда, выполнять требования по защите окружающей среды	Требования ФГОС (ОПК-1, 2), Критерий 5 АИОР (пп. 5.2.5, 5.2.6), согласованный с требованиями международных стандартов <i>EUR-ACE</i> и <i>FEANI</i>
<i>Универсальные компетенции</i>		
P7	Использовать глубокие знания в области проектного менеджмента для ведения инновационной инженерной деятельности с учетом юридических аспектов защиты интеллектуальной собственности	Требования ФГОС (ОПК-2; ПК-14, 15). Критерий 5 АИОР (п. 5.3.1), согласованный с требованиями международных стандартов <i>EUR-ACE</i> и <i>FEANI</i>
P8	Владеть иностранным языком на уровне, позволяющем активно осуществлять коммуникации в профессиональной среде и в обществе, разрабатывать документацию, презентовать и защищать результаты инновационной инженерной деятельности	Требования ФГОС (ОК-1), Критерий 5 АИОР (п. 5.3.2), согласованный с требованиями международных стандартов <i>EUR-ACE</i> и <i>FEANI</i>
P9	Эффективно работать индивидуально и в качестве члена и руководителя команды, состоящей из специалистов различных направлений и квалификаций, с делением ответственности и полномочий при решении инновационных инженерных задач	Требования ФГОС (ОК-3, ОПК-3; ПК-3, 12, 13), Критерий 5 АИОР (п. 5.3.3), согласованный с требованиями международных стандартов <i>EUR-ACE</i> и <i>FEANI</i>
P10	Демонстрировать личную ответственность, приверженность и готовность следовать профессиональной этике и нормам ведения инновационной инженерной деятельности	Критерий 5 АИОР (п. 5.3.4), согласованный с требованиями международных стандартов <i>EUR-ACE</i> и <i>FEANI</i>
P11	Демонстрировать глубокие знание правовых, социальных, экологических и культурных аспектов инновационной инженерной деятельности, компетентность в вопросах охраны здоровья и безопасности жизнедеятельности	Критерий 5 АИОР (п. 5.3.5), согласованный с требованиями международных стандартов <i>EUR-ACE</i> и <i>FEANI</i>
P12	Самостоятельно учиться и непрерывно повышать квалификацию в течение всего периода профессиональной деятельности	Требования ФГОС (ОК-2, 4; ОПК-4), Критерий 5 АИОР (п.5.3.6), согласованный с требованиями международных стандартов <i>EUR-ACE</i> и <i>FEANI</i>

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 Direction of training 12.04.04 «Biotechnical systems and technologies»
 Department of Electronic Engineering

APPROVED BY
 Head of the Program
 _____ F.A.Gubarev
 (Signature) (Date)

**ASSIGNMENT
 for the Master's Thesis completion**

In the form:

Master's Thesis

For a student:

Group	Full Name
1DM7I	Bykova Maria Victorovna

Topic of the work:

Detection of changes in brain structures on MRI for various diseases (Выявление изменений структур головного мозга на МРТ при различных заболеваниях)
Approved by the order of the Head (date, number)

Deadline for completion of the Master's Thesis:	
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TERMS OF REFERENCE:

<p>Initial data for work: <i>(the name of the object of research or design; performance or load; mode of operation (continuous, periodic, cyclic, etc.); type of raw material or material of the product; requirements for the product, product or process; special requirements to the features of the operation of the object or product in terms of operational safety, environmental impact, energy costs; economic analysis, etc.).</i></p>	<ol style="list-style-type: none"> 1. The results of T1-T2 weighted images of patients with diabetes mellitus type 1 and 2 and people without endocrine diseases; 2. Magnetic resonance spectrogram of patients with diabetes mellitus type 1 and 2 and people without endocrine diseases; 3. Software applications for autosegmentation of medical images.
<p>List of the issues to be investigated, designed and developed <i>(analytical review of literary sources in order to elucidate the achievements of world science and technology in the field under consideration, the formulation of the problem of research, design, construction, the content of the procedure of the research, design, construction, discussion of the performed work results, the name of additional sections to be developed; work conclusion).</i></p>	<p>To accomplish the task, it is necessary to investigate a number of questions:</p> <ol style="list-style-type: none"> 1. Search for information on brain structures related to cognitive function; 2. The study of algorithms for autosegmentation of brain structures; 3. Analysis of the MPC study groups; 4. Calculation of the ratio of gray / white matter and the volume of the hippocampus for research groups. 6) Visualization and mathematical analysis of the obtained data. 7) Feasibility study

	8) Industrial and environmental safety.
List of graphic material <i>(with an exact indication of mandatory drawings)</i>	
Advisors on the sections of the Master's Thesis	
Chapter	Advisor
Section «Financial Management, Resource Efficiency and Resource Saving»	Senior Lecturer, Department of Social and Human Sciences Potekhina Nina Vasilyevna
Section «Social Responsibility»	Associate Professor of General Technical Disciplines Mikhail Vladimirovich Gorbenko

Date of issuance of the assignment for Master's Thesis completion according to a line schedule	
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The task was issued by the Scientific Supervisor and Technical Advisor:

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Assistant professor	Gubarev Fedor Aleksandrovich	Candidate of Technical Sciences		
Assistant professor	Tolmachev Ivan Vladislavovich	Candidate of Medical Sciences		

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**ASSIGNMENT FOR THE SECTION
«FINANCIAL MANAGEMENT»**

For a student:

Group	Full name
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School	RSCBMT	Department (SEC)	Electronic engineering
Level of education	Magistracy	Direction of training/Specialty	12.04.04 Biotechnical systems and technologies

Initial data to the section "Financial management, resource efficiency and resource saving":

<i>1. The cost of scientific research resources: material, energy, financial, informational and human</i>	Salary of the head - 33664 rub. Salary of the student - 21,760 rub. The cost of material resources is determined on the basis of open prices.
<i>2. Norms and standards of resource usage</i>	Additional salary 13%; Overhead costs 16%; District coefficient of 30%.
<i>3. The used tax system, rates of taxes, deductions, discounting and lending</i>	The ratio of deductions for payment in extra-budgetary funds 30%.

The list of issues to be investigated, designed and developed:

<i>1. Pre-project analysis</i>	Description of the potential consumer of the research results, Analysis of the competitiveness of technical solutions SWOT analysis
<i>2. Initiation of the project</i>	Definition of the working group of the project, building a tree of project goals.
<i>3. Planning research projects</i>	Planning work stages, determining the schedule of the study Definition of project risks, assessment of risk and loss probability
<i>4. Determination of the potential effect of a research project.</i>	Determination of the potential effect of a research project.

List of graphic materials (with exact indication of required drawings):

<ol style="list-style-type: none"> 1. "Portrait" of a consumer of NTI results 2. Map of market segmentation; 3. Evaluation map for comparison of competitive technical solutions 4. SWOT matrix 5. Temporary indicators of research 6. Schedule of the study 7. Budget of research project costs 8. Determination of risks
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Date of assignment for the section on a linear schedule	
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**ASSIGNMENT FOR THE SECTION
«SOCIAL RESPONSIBILITY»**

For a student:

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School	RSCBMT	Department (SEC)	Electronic engineering
Level of education	Magistracy	Direction of training/Specialty	12.04.04 Biotechnical systems and technologies

Initial data to the section «Social responsibility»:	
1. Characteristics of the object of study (substance, material, device, algorithm, method, working area) and its areas of application	Development of software for the rehabilitation of motor functions of patients with neurological diseases.
The list of issues to be investigated, designed and developed:	
1. Legal and organizational safety issues: <i>1.1. Special legal norms of labor legislation.</i> <i>1.2. Organizational activities in the layout of the working area.</i>	Special legal norms of labor legislation (medical examination of employees, psychiatric examination, safety instructions, provision of personal protective equipment). Requirements for the organization of the workplace.
2. Production safety: <i>2.1. Analysis of harmful and dangerous factors that can be created by object of study.</i> <i>2.2. Analysis of harmful and dangerous factors that may arise in the laboratory during research.</i> <i>2.3. Justification of measures to protect the researcher from the effects of dangerous and harmful factors.</i>	Harmful production factors: 1) Insufficient illumination of the working area; 2) Increased level of electromagnetic radiation; 3) Lack or lack of natural light; 4) Increased air temperature in the workplace Hazardous production factors: 1) The increased value of the voltage in the electrical circuit, the circuit.
3. Ecological safety: <i>3.1. Analysis of the impact of the object of research on the environment.</i> <i>3.2. Analysis of the "life cycle" of the object of study.</i> <i>3.3. Justification of measures to protect the environment.</i>	When using devices necessary for the implementation of FQW, the atmosphere, hydrosphere or lithosphere is not harmed, since no harmful substances are released into the air and water. In the event of a malfunction of the device, this technology also passes recycling.

<p>4. Safety in emergency situations: <i>4.1. Analysis of probable emergencies that may occur in the laboratory during research.</i> <i>4.2. Justification of measures to prevent emergencies and the development of procedures in case of an emergency.</i></p>	<p>When developing and operating a designed solution, the most possible emergency is fire. The list of measures to reduce the threat of possible emergencies.</p>
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Date of assignment for the section on a linear schedule	
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Assignment was issued by an advisor:

Position	Full name	Degree	Signature	Date
Associate professor of general technical disciplines	Mikhail Vladimirovich Gorbenko	Candidate of technical sciences		

Assignment was accepted for execution by the student:

Group	Full name	Signature	Date
1DM7I	Bykova Maria Victorovna		

Essay

This final qualifying work contains 110 p., 39 fig., Table 30, 29 sources.

Keywords: diabetes mellitus, magnetic resonance imaging, magnetic resonance spectroscopy, automatic segmentation, cognitive functions.

The object of the study is the data of MRI, MRS of patients suffering from diabetes mellitus type 1 and 2 and the control group.

The purpose of this work is to identify differences in indicators of the structure and metabolism of the brain according to MRI and MRS data in patients with diabetes and healthy.

As a result of the study, based on an analysis of the literature, brain structures of damage that are associated with cognitive impairments were identified, data obtained by the MRS method were analyzed, automatic segmentation of images obtained from MRI studies of patients with diabetes was performed, and, according to FreeSurfer, the volumes of gray were calculated and the white matter of the brain.

Degree of implementation: the data obtained are of a fundamental nature, publications are planned in the rating Journal of neurological sciences.

The main design, technological and technical and operational characteristics: laboratory conditions of operation.

Scope: medical centers, private clinics, public clinics, as well as practicing doctors working with endocrinological diseases, in particular, diabetes mellitus type 1 and 2.

Cost-effective work saves time for research and labor.

Definitions, designations, abbreviations, normative references

References to the following standards are used in this work:

GOST 12.1.006-84 “SSBT. Electromagnetic fields of radio frequencies. Permissible levels at workplaces and requirements for monitoring”

GOST 12.1.003-83 “SSBT. Noise. General safety requirements”

GOST 12.0.003-74 “SSBT. Dangerous and harmful production factors. Classification”

GOST 12.1.019-79 “SSBT. Electrical safety. General requirements and nomenclature of types of protection”

GOST 12.1.006-84 “SSBT. Electromagnetic fields of radio frequencies. Permissible levels at workplaces and requirements for monitoring”

GOST R 22.0.02-94 “SSBT. Safety in emergency situations. Terms and definitions of basic concepts”

GOST 12.2.032-78 “SSBT. Workplace when working sitting. General ergonomic requirements”

The following abbreviations are used in this paper:

MRI – Magnetic resonance imaging

MRS - Magnetic Resonance Spectroscopy

NMR - Nuclear Magnetic Resonance

MR - Magnetic resonance

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Introduction

Diabetes mellitus is a disease that humankind encountered thousands of years ago before our era. The doctor, whose name Arethaius, gave the disease the name "diabetes", which in Greek means "flow, pass through." In those days, the causes of diabetes were called the most different, doctors tried to show ingenuity and ingenuity in trying to diagnose it, but, nevertheless, their study and the consequences of the disease are still being studied.

The term Diabetes mellitus is commonly understood as a group of endocrine diseases that are associated with impaired glucose uptake and, as a result, relative development (impaired interaction with target cells) or absolute insulin deficiency. As a consequence, a disease called hyperglycemia, characterized by a high content of glucose in the blood, develops. This disease violates all types of metabolism: protein, fat, carbohydrate, mineral and water-salt, as well as characterized by a chronic course.

There are 2 of the most popular types of diabetes mellitus: the first type and the second type, which are also called insulin-dependent and insulin-independent, respectively.

Diabetes mellitus of the first type refers to a group of diseases that develop due to the rapid destruction of the beta cells of the pancreas. This leads to a deficiency in the synthesis of proinsulin and hyperglycemia, the symptoms of which have been described above. This type of diabetes requires hormone replacement therapy.

Type 2 diabetes mellitus or non-insulin dependent diabetes is a disease that usually develops in people with excessive fat accumulation and insulin resistance is a physiological condition in which cells do not respond to the usual actions of the hormone insulin, i.e. cells are not able to use the insulin obtained effectively, and these leads, again, to hyperglycemia. As a result of all this, the synthesis of proinsulin and amylin is enhanced by beta cells and the so-called "relative deficit" occurs. [1]

In the last revision of the classification of diabetes mellitus made by the American Diabetes Association in January 2010, diabetes mellitus of the first and

second types, diabetes of pregnant women, a number of rare forms of diabetes, like «diabetes type and a half» and «other specific types of diabetes» were identified. [2]

Prolonged exposure to this disease can lead to such violations of the state of human health, such as, for example, renal failure, blindness and damage to the central nervous system (CNS). They arise as a result of the defeat of small vessels, such as capillaries and arterioles, of these organs. Such a lesion is called microvascular or microvascular.

In addition, diabetes is involved in accelerating the lesion of larger arteries and the development of atherosclerosis in them, which in clinical studies manifested such conditions as coronary heart disease, stroke, and other diseases of the cardiovascular system. [3]

In the event that large vessels were affected due to the influence of diabetes mellitus, such a lesion would be called a macrovascular one.

At the moment, diabetes treatment is one of the most expensive items in the budget of medicine in almost all countries of the world. For example, in 1997, about 98 billion dollars was spent on the treatment of diabetes in the United States. After 20 years, the costs have almost not decreased, and diabetes still continues to destroy the organisms of patients.

Nowadays, diabetes is the third leading cause of death in the United States after heart disease and cancer. [4]

In this final qualifying work, the analysis of the effect on the human body of diabetes of the first and second types, that is, insulin-dependent and insulin-independent, is carried out. Diabetes leads to irreversible cognitive impairment in patients suffering from this type of disease. [5]

Cognitive impairment is called the phenomenon of memory loss, mental performance and other cognitive functions in comparison with the initial level determined by the individual norm. Cognitive functions are the most complex functions of the brain that allow the process of rational knowledge of the world and provide targeted interaction with it: analysis and processing of information, its perception,

storage and memorization, as well as the exchange of information and the construction and implementation of an action program.

The purpose of this work is to identify differences in indicators of the structure and metabolism of the brain according to MRI and MRS data in diabetic and healthy patients.

The tasks of this final qualifying work:

- 1) Analysis of the literature and the search for information about the structures of the brain associated with cognitive functions;
- 2) Evaluation of the concentration of metabolites (NAA - N-acetyl-aspartate, Cr - creatine, Cho - choline) in significant areas of the brain according to spectral MRI;
- 3) Conduct automatic segmentation of images obtained as a result of MRI studies;
- 4) Calculation of the ratios of the volumes of gray and white matter of the brain in different parts of it and the volume of the hippocampus.

To conduct this study, data from patients with diabetes mellitus and data from the control group were required to assess the deviation of indicators from the norm. The results are collected from magnetic resonance imaging (MRI), including magnetic resonance spectroscopy (MRS).

1 Literature Review

1.1 Relevance

Diabetes mellitus and its complications can cause permanent or transient cognitive changes resulting from chronic or acute disorders of the relative constancy of blood glucose levels. Ever since 1992, the scientific community has been interested in the relationship between diabetes and cognitive functions. The term "diabetic encephalopathy" was proposed for the first time in 1950. It meant by a cognitive impairment that complicate the course of the disease. Mijnhout and co-authors in 2006 proposed a new term that sounds like "diabetes-associated cognitive decline" (DACD). In their opinion, this term describes a condition from mild to moderate cognitive impairment, in particular a decrease in cognitive flexibility and psychomotor retardation, which is not related to other causes, but does not imply a specific pathogenetic cause.

However, at the moment there are no clear criteria for the diagnosis of cognitive impairment, and therefore this pathology remains rarely diagnosed and underestimated. To date, there are a number of studies that prove that diabetes has a direct impact on changes in the central nervous system.

Thus, the exact cause of the development of cognitive impairment in patients with insulin-dependent diabetes mellitus has not yet been established. The effects of both hypoglycemia and hyperglycemia, as well as the severity of vascular diseases and glycemia variability, are considered. It is indisputable that, as a combination of these conditions, each of these factors separately can influence, and also the age, social status of the patient, the method of treatment of the underlying disease and the presence of concomitant pathology cannot be excluded.

Diabetes mellitus of the first type most often develops in young, adolescent or childhood and always requires replacement therapy with insulin. Chronic hyperglycemia, which is associated with inadequate selection of insulin doses, is the risk of developing various microvascular complications. However, on the other hand,

the frequency of severe hypoglycemia leads to intensive insulin therapy, which is aimed at achieving normal glycemia indices, which contribute to reducing the severity and development of these complications, as well as further studies that clarify the study.

Type 2 diabetes mellitus is caused by a combination of genetic and lifetime factors. Most people with these types of diabetes are overweight. Obesity itself is one of the serious risk factors for the development of type 2 diabetes. In children who are obese, the risk of developing type 2 diabetes is increased 4 times. [6]

1.2 Magnetic resonance spectroscopy

Magnetic resonance spectroscopy is an additional magnetic resonance imaging (MRI) technique, which allows non-invasive assessment of the concentration of a number of compounds in a selected tissue volume.

The data set depends primarily on the choice of the nucleus, at the resonant frequency of which the spectroscopic study will be performed (the most common ^1H , ^{31}P), dictated, usually, by the hardware capabilities of a particular tomograph.

When using ^1H -single-voxel spectroscopy, one can obtain data on relative concentrations of 3 or more metabolites in the entire specified volume, whereas the use of multi-voxel allows you to multiply the amount of data obtained, because they are collected for each unit of the selected volume. In a single-slice multi-voxel spectroscopy sample estimated, there are usually more than 50 voxels. Compared with one voxel, the amount of information increases dramatically, which creates difficulties in their clinical evaluation.

The advantages of this method include the ability to evaluate complex and small structures. The disadvantage is that the method is rather time-consuming (with a large number of voxels evaluated); laborious; automation is possible, but highly dependent on the task. [9]

1.3 Magnetic resonance imaging

Magnetic resonance imaging is a method of scanning a person's body using radio waves and strong magnetic fields to obtain high-quality images that help in diagnosing a wide range of human health conditions. This is a complex, but safe and effective diagnostic method that is not associated with the introduction of any radioactive substances or with ionizing radiation. Magnetic field and radio frequency pulses are the basis for MRI imaging.

MRI is based on the effects of nuclear magnetic resonance (NMR). It consists in the possibility of absorption and emission of the energy of radio frequency pulses by the nuclei of certain substances — such as, for example, hydrogen — that are in a magnetic field when the frequency of the pulses and the frequency of rotation of the nuclei coincide.

MRI has 2 main advantages: 1) high soft tissue contrast, and this allows to obtain high-quality images of various soft tissues, while the introduction of a contrast agent is not necessary; 2) no radiation exposure.

As a rule, MRI is not used for studies of the lungs, stomach and intestines, bones.
[7]

1.4 MR-images

The MR image is a radio wave that is generated by protons at the moment when the very phenomenon of NMR disappears during a certain period. This period is called the relaxation time. The generated radio wave is picked up by a radio frequency coil, as a result of which an electric current is induced, the amplitude of which is directly proportional to the intensity of the MR signal. As a result, the intensity of this MR signal is estimated.

However, protons emitted by different types of tissue (for example, liquid formations or adipose tissue) emit different MR signals. They differ from each other not only in intensity, but also in duration. The reason is that during relaxation, chemically strongly bound protons (as in adipose tissue) give off energy emitted by radio waves much faster than less bound ones (as in water). Consequently, the period of relaxation of fat is much less than that of water.

At the heart of the phenomenon of relaxation lies 2 parallel flow processes:

- 1) The return of the magnetization vector created by the rotation of the protons to the initial state, that is, before the appearance of NMR;
- 2) Dephasing.

As a result, two basic concepts are distinguished, the so-called T1 and T2 relaxation times:

- 1) The T1 relaxation time is the time required to reach 63% of the magnitude of the proton magnetization vector that existed before the appearance of the NMR phenomenon.

- 2) The T2 relaxation time is the time required to reach the state when, in the process of dephasing, only 37% of the protons synchronized in phase from the initial value are saved.

At that moment, when the patient is placed inside an MRI tomograph (inside a magnetic field), as a whole, a total magnetic moment is created in the patient's body, which coincides with the direction of the external magnetic field. This value depends primarily on the proton density and it is customary to denote PD.

The layer of tissues obtained using MRI can be represented as a set of elements of the electronic matrix equal in volume - voxels. Each such voxel corresponds to a pixel — an element of the planar image, which is characterized by its proton density, T1 and T2 relaxation time.

With the help of special methodological approaches that create conditions for NMR only in a strictly defined voxel, the MR signals generated by the protons of other voxels are eliminated. As a result of repeated repetitions of radio frequency pulses,

each voxel receives a unique spatial coding, on the basis of which the intensity of the MR signal is estimated.

Accordingly, there are three different types of MRI images. MR imaging can be visualization of proton density (PD) or T1- and T2-weighted images. The intensity of the MR signal in the image is encoded by a certain shade of black and white gamma. [8]

1.5 Brain metabolites

NAA - N-acetyl aspartate. It is a derivative of aspartic acid. This is the second most concentrated molecule in the brain after the amino acid glutamate. It is synthesized in neurons from the amino acid aspartate and acetyl - coenzyme A. The various functions of the NAA are not yet fully understood, but such metabolite functions are already known, such as:

- 1) a neural osmolyte in which the NAA participates in the balance of fluid in the brain;
- 2) Acetate source for lipids and myelin synthesis in oligodendrocytes, glial cells;
- 3) the precursor of the important neural dipeptide, N-acetylaspartartilglutamate;
- 4) NAA is also involved in the production of energy from the amino acid glutamate in neuronal mitochondria.

The decrease in NAA metabolite is correlated as an indicator of neuronal dysfunction and neuron death. It has been shown that in MLS - a study of patients with schizophrenia, zones of deficiency of N-acetyl aspartate, localized in the prefrontal cortex, temporal lobes, hippocampus, are detected.

Cho - choline. It is the precursor of the major neurometirator acetylcholine, which transmits nerve impulses, as well as an important element of the nervous system. Functions of choline:

- 1) Improves memory;
- 2) Included in the cell membrane in the composition of phospholipids, which are markers of gliosis;
- 3) Participates in the regulation of insulin levels in the body, while normalizing carbohydrate metabolism;
- 4) It promotes the metabolism and transport of fats in the liver, being a hepatoprotector and a lipotropic agent.

With a decrease or absence of choline, the kidneys are affected, blood circulation deteriorates and fats are deposited in the liver.

Cr - Creatine and Cr2 - Phosphocreatine. Functions:

- 1) Creatine plays an important role in energy metabolism in muscle and nerve cells. Carrying out the function of the energy depot, it maintains ATP / ADP at a sufficient level, providing cells in which it is necessary with a high level of ATP.
- 2) Phosphate form of creatine - phosphocreatine, acts as a high-energy phosphate reserve in the cells. The phosphocreatinase system is responsible for intracellular energy metabolism.
- 3) Creatine phosphate also neutralizes acids formed during exercise in muscle cells.
- 4) Creatine activates glycolysis.

When conducting MRS studies, the protons of the nuclei of atoms of different substances absorb the energy of radio-frequency pulses at different frequencies and then emit it. The amount of the corresponding chemical substance in the tissue volume under investigation can be determined from the value of the signal emitted at a given frequency. The unit of measurement for “chemical shift” is part per million. Each metabolite in brain tissue has its own characteristic ppm value. In MR spectroscopy, a relative “chemical shift” scale is adopted, on which the zero value is on the right side of the scale. [9]

- 1) The peaks of the following metabolites are determined on the spectrum of a normal brain substance:
- 2) 1) N-acetyl-aspartate (NAA): resonates at 2.0 ppm

- 3) 2) Creatine: resonates at 3.0 ppm
- 4) 3) Choline: resonates at 3.2 ppm [10]

1.6 Hippocampus

The hippocampus refers to an element that enters the limbic system of the brain (olfactory brain) and is responsible for the formation of emotions, the transition of short-term memory into long-term memory and the generation of the theta rhythm while maintaining attention.

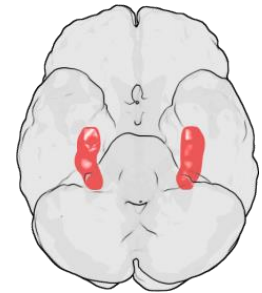


Figure 1 - Anatomy of the location of the hippocampus

Functions of the hippocampus:

- 1) Presumably, the hippocampus plays an important role in the formation of short-term memory by isolating and retaining important information in a stream of external stimuli, and also translates it into a long-term one. The complete mechanism of the hippocampus is not yet clear, but some scientists believe that the hippocampus holds information in wakefulness, and during sleep translates it into the bark of the big hemispheres.
- 2) Participates in the formation of spatial memory;
- 3) It is a filter for memory, that is, it participates in the processes of memorizing and forgetting information.

When the hippocampus malfunctions, Korsakov syndrome occurs, a disease that results in impairment of memory of current events while maintaining traces of long-term memory. When reducing the volume of the hippocampus, Alzheimer's disease should be suspected. [11]

It is because of the special functions of the hippocampus that its area was chosen to conduct research and collect data on the volume of metabolites in the performance of this final qualifying work.

2 Materials and methods

2.1 FreeSurfer

For the processing of MRI data using the program FreeSurfer. FreeSurfer is a software package designed to analyze and visualize structural and functional neuroimaging data from cross-sectional or longitudinal studies. It was developed by the Computational Neuroimaging Laboratory at the Center for Biomedical Imaging. FreeSurfer is an MRI structural analysis software selected for the Human Connector project.

Thanks to this program, it became possible to conduct T1-T2 segmentation - weighted MRI images. FreeSurfer provides a complete processing flow for MRI structural data, including:

- 1) Isolation of the skull, B1 - offset field correction, and segmentation of gray and white matter;
- 2) Reconstruction of cortical surface models;
- 3) Marking of areas on the surface of the cortex, as well as subcortical structures of the brain. Figure 2 shows a picture of the selection of the hippocampus using this program;
- 4) Nonlinear registration of the cortical surface of an individual with stereotactic atlas;
- 5) Statistical analysis of group differences in morphometry; [12]

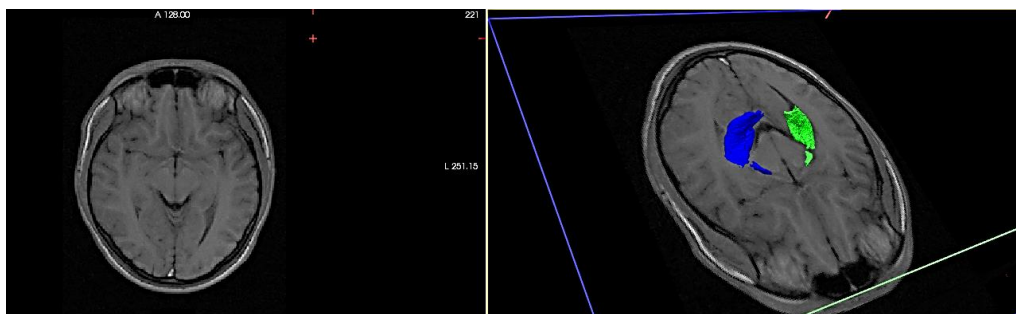


Figure 2 - Selection of a separate area of the hippocampus

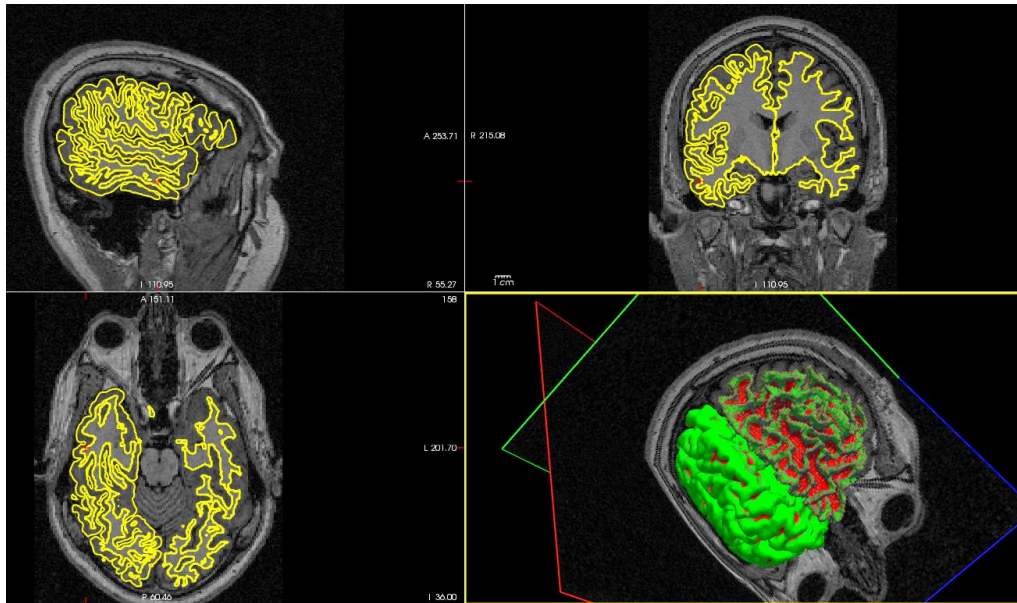


Figure 3 - MRI image processed with FreeSurfer

2.1.1 Algorithm of the recon-all script

Recon-all is a batch program containing more than 30 steps. One treatment takes about 30 hours. The full code of the algorithm for the script recon-all is presented in Appendix 1.

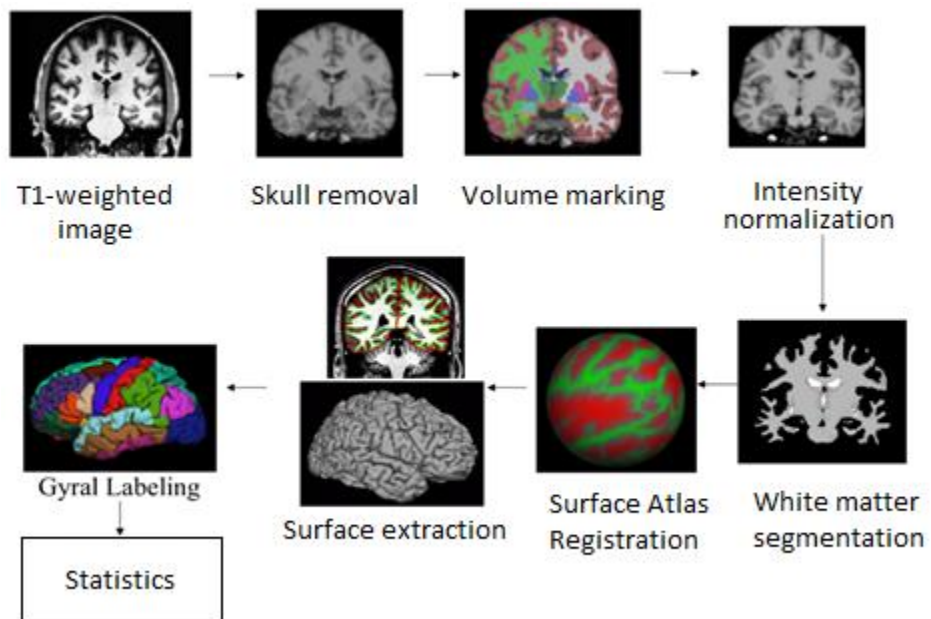


Figure 4 - Processing Flow Diagram

Stages of automatic image segmentation Free surfer:

I. The stage of registration of incoming data:

- 1) 1) Correction of data format compliance, in case of non-conformity, conversion is necessary;
- 2) 2) Talairach transformation, which is necessary to transfer all coordinates;
- 3) Normalization of image intensity (Fig. 5).

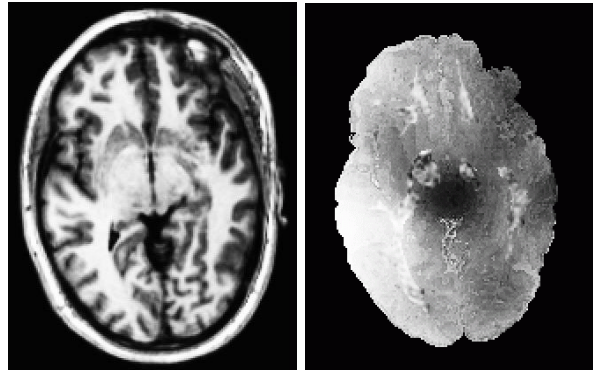


Figure 5 - Normalization of intensity

- II. Removal of the skull (Fig. 6).
- III. Removes all extracerebral structures: skull, eyes, neck, substances.

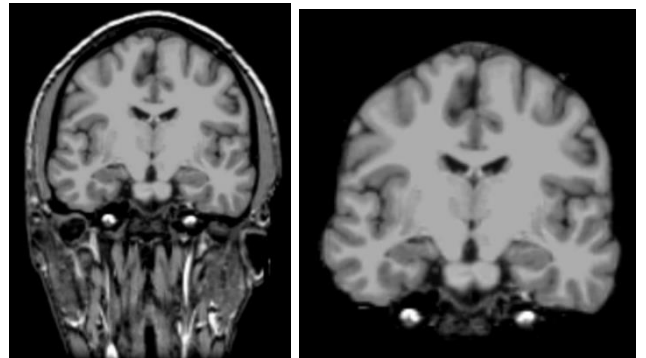


Figure 6 - Removal of the skull

IV. Automatic labeling of volume (Fig. 7). Used to fill the subcortical structures and to create a subcortical mass. Normalization of the intensity of the resulting image.

V. Segmentation stage.

1. White matter segmentation (Fig. 8). Separates white matter from everything else.

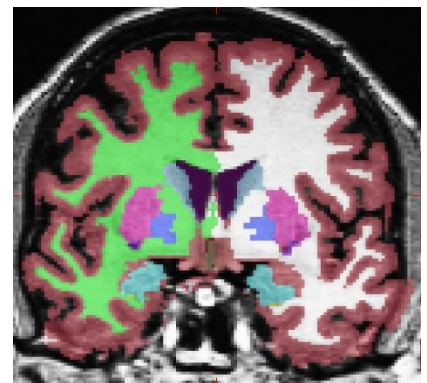


Figure 7 - Automatic labeling of volume

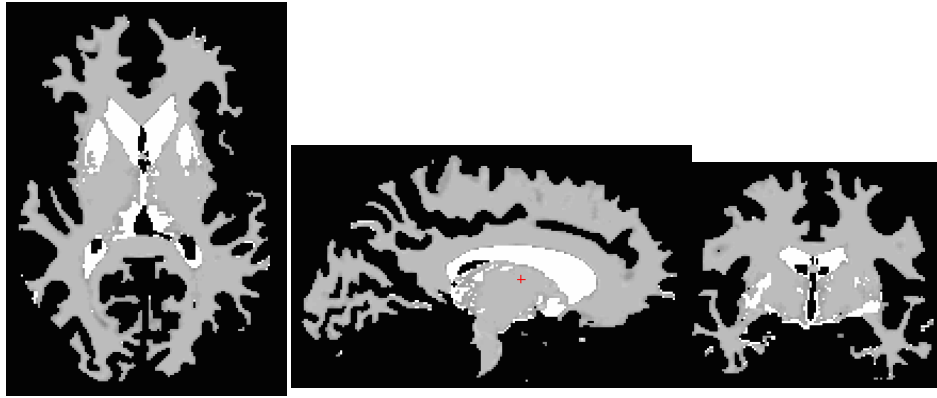


Figure 8 - White matter segmentation

2. Filling and cutting out (Fig. 9, Subcortical mass).

Fills any holes, removes the brain stem, divides it into hemispheres.

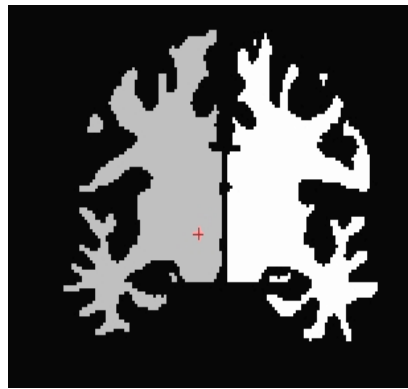


Figure 9 - Hemispheres

3. Surface extraction (Fig. 10). Divided hemispheres correlate with segmented white matter. The image is rough and jagged.

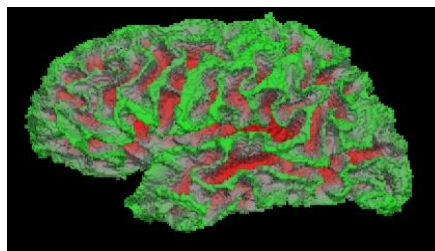


Figure 10 - Surface Selection

4. The surface of the white matter (Fig. 11). The original surface shifts, following the intensity gradient according to the T1 weighted image. Then smoothing the resulting boundary.

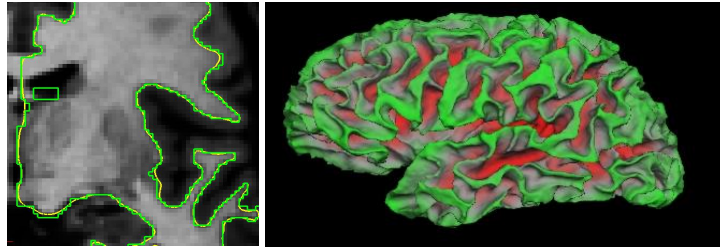


Figure 11 - Smoothing the surface of the white matter

5. The surface of the pia mater (Fig. 12).

The surface of the pia mater "grows" from the surface of the white matter. Errors are possible that can be fixed by specifying the control points of the white matter boundaries.

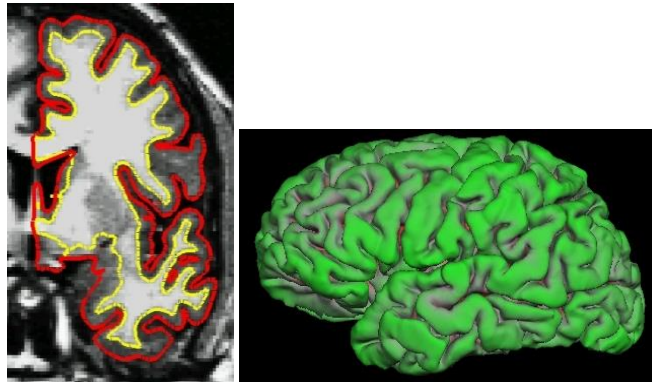


Figure 12 - The surface of the pia mater

6. Cortical thickness (Fig. 13).

Gray matter. The distances between the boundary of the white matter and the boundary of the pia mater are calculated. One value for each vertex.

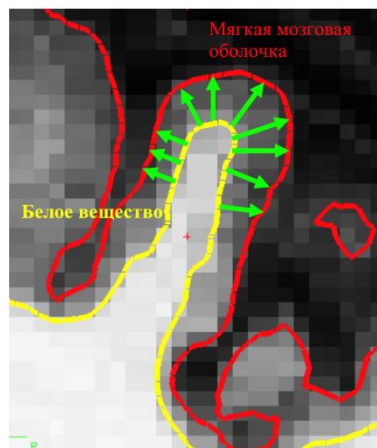


Figure 13 - Cortical Thickness

7. Radial curvature (Fig. 14).

Circles are formed that are tangent to the surface at each vertex. Measure of curvature = $1 / \text{radius}$ of the obtained circle.

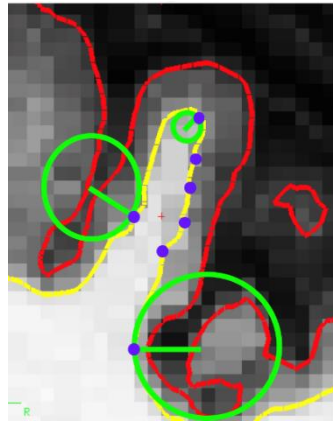


Figure 14 - Radial Curvature

VI. Spherical registration

«Inflating» (Fig. 15).

The inflation mechanism tries to minimize metric distortion so that distances and areas are preserved (that is, surfaces do not stretch). Basically, how to inflate a paper bag, not a balloon.

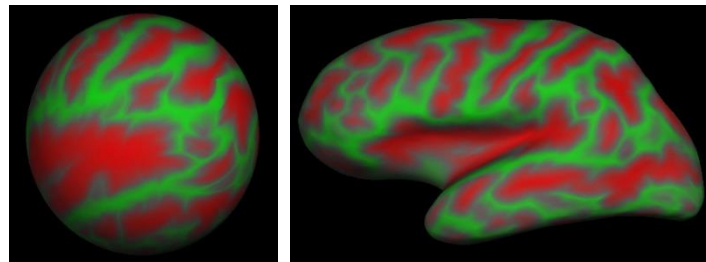


Figure 15 - "Inflating"

VII. A model of the entire surface is created (Fig.16).

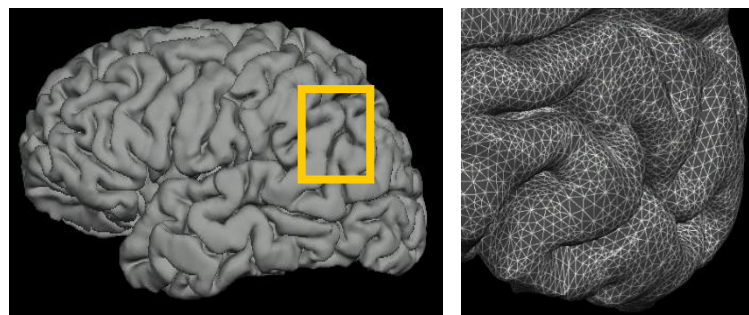


Figure 16 - Model of the entire surface

VIII. The surface is created by covering the filled hemisphere with triangles, thereby creating a grid, as the final element.

- Vertices are intersections of triangles;
- Each vertex has an index;
- Distance between vertices ~ 1 mm.
- A voxel is the intersection of the grid lines (Figure 17).

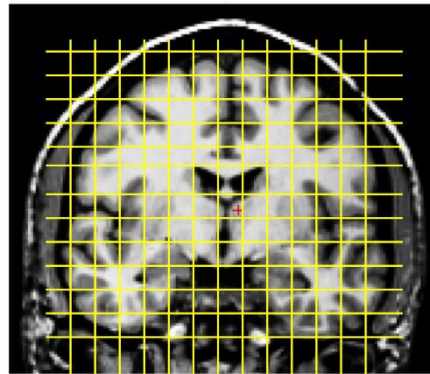


Figure 17 - Voxel Wire

IX. Division of the cerebral cortex.

1. Spherical atlas based on manual marking (Fig. 18).
2. Exact adjustment to the obtained surface model (Fig. 19).
3. Conformity with an individual anatomical structure (Figure 20). [13]

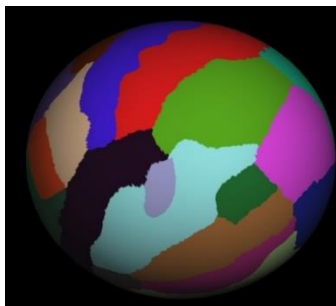


Figure 18 - Manual marking

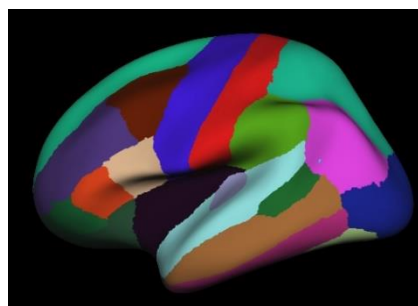


Figure 19 - Fine Tuning

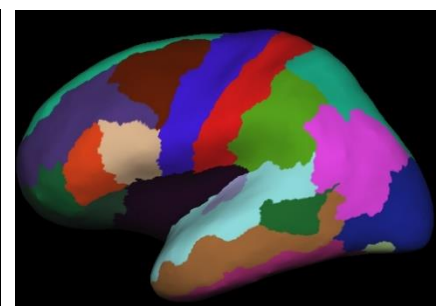


Figure 20 - Individual tuning

2.2 Methods of grouping data in assessing the results of multi-index spectroscopic studies of the brain

Magnetic resonance spectroscopy, as an additional technique of magnetic resonance imaging, in recent years has become increasingly popular and informative in clinical practice. In connection with the improvement of new models of magnetic resonance tomographs, the capabilities of the MRS method are increasing, in particular, in multi-voxel spectroscopy.

In multi-voxel spectroscopy, not only the correct interpretation of the data is important, but also their rational grouping for accurate estimates of various metabolic deviations or regional differences in metabolism.

There are several recommendations for grouping data obtained from a multi-voxel spectroscopic study. Grouping methods are considered on the example of single-slice multi-voxel spectroscopy of the brain.

Based on the collection of information, the method is divided into single-voxel, that is, one selected tissue volume - voxel, and multi-voxel spectroscopy, when the selected volume is divided into equal volumetric units - voxels. It should be noted that for multi-voxel spectroscopy there are a number of significant limitations: with similar parameters, namely the same volume-selection method (Tr), the signal-to-noise ratio is significantly lower than with single-voxel spectroscopy, the acquisition time increases in proportion to the scan field. In addition, the minimum Te is usually limited to 35ms, and for turbo sequences of the order of 100ms and even more. On the other hand, using ^1H -single-voxel spectroscopy, one can obtain data on relative concentrations of 3 or more metabolites in the entire specified volume, whereas the use of multi-voxel allows you to multiply the amount of data obtained, because they are collected for each unit of the selected volume. In a single-slice multi-voxel spectroscopy sample estimated, there are usually more than 50 voxels. In contrast to a single-voxel, the amount of information increases dramatically, resulting in difficulties in their clinical evaluation. [9]

2.2.1 Principles of grouping data in assessing the results of a multi-voxel spectroscopic study of the brain

In connection with the expansion of complete sets of newly installed MRI tomographs and with the capabilities of the method of magnetic resonance spectroscopy, in recent years, interest has increased in the use of proton MRS in clinical practice. Multi-voxel spectroscopy is becoming increasingly popular, in which, besides interpreting the data, rational grouping of these data is also important for an accurate assessment of deviations in metabolism and regional differences in metabolism, if necessary. The grouping options given in the description below were considered on the example of single-slice multi-voxel spectroscopy of the brain.

At first glance, the assessment of each voxel separately, despite the huge amount of time spent on the analysis, seems to be the most accurate, but this is not quite so. The areas of the metabolites to be determined (for example, water) are shifted relative to the main metabolite (specified in the system parameters). The degree of displacement is higher, the farther away the non-basic metabolite is in relation to the main one on the ppm scale (the unified frequency scale for magnetic resonance spectroscopy on a 1.5 T tomograph). Thus, evaluating myoinositol (mI) in relation to N-acetyl-aspartate (NAA), we correlate metabolites from partially different anatomical volumes. This circumstance may be critical in the case of an assessment of minor structural changes.

At the same time, this approach is most successful in assessing small in volume (and sometimes complex anatomically) structures, such as the head and body of the hippocampus (Fig. 23), or repeated minor structural changes (for example, demyelination foci). The advantages of this method include: the ability to evaluate complex and small structures. Disadvantages: time consuming (with a large number of voxels evaluated); laborious; Automation is possible, but depends heavily on the task. [9]

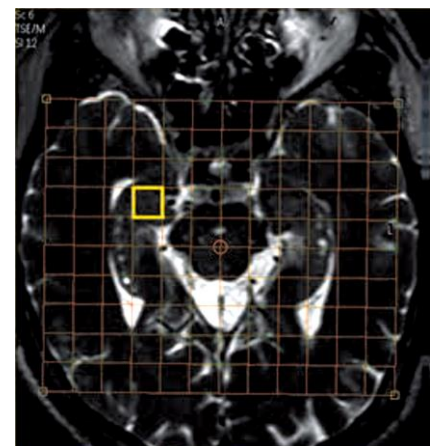


Figure 21 - Selected volume corresponding to the head of the right hippocampus

2.2.2 Voxel grouping options

2.2.2.1 Linear grouping

The ability to form static data groups for a comfortable subsequent comparison between the obtained groups gives the principle of linear grouping.

When laying a grid of research areas and interest for conducting multi-voxel spectroscopic research, it is important to take into account the symmetry of the voxel groups that are planned for evaluation. The image shows that the white matter fits into the planned voxel groups, and, separately, the gray matter of the medial cortex of the frontal and parietal lobes. This allows the comparison of averaged data from the entire range, while tying the data to brain structures, both between themselves (contralateral regions) and similar groups between subjects. This principle of grouping data allows the separation of values from tissues with different metabolism (in this example, the gray matter of the medial cortex and the white matter of the brain), however, still does not allow for regional differences in metabolism (for example, the ratio of NAA / Cr for white matter of frontal and the parietal lobes of the brain varies).

Advantages: differentiation of metabolic parameters of linearly located structures and tissues. Disadvantages: lack of consideration of regional heterogeneity. Scope: comparison of asymmetric changes in the gray matter of the medial cortex, the white matter of the big hemispheres. [9]

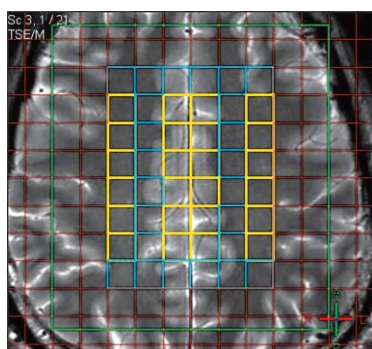


Figure 22 - Linear grouping with comparison of gray and white matter of the brain hemisphere.

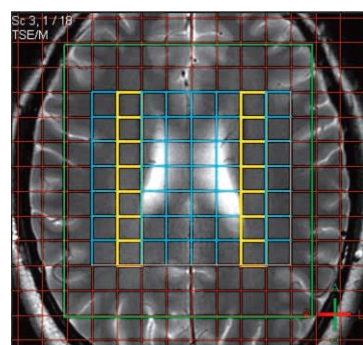


Figure 23 - Linear grouping, data of the paraventricular white matter are evaluated.

2.2.2.2 Regional approach

Grouping voxels in a certain way and dividing into several areas of interest is possible only with sufficient size of the study area. This step not only simplifies the assessment of results by reducing the amount of data due to averaging the values within the area, but also allows you to compare the areas of interest among themselves and in the ipsilateral and contralateral areas of the brain.

In this example, where the metabolism of structurally unchanged brain tissues of patients with multiple sclerosis was investigated, the entire study area was divided into 9 areas of interest, of which 6 included white matter (voxels that included the convexital cortex were excluded from the calculation), 3 areas in each hemisphere, and 3 regions included the medial cortex of the supraventricular spaces of the large hemispheres (Fig. 24, left). Regional heterogeneity of metabolic indices was shown in both healthy and patients with multiple sclerosis. Differences were found in the main ratios of metabolites not only between the white matter of the frontal and parietal lobes, but also between the middle and posterior third of the frontal lobe of one brain hemisphere. As a result, a comparative assessment of changes in metabolism ratios was carried out separately for each region of interest.

The regional grouping method allows you to compare the results within a single study in any direction, which allows you to evaluate changes taking into account differences in the metabolism of different brain regions, while averaging the values within the zones of interest.

So, we highlight the disadvantages: the need for manual sampling of voxels within each zone; in comparison with other principles of grouping, a large amount of data - advantages: the ability to assess metabolic changes separately for each zone of interest.

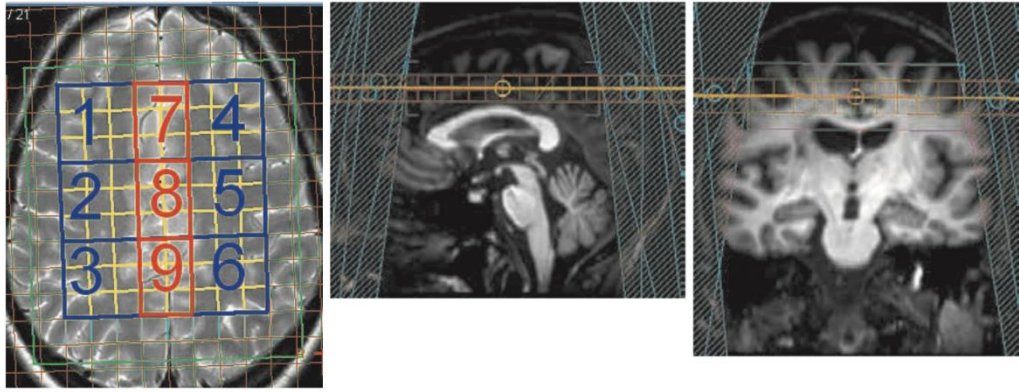


Figure 24 - Division of the study area into 9 zones of interest.

Below is a comparative table of the principles of grouping data when evaluating the results of a multi-voxel 1H-MRS-brain study. [9]

Table 1 - Comparison of the principles of grouping data when evaluating the results of a multi-voxel 1H-MRS study

Grouping method	Benefits	Disadvantages	Application options
Voxel estimate	Ability to evaluate complex and small structures	Time consuming, laborious	Hippocampus, subcortical nuclei, multiple focal changes
Data averaging	The speed of processing, the possibility of excluding the volume of the region of interest, a small amount of data for subsequent interpretation	Low sensitivity to localized changes, lack of assessment of tissue and regional heterogeneity	Significant cerebral changes, quality control of therapy
Linear grouping	Differentiation of metabolic parameters of linearly located structures and tissues	Lack of regional heterogeneity	Comparison of asymmetric changes in the medial cortex, white matter
Regional approach	Ability to assess metabolic changes separately for each zone of interest	A large amount of data, the need for manual sampling of voxels	Evaluation of regional brain substance changes

2.3 Automatic image segmentation

MRI is one of the most modern methods of neuroimaging, which allows to obtain three-dimensional images with high inter-tissue contrast. To improve the efficiency of diagnosis and the most effective use of the MRI method, the need arises for a more complete extraction of information and for carrying out complex computerized quantitative measurements of various brain structures. The main method for quantitative assessment of brain structures is segmentation - the classification of tissues, in particular gray matter, white matter and cerebrospinal fluid, with the purpose of their quantitative analysis.

The task of automatic segmentation of brain MRI images is complicated by such factors as uneven illumination of images, interpolation artifacts when constructing a three-dimensional image from a sequence of flat sections, the same intensity values for different anatomical structures. Therefore, the task becomes practically intractable in the absence of a priori anatomical information. Such information can be presented in the form of a set of rules formulated by experts. But the most effective approach was to compare with atlas.

The atlas, in this case, is a set of two three-dimensional images of the brain, one of which is an MRI image (as a template), and the second stores in each voxel the value of the label of the corresponding anatomical structure (as markup). If there is an atlas, the segmentation task is reduced to the task of comparing the MRI image from the atlas and the input image that needs to be tagged. A transformation is applied to the image from the atlas, which makes it as similar to the input image as possible.

Using more than one atlas improves the accuracy of automatic anatomical markings. In this case, several atlases are recorded with the input image, and their markup is merged to obtain the input image markup. Most of the existing algorithms use a weighted voting scheme, where each atlas contributes to the decision to assign each point an input image of a particular label in proportion to its weight. The weight of the atlas is determined by the similarity with the input image.

The most successful of these algorithms in practice were those that calculate

weights not for the entire image, but at each point separately, depending on the local similarity of the atlas and the input image. A common problem with this group of algorithms is that they do not take into account the fact that errors introduced by different atlases may correlate. If there are several atlases participating in the voting, offering an incorrect mark at the same point, the accuracy of the algorithm decreases.

Until now, most methods for quantitative analysis of the volumetric characteristics of MRI images are manual or semi-automatic. These methods are time consuming, depend on the subjective factor and are characterized by low reproducibility. In this regard, the introduction into clinical practice of methods based on automatic segmentation is extremely important, the algorithm of which must meet the following requirements: accuracy, the ability to measure the volumes of the maximum number of brain structures, reproducibility. [15]

Currently, various software versions for automatic segmentation of brain structures have been developed and continue to be improved, which differ in classification, error handling, and results control algorithms. With a wide variety of software, the results obtained are not always accurate and often contradictory. For software products, the focus is on narrow tasks, the complexity of setting up for use in everyday practice and the lack of documentation. In this regard, for a full morphometric analysis of brain structures, it is necessary to use a consistent series of specialized applications that are selected and configured to perform certain tasks.

Using the results of morphometry obtained in this way for further, including dynamic, analysis requires the formation of a general report that would include all the data obtained as a result of processing after the process. [16]

2.4 Neuropsychological tests

2.4.1 Montreal cognitive assessment scale

The Montreal Cognitive Function Assessment Scale (MoCA) was established in 1996 by Ziad Nasreddine in the city of Montreal, in the province of Canada Quebec. This test is designed to assess moderate cognitive impairment, and, subsequently, adopted as a standard, in particular used in the study of Alzheimer's disease.

She assesses various cognitive spheres: attention and concentration, executive functions, memory, language, visual and constructive skills, abstract thinking, counting and orientation. The time for the MoCA is approximately 10 minutes. The maximum possible number of points - 30; 26 points or more is considered normal.

The MoCA test is conducted in approximately 10 minutes, as a result of which you can score a maximum of 30 points, 26 points or more is considered the norm. The test itself is available to doctors in any form and in 55 different languages. There are also alternative, time-consuming forms designed for research for more detailed parameters. In addition, there is also a basic form for testing illiterate or lower educated people.

MoCA assesses several cognitive areas: attention and concentration, executive functions, memory, language, visual and constructive skills, abstract thinking, counting and orientation. [17]

3. Results

3.1. Neuropsychological Testing

Patients with diabetes mellitus type 1 and type 2 and the control group (healthy) underwent neuropsychological MoCA testing with neurologists. Test results: among patients with the first type of diabetes, only one patient turned out to be higher than normal, and the rest - lower (normally 26 points and higher). The test results in patients with type 2 diabetes were several times worse: more than half of the patients received a score below 26. In healthy patients, the test result was normal.

3.2 Processing of data obtained by the method of MRS

The linear grouping method selected the metabolites Cho (choline), Cr (creatine), Cr2 (phosphocreatine), NAA (N-acetyl-aspartate), localized in the gray matter of the medial cortex, in the white matter on the left and right in lateral areas, as shown in figure 25.

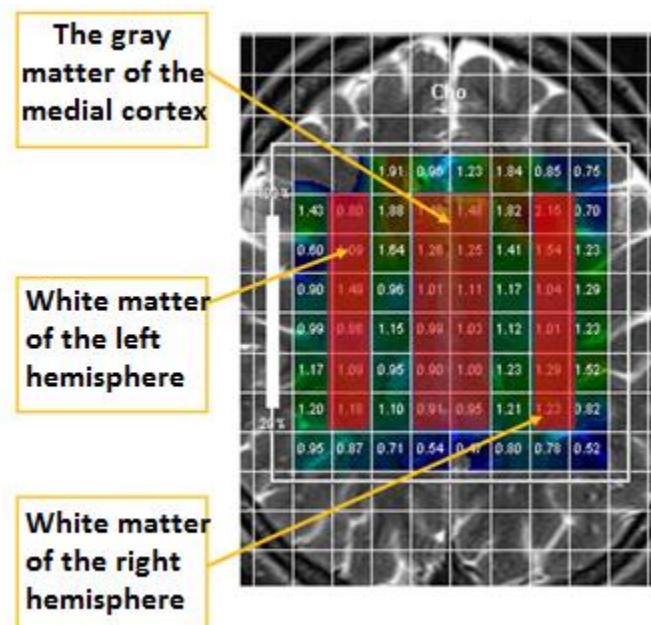


Figure 25 - Linear grouping method

Using a regional approach, data were selected for Cho (choline), Cr (creatine), Cr2 (phosphocreatine), NAA (N-acetyl-aspartate) metabolites located in the left and right areas of the hippocampus, as shown in Figure 26.

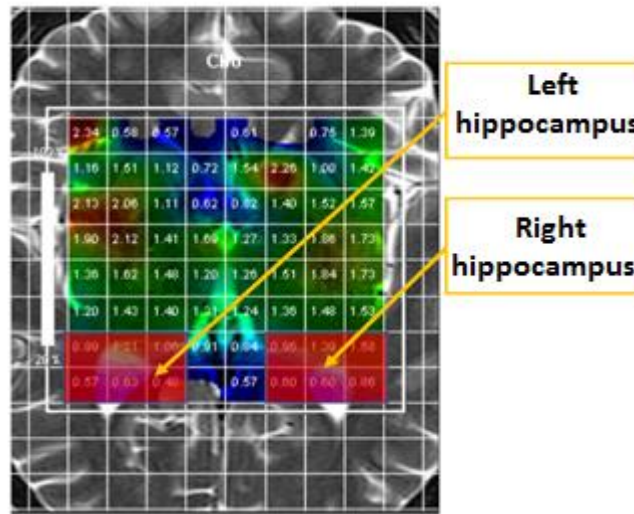


Figure 26 - Regional approach

After averaging the concentration data in each region for each metabolite (Cho, NAA, Cr, Cr2), 20 indicators were obtained, the names of which are given below:

Table 2 - Designations of averaged values of metabolites by groups

Metabolite	Hippocampus area on the left	Hippocampal area on the right	The white matter area on the left	The gray matter of the medial cortex	White matter area on the right
Cho	ChoHypLeft	ChoHypRight	ChoWhiteLeft	ChoGrayCenter	ChoWhiteRight
Cr	CrHypLeft	CrHypRight	CrWhiteLeft	CrGrayCenter	CrWhiteRight
Cr2	CrPHypLeft	CrPHypRight	CrPWhiteLeft	CrPGrayCenter	CrPWhiteRight
NAA	NAAHypLeft	NAAHypRight	NAAWhiteLeft	NAAGrayCenter	NAAWhiteRight

Statistical data processing was performed in the SPSS Statistics program. When comparing patients with type 1 diabetes (36 people), type 2 (24 people), and the control group (20 people) for the metabolites Cho (choline), Cr (creatine), Cr2 (phosphocreatine), NAA (N-acetyl-aspartate), grouped by the method of linear grouping and regional approach, according to table 3 it can be seen that there were no

statistically significant differences, based on non-parametric criteria for two independent samples of the Mann-Whitney U-test (for all indicators $p > 0.05$).

Table 3 - “Chemical Shift” ppm of metabolites grouped regionally in the hippocampus and linearly on the cortex (Me; Q₁:Q₃)

Indicator	Patients with diabetes mellitus type 1 (n=36)	Patients with diabetes mellitus type 2 (n=24)	Control group (n=20)	Comparison p
ChoHypLeft	0,96(0,84-1,01)	0,98(0,83-1)	0,94(0,93-0,98)	0,686
ChoHypRight	1,03(0,97-1,13)	1(0,94-1,15)	1,12(1,03-1,26)	0,124
ChoWhiteLeft	1,09(1,01-1,31)	1,1(1,11-1,22)	1,21(1,09-1,41)	0,647
ChoGrayCenter	1(0,98-1,22)	1,2(0,96-1,12)	1,03(0,91-1,15)	0,808
ChoWhiteRight	1,1(1-1,34)	1,15(1,2-1,3)	1,22(1,02-1,44)	0,467
CrHypLeft	0,91(0,78-0,99)	0,87(0,79-0,88)	0,88(0,81-1,06)	0,936
CrHypRight	0,87(0,81-0,94)	0,9(0,82-0,96)	0,92(0,87-1,02)	0,247
CrWhiteLeft	1,3(1,12-1,62)	1,32(1,21-1,42)	1,37(1,22-1,52)	0,829
CrGrayCenter	1,06(1,02-1,29)	1 (1,05-1,24)	1,24(1,23-1,29)	0,269
CrWhiteRight	1,24(1,03-1,48)	1,3(1,05-1,44)	1,39(1,34-1,44)	0,187
CrPHypLeft	1,34(1,17-1,64)	1,28(1,24-1,44)	1,27(0,94-1,47)	0,247
CrPHypRight	2,05(1,52-2,25)	2 (1,50-2,24)	1,36(1,26-1,64)	0,056
CrPWhiteLeft	1,35(0,99-1,82)	1,3 (0,95-1,8)	1,34(1,29-1,39)	0,808
CrPGrayCenter	1,58(1,2-1,68)	1,55(1,12-1,58)	1,39(1-1,69)	0,936
CrPWhiteRight	1,35(1,21-1,74)	1,3(1,22-1,73)	1,69(1,63-1,8)	0,187
NAAHypLeft	1,66(1,55-1,88)	1,62(1,53-1,86)	1,58(1,42-1,72)	0,467
NAAHypRight	1,72(1,55-1,98)	1,74(1,57-1,96)	1,76(1,67-1,97)	0,808
NAAWhiteLeft	2,38(2,31-2,68)	2,36(2,29-2,7)	2,51(2,32-2,77)	0,726
NAAGrayCenter	2(1,83-2,28)	2,2(1,85-2,3)	1,89(1,84-1,93)	0,293
NAAWhiteRight	2,41(2,23-2,7)	2,39(2,21-2,68)	2,5(2,23-2,7)	0,647

Note: p - significance of differences with the values of the control group.

In the same areas (medial cortex, white matter of both hemispheres and hippocampus), as indicated above, the voxel assessment method was also considered. Figure 28 below shows the voxel numbering. According to the numbering, each metabolite in each voxel is indicated by an index: Cho1- Cho36, Cr1- Cr 36, CrP1- CrP36, NAA1- NAA36.

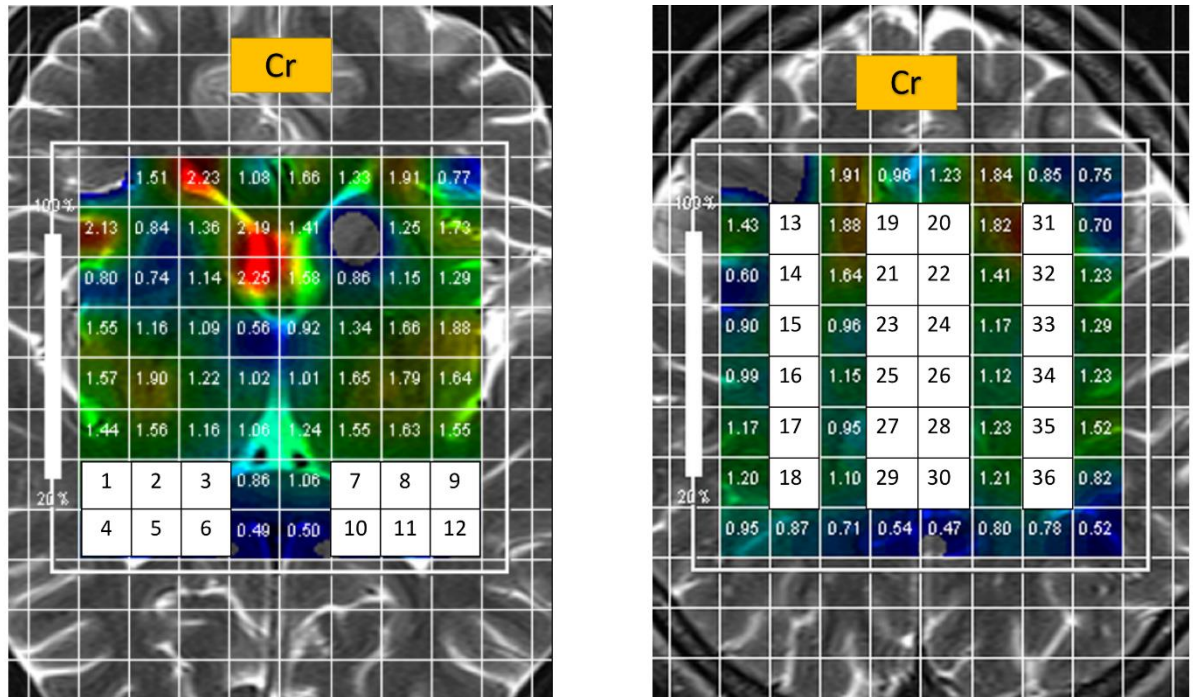


Figure 27 - Voxel numbering. On the left - the area of the hippocampus, on the right - the cerebral

Performed statistical data processing in the program SPSS Statistics:

- 1) 1) When comparing Cho metabolite (choline) of patients with type 1 diabetes (36 people) and the control group (20 people), identified with voxel scores, table 3 shows that a statistically significant difference was found: Cho12 in patients with 0.82 (0.75–0.84) is less than in healthy 0.87 (0.81–2.02), based on nonparametric test for two independent samples of the Mann – Whitney U test ($p < 0.05$). No statistically significant differences were found for the remaining voxels ($p > 0.05$).

Table 4 - “Chemical Shift” ppm of choline in the isolated 36 voxels (Me; Q1:Q3)

Indicator	Patients with diabetes mellitus type 1 (n=36)	Patients with diabetes mellitus type 2 (n=24)	Control group (n=20)	P
Cho1	1,26(1,07-1,4)	1,24(1,06-1,34)	1,21(1,15-1,26)	0,589
Cho2	1,3(1,21-1,43)	1,32(1,23-1,46)	1,3(1,25-1,59)	0,706
Cho3	1,11(1,03-1,22)	1,1(1,05-1,24)	1,16(0,98-1,23)	0,936
Cho4	0,73(0,65-0,75)	0,7(0,62-0,73)	0,7(0,66-0,7)	0,499
Cho5	0,74(0,65-0,75)	0,76(0,67-0,77)	0,69(0,66-0,72)	0,705
Cho6	0,65(0,6-0,67)	0,63(0,63-0,7)	0,59(0,57-0,6)	0,082
Cho7	1,12(0,97-1,22)	1,15(1-1,25)	1,19(1,09-1,42)	0,269
Cho8	1,3(1,23-1,39)	1,27(1,2-1,36)	1,47(1,36-1,54)	0,161
Cho9	1,52(1,41-1,58)	1,5(1,39-1,56)	1,47(1,43-1,56)	0,686
Cho10	0,81(0,68-0,81)	0,8 (0,67-0,8)	0,69(0,61-0,74)	0,08
Cho11	0,78(0,68-0,81)	0,8(0,7-0,8)	0,81(0,73-0,87)	0,279
Cho12	0,82(0,75-0,84)	0,84(0,77-0,86)	0,87(0,81-2,02)	0,033
Cho13	1,38(1,11-1,54)	1,35(1,07-1,51)	1,29(1,14-1,39)	0,893
Cho14	1,09(0,77-1,31)	1 (0,76-1,34)	1,29(1,2-1,47)	0,225
Cho15	1,14(0,92-1,38)	1,16(0,9-1,35)	1,28(1,19-1,38)	0,787
Cho16	1,21(0,93-1,33)	1,23(0,9-1,3)	1,17(1,07-1,38)	0,787
Cho17	1,08(0,89-1,29)	1,1(0,91-1,31)	1,18(0,91-1,41)	0,517
Cho18	1,1(1-1,28)	1,12(1,2-1,3)	1,14(0,94-1,3)	0,914
Cho19	1,28(1,17-1,39)	1,26(1,15-1,37)	1,25(1,18-1,35)	0,787
Cho20	1,35(1,26-1,62)	1,33(1,24-1,64)	1,21(0,99-1,39)	0,187
Cho21	1,14(1,03-1,26)	1,17(1,06-1,29)	1,14(1,07-1,18)	0,978
Cho22	1,24(0,98-1,39)	1,22(0,96-1,37)	1,07(0,92-1,3)	0,235
Cho23	1,04(0,86-1,11)	1,05(0,86-1,15)	0,99(0,91-1,07)	0,608
Cho24	0,97(0,87-1,09)	0,95(0,85-1,07)	0,96(0,9-1,12)	0,957
Cho25	0,95(0,85-1,09)	0,97(0,87-1,11)	0,99(0,94-1,08)	0,829
Cho26	0,92(0,88-1,03)	0,93(0,87-1,05)	1,01(0,88-1,11)	0,726
Cho27	0,94(0,9-1,09)	0,96(0,92-1,1)	1(0,96-1,11)	0,553
Cho28	0,94(0,89-1,15)	0,95(0,9-1,17)	1,04(0,9-1,11)	0,767
Cho29	0,9(0,83-1,03)	0,92(0,85-1,05)	0,86(0,65-0,93)	0,609
Cho30	0,95(0,85-1,07)	0,93(0,83-1,04)	0,89(0,73-1,03)	0,608

Continuation of Table 4

Cho31	1,22(1,01-1,75)	1,24(1,01-1,78)	1,43(1,41-1,69)	0,914
Cho32	1,12(0,96-1,25)	1,1(0,94-1,27)	1,31(1,19-1,6)	0,112
Cho33	1,04(0,85-1,22)	1,06(0,87-1,2)	1,16(1,07-1,36)	0,145
Cho34	1,02(0,95-1,12)	1(0,94-1,13)	1,14(0,97-1,27)	0,246
Cho35	1,1(0,94-1,29)	1,12(0,96-1,31)	1,21(1,06-1,39)	0,332
Cho36	1(0,88-1,26)	1,01(0,87-1,27)	1,11(1,03-1,29)	0,517

Note: p - significance of differences with the values of the control group

2) When comparing the metabolite Cr (creatine) of patients with type 1 diabetes (36 people), type 2 (24 people), and the control group (20 people), identified with a voxel assessment, table 4 shows that statistically significant differences were found:

- a) Cr5 in patients 0.74 (0.7-0.75) more than in healthy 0.66 (0.66-0.66);
- b) Cr10 indicator in patients 0.66 (0.66-0.68) more than in healthy 0.56(0.55-0.56);
- c) Cr25 indicator in patients 0.96 (0.88-1.05) is less than in healthy 1.14 (1.06-1.14);
- d) Cr26 in patients 0.97 (0.85-1.16) less than in healthy 1.19 (1.17-1.19);
- e) Cr28 in patients with 1.14 (0.97-1.21) less than in healthy 1.3 (1.21-1.35);
- f) Cr31 in patients 1.34 (1.02-1.48) less than in healthy 1.59 (1.55-1.62);
- g) Cr36 in patients 1.13 (1.02-1.21) less than in healthy 1.35 (1.25-1.39), - based on non-parametric test for two independent samples of the Mann-Whitney U-test ($p < 0.05$).

No statistically significant differences were found for the remaining voxels. ($p > 0,05$).

Table 5 - “Chemical Shift” ppm of creatine in the isolated 36 voxels (Me; Q₁:Q₃)

Indicator	Patients with diabetes mellitus type 1 (n=36)	Patients with diabetes mellitus type 2 (n=24)	Control group (n=20)	P
Cr1	1,12(0,94-1,29)	1,1(0,92-1,27)	1,25(1,14-1,31)	0,403
Cr2	1,15(0,96-1,26)	1,13(0,93-1,23)	1,15(1,01-1,29)	0,957
Cr3	1,02(0,8-1,1)	1,025(0,81-1,12)	0,94(0,89-1,34)	0,893
Cr4	0,78(0,67-0,8)	0,8(0,7-0,83)	0,69(0,69-0,74)	0,233
Cr5	0,74(0,7-0,75)	0,75(0,71-0,76)	0,66(0,66-0,66)	0,011
Cr6	0,64(0,59-0,66)	0,63(0,6-0,63)	0,68(0,56-0,68)	0,645
Cr7	1,04(0,85-1,1)	1,05(0,87-1,12)	0,9(0,73-1,12)	0,893
Cr8	1,06(0,96-1,31)	1,05(0,95-1,3)	1,19(1,09-1,49)	0,153
Cr9	1,12(0,99-1,28)	1,1 (0,97-1,26)	1,27(1,26-1,35)	0,059
Cr10	0,66(0,66-0,68)	0,62(0,62-0,64)	0,56(0,55-0,56)	0,001
Cr11	0,69(0,69-0,75)	0,7 (0,7-0,76)	0,68(0,6-0,71)	0,433
Cr12	0,75(0,71-0,84)	0,76(0,72-0,85)	0,77(0,7-0,78)	0,482
Cr13	1,61(1,39-1,87)	1,6 (1,4-1,9)	1,82(1,41-2,05)	0,467
Cr14	1,46(1,17-1,67)	1,43(1,2-1,7)	1,28(1,17-1,35)	0,257
Cr15	1,23(1,06-1,59)	1,2 (1,09-1,6)	1,24(1,11-1,26)	0,872
Cr16	1,12(0,96-1,28)	1,1(0,98-1,26)	1,26(1,08-1,39)	0,45
Cr17	1,24(1,16-1,47)	1,22(1,14-1,45)	1,39(1,24-1,57)	0,305
Cr18	1,23(1,02-1,33)	1,2(1 -1,3)	1,23(1,23-1,32)	0,553
Cr19	1,42(1,14-1,64)	1,4 (1,12-1,62)	1,4(1,27-1,51)	0,766
Cr20	1,27(1,19-1,44)	1,3(1,22-1,46)	1,36(1,3-1,54)	0,627
Cr21	1,21(1,08-1,45)	1,2 (1,09-1,46)	1,22(1,2-1,27)	0,914
Cr22	1,14(1,03-1,25)	1,12(1,01-1,23)	1,26(1,23-1,36)	0,195
Cr23	0,97(0,88-1,14)	0,95(0,86-1,12)	1,14(1,02-1,24)	0,257
Cr24	0,91(0,86-1,12)	0,9 (0,85-1,11)	1,09(1,09-1,2)	0,16
Cr25	0,96(0,88-1,05)	0,95(0,89-1,06)	1,14(1,06-1,14)	0,018
Cr26	0,97(0,85-1,16)	0,95(0,87-1,18)	1,19(1,17-1,19)	0,049
Cr27	1,1(0,94-1,25)	1,12(0,96-1,23)	1,24(1,12-1,36)	0,153
Cr28	1,14(0,97-1,21)	1,11(0,94-1,18)	1,3(1,21-1,35)	0,035
Cr29	1,13(0,98-1,29)	1,1 (0,95-1,26)	1,21(1,07-1,22)	0,419
Cr30	1,11(1,02-1,19)	1,1(1-1,2)	1,23(1,1-1,34)	0,257
Cr31	1,34(1,02-1,48)	1,31(1,01-1,45)	1,59(1,55-1,62)	0,007
Cr32	1,41(0,99-2,06)	1,4(1-2,02)	1,43(1,36-1,54)	0,726
Cr33	1,11(1,03-1,33)	1,1 (1 -1,31)	1,31(1,15-1,4)	0,269
Cr34	1,09(0,97-1,42)	1,1(0,98-1,4)	1,27(1,14-1,41)	0,466
Cr35	1,15(0,94-1,47)	1,17(0,96-1,45)	1,34(1,32-1,42)	0,225
Cr36	1,13(1,02-1,21)	1,1(1-1,2)	1,35(1,25-1,39)	0,02

Note: p - significance of differences with the values of the control group: p > 0.05 - no differences are observed, p < 0.05 - differences are observed.

3) When comparing the CrP metabolite (phosphocreatine) in patients with type 1 diabetes mellitus (36 people), type 2 (24 people), and the control group (20 people) identified with a voxel score, table 5 shows that statistically significant differences were found:

- a) a) CrP3 in patients 1.18 (0.99-1.18) more than in healthy 0.61 (0.61-0.61);
- b) CrP4 in patients with 0.84 (0.84-0.84) is lower than in healthy 1.26 (1.26-1.26);
- c) CrP5 in patients with 1.94 (1.94-1.94) is higher than in healthy 1.2 (1.2-1.2);
- d) CrP6 in patients with 1.81 (1.72-1.81) more than in healthy 1.14 (1.14-1.14);
- e) CrP7 in patients with 2.03 (2.03-2.12) is higher than in healthy 1.75 (1.75-1.75);
- f) CrP10 in patients 1.89 (1.89-1.89) is higher than in healthy 1.36 (1.26-1.64);
- g) CrP12 in patients 2.48 (2.48-2.48) is higher than in healthy 1.25 (1.25-1.25);
- h) CrP15 in patients 1.21 (0.84-1.21) is lower than in healthy 1.92 (1.34-2);
- i) CrP18 in patients 1.31 (0.9-1.43) is higher than in healthy 0.76 (0.76-0.76);
- j) CrP28 in patients with 1.33 (1-1.33) more than in healthy 0.89 (0.89-0.91);
- k) CrP29 in patients 1.18 (1.07-1.18) more than in healthy 0.69 (0.69-0.69);
- l) CrP30 in patients with 1.45 (1.13-1.45) more than in healthy 0.95 (0.65-0.95);
- m) CrP31 in patients 1.46 (1.22-1.67) is less than in healthy 2.49 (2.49-2.49);
- n) CrP32 in patients with 1.42 (1.12-1.42) is less than in healthy 2.18 (1.91-2.18), - based on non-parametric test for two independent samples of the Mann-Whitney U-test ($p < 0.05$).

For the remaining voxels, no statistically significant differences were found ($p > 0.05$).

Table 6 - “Chemical Shift” ppm of phosphocreatine in isolated 35 voxels (Me; Q1:Q3)

Indicator	Patients with diabetes mellitus type 1 (n=36)	Patients with diabetes mellitus type 2 (n=24)	Control group (n=20)	P
CrP1	1,18(1,18-1,25)	1,15(1,15-1,22)	1,51(1,23-1,51)	0,066
CrP2	1,48(1,03-1,48)	1,45(1,01-1,44)	1,51(0,72-2,18)	0,682
CrP3	1,18(0,99-1,18)	1,19(1-1,15)	0,61(0,61-0,61)	0,001
CrP4	0,84(0,84-0,84)	0,81(0,81-0,84)	1,26(1,26-1,26)	<0,001
CrP5	1,94(1,94-1,94)	1,95(1,95-1,94)	1,2(1,2-1,2)	0,006
CrP6	1,81(1,72-1,81)	1,8(1,7-1,8)	1,14(1,14-1,14)	<0,001
CrP7	2,03(2,03-2,12)	2,01(2,01-2,1)	1,75(1,75-1,75)	0,034
CrP8	1,87(1,06-2,25)	1,85(1,05-2,23)	1,66(1,21-2,01)	0,607
CrP9	2,02(1,51-2,4)	2 (1,5-2,42)	1,53(0,96-1,53)	0,15
CrP10	1,89(1,89-1,89)	1,9(1,9-1,9)	1,36(1,26-1,64)	0,043
CrP11	1,98(1,8-1,98)	2(1,82-1,96)	1,36(1,26-1,64)	0,174
CrP12	2,48(2,48-2,48)	2,44(2,45-2,45)	1,25(1,25-1,25)	<0,001
CrP13	1,39(1,3-1,44)	1,4(1,32-1,42)	1,28(1,25-1,28)	0,288
CrP14	1,31(1,31-1,31)	1,3(1,3-1,3)	1,54(1,11-1,54)	0,201
CrP15	1,21(0,84-1,21)	1,2(0,84-1,2)	1,92(1,34-2)	0,027
CrP16	1,04(0,77-1,74)	1,01(0,75-1,71)	1,58(1,58-1,66)	0,499
CrP17	1,54(0,97-2,05)	1,51(0,95-2,056)	0,98(0,98-0,98)	0,065
CrP18	1,31(0,9-1,43)	1,3(0,91-1,43)	0,76(0,76-0,76)	0,007
CrP19	1,18(0,74-1,18)	1,2(0,74-1,17)	1,11(0,86-1,11)	0,329
CrP20	1,62(0,97-1,69)	1,6 (0,95-1,69)	1,55(1,24-1,55)	0,808
CrP21	1,39(1,03-1,39)	1,36(1-1,39)	1,84(1,39-2,53)	0,061
CrP22	1,46(0,87-3,26)	1,45(0,86-3,27)	2,66(1,91-3,58)	0,205
CrP23	2,06(0,87-3,04)	2,01(0,88-3)	1,6(1,23-1,73)	0,646
CrP24	1,74(0,96-2,14)	1,75(0,97-2,17)	2,01(0,87-2,72)	0,957
CrP25	1,37(1,18-1,9)	1,35(1,2-1,91)	1,31(0,9-1,31)	0,465
CrP26	1,45(1,11-1,63)	1,41(1,13-1,6)	1,13(0,83-1,13)	0,202
CrP27	1,3(0,67-1,3)	1,31(0,68-1,33)	0,93(0,71-0,93)	0,313
CrP28	1,33(1-1,33)	1,31(1,2-1,31)	0,89(0,89-0,91)	0,006
CrP29	1,18(1,07-1,18)	1,2(1,09-1,18)	0,69(0,69-0,69)	0,002
CrP30	1,45(1,13-1,45)	1,44(1,1-1,42)	0,95(0,65-0,95)	0,013
CrP31	1,46(1,22-1,67)	1,47(1,2-1,65)	2,49(2,49-2,49)	0,015
CrP32	1,42(1,12-1,42)	1,4(1,1-1,4)	2,18(1,91-2,18)	0,047
CrP33	1,62(0,77-1,73)	1,64(0,79-1,75)	1,4(1,34-1,44)	0,766

Note: p - significance of differences with the values of the control group.

4) When comparing patients with type 1 diabetes (36 people), type 2 (24 people), and the control group (20 people) for the metabolite NAA (N-acetyl-aspartate), selected with a voxel score, table 6 shows that no significant voxel differences were found, based on the non-parametric criterion for two independent samples of the Mann-Whitney U-test (for all indicators $p > 0.05$).

Table 7 - “Chemical Shift” ppm of phosphocreatine in isolated 36 voxels (Me; Q1:Q3)

Indicator	Patients with diabetes mellitus type 1 (n=36)	Patients with diabetes mellitus type 2 (n=24)	Control group (n=20)	P
NAA1	1,99(1,8-2,21)	1,95(1,8-2,2)	1,85(1,61-1,9)	0,178
NAA2	2,04(1,9-2,24)	2,01(1,91-2,2)	2,04(1,74-2,34)	1,000
NAA3	1,84(1,54-2,08)	1,81(1,55-2,07)	1,6(1,5-2,11)	0,850
NAA4	1,48(1,4-1,54)	1,47(1,41-1,55)	1,38(1,3-1,45)	0,169
NAA5	1,43(1,33-1,74)	1,42(1,31-1,75)	1,44(1,28-1,52)	0,647
NAA6	1,38(1,14-1,6)	1,36(1,15-1,61)	1,21(1,04-1,54)	0,403
NAA7	1,87(1,61-2,17)	1,9(1,6-2,15)	1,85(1,77-2,05)	0,978
NAA8	2,28(1,9-2,38)	2,3(1,92-2,38)	2,23(2,12-2,43)	0,647
NAA9	2,24(1,93-2,41)	2,21(1,91-2,4)	2,15(2,09-2,23)	0,957
NAA10	1,3(1,21-1,67)	1,32(1,23-1,65)	1,36(1,15-1,61)	0,872
NAA11	1,46(1,31-1,83)	1,45(1,3-1,85)	1,56(1,4-1,58)	0,483
NAA12	1,51(1,38-1,75)	1,5(1,37-1,75)	1,51(1,47-1,55)	0,978
NAA13	2,25(2,02-2,53)	2,26(2-2,51)	2,27(2,14-2,38)	0,767
NAA14	2,37(2,25-2,57)	2,35(2,26-2,55)	2,56(2,36-2,76)	0,169
NAA15	2,31(2,23-2,8)	2,3(2,21-2,82)	2,59(2,33-2,9)	0,418
NAA16	2,46(2,19-2,98)	2,43(2,2-3)	2,55(2,34-2,77)	0,767
NAA17	2,42(2,27-2,81)	2,41(2,28-2,8)	2,58(2,4-2,85)	0,525
NAA18	2,35(2,24-2,65)	2,31(2,21-2,62)	2,48(2,39-2,72)	0,535
NAA19	1,9(1,82-2,13)	1,92(1,84-2,15)	1,92(1,89-1,98)	0,978
NAA20	2,05(1,9-2,25)	2,03(1,92-2,22)	1,86(1,86-2,03)	0,177
NAA21	2(1,88-2,18)	2,2(1,9-2,2)	1,89(1,78-2,07)	0,281
NAA22	1,99(1,82-2,3)	2(1,85-2,33)	1,88(1,73-2,07)	0,215
NAA23	1,88(1,76-2,17)	1,87(1,75-2,15)	1,8(1,75-1,82)	0,246
NAA24	1,83(1,67-2,21)	1,8(1,64-2,18)	1,82(1,76-1,87)	0,590
NAA25	2(1,66-2,12)	2,1(1,67-2,12)	1,8(1,73-1,87)	0,518
NAA26	1,91(1,64-2,14)	1,9(1,65-2,15)	1,81(1,73-1,83)	0,746
NAA27	1,97(1,79-2,25)	1,99(1,81-2,25)	1,93(1,85-1,94)	0,403
NAA28	2,06(1,9-2,36)	2,03(2-2,36)	2(1,92-2,02)	0,434
NAA29	1,97(1,9-2,27)	2(2-2,3)	1,9(1,88-2,04)	0,225

Continuation of Table 7

NAA30	2,18(2-2,27)	2,2(2-2,27)	2,05(1,97-2,07)	0,331
NAA31	2,29(2,04-2,49)	2,3(2,05-2,49)	2,24(1,97-2,39)	0,726
NAA32	2,39(2,2-2,8)	2,4(2,2-2,7)	2,54(2,31-2,65)	0,450
NAA33	2,52(2,18-2,74)	2,5 (2,18-2,75)	2,46(2,31-2,68)	0,936
NAA34	2,5(2,07-2,79)	2,52(2,05-2,77)	2,51(2,27-2,78)	0,590
NAA35	2,43(2,19-2,77)	2,41(2,2-2,75)	2,66(2,56-2,81)	0,257
NAA36	2,52(2,27-2,6)	2,5 (2,29-2,61)	2,58(2,46-2,79)	0,215
NAA21	2(1,88-2,18)	2,1(1,9-2,18)	1,89(1,78-2,07)	0,281
NAA22	1,99(1,82-2,3)	2(1,82-2,31)	1,88(1,73-2,07)	0,215
NAA23	1,88(1,76-2,17)	1,9(1,76-2,2)	1,8(1,75-1,82)	0,246
NAA24	1,83(1,67-2,21)	1,8 (1,64-2,2)	1,82(1,76-1,87)	0,590
NAA25	2(1,66-2,12)	2,1(1,65-2,12)	1,8(1,73-1,87)	0,518
NAA26	1,91(1,64-2,14)	1,9 (1,65-2,15)	1,81(1,73-1,83)	0,746
NAA27	1,97(1,79-2,25)	1,96(1,8-2,25)	1,93(1,85-1,94)	0,403
NAA28	2,06(1,9-2,36)	2,08(2-2,36)	2(1,92-2,02)	0,434
NAA29	1,97(1,9-2,27)	1,99(2-2,27)	1,9(1,88-2,04)	0,225
NAA30	2,18(2-2,27)	2,2(2,1-2,27)	2,05(1,97-2,07)	0,331
NAA31	2,29(2,04-2,49)	2,3(2,05-2,5)	2,24(1,97-2,39)	0,726
NAA32	2,39(2,2-2,8)	2,4(2,2-2,8)	2,54(2,31-2,65)	0,450
NAA33	2,52(2,18-2,74)	2,5(2,2-2,75)	2,46(2,31-2,68)	0,936
NAA34	2,5(2,07-2,79)	2,51(2,1-2,79)	2,51(2,27-2,78)	0,590
NAA35	2,43(2,19-2,77)	2,45(2,2-2,77)	2,66(2,56-2,81)	0,257
NAA36	2,52(2,27-2,6)	2,5(2,3-2,6)	2,58(2,46-2,79)	0,215

Note: p - significance of differences with the values of the control group

For clarity, the obtained results obtained by the voxel assessment method, in Figs 28, 29, 30, highlighted in red are the voxels of Cho (choline), Cr (creatine), Cr2 (phosphocreatine) metabolites, in which statistically significant differences were found based on the non-parametric test for two independent samples of the Mann-Whitney U test ($p < 0.05$).

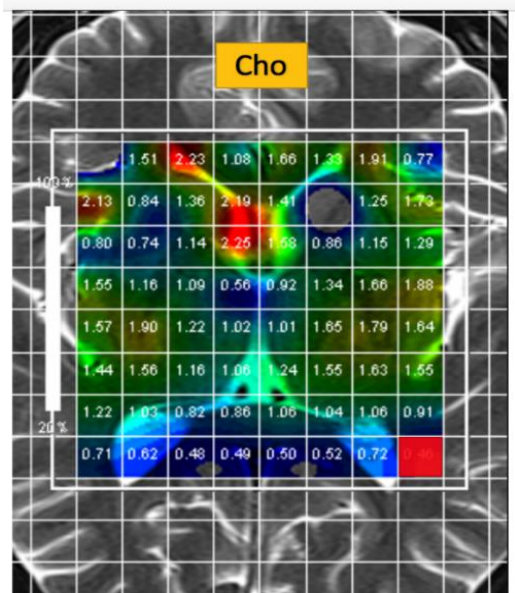


Figure 28 - Choline. Cho12 (voxel marked in red)

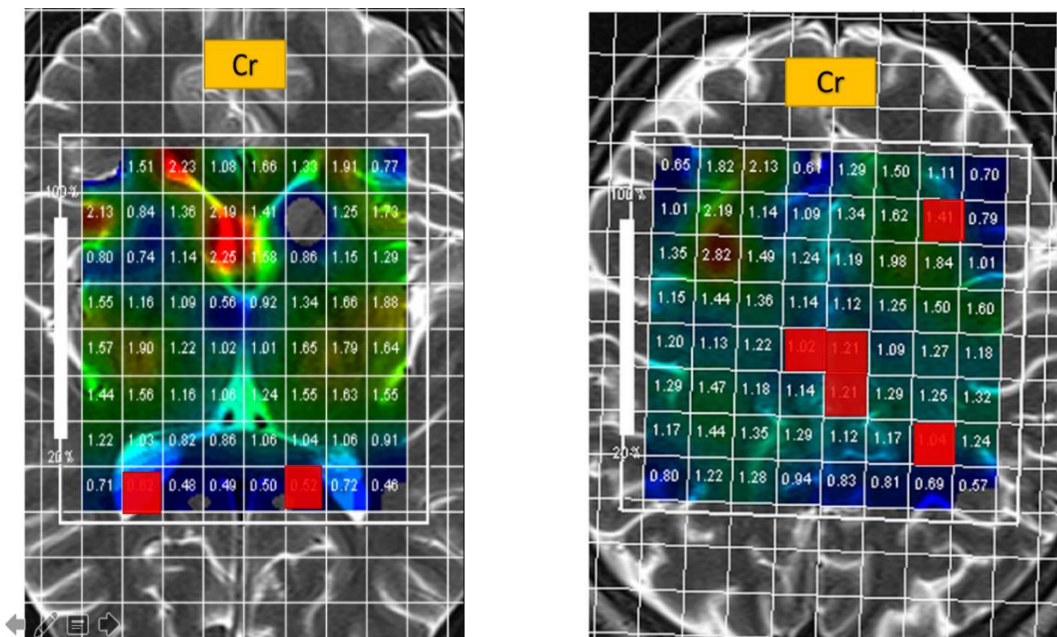


Figure 29 - Creatine. CR5, CR10, CR25, CR26, CR28, CR31, CR36 (voxels are marked in red)

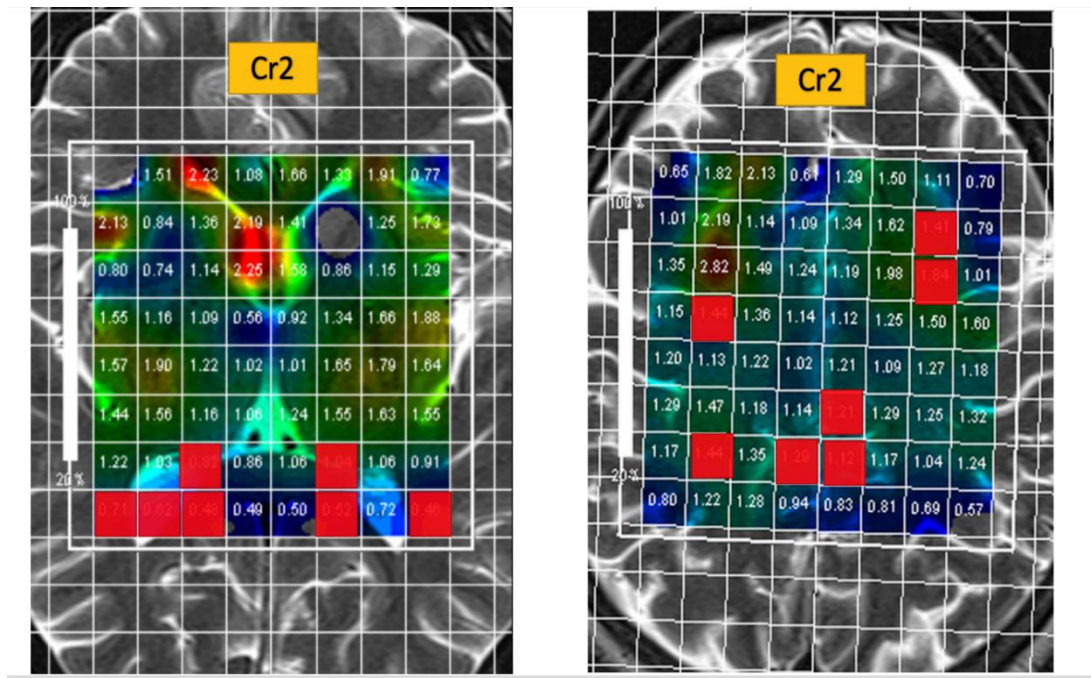


Figure 30 - Phosphocreatine. Cr3, Cr4, Cr5, Cr6, Cr7, Cr10, Cr12, Cr15, Cr18, Cr28, Cr29, Cr30, Cr31, Cr32 (voxels are marked in red)

Also, statistical processing of metabolites ratios was carried out in the SPSS Statistics program:

Table 8 - Ratio of "chemical shifts" ppm of metabolites grouped regionally in the hippocampus and linearly on the cortex (Me; Q₁:Q₃)

Indicator		Patients with diabetes mellitus type 1 (n=36)	Patients with diabetes mellitus type 2 (n=24)	Control group (n=20)	P
Cho/Cr	ChoHypLeft/CrHypLeft	1,07(0,99-1,24)	1,05(1 -1,24)	1,05(0,96-1,11)	0,726
	ChoHypRight/CrHypRight	1,21(1,08-1,32)	1,2(1,09-1,3)	1,21(1,13-1,29)	0,686
	ChoGrayLeft/CrGrayLeft	0,83(0,73-1)	0,81(0,73-1,2)	0,88(0,69-1,01)	0,936
	ChoWhiteCent/CrWhiteCent	0,96(0,87-1,01)	0,98(0,86-1)	0,84(0,66-1)	0,225
	ChoGrayRight/CrGrayRight	0,91(0,75-1)	0,9(0,75-1,1)	0,88(0,76-1,04)	0,893
Cho/CrP	ChoHypLeft/CrHypLeft	0,69(0,55-0,88)	0,7(0,56-0,9)	0,87(0,65-0,89)	0,205
	ChoHypRight/CrPHypRight	0,47(0,44-0,73)	0,45(0,42-0,7)	0,84(0,74-0,97)	0,008
	ChoGrayLeft/CrPGrayLeft	0,83(0,63-1,3)	0,8(0,6-1,31)	0,9(0,78-1,06)	0,5
	ChoWhiteCent/CrPWhiteCent	0,8(0,55-1,03)	0,81(0,56-1)	0,74(0,65-0,91)	0,936
Cho/NAA	ChoGrayRight/CrPGrayRight	0,81(0,56-1)	0,8(0,56-1,1)	0,75(0,57-0,83)	0,571
	ChoHypLeft/NAAHypLeft	0,54(0,5-0,61)	0,55(0,52-0,6)	0,59(0,58-0,66)	0,247
	ChoHypRight/NAAHypRight	0,58(0,52-0,67)	0,6(0,5-0,7)	0,67(0,58-0,76)	0,225
	ChoGrayLeft/NAAGrayLeft	0,47(0,42-0,53)	0,5(0,4-0,5)	0,48(0,47-0,51)	0,767
	ChoWhiteCent/NAAGrayRight	0,53(0,49-0,56)	0,5(0,5-0,56)	0,55(0,48-0,6)	0,726
ChoGrayRight/NAAGrayRight	0,45(0,39-0,54)	0,46(0,4-0,54)	0,49(0,39-0,52)	0,767	

Continuation of Table 8

Cr/CrP	CrHypLeft/CrPHypLeft	0,71(0,49-0,78)	0,7(0,5-0,8)	0,84(0,76-0,93)	0,09
	CrHypRight/CrPHypRight	0,41(0,35-0,59)	0,4(0,36-0,6)	0,62(0,57-0,74)	0,025
	CrGrayLeft/CrPGrayLeft	0,93(0,77-1,32)	0,93(0,8-1,3)	1,18(1,02-1,21)	0,571
	CrWhiteCent/CrPWhiteCent	0,81(0,62-0,9)	0,88(0,62-0,91)	0,89(0,8-1,19)	0,293
	CrGrayRight/CrPGrayRight	0,85(0,72-1,12)	0,85(0,7-1,1)	0,8(0,74-0,87)	0,609
Cr/NAA	CrHypLeft/NAAHypLeft	0,5(0,48-0,61)	0,51(0,5-0,6)	0,56(0,46-0,62)	0,535
	CrHypRight/NAAHypRight	0,51(0,42-0,54)	0,5(0,4-0,54)	0,56(0,43-0,6)	0,435
	CrGrayLeft/NAAGrayLeft	0,55(0,48-0,62)	0,55(0,5-0,64)	0,55(0,51-0,58)	0,893
	CrWhiteCent/NAAWhiteCent	0,57(0,53-0,61)	0,58(0,53-0,6)	0,64(0,6-0,65)	0,019
	CrGrayRight/NAAGrayRight	0,5(0,46-0,57)	0,52(0,46-0,58)	0,56(0,52-0,56)	0,246
CrP/NAA	CrPHypLeft/NAAHypLeft	0,81(0,63-1,01)	0,8(0,63-1)	0,74(0,65-0,96)	0,686
	CrPHypRight/NAAHypRight	1,23(0,8-1,3)	1,25(0,81-1,3)	0,79(0,63-0,91)	0,112
	CrPGrayLeft/NAAGrayLeft	0,62(0,38-0,7)	0,6(0,38-0,71)	0,54(0,49-0,6)	0,535
	CrPWhiteCent/NAAWhiteCent	0,76(0,63-0,86)	0,71(0,6-0,86)	0,74(0,53-0,75)	0,726
	CrPGrayRight/NAAGrayRight	0,6(0,5-0,66)	0,61(0,51-0,65)	0,64(0,59-0,81)	0,403

When comparing groups of patients with diabetes mellitus and healthy ratios of Cho (choline), Cr (creatine), Cr2 (phosphorcreatin), NAA (N-acetyl-aspartate) metabolites, Table 8, statistically significant differences were found:

1. The ratio of ChoHypRight / CrPHypRight metabolites (Choline in the hippocampus to Phosphorcreatine in the hippocampus on the right) in patients (0.47 (0.44-0.73)) is less than in healthy ones (0.84 (0.74-0.97)), based on non-parametric test for two independent samples (Mann-Whitney U-test, $U = 27$; $p = 0.008$).
2. The ratio of CrHypRight / CrPHypRight metabolites (Creatine in the hippocampus to Phosphorcreatine in the hippocampus on the right) in patients (0.41 (0.35-0.59)) is less than in healthy ones (0.62 (0.57-0.74)), based on a non-parametric criterion for two independent samples (Mann-Whitney U-test, $U = 35$; $p = 0.025$).
3. The ratio of CrWhiteCenter / NAAWhiteCenter metabolites (Creatine white matter in the central region to N-acetyaspartate white matter in the central region) in patients (0.57 (0.53-0.61)) is less than in healthy (0.64 (0, 6-0.65)), based on a non-parametric test for two independent samples (Mann-Whitney U-test, $U = 33$; $p = 0.019$).

In the remaining ratios of metabolites, no statistically significant differences were found, since p is greater than the 0.05 significance level.

In view of the results obtained, it was necessary to consult with experts in the field: neurologists and endocrinologists. Given the opinion of experts and the literature studied on this issue, we can conclude:

- 1) The main differences in patients with type 1 diabetes, type 2 and in the control group were found in the metabolites creatine and phosphocreatine. However, these metabolites in their function are markers of energy metabolism and contribute to glycolysis, which may be due to differences in the concentration of creatine and phosphocreatine in patients with diabetes, in whom the violation of the carbohydrate metabolism is the basis of the disease itself.
- 2) It was found that in the hippocampus the concentration of creatine and phosphocreatine in patients with diabetes is greater than in healthy ones, but in the cortex there is a gradient of changes in these metabolites (in some voxels the concentration of creatine and phosphocreatine is greater and in some less). Since the hippocampus is one of the ancient structures of the nervous system, it can be assumed that functional changes affect it in the first place, which is confirmed by the data obtained by neurologists (patients had a deterioration in memory and attention).
- 3) However, the situation is different in the bark. Based on the concentration gradient in patients and the fact that the cortex is the younger element of the nervous system, it can be assumed that this is due to the compensatory mechanisms of the cerebral cortex. And at the compensatory stage, clinical manifestations are not detected.

3.3 Automatic segmentation of FreeSurfer MRI images

3.3.1 Automatic Segmentation of FreeSurfer MRI Images

The automatic segmentation of MRI images of patients with diabetes mellitus type 1 and 2 and the control group was carried out, as a result of which images and quantitative data were obtained on the volumes of gray, white matter of the cerebral hemispheres and on the volume of the hippocampus in milliliters.

Below is an example of processing MRI images of one of the patients:

- 1) Isolation and removal of extracerebral structures (Fig. 31);
- 2) Segmentation of the white matter of the brain (Fig. 32). Determination of white matter surface boundaries and volume calculation.



Figure 31 - Isolation and removal of extracerebral structures

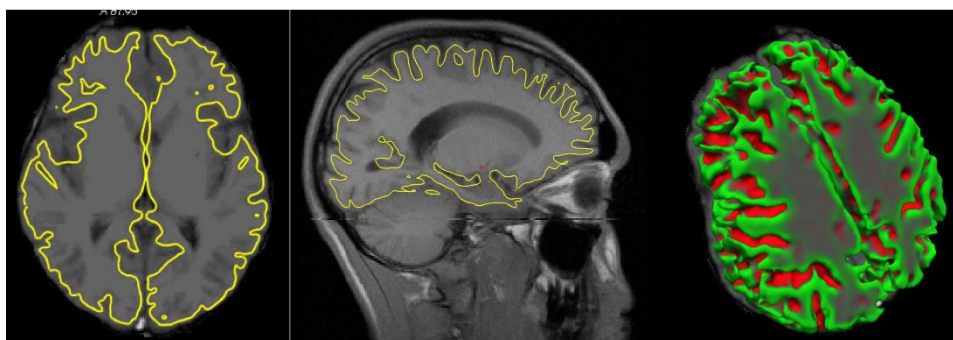


Figure 32 - Segmentation of the white matter of the brain in section and in volume representation

- 3) Determining the boundaries of the pia mater in the right and left hemispheres (Fig. 33).
- 4) Segmentation of the gray matter of the brain (Fig. 34). Determining the boundaries of gray and white matter, the calculation of the volume of gray matter.

- 5) Hippocampal segmentation (Fig. 35). Determination of the boundaries, the volume of the right and left hippocampus.

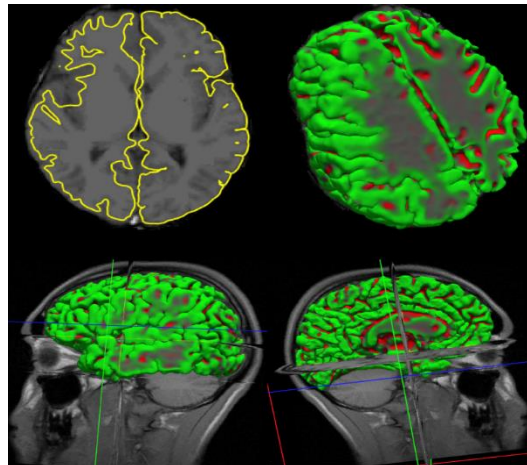


Figure 33 - Border of the pia mater of the left hemisphere of the brain in section

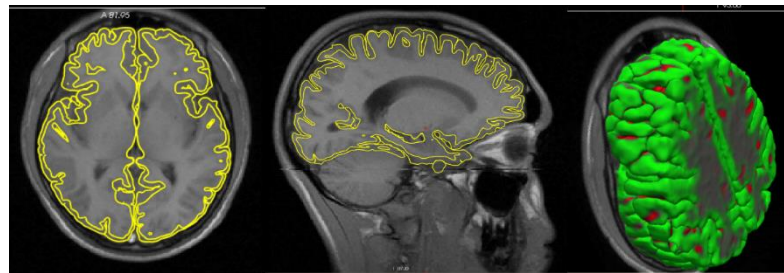


Figure 34 - Segmentation of the gray matter of the brain in section and in volume representation

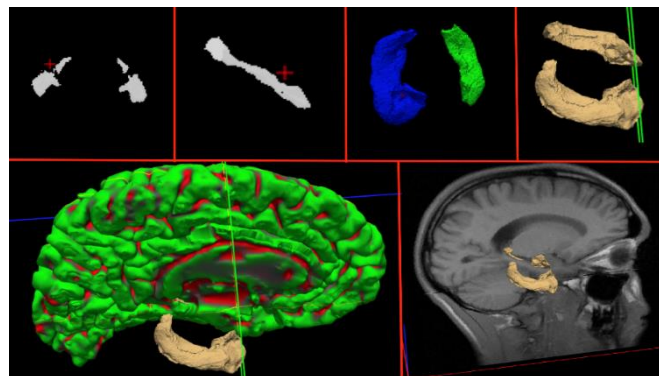


Figure 35 - Segmentation of the hippocampus in the slice and in the volumetric representation

Statistical processing of gray, white matter and hippocampus in SPSS Statistics:

Since there is evidence that the brain of men has an average weight of 100-150 grams more and the ratio of gray and white matter is different in men and women, it was necessary to divide the groups into men and women.

When comparing patients with diabetes mellitus and the control group in terms of white, gray matter, statistically significant differences were detected (Table 9):

- 1) The gray matter volume of the cerebral hemispheres in diabetic patients in men (534 (519-560)) and women (513 (499-538)) is statistically significantly less than in the control group in men (560 (544-572)) and women (524 (523-547)), respectively, on the basis of non-parametric criteria for two independent samples (Mann-Whitney U-test, $p < 0.05$).
- 2) The white matter volume of the cerebral hemispheres in diabetic patients in men (670 (548-708)) and women (676 (544-711)) is statistically significantly higher than in the control group in men (624 (534-698)) and women (632 (557-702)), respectively, based on a non-parametric test for two independent samples (Mann-Whitney U-test, $p < 0.05$).

When comparing patients with diabetes men (144 (133-163)) and women (140 (134-159)), and the control group of men (141 (130-164)) and women (138 (132-156)) by volume of the hippocampus no statistically significant differences were found (Table 9), based on non-parametric criteria for two independent samples (Mann-Whitney U-test, $p > 0.05$).

Table 9 - Volumes of gray, white matter and hippocampus in milliliters segmented in FreeSurfer for patients with type 1 diabetes (Me; Q₁:Q₃)

Indicator	Sick		Healthy		P	
	M	F	M	F	M	F
The volume of gray matter of the big hemispheres (ml)	534(519-560)	513(499-538)	560(544-572)	524(523-547)	0.027	0.041
The volume of white matter (ml)	670(548-708)	676(544-711)	624(534-698)	632(557-702)	0.022	0.038
The volume of the hippocampus (ml)	144(133-163)	140(134-159)	141(130-164)	138(132-156)	0.189	0.452

Table 10 - Volumes of gray, white matter and hippocampus in milliliters segmented in FreeSurfer for patients with type 2 diabetes (Me;Q₁:Q₃)

Indicator	Sick		Healthy		P	
	M	F	M		M	F
The volume of gray matter of the big hemispheres (ml)	534(519-560)	513(499-538)	560(544-572)	524(523-547)	0.027	0.041
The volume of white matter (ml)	670(548-708)	676(544-711)	624(534-698)	632(557-702)	0.022	0.038
The volume of the hippocampus (ml)	144(133-163)	140(134-159)	141(130-164)	138(132-156)	0.189	0.452

- 1) Statistically processing the data obtained from the automatic segmentation of MRI images of patients with diabetes mellitus type 1 and the control group, it was found that the volume of gray matter in patients less than in healthy ones. It can be assumed that atrophy of the cerebral cortex in patients with diabetes mellitus type 1 and 2.
- 2) Automatic segmentation allowed to state about changes in the brain at the anatomical level.
- 3) Since there is already evidence that patients with type 1 and type 2 diabetes have a decrease in the gray matter of the brain, we were able to confirm this in a different way. Automatic segmentation of FreeSurfer allowed to analyze faster and more accurately than the manual method.

3.3.2 Application of the neural network model for predicting cognitive impairment in diabetes mellitus

To conduct statistical processing of data, a multilayer perceptron with the number of input neurons equal to 256 and 1 hidden layer was chosen as a state recognition algorithm. The hyperbolic tangent was used as the activation function for hidden layers. The criterion for stopping the training was to achieve maximum recognition accuracy of the training set. An approximating type of neural network was used. According to the generalized data of the MPC, the number of MOKA test scores was predicted. Based on groups of patients with diabetes mellitus type 1 and type 2, two samples were compiled: training and test (220 people each).

In the process of implementing the DSS (decision support system) model, a neural network of approximating type was constructed to predict the score of MoCA. As input data, the MRS layer data, metabolites: Cho, Cr2, CrP, NAA were used. As an output parameter, the predicted value of the MoCA cognitive test was used. The accuracy of the model for the test sample was 79%, the root-mean-square error 1.

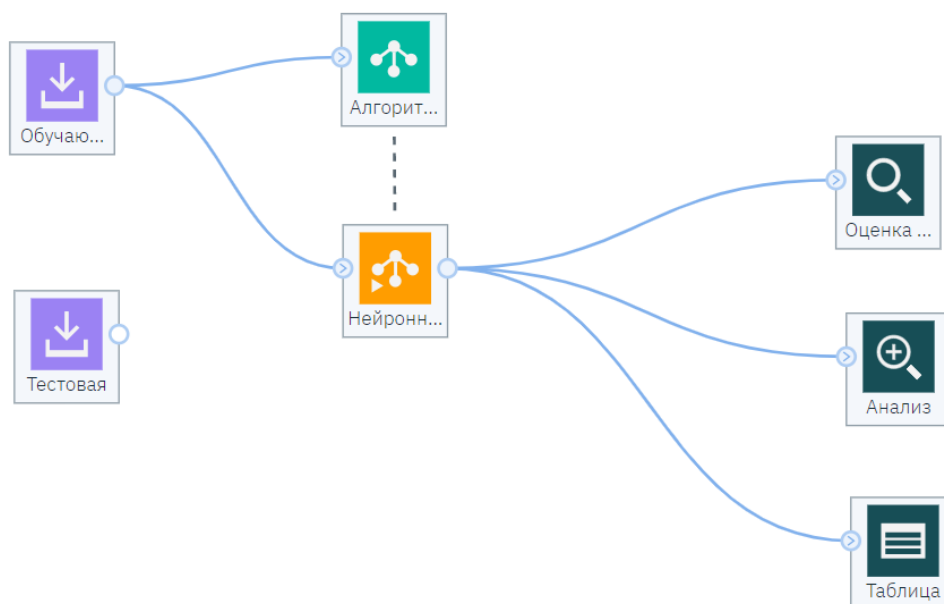


Figure 36 - Diagram of learning neural network

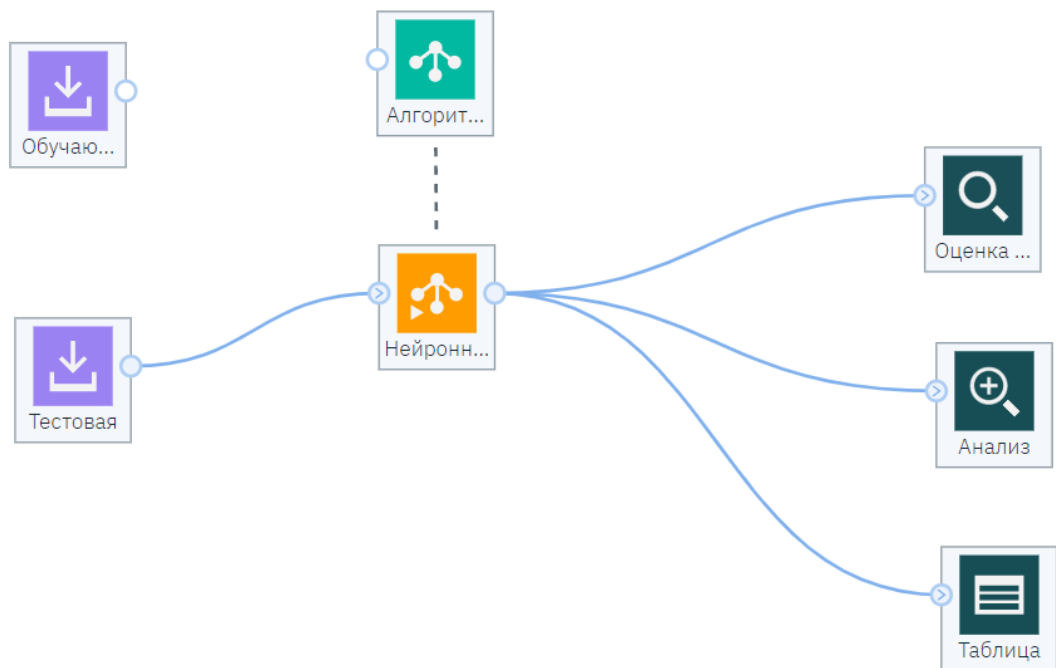


Figure 37 - Diagram of neural network testing

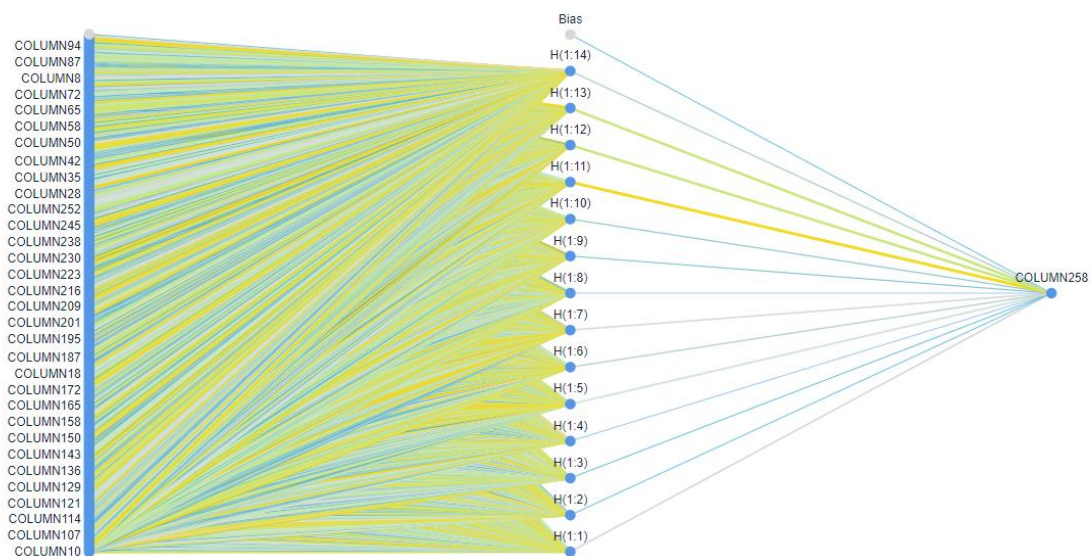


Figure 38 - Diagram of a multilayer perceptron for the approximation of data

Interpreting the result we can say about the following: the use of machine learning methods can be applied to assess the level of cognitive impairment according to MLS data. Unfortunately, the sample size for building an adequate model is insufficient, but even at the level of a relatively small sample, the hypothesis of the relationship between the level of cognitive impairment and brain metabolism indicators was confirmed. Direct correlation methods did not show such a connection. In fact, the resulting picture indicates a significantly non-linear processes at the metabolic level that characterize a person's cognitive function.

4. Financial management, resource efficiency and resource saving

4.1.1 Potential results of research results

The purpose of this section is to confirm the technical solutions described in the final qualifying work, justifying the economic necessity and feasibility of scientific and technical research.

This study was conducted to identify differences in indicators of the structure and metabolism of the brain according to MRI and MRS data of patients with diabetes mellitus type 1 and 2 and the control group (healthy people). Endocrinologists and neuropathologists to build a predictive statistical model to support decision-making can use the results obtained during the study. The work can apply further in medical research centers, clinics and other medical institutions.

The target market called the market segments, which will be the main consumer of the development in the future, and the market segment called the part of the market or a group of consumers, identified by special common features.

Firstly, we choose the medical field as a general application area for selection, since the results of this study will be further applying as support for the decision-making of a doctor.

Secondly, the results of this study intended to enable the construction of a predictive statistical model to support the decision-making of a doctor, that is, they will be use in various medical institutions, which will be a narrower area of selection: hospitals, medical research centers and clinics.

The target market is called the market segments, which will be the main consumer of the development in the future, and the market segment is called the part of the market or a group of consumers, identified by special common features.

Firstly, we choose the medical field as a general application area for selection, since the results of this study will be further applied as support for the decision-making of a doctor.

Secondly, the results of this study are designed to be able to build a predictive statistical model to support the decision-making of a doctor, that is, they will be used

in various medical institutions, which will be a narrower area of selection: hospitals, medical research centers and clinics.

And finally, thirdly, the study is aimed at patients suffering from diabetes mellitus of the first and second types, and, therefore, its application will be concentrated in the endocrinological departments of medical institutions of different plan.

Map of market segmentation is presented in Table 11

Table 11 - Market Segmentation Map

	Scope of application	
	Research	Diagnostics
Individuals		
Medical research centers		
Medical institutions		

Thus, it can be concluded that the main segment of the market is represented by medical research centers that this development is focused on, as well as institutions that provide medical services, such as clinics and hospitals. In particular, this study will be applied in clinics of the Siberian State Medical University, as well as in the Sergey Berezin Medical Institute, Tomsk.

4.1.2 Analysis of competitive technical solutions from the position resource efficiency and resource saving

Analysis of competitive technical solutions from the standpoint of resource efficiency and resource saving allows us to assess the comparative effectiveness of scientific development and determine the direction for its future improvement.

To do this, we will carry out this analysis using the scorecard presented below in Table 12.

Table 12 - Evaluation map for comparing competitive technical making

Criteria for evaluation	Weight criterion	Points			Competitiveness		
		Pf	Pc1	Pc2	Cf	Cc1	Cc2
1	2	3	4	5	6	7	8
Technical criteria for evaluating resource efficiency							
1. Ease of getting results	0,15	5	1	3	0,3	0,2	0,5
2. Detection of cognitive disorders in the early stages	0,3	2	3	5	1	0,2	1
3. Accuracy of results	0,15	2	4	5	0,3	0,1	0,5
Economic criteria for evaluating results							
1. Price	0,15	5	2	4	0,25	0,25	0,25
2. Demand on the market	0,25	5	3	5	0,3	0,3	0,5
Total	1	19	13	22	2,15	1,05	2,75

where abbreviations are:

- Pf - neuropsychological examination (Moca test);
- Pc1– identification of liquorological biomarkers (they allow one to judge the supposed form of the disease with cognitive impairment);
- Pc2 - magnetic resonance spectroscopy (a method that allows to determine the biochemical changes in tissues in various diseases according to the concentration of certain metabolites).

Analysis of competitive technical solutions determined by the formula:

$$K = \sum B_i \cdot \bar{B}_i, (1.1)$$

- where K is the competitiveness of scientific research or a competitor;
- B_i – weight of the indicator (in fractions of a unit);
- B_i - the score of the i-th indicator.

The result of this analysis is that the magnetic resonance method

The result of this analysis is that the MRS method proposed in this paper is more effective than the methods of competitors.

4.1.3 SWOT analysis

SWOT analysis is one of the most effective tools in strategic management, which consists in analyzing the external and internal factors of a company, assessing the competitiveness and risks of goods in the industry. The paper conducted a SWOT analysis, the results of which are presented in Table 13.

Table 13 - SWOT Matrix

	<p>Strengths of a research project: S1. Demand for research; S2. The relevance of the study; S3. Availability of budget financing; S4. The possibility of conducting research without additional equipment, fixed on the human body; S6. Novelty research</p>	<p>Weaknesses of a research project: W1. The lack of a prototype of scientific development; W2. The relative accuracy of the results; W3. Difficulty in obtaining the necessary data; W4. Time consuming W5. Limitations in conducting this study for certain groups of individuals.</p>
<p>Opportunities: O1. The widespread dissemination of research methods for diseases used in the STI; O2. The introduction of various studies of the disease as a supplement to support the decision of the doctor; O3. The appearance of additional demand; O4. Increase the number of trained personnel;</p>	<p>This study is relevant and relevant, therefore its wide distribution and introduction into other studies is possible. In this regard, it is also possible to increase the number of trained personnel, which would entail a reduction in the time that will be spent on this research.</p>	<p>Since there are no prototypes of this study, it is likely that the spread of the methods will take place at a very low speed, like the introduction of this method into other studies. This also causes additional demand.</p>

Continuation of Table 13

<p>Threats: T1. The emergence of a more advanced competitive diagnostic method; T2. Insufficient number of trained specialists; T3 Lack of sufficient funding.</p>	<p>Such studies are quite relevant and in demand, and this means that there is a likelihood of the emergence of a more advanced competitive diagnostic method, and, as a result, there is a probability of lack of funding.</p>	<p>The lack of prototypes of this work may lead to a decrease in funding, which means that among qualified personnel, an increase will also not be observed.</p>
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Based on the results of the SWOT analysis, it can be concluded that it is necessary to develop and improve the methods of the performed scientific and technical research, as well as to seek funding sources for the development and improvement of this research, including an increase in the number of trained personnel.

When considering weaknesses, we can conclude that the problem is also in the issue of funding, which will help to increase the number of trained employees, and, consequently, the time spent on conducting STR will be reduced.

Strengths, such as the relevance of the study, its novelty and relevance can ensure that the research will be in demand, which will also lead to an influx of funding. These factors will help to develop opportunities for promoting research in a dedicated market segment, as well as reduce the number of weaknesses and threats that affect the ability of this work to compete.

4.2 Initiation of the project

The purpose of the work performed is to identify differences in indicators of the structure and metabolism of the brain according to MRI and MRS data in patients with type 1 and type 2 diabetes and the control group.

The goals of the project, the structure of the project and the organization of the project participants can be described by interrelated hierarchical (tree-like) structures in which the relations between the components can be established: goals - parts of the project - participants, etc.

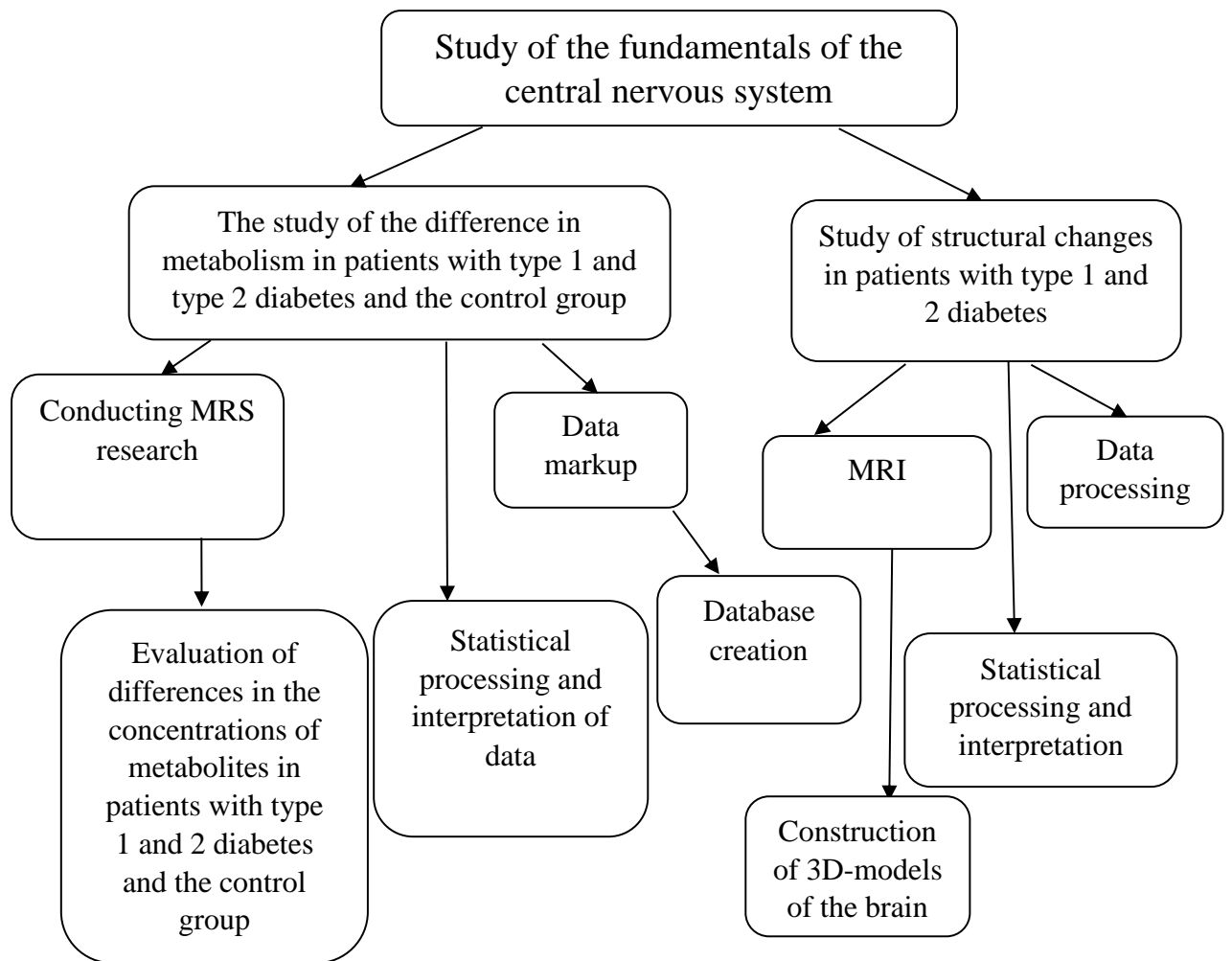


Figure 39 - Project Objective Tree

Table 14 - Stakeholders of the project

Project stakeholders	Stakeholder expectations
Clinics of SSMU	Obtaining reliable results of the study to support the decision of the doctor
Sergey Berezin Medical Institute	

Table 15 - Project Working Group

Item number	FULL NAME, main place of work position	Role in the project	Functions	Labor costs, an hour.
1	Tolmachyov I.V., Candidate of Medical Sciences, SSMU	Scientific supervisor	Approval of the main sections, issue of tasks for execution	14
2	Bykova M.V., student of TPU, RSCABS	Graduate student	Execution of tasks	75
TOTAL:				89

This section reflects the fact that the work performed is quite large. Stakeholders of the project expect quite accurate results, which is a big challenge for a small project team.

4.3 Planning the management of scientific and technical project

4.3.1 Project Plan

A group of planning processes consists of processes that are carried out to determine the overall content of the work, clarify the objectives and develop a sequence of actions required to achieve these goals.

As part of the planning of a research project, it is necessary to build a project calendar and network schedules. The list of stages, works and distribution is presented below in Table 16.

Table 16 - List of stages, work and distribution of performers

Main steps	№	Content of work	Position performer
Development of technical specifications	1	Drafting and approval of technical specifications	Tolmachev I.V.
Choice of direction research	2	Selection and study of materials on the research topic	Bykova M.V.

Continuation of Table 16

	3	Choosing the direction of research	Tolmachev I.V.
	4	Scheduling work on a research topic	Tolmachev I.V.
Theoretical studies	5	Search for information about the types of disease	Bykova M.V.
	6	Systematization of the information received	Bykova M.V.
	7	Analysis of the information received	Tolmachev I.V., Bykova M.V.
	8	Selection of the most appropriate research methodology	Tolmachev I.V., Bykova M.V.
	9	Exploring data extraction methods	Tolmachev I.V., Bykova M.V.
	10	Installing the necessary software to perform research	Tolmachev I.V.
Practical research	11	MRI data collection for diabetics, stroke patients, and control group	Tolmachev I.V.
	12	Data analysis	Tolmachev I.V., Bykova M.V.
	13	Grouping and highlighting especially basic parameters	Bykova M.V.
	14	Verification of autosegmentation	Tolmachev I.V., Bykova M.V.
	15	Evaluation of the accuracy of the data	Tolmachev I.V., Bykova M.V.
Registration of the research results	16	Compilation of the final version of the study	Bykova M.V.
	17	Verification of completed research	Tolmachev I.V., Gubarev F.A.

4.3.2 Determination of the complexity of the work

To determine the expected value of the complexity we use the formula below:

$$t_w = \frac{3t_{\min} + 2t_{\max}}{5}, \text{ where} \quad (1)$$

- 1) t_w - the expected complexity of the i -th work, man-days;
- 2) t_{\min} - the minimum possible labor-intensiveness of performing a given i -th job (optimistic estimate: assuming the most favorable set of circumstances), man-days;

- 3) t_{max} - the maximum possible complexity of performing the given i -th work (pessimistic estimate: assuming the most unfavorable set of circumstances), man-day.

After you have calculated t_w , the duration of each work in working days is calculated:

$$T_{pi} = \frac{t_w}{q_i}, \text{ where} \quad (2)$$

- 1) T_{pi} – the duration of one job, working days;
- 2) t_w – the expected complexity of doing one job, man-days.
- 3) q_i – the number of performers performing simultaneously the same work at this stage, pers.

4.3.3 Development of a research schedule

When developing a schedule for conducting a scientific study, it is advisable to use a Gantt chart - a horizontal tape chart, on which work on a topic appears to be lengthy segments, characterized by dates of the beginning and end of the work.

To calculate the calendar factor:

According to the production calendar (for a 6-day working week) in 2019, 365 calendar days, 299 working days, 66 days off / holidays.

$$kcal = \frac{T_{cal}}{T_{cal} - T_{off} - T_{hol}} = \frac{365}{365 - 66} = 1,22, \text{ where} \quad (3)$$

- 1) T_{cal} – number of calendar days per year;
- 2) T_{off} – number of days off per year;
- 3) T_{hol} – the number of holidays in the year.

All results obtained during the calculations are listed in the table below.

Table 17 - Temporary indicators of research

Title work	The complexity of the work									Duration of work in working days T_{pi}			Duration of work in calendar days T_{ki}		
	t_{min} , man-days			t_{max} , man-days			t_w , man-days			Tolma chev	Byko va	Guba rev	Tolma chev	Byko va	Gubar ev
Drafting and approval of technical specifications	1	-	-	2	-	-	1	-	-		-	-	1	-	-
Selection and study of materials on the research topic	-	10	-	-	15	-	-	14	-	-	14	-	-	17	-
Choosing the direction of research	1	-	-	1	-	-	1	-	-	1	-	-	1	-	-
Scheduling work on a research topic	1	-	-	1	-	-	1	-	-	1	-	-	1	-	-
Search for information about the types of diseases	-	5	-	-	7	-	-	6.5	-	-	7	-	-	8	-
Systematization of the information received	-	5	-	-	7	-	-	6.5	-	-	7	-	-	9	-
Analysis of the information received	1	4	-	1	5	-	1	4.7	-	1	2	-	1	3	-
Selection of the most appropriate research methodology	1	3	-	1	4	-	1	2.8	-	1	2	-	1	2	-
Exploring data extraction methods	1	4	-	1	5	-	1	4.6	-	1	4	-	1	5	-
Installing the necessary software to perform research	1	-	-	2	-	-	1	-	-	1	-	-	1	-	-

Continuation of Table 17

MRI data collection for diabetics, stroke patients, and control group	2	-	-	3	-	-	2	-	-	2	-	-	2	-	-
Data analysis	1	6	-	1	8	-	1	6.7	-	1	6	-	1	7	-
Grouping and highlighting especially basic parameters	-	3	-	-	5	-	-	4.8	-	-	2	-	-	3	-
Verification of autosegmentation	1	3	-	2	4	-	1.5	3.9	-	1	2	-	1	2	-
Evaluation of the accuracy of the data	1	2	-	2	3	-	1.1	2.7	-	1	1	-	1	2	-
Compilation of the final version of the study	-	12	-	-	16	-	-	15	-	-	14	-	-	17	-
Verification of completed research	1	-	1	2	-	2	1.4	-	1.4	1	-	1	2	-	2

Table 18 - The calendar schedule of the study

№ of works	Type of work	Performers	T_{ki} , Cal.days	Duration of work										
				March			April			May				
				1	2	3	1	2	3	1	2	3		
1	Drafting and approval of technical specifications	Tolmachev I.V.	1	█										
2	Selection and study of materials on the research topic	Bykova M.V.	17	██████████										
3	Choosing the direction of research	Tolmachev I.V	1		█									
4	Scheduling work on a research topic	Tolmachev I.V	1		█									
5	Search for information about the types of diseases	Bykova M.V.	8			██████								
6	Systematization of the information received	Bykova M.V.	9			██████								
7	Analysis of the information received	Tolmachev I.V., Bykova M.V.	1 3				█	██						
8	Selection of the most appropriate research methodology	Tolmachev I.V., Bykova M.V.	1 2				█	██						
9	Exploring data extraction methods	Tolmachev I.V., Bykova M.V.	1 5					█	████					
10	Installing the necessary software to perform research	Tolmachev I.V.	1					███						
11	MRI data collection for diabetics, stroke patients, and control group	Tolmachev I.V	2						█					
12	Data analysis	Tolmachev I.V., Bykova M.V.	1 7						█	██████				

4.3.4 The budget of scientific and technical research (STR)

A reliable and complete reflection of all types of costs associated with its implementation should be ensured. When planning the budget of scientific and technical research. The cost grouping is used according to the following items in the formation of the STR budget:

- 1) material costs;
- 2) the basic salary of the performers of the topic;
- 3) additional salary of the performers of the topic;
- 4) depreciation deductions;
- 5) contributions to extra-budgetary funds (insurance contributions);
- 6) overhead costs.

4.3.4.1 Calculation of material costs of STR

This article includes the cost of all materials used in project development. Calculation will be made on all performers.

Table 19 - Material costs

Name	Unit of measurement	Amount	Price per one., rub.	The cost of materials, (Cm), rub.
Packed paper (Format A4)	Rub.	1	290	290
Шариковая ручка	Rub.	2	20	40
Total:			330	

Total for the item "Material costs" - 330 rubles.

4.3.4.2 Calculation of depreciation

Considering the fact that the PC that was used to write the work, has an initial cost of 45,000 with a useful life of 3 years and the writing of the work took place within 3 months. Then:

- depreciation rate:

$$An = \frac{1}{n} * 100\% = \frac{1}{3} \times 100\% = 33,33\%$$

- annual depreciation:

$$Ay = 45000 \times 0,33 = 14850 \text{ rubles}$$

- monthly depreciation:

$$Am = \frac{14850}{12} = 1237,5 \text{ rubles}$$

- total depreciation of fixed assets:

$$A = 1237,5 \times 3 = 3712,5 \text{ rubles}$$

Total for the article "Calculation of depreciation" - 3712.5 rubles.

4.3.4.3 Basic wages of the performers of the topic

This article includes the remuneration of the research supervisor and the engineer. The salary of the head is 33664 rubles without the regional coefficient, and the engineer 21760 rubles without the regional coefficient.

Thus, the salary is calculated according to the following formula:

$$S_{sal} = S_b + S_{add}, \text{ ГДЕ} \quad (5)$$

1) S_b – basic salary;

2) S_{add} – additional salary.

$$S_{sal} = S_d \times T_w, \text{ ГДЕ} \quad (6)$$

1) S_d – average daily salary of an employee, rubles;

2) T_w - the duration of work performed by the employee, work days

The average daily salary is calculated by the formula:

$$S_d = \frac{S_m \cdot M}{F_a}, \text{ ГДЕ} \quad (7)$$

1) S_m – monthly salary of an employee, rub.;

- 2) M – the number of months of work without vacation during the year (with a vacation of 24 working days $M = 11.2$ months, 5 days a week; with a vacation of 48 working days $M = 10.4$ months, a 6-day week);
- 3) $F_{\text{д}}$ – valid annual fund of working time of scientific and technical personnel, work days.

Table 20 - the balance of the working day

Working time	Tolmachev	Bykova	Gubarev
Calendar number of days	365	365	365
The number of non-working days - weekend - holidays	66	66	66
Loss of working time - vacation - absences due to illness	56	56	56
Valid annual working time fund	243	243	243

Monthly salary of an employee:

$$S_m = S_{tr} \cdot (1 + k_{pc} + k_{add}) \cdot k_p, \text{ where} \quad (8)$$

- 1) S_{tr} – salary at the tariff rate, rub.;
- 2) k_{pc} – premium coefficient equal to 0,3 (i.e 30% from S_{tr});
- 3) k_{add} – coefficient of surcharges and allowances is approximately 0,2 – 0,5 (in scientific research institutes and at industrial enterprises - for the expansion of service industries, for professional skills, for harmful conditions: 15-20 % from S_{tr});
- 4) k_d – district coefficient equal to 1,3 (for Tomsk).

Table 21 - Calculation of basic salary

Performers	S_{tr} , rub.	S_m , rub.	S_d , rub.	T_w , work.days	k_d	S_b
Engineer	21760	28288	1210.68	75	1.3	90801
Supervisor	33664	43763	1140.76	14	1.3	15970.6
Consultant	33664	43763	1140.76	2	1.3	2281.5
Total	109053.1					

Total for the article "Basic salary" - 109053.1 rubles.

4.3.4.4 Additional salary of the executive system

The costs of additional salary for the executors of the topic consider the amount of additional payments for deviation from the normal working conditions, as well as payments related to the provision of guarantees and compensations, provided for by the Labor Code of the Russian Federation.

The calculation is made according to the following formula:

$$S_{add} = k_{add} \cdot S_b, \text{ where} \quad (9)$$

k_{add} – the coefficient of additional salary is taken equal 0,13.

$$S_{add}(\text{Supervisor}) = 2076.18(\text{rub.})$$

$$S_{add}(\text{Engineer}) = 11804.13(\text{rub.})$$

$$S_{add}(\text{Consultant}) = 296.6(\text{rub.})$$

Total for the article "Additional salary" - 14473.5 rubles.

4.3.4.5 Deductions to extra-budgetary funds (insurance deductions)

This item of expenditure reflects obligatory deductions, according to the standards established by the legislation of the Russian Federation, to the state social insurance (SSI), pension fund (PF) and medical insurance (FFOMI) from the costs of workers. The amount of contributions to extra-budgetary funds is determined on the basis of the following formula:

$$S_e = k_e \cdot (S_b + S_{add}), \text{ where} \quad (10)$$

k_e – coefficient of deductions for payment to extra-budgetary funds, equal to 30% (0,3).

$$S_e(\text{Supervisor}) = 5414(\text{rub.})$$

$$S_e(\text{Engineer}) = 30781.5(\text{rub.})$$

$$S_e(\text{Consultant}) = 773.4(\text{rub.})$$

Total for the item "Deductions to extra-budgetary funds" - 36968.9 rubles.

4.3.4.6 Overhead costs

Overhead costs consider other expenses of the organization that are not included in the previous cost items: printing and photocopying of research materials, payment of communication services, electricity, postal and telegraph expenses, reproduction of materials, etc. Their value is determined by the following formula:

$$S_o = (\text{amount of articles} \div 6) \cdot k_o, \text{ where} \quad (11)$$

k_o - coefficient considering overhead.

The overhead coefficient can be taken in the amount 16%.

Total for the item "Overhead" - 26458 rubles.

4.3.4.7 Forming a budget for a research project

Table 22 - the cost of the research project

Article title	Amount, rub.	Cost share, %
1. Material costs of STR	330	0.17
2. Depreciation	3712.5	1.94
3. The costs of the basic salary of the performers of the topic.	109053.1	57
4. Costs for additional salary of the topic performers	14473.5	7.58
5. Deductions to extra-budgetary funds	36968.9	19.36
6. Overhead costs	26458	13.86
Total:	190996	100

4.3.5 Project Risks

Risk is the possibility of the occurrence of some adverse event that entails the occurrence of various kinds of losses. A unified risk classification project does not exist. We can single out the following main groups of risks inherent in almost all projects: political, economic, social, technological, environmental, financial, organizational, marketing, personnel, technical.

To begin with, the main risk groups of the project are determined, it is explained what each risk group is.

Table 23 - the definition of risk

№	Risk name	Risk description
1	Political	No risk
2	Economic	No risk
3	Social	Restriction of research for some patients
4	Ecological	Negative impact of equipment used in the study
5	Technological	Violation of equipment, software used for research
6	Financial	Insufficient research funding
7	Organizational	The difficulty of collecting data from patients participating in the study
8	Marketing	The study has no analogues, and, therefore, there is no possibility of comparing the results
9	HR	Lack of trained staff
10	Technical	Equipment breakdown

Then, the risk probability is estimated using the risk probability scale and the loss level assessment scale. The result of this stage is presented in the form of Table 24.

Table 24 - Risk Probability Assessment

№	Risk name	Risk probability estimate (low, medium, high)
1	Political	Low
2	Economic	Low

Continuation of Table 24

3	Social	Medium
4	Ecological	Low
5	Technological	Medium
6	Financial	Medium
7	Organizational	Low
8	Marketing	High
9	HR	Low
10	Technical	Low

Table 25 - Estimation of the level of losses

№	Risk name	Loss assessment (low, medium, high)
1	Political	Low
2	Economic	Low
3	Social	Medium
4	Ecological	Low
5	Technological	High
6	Financial	High
7	Organizational	High
8	Marketing	High
9	HR	Medium
10	Technical	High

After that, we fill in the table “Matrix of the probability of risks / losses” on the basis of the scale and develop the main measures to reduce the risk.

Table 26 - Key risk reduction measures

№	Risk name	Risk reduction measures
1	Political	Not required
2	Economic	Not required
3	Social	An assessment of the health status of patients who intend to participate in the study is required.
4	Ecological	It is necessary to familiarize with the ways of utilization of the equipment used for carrying out STR in case of its failure

Continuation of Table 26

5	Technological	Preliminary training of the doctor is necessary before starting work with the equipment and software used in the study.
6	Financial	Publication of the study with an emphasis on the need for it in connection with the prevalence of the disease
7	Organizational	Additional training for personnel involved in data collection and processing
8	Marketing	It is necessary to widely disseminate information about the danger of the disease and the need for research to prevent deterioration of patient health.
9	HR	Lectures, additional training of staff participating in the study
10	Technical	Timely maintenance, careful handling and repair of equipment as needed

Thus, the risks associated with conducting this scientific and technical research, as well as measures to reduce them, were considered in this section.

4.4 Description of potential effect

The effect of diabetes on the body today is still not fully understood, but since this disease is one of the most common diseases on the planet, this study is socially effective and in demand in modern society. Diabetes has a negative effect on the body, which requires close monitoring of the patient.

The effectiveness of this work lies in the fact that such studies have never been conducted before. Since the evidence of this method has not been fully investigated, there are practically no works like this. In addition, conducting research of this type

in collaboration with the Siberian State Medical University attracts sufficient attention from outside, which may entail additional funding.

In this section of the work, potential consumers of the research results were identified, a SWOT analysis was performed, which showed that it is necessary to develop and improve the methods of the performed scientific and technical research, as well as to seek funding sources for the development and improvement of this research, including an increase in the number of trained personnel. Consideration of weaknesses showed that the problem also lies in the issue of funding, which will help to increase the number of trained employees, and, consequently, the time spent on conducting STR will be reduced. Strengths, such as the relevance of the study, its novelty and relevance can ensure that the research will be in demand, which will also lead to an influx of funding. These factors will help to develop opportunities for promoting research in a dedicated market segment, as well as reduce the number of weaknesses and threats that affect the ability of this work to compete.

In addition, an analysis of competitive technical solutions was carried out from the point of view of resource efficiency and resource saving with the help of an evaluation card, and the research subjects were identified (3 people). The total duration of the project was 3 months. The budget of scientific and technical research amounted to 190996 rubles. Well, and, to finish this section, the risks for this scientific and technical study were considered: they showed that this work does not bear risks from the environmental, political and economic parts, while marketing, financial and organizational risks can bring problems performing research. Measures to reduce these risks were also reviewed and described.

5. Social responsibility

Introduction

The object of research in this final qualifying work is the data of MRI and MRS of patients suffering from diabetes mellitus of the first and second types, and the control group needed to compare the results of the study. This work characterized by spending a lot of time at the computer indoors.

In the course of this work, we studied the data obtained using magnetic resonance imaging and magnetic resonance spectroscopy, and we tested a neural network aimed at predicting poor results in the MoCA test. From all of the above, we can conclude that there is a need to organize a workplace at the computer in accordance with the regulations. All research and work are carried out in an educational institution in the laboratory for computers, therefore, the working area will be the space corresponding to a small room, up to 2 meters high.

5.1 Legal and organizational security issues

Most of the work that is performed in production is directly related to the presence of dangerous and (or) harmful production factors. Working conditions according to the degree of harmfulness and (or) danger are divided into four classes - optimal, permissible, harmful and dangerous working conditions.

In accordance with art. 221 - 225 of the Russian Federation Labor Code, at work with harmful and (or) hazardous working conditions, as well as at work performed in special temperature conditions or related to pollution, employees are given free compulsory certification or declaration of compliance with special clothing, special shoes and other means personal protection, as well as washing and (or) neutralizing agents in accordance with the model rules, which are established in the manner determined by the Government of the Russian Federation.

It is also envisaged to undergo a medical examination for workers who perform work in conditions with hazardous and (or) harmful production factors, which is specified in article 213 of the Russian Federation Labor Code. Moreover, and in employment, and in the process. In the order of the Ministry of Health and Social Development of the Russian Federation of 12.04.2011 No. 302n. specified procedure for conducting a medical examination. The requirements of this document provide that a medical examination should be carried out once a year, or twice a year. It depends on the type of activity of the worker in production, as well as on the presence of specific harmful factors.

According to Part 6 of Article 213 of Russian Federation Labor Code, workers engaged in certain types of activities, including those associated with sources of increased danger (with the influence of harmful substances and adverse production factors), as well as working in conditions of increased danger, undergo an obligatory psychiatric examination at least once every five years in the manner established by the federal executive body authorized by the Government of the Russian Federation.

5.1.1 Organizational measures in the working area layout

The working zone is a space up to 2 m high above the site of permanent or temporary stay of workers. The place of stay considered permanent if the employee is on it for more than 50% of the total, or 2 hours of continuous working time. A workplace is a place of temporary or permanent stay of production workers in the course of their employment.

The organization of the workplace is a complex of measures for equipping the workplace with objects and means of labor, as well as their placement in a specific order.

The organization of the workplace is a set of activities that include:

- 1) Rational workplace specialization;
- 2) Equipping it with the required sets of main and auxiliary equipment;

- 3) Technological equipment and inventory;
- 4) Creating comfortable working conditions; optimal arrangement of equipment, convenient placement of equipment and objects of labor in the workplace;
- 5) Uninterrupted service of the worker in accordance with his functional needs.

The specific composition and content of work on the rational organization of the workplace depends on a number of factors: industry, type of production, type of labor, degree of cooperation and division of labor, levels of technical equipment and mechanization of labor, working conditions, etc.

We must not forget about microclimatic factors in the design of the workplace: temperature, noise, light, dust and other sanitary and hygienic requirements for the organization of workplaces.

It is necessary that the working room be provided with the correct location and layout of the workplace. GOST 12.2.032-78 "OSSS. Workplace when working sitting. General Ergonomic Requirements" establishes general ergonomic requirements for workplaces when working in the sitting position when designing a new and modernizing existing equipment and production processes. It is stipulated that the mutual arrangement of all its elements must comply with the physiological, psychological and anthropometric requirements. And, in addition, to conform to the nature of the work.

Quite an important aspect in the organization of the workplace is the periodic ventilation of the working room, established by the schedule of technological breaks. For women and men, the height of the working surface when doing computer work should be 655 mm. Work is done only at a personal computer, therefore, the working surface will be rectangular in shape. The permissible location of the monitor is a vertical plane at an angle of $\pm 30^\circ$ from the normal line of sight and in a horizontal plane at an angle of $\pm 30^\circ$ from the sagittal plane.

5.2 Industrial safety

Industrial safety is the system of organizational measures and technical means that prevent or reduce the likelihood of exposure to working personnel of the dangerous traumatic factors that arise in the working area during work.

In this section of work, it is necessary to find out the dangerous and harmful factors that may arise when working with an information system. Further selection is made using GOST 12.0.003-74 "Dangerous and harmful production factors. Classification". The selection results are shown in the table below.

Table 27 - Harmful and dangerous factors when working with a computer

Source factor, the name of the type of work	The list of factors (according to GOST 12.0.003-74)		Relevant regulatory documents
	Harmful	Dangerous	
1) Performance of work at the personal computer	1) Insufficient illumination of the working area; 2) Increased level of electromagnetic radiation; 3) Lack or lack of natural light; 4) Increased air temperature in the workplace	1) The increased value of the voltage in the electrical circuit, the circuit.	1) GOST 12.1.006-84; 2) SanPiN 2.2.4.1191-03 SanPiN 2.2.4.548-96; 3) GOST 12.1.003-83

5.2.1 Analysis of hazardous and harmful production factors

Since all work is done at a personal computer, we exclude chemical, psychophysiological and biological harmful and dangerous factors.

Physical hazards, as a rule, include:

- 1) increased noise level in the room;
- 2) insufficient illumination of the working area;
- 3) increased air temperature;
- 4) electromagnetic radiation and other factors.

The last factor, electromagnetic radiation, has the greatest impact on the human body compared to the other factors described. Prolonged exposure to electromagnetic radiation can cause various serious illnesses.

5.2.2 Justification of measures to reduce the levels of exposure to hazardous and harmful factors on the researcher (working)

Working with a computer takes most of the time when performing this scientific and technical research, so it is important to consider the influence of the electromagnetic field for several reasons:

- 1) The system unit and PC monitor are sources of electromagnetic radiation;
- 2) Works are performed at a close distance from the sources described above and there is no possibility to increase this distance to a safe one;
- 3) Work at the computer is sufficiently long in time, and, consequently, the time of exposure to the electromagnetic field.

GOST 12.1.006-84 provides the following limit values for the level of electromagnetic radiation:

- 1) On the magnetic component – 0.3 A/m;
- 2) On the electrical component - 5 V/m.

With the development of various electronic equipment, liquid crystal monitors have replaced the cathode-ray tube monitors. Their level of electromagnetic radiation is lower than that of older ones.

The level of electromagnetic radiation still exceeds the standards. To avoid its negative influence, screening of current-carrying parts of the computer, as well as its entire body used. In addition, it is necessary to limit the time spent at work on a PC, and introduce short breaks in the work of staff for recreation.

In terms of occupational safety, visual ability and visual comfort are extremely important. Many accidents occur, in addition to all because of poor lighting or because of errors made by the worker, because of the difficulty of recognizing a

particular object or awareness of the degree of risk associated with the workplace. Lighting creates normal working conditions.

Poor illumination in the workplace or in the work area can cause a decrease in productivity and quality of work, as well as injury.

In order to provide the conditions necessary for visual comfort, the following prerequisites must be implemented in the lighting system:

- 1) sufficient and uniform lighting;
- 2) optimum brightness;
- 3) the absence of glare and blindness;
- 4) appropriate contrast;
- 5) correct color range;
- 6) the absence of a stroboscopic effect or pulsation of light.

In order to improve the uniformity of the lighting, it is necessary that the walls and ceiling of the working room be painted in light colors. You also need to use a combined lighting - lighting, in which local lighting is added to the general lighting. Also, the correct distribution of illumination contributes to the absence of sharp shadows, reflected and direct brilliance (i.e., increased brightness of the luminous surfaces) and the constancy of illumination in time.

According to SanPiN 2.2.1 / 2.1.1.1278-03 the following norms are indicated:

Table 28 - Standardized indicators of combined lighting of the main premises

The room	Minimum illumination of the working surface (E), lx	Coefficient of daylight for combined illumination (CDL), %	Pulsation coefficient of illumination (PC), %, no more than
Cabinets, offices	300	1.8	15
Rooms for working with PC displays	300-500	3.5	5
Laboratories	400	3.5	10

Favorable weather conditions in production are an important factor in ensuring high productivity and preventing diseases. Failure to comply with the hygienic norms of the microclimate not only reduces the efficiency of a person, but also increases the risk of injury and a number of diseases, including professional ones.

The microclimate in the production area is characterized by such indicators as:

- 1) Relative humidity. In the air, excessively saturated with water vapor, it is difficult for evaporation of moisture from the surface of the skin and lungs, which can dramatically worsen the condition and reduce human performance.
- 2) Air velocity. The human body begins to feel air currents at a speed of about 0,15 m/s. Moreover, if these streams have a temperature of up to 360°C, the body feels a refreshing effect, and at temperatures above 400° C they act depressingly.
- 3) Air temperature. During work in a “hot” microclimate, labor productivity drops rapidly and decreases to 20–30% at 300° C. This applies to both physical and mental work.

Optimum values of microclimate indicators should be observed at workplaces of industrial premises where operator-type work is performed, associated with neuro-emotional stress (in cabins, consoles and process control posts, in computer halls, etc.).

SanPiN 2.2.4.548–96 shows the optimal values of the microclimate indicators at the workplaces of industrial premises. These parameters can be achieved with the help of air conditioning systems during the warm period of the year and with the help of water heating during the cold period of the year.

The mechanisms of thermoregulation when performing this type of work will not depend on physical exertion, since working at a computer does not provide for them as such, therefore, this type of work falls into category Ia. Below, in the table, the optimal values of the microclimate indicators for the workplace in the production area for this type of work are given.

Table 29 - The optimal values of microclimate indicators for the workplace in the production area

Period of year	Category of work on the level of energy consumption, W	Air temperature, °C	Relative humidity, %	Flow rate, m/s
Cold period	Ia (up to 139)	22 – 24	40 – 60	0.1
Warm period	Ia (up to 139)	23 – 25	40 – 60	0.1

Table 30 - Permissible values of microclimate indicators for the workplace in the production area

Period of year	Category of work on the level of energy consumption, W	Air temperature, °C	Relative humidity, %	Flow rate, m/s
Cold period	Ia (up to 139)	20 – 25	15 – 75	0.1
Warm period	Ia (up to 139)	21 – 28	15 – 75	0.1 – 0.2

Noise is a random mix of different levels and frequencies of sounds. Noise can occur during operation of electromagnetic devices, with the outflow of air and gases, as well as with the movement of water and liquid.

From a physiological point of view, noise is any unwanted noise that is unpleasant for human perception. Noise worsens working conditions, having a harmful effect on the human body. With prolonged exposure to noise on the human body, undesirable phenomena occur:

- 1) decreased visual acuity, hearing;
- 2) blood pressure rises;
- 3) attention decreases.

Strong prolonged noise can cause functional changes in the cardiovascular and nervous systems, leading to heart disease and increased nervousness.

Normal noise level: up to 50-55 dB. Corresponds to the conversation of moderate volume, low background noise of the working mechanisms. According to

GOST 12.1.003-83, the extreme noise level in laboratories is 60 dB when a person performs work on a PC.

Since the work is done at the computer, it is likely an electric shock. Therefore, it is necessary to identify safety requirements for electrical installations that are sources of hazards. To exclude electric shock:

- 1) often turn on and off the computer without the need;
- 2) touch the screen and the back of the computer units;
- 3) work on computer equipment and peripheral equipment with wet hands;
- 4) work on computer equipment and peripheral equipment that have a violation of the integrity of the case, a break in the insulation of wires, a faulty power-up indication, with signs of electrical voltage on the case;
- 5) put foreign objects on computer equipment and peripheral equipment.

It is prohibited under voltage:

- 1) to clean dust and dirt from electrical equipment.
- 2) to check the operability of electrical equipment in unsuitable for operation premises with conductive floors, raw, not allowing grounding accessible metal parts.
- 3) to carry out repairs of computer equipment and peripheral equipment.

Repair of electrical equipment is carried out only by technicians in compliance with the necessary technical requirements.

In order to avoid electric shock, when using electrical appliances, one should not touch simultaneously any pipelines, radiators, metal structures connected to the ground.

In order to eliminate the danger of electric shock, the following electrical safety rules must be observed:

- 1) Visual inspection of the electrical wiring of the equipment in the absence of any insulation problems before switching on the electrical device to the supply network.
- 2) In the case of detection of those, you must immediately disconnect the electrical device from the mains before correcting the problem.

- 3) The prohibition of contact with devices that are naturally grounded when electrical equipment is on.

GOST 12.1.019-79 contains the following items:

- 1) it is necessary to apply protective sheaths to live parts;
- 2) ensure the safe location of live parts;
- 3) use insulation for them, which can be working, additional, double and reinforced;
- 4) apply workplace insulation;
- 5) to control the current-carrying parts.

According to SanPiN 2.2.2 / 2.4.1340-03, the following requirements must be observed when operating a computer:

- 1) Electrical equipment must be factory-made. And there must be compliance of electrical equipment with the requirements of state standards and technical conditions;
- 2) During operation and maintenance, it is necessary to comply with the requirements of the passport of electrical equipment and operating manuals, which were developed by the manufacturer.

In addition to all of the above, you can apply organizational and technical measures to ensure electrical safety, for example, affix marking parts of electrical equipment; use warning signals, signs, labels, warning signs; paint over current-carrying parts and resort to light-signaling.

SanPiN 2.2.2 / 2.4.1340-03 regulates the following security measures when working with a computer:

- 1) The presence of artificial and natural lighting in the workplace during the operation of a personal computer;
- 2) The maximum duration of continuous work with the monitor without a regulated break is 1 hour.
- 3) Providing window openings with such adjustable devices as: blinds, curtains, external visors to eliminate the direct brilliance due to the sun's rays;

- 4) The presence of a non-reflecting reflector having a protective angle of at least 40 degrees for local lighting fixtures.
- 5) The distance from the monitor screen to the eyes should be in the range of 600-700 mm, but no closer than 500 mm.

5.3 Ecological safety

This subsection considers the nature of the impact of the projected solution on the environment. When using these devices, there is no harm to the atmosphere and hydrosphere, since there are no emissions of harmful substances into the air and water.

In the event of a malfunction of the device, this technology also passes recycling. Before disposing of the equipment, it is necessary to write off, to confirm the equipment malfunction, to disassemble the specialists, to determine what will be recycled and refined. Processing of materials such as plastic, metal, is carried out on special equipment, and turns into raw materials for the manufacture of new technology.

5.4 Safety in emergency situations

5.4.1 Analysis of probable emergencies that may be initiated by the object of research

According to GOST R 22.0.02-94, an emergency situation is defined as a situation in a certain territory that has developed as a result of an accident, a catastrophe, a dangerous natural phenomenon, a natural or other disaster that may or has already caused human casualties, damage to human health or the surrounding nature. environment, violation of living conditions of people and significant material losses.

In case of consideration of emergencies, the cause of which may be the object of research, and the object, in turn, is the data of patients with diabetes, the occurrence of emergency situations is impossible.

5.4.2 Analysis of probable emergencies that may occur in the laboratory during research

Emergency situations in the laboratory may be the result of emergencies of a technogenic nature, the causes of which may be:

- a. Broken power wires, ground faults and other damage;
- b. Work on faulty equipment;
- c. Severe safety violations.

One of the consequences of emergency situations in the laboratory can be a fire, which can cause numerous losses among people, equipment and facilities in general.

5.4.3 Justification of measures to prevent emergencies and the development of procedures in the event of an emergency

1. In all cases of broken power wires, ground faults and other damage, the appearance of burning, immediately turn off the power and inform the manager about the emergency situation;
2. Do not start work until troubleshooting;
3. In case of fire, smoke:
 - 1) Immediately inform the fire brigade by telephone “01”, notify the workers, inform the head of the department, report a fire to the security post.
 - 2) Open the emergency exits from the building, de-energize the power supply, close the windows and close the doors.

- 3) Start fire extinguishing with primary fire extinguishing agents, if this is not associated with a risk to life.
 - 4) Arrange a fire brigade meeting.
 - 5) Leave the building and be in the evacuation zone.
4. In the event of an accident:
- 1) Immediately organize first aid to the victim and, if necessary, deliver it to the medical organization.
 - 2) Take urgent measures to prevent the development of an emergency or other emergency situation and the impact of traumatic factors on other persons.
 - 3) Save the situation as it was at the time of the incident, if it does not threaten the life and health of other people and does not lead to a catastrophe, an accident or other extraordinary circumstances, and if it is impossible to save it, fix the situation until make plans, carry out other activities).

Conclusion on the section Social responsibility

This section provided a description of social responsibility that accompanies the implementation of final qualifying work.

Industrial and environmental safety were described, various harmful and dangerous factors and methods of combating them were identified. In addition, a list of measures to reduce the threat in the event of an emergency was given, and legal and organizational security issues were examined. On top of this, the most important points of the organizational arrangements for the design of the working area are presented.

Conclusion

- 1) A review of the literature on relevant topics was made, information was obtained about brain structures that are associated with cognitive functions;
- 2) Analyzed data obtained by the method of MRS. Significant increases were found for metabolites creatine, creatine phosphate in the posterior part of the hippocampus in patients with type 1 and type 2 diabetes;
- 3) Automatic segmentation of images obtained as a result of MRI studies of patients with diabetes mellitus;
- 4) According to the Free Surfer, the volumes of gray and white matter of the brain are calculated and a significant decrease in the volume of gray matter and an increase in white matter in diabetic patients is revealed.

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Appendices

Appendix 1

Counter-all script operation algorithm

Recon-all is a batch program whose work consists of 30 steps, the execution of which takes an average of 30 hours to complete one image processing.

Structural images are placed in a specific directory hierarchy and set in a variable environment. Suppose there is a folder "structural", where the structural images of objects. Under "structural", there are folders "SUBJ1", "SUBJ2", "CON14", etc. for each item. Structural images are placed in "structural / SUBJ1 / mri / orig / 001.mgz". If there are several images for of this processing, "002.mgz" is used, etc. (If the original format of the file is not MGZ, you need to convert it).

structural

|--SUBJ1

|--mri

|--orig

|--001.mgz

|--002.mgz

Then the environment variables are set in the Linux shell:

```
setenv SUBJECTS_DIR $PWD
```

1. Motion correction MC (motion correction and compliance).

- Entrance: mri/orig/00?.mgz
- Output: mri/orig.mgz (через mri/rawavg.mgz)

If there are several structural images (001.mgz, 002.mgz, etc.), then motion correction will be made and created rawavg.mgz.

If only one image (001.mgz), it simply copies the file and renames it to rawavg.mgz.

```
cp CON14/mri/orig/001.mgz CON14/mri/rawavg.mgz
```

Then it matches mri_convert:

```
mri_convert CON14/mri/rawavg.mgz CON14/mri/orig.mgz --conform
```

Conform is performed to make a voxel size of $1 \times 1 \times 1$ mm and the same number of voxels (256) along the x, y, z directions (iso). Data is recorded in orig.mgz.

2. Uneven intensity normalization (non-uniform (NU) intensity normalization)

- Entrance: mri/orig.mgz
- Output: mri/nu.mgz

```
mri_nu_correct.mni --i orig.mgz --o nu.mgz --n 2
```

Nonparametric (non-uniform) intensity normalization (N3) corrects the intensity non-uniformity in the MR data, which is done relative to several data assumptions. This item runs the MINC program 'nu_correct', in which, by default, four iterations. The -niterations specification checkbox occurs in a slightly different number of iterations.

3. Transformation Talairach.

- Entrance: mri/nu.mgz
- Output: transform/talairach.auto.xfm

```
talairach_avi --i nu.mgz --xfm transforms/talairach.auto.xfm
```

It calculates affine transformation from volume to the Orig Atlas MNI305 using the MINC mritotal program via the FreeSurfer script, which is called talairach. Several subsequent programs use talairach coordinates as seed points.

It is possible, and even necessary, to check how well the talairach registration is used:

```
tkregister2 --s subjid -fstal
```

tkregister2 allows you to compare Orig volume and volume talairach, then re-creates Orig space. Running "tkregister2 -help" provides additional information. It is created mri / transform / talairach.auto.xfm and talairach.xfm. This step is long lasting.

4. Intensity normalization (INorm 1) – Intensity normalization.

- Entrance: mri/nu.mgz
- Output: mri/T1.mgz

```
mri_normalize -g 1 nu.mgz T1.mgz
```

This step normalizes the intensity of the Orig volume and places the result in mri / T1.mgz. Attempts to correct fluctuations in intensity that could make segmentation based on intensity are much more difficult. The intensities for all voxels are scaled so that the average intensity of the white matter is 110. If there are problems with normalization, users can add control points. See also Normalization2.

5. Skull strip – Skull selection.

- Entrance: mri/nu.mgz
- Output: mri/brainmask.mgz, mri/brainmask.auto.mgz

```
mri_em_register -skull nu.mgz
```

```
/usr/local/freesurfer/average/RB_all_withskull_2008-03-26.gca
```

```
transforms/talairach_with_skull.lta
```

Removes the skull from mri / T1.mgz and saves the result in mri /

brainmask.auto.mgz and mri / brainmask.mgz. Runs the mri_watershed program. If

the skull compartment fails, users can specify the starting points (-wsseed) or

change the threshold (-wsthresh, -wsmore, -wsless).

Stage -autorecon1 ends here.

6. EM (GCA) Registration (-<no>gcareg) – EM (GCA) registration.

- Entrance: mri/nu.mgz, mri/brainmask.mgz
- Output: mri/transforms/talairach.lta

```
mri_em_register -mask brainmask.mgz nu.mgz
```

```
/usr/local/freesurfer/average/RB_all_2008-03-26.gca transforms/talairach.lta
```

Computes a transform for leveling mri / nu.mgz in GCA atlas, which by default is located in FREESURFER_HOME / average (see -gca flag for more information). Creates a file mri / transforms / talairach.lta.

Stage -autorecon2 starts here.

7. CA Normalize (-<no>canorm) – CA Normalization.

- Entrance: mri/nu.mgz, mri/brainmask.mgz
- Output: mri/norm.mgz

```
mri_ca_normalize -mask brainmask.mgz nu.mgz
/usr/local/freesurfer/average/RB_all_2008-03-26.gca transforms/talairach.lta
norm.mgz
```

Further normalization based on the GCA model. Creates mri / norm.mgz.

8. CA Register (--<no>careg) – CA Регистрация.

- Entrance: mri/norm.mgz, mri/brainmask.mgz
- Output: talairach.m3z

```
mri_ca_register -align-after -nobigventricles -mask brainmask.mgz -T
transforms/talairach.lta norm.mgz /usr/local/freesurfer/average/RB_all_2008-03-
26.gca transforms/talairach.m3z
```

Computes a nonlinear transformation for matching with a GCA Atlas (Groupe Scolaire ATLAS). Creates the file mri / transform / talairach.m3z.

This step lasts a long time, about 10 hours.

9. Remove neck (--<no>rmneck) – Neck removal.

- Entrance: mri/nu.mgz
- Output: mri/nu_noneck.mgz

```
mri_remove_neck -radius 25 nu.mgz transforms/talairach.m3z
/usr/local/freesurfer/average/RB_all_2008-03-26.gca nu_noneck.mgz
```

The neck area is removed from the NU-corrected volume mri / nu.mgz. Allows the use of the transformation calculated from the previous CA register. Creates a file mri/nu_noneck.mgz.

10. EM Registration, with Skull (--<no>skull-lta) – EM registration, with skull.

- Entrance: mri/nu_noneck.mgz
- Output: mri/transforms/talairach_with_skull.lta

```
mri_em_register -skull -t transforms/talairach.lta nu_noneck.mgz
/usr/local/freesurfer/average/RB_all_withskull_2008-03-26.gca
transforms/talairach_with_skull.lta
```

Computes a transform to align the volume of `mri / nu_noneck.mgz` with the volume of the GCA, where there is a skull. Creates a file `mri/transforms/talairach_with_skull.lta`.

11. CA Label (-<no>calabel) – CA Метка.

- Entrance: `mri/norm.mgz`, `mri/transforms/talairach.m3z`
- Output: `mri/aseg.auto.mgz`, `mri/aseg.mgz`, (through `mri/aseg.auto_noCCseg.mgz`)

```
mri_ca_label -align -nobigventricles norm.mgz transforms/talairach.m3z
/usr/local/freesurfer/average/RB_all_2008-03-26.gca aseg.auto_noCCseg.mgz
mri_cc -aseg aseg.auto_noCCseg.mgz -o aseg.auto.mgz CON14
```

Выполняется метка подкорковых структур, основанная на модели GCA. Создает файлы `mri/aseg.auto.mgz` and `mri/aseg.mgz`.

12. ASeg Stats (-<no>segstats) – ASEG Статистика.

Вычисляет статистику по сегментированным подкорковым структурам, найденных в `mri/aseg.mgz`. Записывает вывод в файл `stats/aseg.stats`.

13. Normalization2 (-<no>normalization).

- Entrance: `mri/norm.mgz`, `mri/aseg.mgz`, `mri/brainmask.mgz`
- Output: `mri/brain.mgz`

```
mri_normalize -aseg aseg.mgz -mask brainmask.mgz norm.mgz brain.mgz
mri_mask -T 5 brain.mgz brainmask.mgz brain.finalsurfs.mgz
```

Performs a second (primary) intensity correction using only the brain volume as an Entrance (so this should be done after the skull is separated). Intensity correction works better when the skull is removed. Creates a new volume `brain.mgz`. The `-autorecon2-cp` stage starts here. If the `-noaseg` flag is used, then `aseg.mgz` is not used in `mri_normalize`.

14. WM Segmentation (-<no>segmentation) – WM Segmentation.

- Entrance: `brain.mgz`

- Output: wm.seg.mgz

mri_segment brain.mgz wm.seg.mgz

mri_edit_wm_with_aseg -keep-in wm.seg.mgz brain.mgz aseg.mgz

wm.asegedit.mgz

mri_preteess wm.asegedit.mgz wm norm.mgz wm.mgz

Tries to separate white matter from everything else. Entrance mri / brain.mgz, and Output mri / wm.mgz. Uses intensity, neighborhood, and smoothness limits. This is the volume that is edited when manually fixing defects. Calls mri_segment, mri_edit_wm_with_aseg and mri_preteess. To keep the previous changes, you need to contact -keepwmedits. If -noaseg is used, mri_edit_wm_aseg is skipped..

15. Cut/Fill (-<no>fill)

- Entrance: wm.mgz
- Output: filled.mgz

mri_fill -a ../scripts/ponscc.cut.log -xform transforms/talairach.lta -segmentation aseg.auto_noCCseg.mgz wm.mgz filled.mgz

Subcortical mass is created, from which the Orig surface is created. The midbrain is excised from the brain, and the hemispheres are separated from each other. The left hemisphere is converted to binary up to 255. The right hemisphere is converted to binary up to 127. Entrance mri / wm.mgz and the output is mri / filled.mgz Calls mri_fill. If the cut fails, the starting points can be set (see -Cc-CRS, -pons-CRS, -lh-CRS, -rh-CRS). The actual points used for the corpus callosum and bridge cutting planes can be found in scripts / ponscc.cut.log.

The stage -autorecon2-WM starts here. This is the last stage of bulk processing. If -noaseg is used, then aseg.mgz is not used mri_fill.

16. Tessellation (-<no>tessellate) – Mosaic.

- Entrance: filled.mgz, norm.mgz
- Output: urf/lh.orig.nofix (through filled preteess255.mgz)

mri_preteess ../mri/filled.mgz 255 ../mri/norm.mgz ../mri/filled-preteess255.mgz

mri_tessellate ../mri/filled-preteess255.mgz 255 ../surf/lh.orig.nofix

mris_extract_main_component ../surf/lh.orig.nofix ../surf/lh.orig.nofix

This is a step when creating an Orig surface (i.e., surf /? H.orig.nofix). The surface is created by covering the filled hemisphere with triangles. Run mris_tessellate. Places where points of triangles meet are called vertices. Creates a file surf /? H.orig.nofix. Note: Topology fix is created surface ?h.orig.

17.Orig Surface Smoothing (-<no>smooth1, -<no>smooth2) – Smoothing Orig Surface.

- Entrance: surf/lh.orig.nofix
- Output: surf/lh.smoothwm.nofix

```
mris_smooth -nw ../surf/lh.orig.nofix ../surf/lh.smoothwm.nofix
```

After creating the mosaic, the Orig surface is very uneven, because each triangle is on the edge of the voxels of the face and is at a right angle to each other. The position of the vertex is somewhat corrected here to reduce the angle. This is only necessary for the “bloat” process. Creates surf surf /? H.smoothwm (.nofix). Causes mris_smooth. Smooth1 step is performed only after creating a mosaic and smooth2 step only after fixing the topology.

18.Inflation (-<no>inflate1, -<no>inflate2) – « Inflation ».

- Entrance: surf/lh.smoothwm.nofix
- Output: surf/lh.inflated.nofix, lh.sulc, lh.curv, lh.area

```
mris_inflate -no-save-sulc ../surf/lh.smoothwm.nofix ../surf/lh.inflated.nofix
```

Inflating the surf /? H.smoothwm (.nofix) surface to create a surf /? H.inflated. The inflation mechanism tries to minimize metric distortion so that distances and areas are preserved (that is, surfaces do not stretch). In principle, how to inflate a paper bag, not a balloon. Inflate1 step after creating a mosaic and inflate2 step only after fixing the topology. Call mris_inflate. Создаются ?h.inflated, ?h.sulc, ?h.curv, and ?h.area.

19. QSphere (-<no>qsphere).

- Entrance: lh.inflated.nofix
- Output: lh.qsphere.nofix

```
mris_sphere -q ../surf/lh.inflated.nofix ../surf/lh.qsphere.nofix
```


This is the initial stage of automatic topology fixation. This is a quasi-homeomorphic-spherical transformation of the pumped surface, intended for localization of topological defects for the subsequent fixing of the automatic topology. Call `mrisc_sphere`. Creates a surf `/? surf/?h.qsphere.nofix`.

20. Automatic Topology Fixer (`-<no>fix`) – Automatic fixation topology.

- Entrance: `qsphere.nofix`
- Output: `lh.orig`

```
mrisc_fix_topology -mgz -sphere qsphere.nofix -ga CON14 lh
```

```
mrisc_euler_number ../surf/lh.orig
```

```
mrisc_remove_intersection ../surf/lh.orig ../surf/lh.orig
```

It finds topological defects (i.e. holes in the filled hemisphere) using surf `/? H.qsphere.nofix` and changes the surface `Orig` (surf `/? H.orig.nofix`) to remove defects. Changes the number of vertices. All defects will be removed, and the user will have to check the `Orig` surface in volume to make sure that it looks appropriate. Calls `mrisc_fix_topology`. Creates surf `/? H.orig` (by iteratively fixing surf `/? H.orig.nofix`).

21. Final Surfaces (`-<no>finalsurfs`) – End surfaces.

- Entrance: `lh.orig`
- Output: `lh.white`, `lh.pial`, `lh.thickness`, `lh.curv`

```
mrisc_make_surfaces -noaparc -mgz -T1 brain.finalsurfs CON14 lh
```

Creates `H.white` and `H.pial` surfaces, as well as thickness (`? H.thickness`) and curvature (`? H.curv`). The white surface is created by "pushing" the `Orig` surface so that it closely follows the white-gray intensity gradient, as detected in the T1 volume. The surface of the pia mater is created by expanding the white surface so that it accurately follows the intensity gradient of CSF gray, as found in T1 volume. Causes `mrisc_make_surfaces`.

22. Cortical Ribbon Mask (`-<no>cortribbon`) – Stripe cortical mask.

```
mrisc_calc -o lh.area.mid lh.area add lh.area.pial
```

```
mrisc_calc -o lh.area.mid lh.area.mid div 2
```

```
mrisc_calc -o lh.volume lh.area.mid mul lh.thickness
```

Creates binary volumetric masks of the cortical band, that is, each of the voxels is either 1 or 0 depending on whether it falls into the band or not. Stored in? H.ribbon.mgz. Uses mgz regardless of whether the -mgz option is used. -autorecon2 stage ends.

23.Repeat step 17.

- Output: lh.smoothwm

```
mris_smooth -n 3 -nw ../surf/lh.white ../surf/lh.smoothwm
```

24.Repeat step 18.

- Entrance: lh.smoothwm
- Output: lh.inflated

```
mris_inflate ../surf/lh.smoothwm ../surf/lh.inflated
```

```
mris_curvature -thresh .999 -n -a 5 -w -distances 10 10 ../surf/lh.inflated
```

25.Spherical Inflation (-<no>sphere) – Spherical "inflation".

- Entrance: lh.inflated
- Output: lh.sphere

```
mris_sphere ../surf/lh.inflated ../surf/lh.sphere
```

“Inflates” the Orig surface into the sphere while minimizing the distortion metric. This step is necessary in order to register the surface of a spherical atlas (also known as a spherical morph). Call mris_sphere. Creates a surf /? H.sphere.

Stage -autorecon3 starts here.

26.Ipsilateral Surface Registration (Spherical Morph) (-<no>surfreg) –
Registration of ipsilateral surfaces (Spherical Morph).

- Entrance: lh.sphere
- Output: lh.sphere.reg

```
mris_register -curv ../surf/lh.sphere
```

```
/usr/local/freesurfer/average/lh.average.curvature.filled.buckner40.tif
```

```
../surf/lh.sphere.reg
```

Registers the Orig surface to the spherical atlas through the surf /? H.sphere. The first surfaces are coarsely registered by combining large-scale folding models

found in? H.sulc, and then fine tuning using small-scale elements, as in? H.curv.
Causes mris_register. Creates a surf /? H.sphere.reg.

27. Contralateral Surface Registration (Spherical Morph) (-<no>contasurfreg) –
Registration of the contralateral surface (Spherical Morph).

```
mris_jacobian ../surf/lh.white ../surf/lh.sphere.reg ../surf/lh.jacobian_white
```

The same, but to the contralateral atlas. Creates lh.rh.sphere.reg and
rh.lh.sphere.reg.

28. Average Curvature (-<no>avgcurv) – Average Curvature.

- Entrance: lh.sphere.reg
- Output: lh.avg_curv

```
mrisp_paint -a 5
```

```
/usr/local/freesurfer/average/lh.average.curvature.filled.buckner40.tif#6  
../surf/lh.sphere.reg ../surf/lh.avg_curv
```

Oversampling the average curvature of the subject from the atlas. Allows the
user to display activity on the surface of an individual with a folding pattern (ie,
anatomy) of the group. Causes mrisp_paint. Creates surf surf /? H.avg_curv.

29. Cortical Parcellation (-<no>cortparc, -<no>cortparc2) – Кортикальная
парцелляция.

- Entrance: mri/aseg.mgz, surf/lh.sphere.reg
- Output: label/lh.aparc.annot

```
mris_ca_label -aseg ../mri/aseg.mgz CON14 ЛХ ../surf/lh.sphere.reg
```

```
/usr/local/freesurfer/average/lh.curvature.buckner40.filled.desikan_killiany.2007-  
06-20.gcs ../label/lh.aparc.annot
```

Assigns neuroanatomical labels to each location on the surface of the cortex.
It includes both geometric information obtained from the cortical model (grooves
and curvatures), and a neuroanatomical convention. Calls mris_ca_label, -cortparc,
which creates the label /? H.aparc.annot, and -cortparc2, which creates
/label/?h.aparc.a2005s.annot.

30. Parcellation Statistics (-<no>parcstats) – Parcel Statistics.

- Entrance: stats/lh.aparc.stats, label/lh.aparc.annot
- Output: label/aparc.annot.ctab

```
mris_anatomical_stats -mgz -f ../stats/lh.aparc.stats -b -a -c ../label/lh.aparc.annot
../label/aparc.annot.ctab CON14 lh
```

It launches `mris_anatomical_stats` and creates a summary table for bark parcellation statistics for each structure, including: 1. Name of the structure 2. number of peaks 3. total surface area 4. Total volume of gray matter 5. average cortical thickness 6. standard error of cortical thickness 7. integrated rectified average curvature 8. integrated rectified Gaussian curvature 9. folding index 10. inherent curvature index. For `-parcstats`, the file is saved to stats /? H.aparc.stats. For `-parcstats2`, the file is saved in stats /? H.aparc.a2005s.stats.

31.Repeat step 29 - cortical parcellation.

```
mris_ca_label -aseg ../mri/aseg.mgz CON14 LH ../surf/lh.sphere.reg
/usr/local/freesurfer/average/lh.atlas2005_simple.gcs ../label/lh
.aparc.a2005s.annot
```

32.Repeat Step 30 - Parcel Statistics.

```
mris_anatomical_stats -mgz -f ../stats/lh.aparc.a2005s.stats -b -a -c
../label/lh.aparc.a2005s.annot ../label/aparc.annot .a2005s.ctab CON14
lh
```

33.Repeat steps 16-32 for the right hemisphere.

34. ASeg Stats – ASEG Statistics.

```
mri_segstats -seg mri/aseg.mgz -sum stats/aseg.stats -pv mri/norm.mgz -
excludeid 0 -brain-vol-from-seg -brainmask mri/brainmask.mgz -in
mri/norm.mgz -in-intensity-name norm -in-intensity-units MR -etiv -subject
CON14 -surf-wm-vol -ctab /usr/local/freesurfer/ASegStatsLUT.txt
```

35.Cortical ribbon mask – Stripe cortical mask.

```
mris_volmask -label_left_white 2 -label_left_ribbon 3 -
label_right_white 41 -label_right_ribbon 42 -save_ribbon -
save_distance CON14
```

36. AParc κ ASEG

```
mri_aparc2aseg -s CON14 -volmask
```

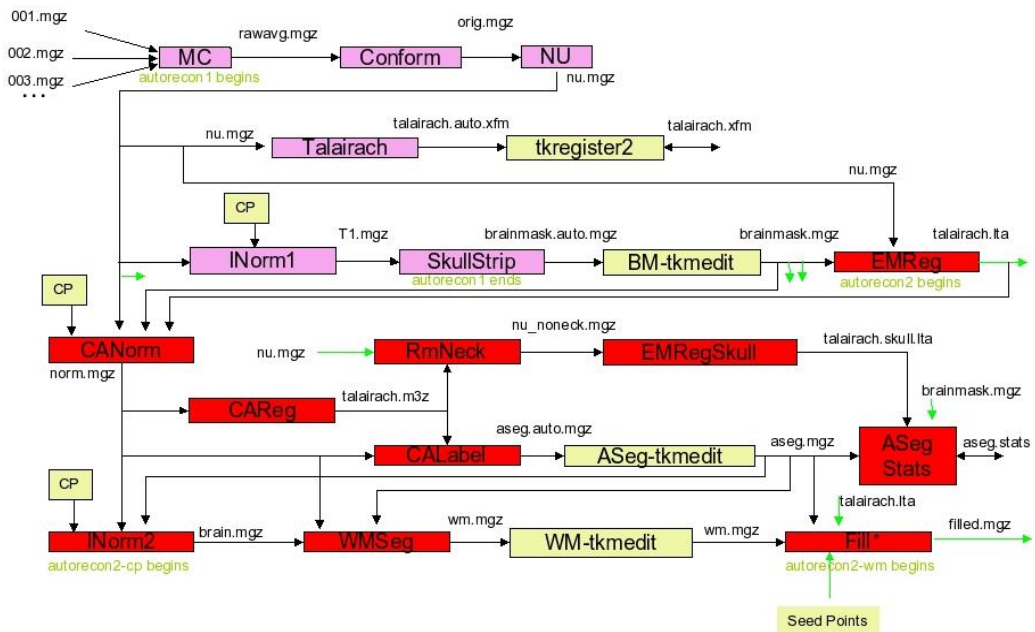
```
mri_aparc2aseg -s CON14 -volmask -a2005s
```

37. WMParc

```
mri_aparc2aseg -s CON14 -labelwm -hypo-a-WM -rip unknown -  
volmask -o mpr / wmparc.mgz -ctxseg aparc + aseg.mgz
```

```
38. mri_segstats --seg mri/wmparc.mgz --sum stats/wmparc.stats --pv
```

```
mri/norm.mgz --excludeid 0 --brain-vol-from-seg --brainmask mri/brainmask.mgz --  
in mri/norm.mgz --in-intensity-name norm --in-intensity-units MR --etiv --subject  
CON14 --surf-wm-vol --ctab /usr/local/freesurfer/
```



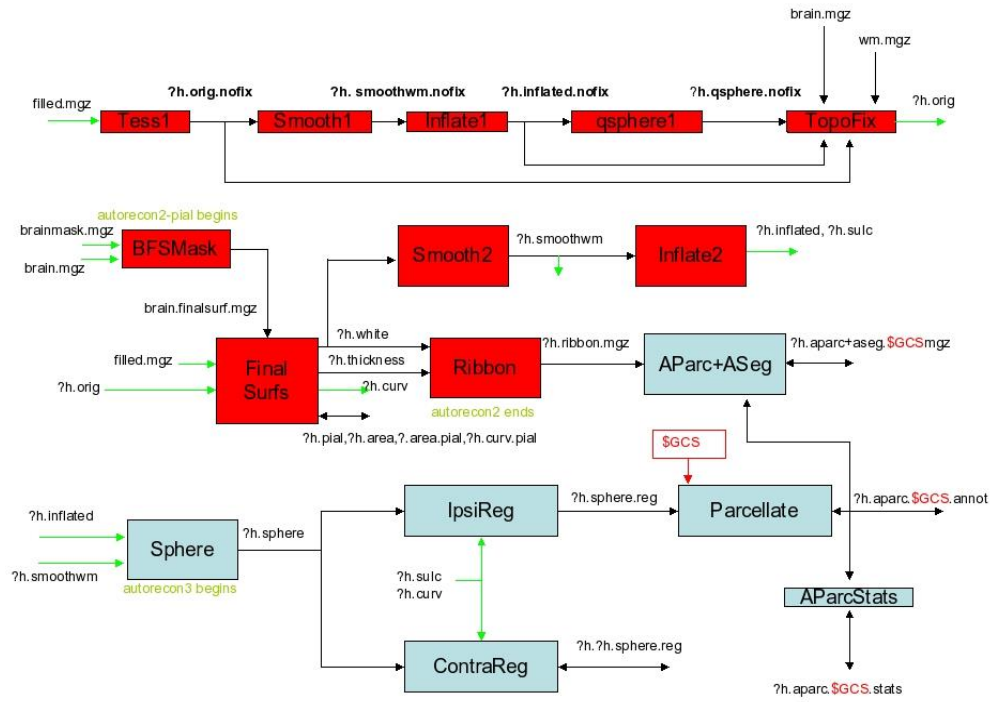


Figure 1 - The process of autoresegmentation using FreeSurfer