ORIGINAL STUDY

Инсулинорезистентность и ее возможные личностные стресс-модераторы

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Актуальность. *Инсулинорезистентность (ИР) в настоящее время активно исследуется специалистами различного профиля. Перспективным представляется изучение роли стресса в формировании ИР.*
Цель. *Изучение ассоциаций ИР с личностными стресс-модераторами (самоотношением, локусом контроля, стратегиями совладания), а также с образом жизни.*
Материалы и методы. *В исследование были включены 63 пациента (средний возраст 48,2±11,7), из них 16 мужчин. У 26 из них был диагностирован сахарный диабет 2 типа (СД2), у 10 – нарушенная толерантность к глюкозе (НТГ), у 6 – нарушенная гликемия натощак (НГН), у 21 на момент включения результаты перорального глюкозотолерантного теста соответствовали норме. Определяли уровень гликированного гемоглобина HbA_{1c} и коэффициент ИР с использованием HOMA (homeostasis model assessment). Для оценки личностных стресс-модераторов использовались валидные опросники, широко применяемые в психологических исследованиях.*
Результаты. *Выявлены значимые связи между ИР и личностными стресс-модераторами. Позитивное самоотношение сопряжено с уменьшением риска развития ИР ($p<0,05$), что можно объяснить снижением риска возникновения стресса. Ассертивная (настойчивая) стратегия совладания наиболее выражена у обследуемых с низкой ИР ($p<0,05$). Личностные характеристики также могут влиять на формирование образа жизни человека, его пищевые привычки, физическую нагрузку и, как следствие, вероятно, на ИР. Обнаружены связи между высоким уровнем ИР и «нездоровыми» алиментарными предпочтениями ($p<0,05$). Такие предпочтения оказались ассоциированы также и с личностными характеристиками, в частности внешним локусом контроля (экстернальностью), менее позитивным самоотношением, пассивными стратегиями совладания ($p<0,05$). Для обследуемых с высокой ИР нехарактерны регулярные физические нагрузки. При этом обнаружена прямая корреляция частоты физических нагрузок и ассертивной стратегии совладания ($p<0,01$). Пол и возраст в выборке не демонстрируют связи с ИР. Семейные люди имеют более высокий уровень ИР ($p<0,05$).*
Заключение. *Выявлена значимая связь между ИР и личностными стресс-модераторами, в число которых входят самоотношение и стратегии совладания. Помимо прямого влияния на уровень стресса, личностные черты могут оказывать на ИР и косвенное влияние, во многом определяя образ жизни человека, в частности особенности питания и физическую активность. Тот факт, что состоящие в браке имеют более высокий уровень ИР, может быть трактован неоднозначно и нуждается в дальнейшем исследовании.*
Ключевые слова: *инсулинорезистентность; стресс-модераторы; сахарный диабет 2 типа; самоотношение; стратегия совладания*

Insulin resistance and its possible personal stress moderators

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Background. *Recently, insulin resistance (IR) has been actively investigated by experts in various fields. Here we aim to study the effect of stress on the development of IR.*
Objective. *To study the associations between IR and personal stress moderators (self-attitude, locus of control and coping strategies) as well as the related performance lifestyles.*
Materials and methods . *The study included 63 patients (16 men; mean age, 48.2 ± 11.7 years). Of these participants, 26 were diagnosed with type 2 diabetes mellitus, 10 with impaired glucose tolerance, 6 with impaired fasting glucose and 21 with normal glucose tolerance. The levels of HbA1c and IR ratio were determined using HOMA. Well-known psychological assessment questionnaires were used to assess the effect of personal stress moderators.*
Results. *There was a significant relationship between IR and personal stress moderators. A positive self-attitude was associated with a lower risk of IR ($p < 0.05$), which can be explained by a decrease in the risk of developing stress. Assertive coping strategies were most pronounced in subjects with a low level of IR ($p < 0.05$). Personal characteristics also determined an individual's lifestyle, which may have an impact on the increase in IR. There was an association between high levels of IR and unhealthy alimentary preferences ($p < 0.05$). Such preferences were also associated with personal characteristics, such as external locus of control, less positive self-attitude and passive coping strategies ($p < 0.05$). People with high IR rarely engage in a regular physi-*

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cal activity; there was a direct correlation between the frequency of physical activity and assertive coping strategies ($p < 0.01$). Married participants had high levels of IR ($p < 0.05$).
***Conclusion**. There were significant relationships between IR and personal stress moderators, such as self-attitude and coping strategies. Besides the direct effects on stress levels, personality traits may also indirectly increase the risk of IR by influencing the individual's lifestyle. There is a need to investigate the fact that married people have higher levels of IR.*
***Keywords:** insulin resistance; stress-moderators; type 2 diabetes; self-attitude; coping strategies*

Insulin resistance (IR) is one of the key factors in the pathogenesis of type 2 diabetes mellitus (DM2), which has attracted great interest in the problem, but at the same time requires a comprehensive approach to its study. One of the most promising fields of research in this area is the study of the role of stress in the development of IR, on which multiple studies have already been published [1-5]. However, in most of these studies stress is regarded as a purely external factor in relation to a person, for example, the living conditions of emigrants or social and economic situation [6-10]. Thus, the role of a subjective factor (associated with the individual characteristics of a patient) in the development of stress and its possible relationship with IR, is unknown.

It is thought that stress develops as a result of interaction between external and internal factors, i.e. particular aspects of the environment and the individual characteristics of a person [11-13]. External factors can have different natures, including economic, political and social factors, but they affect the person indirectly, acting through personal characteristics which can be called stress-moderators. Therefore, the same external factors can provoke significant variations in the dynamics and content of stress in different people. Various individual characteristics can be subjective moderators of stress. Thus, attention should be given to both those moderators which determine the time of stress onset and its severity and those which are responsible for human behaviour under stress and ways of processing it.

The first type of stress moderator includes features of self-awareness[1]: self-attitude, self-esteem and the locus of control. The second type, defining a person's behaviour under stress, is traditionally described in terms of 'coping' or 'coping strategy.' The coping strategies are typical ways a particular person overcomes stressful situations, the actions that they take (or do not take) when faced with stressful factors [2]. The influence of features of self-awareness, as well as coping strategies, on the development of stress has been successfully studied for a long time. It is hypothesised that this research may prove useful in the analysis of factors associated with the development of IR. However, to the best of our knowledge, this topic has not yet become the subject of study in either psychology or medicine.

In addition to direct influence on the level of stress, personal moderators can also indirectly affect the development of IR. Self-attitude and self-esteem act as key regulators of human behaviour [14]. A person's self-perception determines the goals which they set for themselves, the choice of ways to achieve them and the experiences which arise in the process of this achievement. The features of self-awareness ultimately influence the overall lifestyle and participate in the formation of a style of behaviour under certain conditions. In DM, lifestyle has a significant effect on the course of the disease [15]. Behavioural factors including dietary habits, physical activity and adherence to drug therapy, determine the risk of DM progression, as well as aggravation or reduction of IR. Therefore, not only personal characteristics themselves but also the lifestyle that forms as a result of their influence plays an important role in the development of IR.

Thus, the aim of this study was to investigate the associations of IR and personal stress-moderators including self-attitude, the locus of control, coping strategies and associated lifestyle.

MATERIALS AND METHODS

The design of the study was a cross-sectional (one-stage), non-interventional one.

The study included patients over the age of 18 years who were overweight or obese [body mass index (BMI) > 25 kg/m^2], had a HOMA-IR index > 2.77, with any disturbances in glucose metabolism (diagnosed impaired glucose tolerance (IGT), impaired fasting glucose (IFG) or DM2 with a known duration of <5 years, without drug-induced hypoglycaemic therapy) or a history of glucose metabolism disorders.

IR was assessed by determination of glucose and fasting insulin levels [homeostasis model assessment (HOMA)] with the calculation of the IR coefficient (HOMA-IR).

[1]Self-attitude determines a person's overall perception of themselves, the level of trust in themselves, emotions and feelings that arise regarding their own characteristics, and accordingly, the level and nature of experiences in a stressful situation. Self-assessment enables a person to correlate their own resources with the requirements of the situation, which is necessary to make a decision on the nature of actions under stress. The locus of control reflects a sense of control over one's own life, and therefore, the subjective readiness of a person to take responsibility for the development of events.

[2]There are various coping strategies, as well as ways to categorise them. One of the most useful classifications from a practical viewpoint enables structuring of strategies according to the level of a person's activity. Assertive behaviour can be considered as one of the most active ones, such as purposeful preparation and subsequent overcoming the stressful situation. The avoidance strategies are on the opposite pole, when a person prefers not to solve the problem, often due to uncertainty about their own resources to cope with the challenge.

This model developed by D. Matthews [16, 17] is widely used in clinical practice.

$$\text{Insulin Resistance (HOMA-IR)} = \frac{IRI0'}{FPG},$$

Where IRI is immunoreactive insulin and FPG is fasting plasma glucose.

Glycated haemoglobin (HbA1c) was evaluated for all patients on a D-10 analyser (Bio-Rad, Hercules, CA, USA) by high-pressure ion-exchange chromatography.

To evaluate personal stress-moderators, the following questionnaires were used, which are also widely used in psychological research and in clinical practice:

1. 'Questionnaire of self-attitude' (QSA) (V.V. Stolin, S.R. Panteleev) [18]

This questionnaire is designed to evaluate various features of a person's attitude towards themselves, such as self-respect, autosympathy (self-acceptance), self-interest and expectation of positive attitudes from others.

2. 'The level of subjective control' (LSC) (E.F. Bazhin, E.A. Golynkina, L.M. Etkind) [19]

This method enables a person to assess the subjective localisation of control over their own life, i.e. a person's confidence which they control its course (internal locus of control or internality), or that the course of events depends on the influence of external factors (external locus of control, or externality). This method includes numerous scales, such as internality in the field of achievements, failures, interpersonal, professional and family relationships, as well as in the sphere of control over their health.

3. 'Stress avoidance coping strategies' (SACS) by S. Hobfoll in the Russian-language adaptation by N. Vodopyanova, E. Starchenkova [20].

This method aims to identify the inherent behavioural strategies used in difficult life circumstances (under stress). It classifies strategies as assertive (insistent), aggressive, impulsive, antisocial, cautious, manipulative actions, avoidance, entry into social contact and search for social support.

4. To assess overall lifestyle, a questionnaire ('Lifestyle Traits') was developed, which enabled the evaluation of dietary habits and physical activity.
5. To assess individual demographic characteristics (marital status, educational level, employment, nature of professional activity), a questionnaire was also developed.

The data obtained were processed into descriptive statistics (mean, standard deviation, median, quartiles and minimum and maximum values). Statistical analysis was performed using the student's t-test, Mann–Whitney U test, Kruskal–Wallis rank test and Spearman's rs nonparametric correlation, depending on the distribution of the sample. The level of statistical significance selected was = 0.05.

ETHICS STATEMENT

The study was approved by the local ethics committee of the Federal State Budgetary Institution Endocrinology Research Center of the Russian Ministry of Health, Protocol No. 12, 22/10/2014.

RESULTS AND DISCUSSION

The study included 63 patients (mean age 48.20 ± 11.68 years), 16 of which were men. According to the results of the medical examination, including the oral prednisolone glucose tolerance test (PGTT), 26 of them were diagnosed with DM2, 10 with IGT and 6 with IFG, and 21 had normal PGTT results at the time of the test. The proportion of obese patients (BMI ≥ 30 kg/m2) was 69.8% (44 people). The clinical characteristics are summarised in Table 1.

The HOMA-IR index does not show significant associations with either the gender of respondents (p = 0.670, Mann–Whitney U test) or their age (rs = 0.067, p = 0.624).

A correlation analysis with HOMA-IR was performed, and HbA1c and components of two methods were designed for the investigation of self-awareness: QSA and LSC. Figure 1 shows the corresponding correlation galaxy, where only significant correlations are shown.

Fig. 1. Associations of self-attitude (QSA) with levels of IR and HbA1c

As seen in Figure 1, IR has close associations with various characteristics of self-attitude. Importantly, there is a negative correlation with the integral level of self-attitude. That is, the more negative the person refers to themselves, the higher is their IR indicator. Three separate components of the QSA questionnaire reveal associations between self-attitude and IR and suggest how stress can develop, which causes an increase in IR . Fig. 1 demonstrates that the highest correlation of IR and all components of the QSA questionnaire is found with 'Self-confidence.' A possible explanation may be that in a challenging situation, a person with low self-confidence is inclined to view their resources as obviously insufficient to cope with it. As a result, the level of stress is significantly increased. Because self-confidence is a personal characteristic, its impact on the assessment of the ratio of own resources and the requirements of the

Table 1

Clinical characteristics of the study sample

	Median	Mean	Min	Max
BMI, kg/m^2	31.94 (29.80; 41.03)	35.47 ± 9.62	19.57	64.06
HbA1c, %	5.90(5.46; 6.9)	6.53 ± 1.96	5.0	16.1
HOMA-IP	4.21 (3.02; 7.75)	6.08 ± 8.28	2.81	63.0

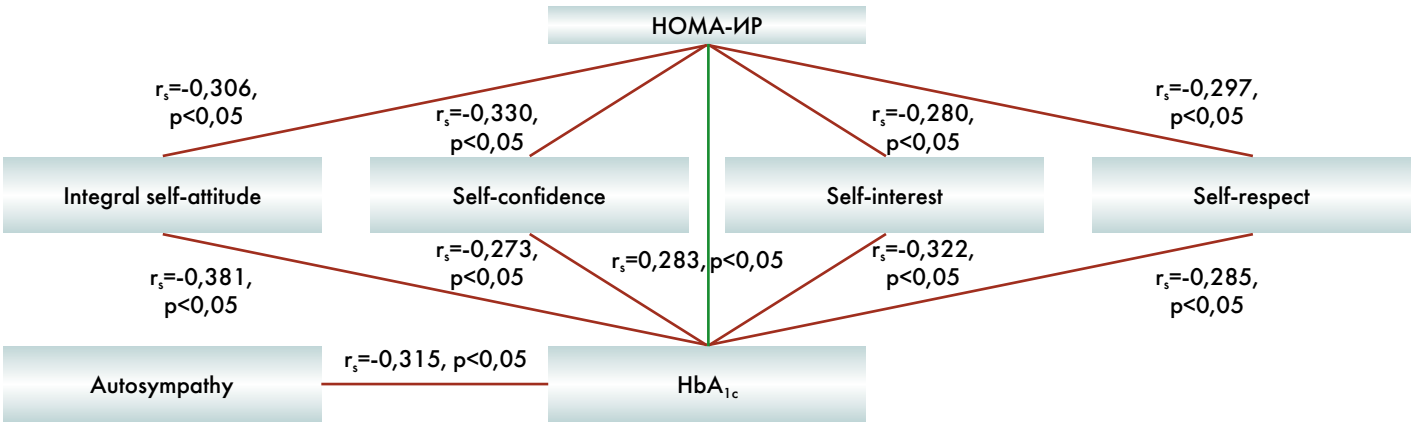


Fig. 1. Associations of self-attitude (QSA) with levels of IR and HbA_{1c}

situation is stable. In many, and probably even in most cases, a person believes that they are not capable (clever, strong) enough to cope with the challenge. The level of stress is chronically increased, which may contribute to the development of IR.

In addition to the lack of self-confidence, a high level of IR is also associated with weak 'Self-interest' and 'Self-respect.' Low values on these scales reflect a person's depreciation of themselves. Of all the scales of the questionnaire, these are the most reflective of the emotional component of self-attitude, the level of its negativity or positivity. Thus, patients with high level of IR are characterised by a more negative self-attitude. It forms a permanent negative background to their world perception, forcing them to expect only unfavourable events. Thus, instead of situational stress, they enter a situation of chronic stress; presumably, this may become an additional factor in IR development.

Figure 1 also shows the correlations of components of the QSA questionnaire with the level of HbA1c. Notably, the correlations coincide with those of IR, which is understandable given the close association between IR and the level of HbA1c (the correlation between them is direct). The only difference is that HbA1c has a negative correlation with the 'Autosympathy' scale, whereas IR has no correlation. However, this single difference does not change the essential interpretation of results and needs to be clarified in further studies.

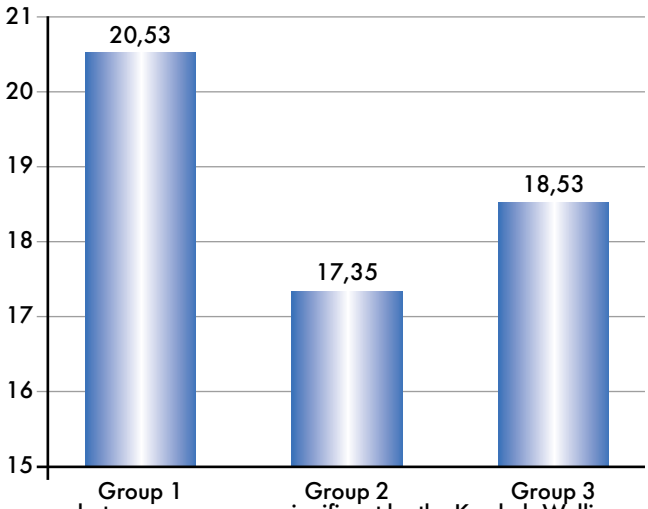
Interestingly, BMI does not show a significant correlation with the components of the QSA questionnaire, except with the scale of 'Self-consistency' ($rs = 0.603$, $p < 0.001$). Thus, the relationship between IR and self-attitude is different between IR and BMI.

Individually, the association of IR and the subjective locus of control is worth considering. Two characteristics of a person's self-consciousness, self-attitude and subjective locus of control, are closely related. Thus, a significant correlation is revealed between the general level of internality of the LSC technique and the integral self-attitude of the QSA technique ($rs = 0.383$, $p < 0.01$). However, despite this, the LSC has no correlation with the IR. It can be hypothesised that this characteristic does not have a significant effect on the development of stress. Therefore, the way a person treats themselves is more important than whether they consider themselves to be the cause of events happening to them.

Regarding associations of IR with coping strategies, it can be hypothesised that active strategies such as assertive behaviour or seeking social contact should reduce the level of stress, and therefore, be associated with a lower level of IR. Conversely, the avoidance strategy (as the most passive of all presented in the SACS methodology) should have a direct relationship with a high level of IR. It should be specifically noted that in this method, the strategy of passivity, in which a person refuses to solve emerging problems or to overcome difficulties, is not presented. The avoidance strategy implies activity anyway such as removal from a dangerous object, due to which the level of stress can be reduced. Therefore, the opposite pole of the assertiveness scale can be considered as passivity scale, the more assertive (insistent) a person is the less passive they are, and vice versa.

The conducted correlation analysis did not reveal significant associations between the scales of the SACS questionnaire and the level of HOMA-IR. At first glance, such results are discouraging and can be explained by either erroneous research hypotheses or by an incorrectly designed methodology, for example, ineffective (in this case) method for diagnosing coping strategies. However, it is possible that the associations between coping strategies and IR are non-linear. To test this hypothesis, the patients were divided into three equivalent-sized groups, according to the level of HOMA-IR (Group 1: 2.34 ± 0.81; Group 2: 4.39 ± 0.59; Group 3: 11.66 ± 12.83), and coping strategy scores were compared. This revealed that there is a non-linear relationship between the level of IR and the assertive behaviour strategy (Fig. 2).

As evident in Figure 2, people with the lowest level of IR are characterised by the highest level of assertive behaviour. This strategy is used least often by respondents with an average level of HOMA-IR. Finally, in the third group, assertive behaviour is slightly increased, while remaining markedly lower than that in the first group. Whatever the explanation for the non-linear relationship between assertiveness and IR, we suggest that active, purposeful behaviour and willingness to overcome the



Differences between groups are significant by the Kruskal–Wallis test, $p < 0.05$.
Differences between the groups 1 and 2 are significant by the Mann–Whitney test, $p < 0.05$.

Fig. 2. Pronouncement of assertive behaviour among respondents grouped according to HOMA-IR scores

obstacles encountered contributes to reducing the level of stress. In contrast, a refusal to do so provokes an increase in negative emotions related to stress, affecting the IR development. Notably, other scales of the SACS methodology do not reveal significant differences, including non-linear, with the level of HOMA-IR, which enables us to confirm the hypothesis that strategies of active/passive behaviour have the greatest influence on the development of IR.

The analysis of lifestyle characteristics and their association with the development of IR are presented in Figure 3 . Among all the questions related to physical activity, only one had significant associations with IR: 'How often do you specifically allocate time for exercise'? with seven gradations from 'never' to 'daily.' The distribution of frequency of responses is shown in Fig. 3.

The respondents most often chose '2 times a week' and '3–4 times a week'. Remaining answers were approximately distributed equally. A significant inverse correlation of frequency of physical activity and the level of HOMA-IR was found. Thus, the level of IR increases in the case when a person does not allocate time for physical activity. It is noteworthy that a direct correlation of frequency of physical activity and assertive coping strategy was also found ($rs = 0.332$, $p < 0.01$). Thus, more assertive patients also exhibit the purposeful management of their own physical activity, thereby reducing the risk of IR development.

A large block of questions in the questionnaire 'Lifestyle Traits' was devoted to nutrition. The answers to these questions reveal certain associations with IR. The answers to the question 'Which fats do you eat more often'? were distributed as seen in Fig. 4.

It is evident that the majority of respondents prefer vegetable fats. At the same time, there are significant differences between those who prefer vegetable fats and those who prefer ready-made sauces. The level of HOMA-IR in the first is 5.85 ± 9.01, while it is 8.69 ± 5.09 in the latter ($p < 0.05$, Mann–Whitney U test).

There is also a trend evident between these two groups on the 'Assertive actions' scale of SACS ($p = 0.065$, Mann–Whitney U test). People who prefer vegetable fats have more pronounced assertiveness compared to those who choose mayonnaise and other ready-made sauces (the average values on the 'Assertive actions' scale are 18.96 ± 3.71 and 16.83 ± 0.75, respectively). Although this difference is not significant, it can reflect a tendency of passivity, which causes difficulties in maintaining a healthy diet.

In the answer to the question 'What are your favourite and frequently eaten foods'? there is a significant association between the level of HOMA-IR and the preferences for certain products (Fig. 5).

Among the wide variety of products offered (16 items of product categories), only two have close associations with the IR level. Patients who prefer bread and sausage products

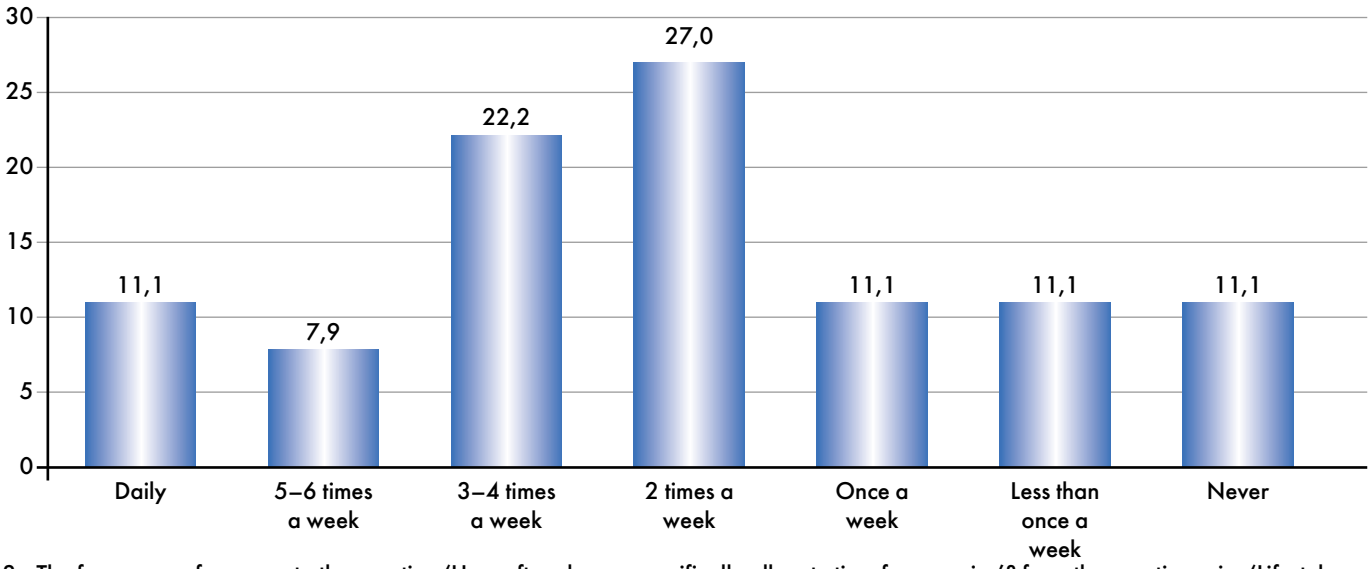


Fig. 3. The frequency of answers to the question 'How often do you specifically allocate time for exercise'? from the questionnaire 'Lifestyle Traits'

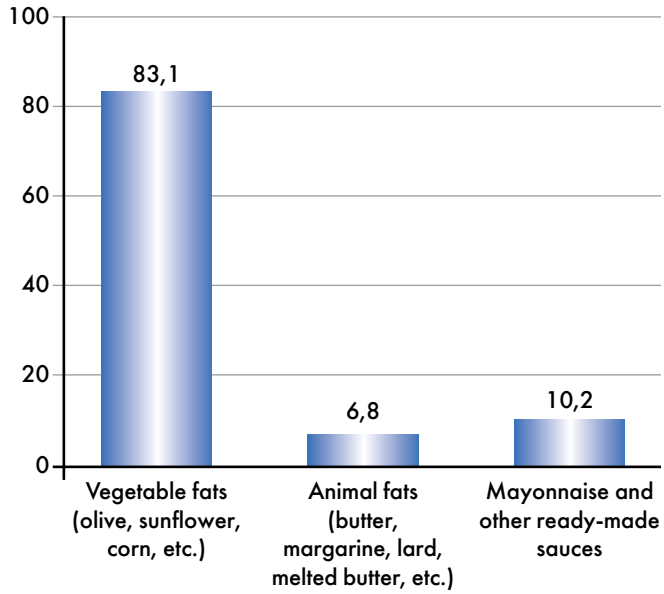


Fig. 4. Distribution of respondents' answers to the question 'Which fats do you eat more often'? from the questionnaire 'Lifestyle Traits'

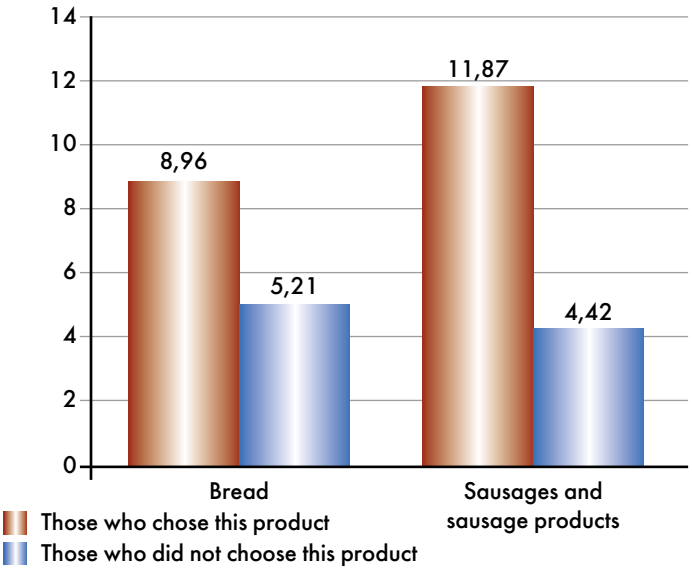


Fig. 5. The values of HOMA-IR in respondents who prefer certain food products in the questionnaire 'Lifestyle Traits'

(25.9% and 24.1% of the total sample, respectively) have significantly higher HOMA-IR values. Here, certain associations of alimentary habits with features of self-consciousness are also found. In particular, the preference for bread and sausage products is more characteristic of people with a lower level of internality in the field of failures. The average values are shown in Table 2.

The respondents who believe that the negative events taking place around them do not depend on themselves, prefer less healthy products (bread and sausage), potentially not considering that their choice can negatively affect health. It should also be added that bread is preferred by people who have a lower value on the scale of the integral self-attitude of the QSA method. Their mean value is 75.58 ± 14.24, whereas for those who did not notice the preferences of this product, it is equal to 82.87 ± 18.17 ($p < 0.05$, Mann–Whitney U test). Negative self-attitude may lead to the use of the most simple and affordable products, without regard for their benefits or harm.

Some associations were also found between the level of IR and individual demographic characteristics. As noted above, sex and age are not associated with HOMA-IR. However, marital status is significantly associated with the development of IR. Figure 6 presents the values of HOMA-IR for respondents with different marital status.

The data provided are somewhat unexpected because they do not coincide with the traditional notion of family as a supporting factor, which reduces the level of stress. Nevertheless, our study revealed that married participants have the highest HOMA-IR score. A possible explanation may be that unmarried people have more opportunities to pay attention to themselves, including taking care of their own health, eating properly and avoiding unnecessary stress associated with other family members. Perhaps the effect of this outbalances the result of the support of relatives in married respondents. However, this assumption seems unlikely because there are no significant relationships between marital status and physical activity and nutrition, at least with those aspects with associations with IR in this study. The revealed regularity requires additional study of the role of family relationships in the development of IR.

The limitations of the study include a small sample size, which did not enable to obtain a sufficient number of associations of IR and lifestyle factors. The enrolment of patients to the study continues, and further such associations can be obtained. In addition, the cross-sectional (one-stage) nature of the study does not enable the assessment of the orientation of associations of IR and other characteristics (personal, demographic, way of life). This report should be regarded as a presentation of the initial results, the interpretation of which is preliminary in nature.

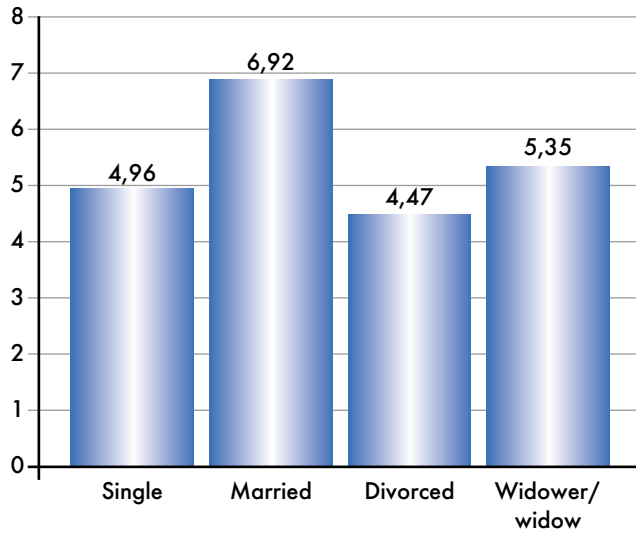
CONCLUSIONS

The results of the study enable the hypothesis that there is a connection between IR and personal characteristics

Table 2.

The level of internality (LSC) in the field of failures of respondents who prefer certain products

	Prefer the product	Do not prefer the product	Significance of differences on the student t-test
Bread	3.53 ± 1.19	4.66 ± 2.27	$p < 0.05$
Sausages and sausage products	3.36 ± 1.60	4.69 ± 2.15	$p < 0.05$



Differences between groups 2 and 3 are significant according to the Mann–Whitney U test, $p < 0.05$.
Differences between groups 2 and 4 are significant according to the Mann–Whitney U test, $p < 0.05$.

Fig. 6. Values of HOMA-IR in respondents with different marital status

(stress-moderators). These characteristics include primarily those which determine the development of stress, such as self-attitude and coping strategies. Positive self-attitude, self-reliance, respect and interest in oneself as a person contribute to the formation of a more favourable worldview, increasing the willingness of a person to cope with emerging challenges. Thus, they reduce the risk of stress, which may be associated with reduction in the risk of developing IR.

Assertive strategy, assuming a purposeful overcoming of emerging difficulties, is also associated with IR. If the situation is considered from the standpoint of the possibility of creating stress, then an active, persistent person has more chances to cope with the emerging stress than a passive one, who is inclined to refuse to overcome it. However, we discovered non-linear relationships between the two studied characteristics. Assertiveness is the most pronounced in people with a low level of IR; however, it is the least pronounced in people with an average IR. Further studies are required to understand the reasons for this.

Personal characteristics can affect IR in two ways. In addition to the fact that the development of stress depends on them, they can affect lifestyle choices; particularly, dietary habits and physical activity. In the study conducted, associations were found between a high level of IR and nutritional preferences for bread, sausage products and mayonnaise. At the same time, these habits also have associations with individual personal characteristics of self-awareness, in particular with a low level of internality in the field of failures, less positive self-attitude and a tendency to more passive forms of behaviour. Thus, presumably, the personality traits of a person have an influence on nutrition, and thus, on IR development.

For people with high IR, allocation of time for exercise is uncommon. A probable cause of unwillingness to do sporting activities is passivity, an inability to be active and purposeful. Thus, personal characteristics can influence the development of IR by influencing their level of physical activity.

Demographic characteristics are the least closely associated with IR. Neither sex nor age demonstrated an association with IR. However, it was found that in the sample studied, married people have a higher level of IR. This finding can be ambiguously interpreted and needs further study.

ADDITIONAL INFORMATION

FINANCING OF WORK

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest related to the writing of this manuscript.

AUTHORS' CONTRIBUTIONS

Motovilin O.G.: development of design, selection of psychological tests, formation of a database, statistical analysis, analysis and interpretation of the results, writing the text; Surkova E.V.: participation in the development of the design, development of questionnaires for patients, typesetting the material, analysis and interpretation of the results, writing the text; Koksharova E.O.: typesetting the material, the formation of a database, writing the text; Mayorov A.Yu.: participation in the development of the study design, typesetting the material, analysis and interpretation of the results, writing the text; Melnikova O.G.: development of questionnaires for patients, typesetting the material, the formation of a database.

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