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RELATIONSHIPS OF SIRT1 AND 8-OHDG WITH RESILIENCE, DEPRESSION AND COGNITION IN THE ELDERLY

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ABSTRACT

The aim of the present study was to evaluate the relationship of serum levels of SIRT1 and 8-OHdG with the psychological variables of resilience, depression and cognitive performance. The study design was quantitative and transversal. Data analyzed from 160 participants of both sexes, aged 60 to 79 years, using the following instruments: SIRT1, 8-OHdG, Resilience Scale, Geriatric Depression Scale and Mini Mental State Examination by the Mann Whitney tests for mean comparison, Spearman correlation and multiple linear regression using the stepwise method. The results demonstrated that there is a significant association between serum SIRT1 levels and resilience, depression and cognitive performance. However, in relation to 8-OHdG only one association with resilience was found. The conclusion was that coping with stressful events through the development of resilience, control of depression symptoms and maintenance of cognitive ability are associated with a good performance in the control of oxidative stress.

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INTRODUCTION

Aging implies changes that affect various aspects of human physiology and behavior, with emphasis on cognition. Thus, with the life expectancy increase of the world population, it is justified the concern with the cognitive deficits of the growing number of elderly people. In pathological aging, cognitive deficits are significant and are associated with dementia. Dementia affects 5% of the elderly at 65 years and 40% of the elderly at 80 years. Considering this fact is that dementia has now become the mental health problem that most rapidly grows in importance and number. Among the dementias with the highest prevalence is Alzheimer's disease, being characterized by the presence of cognitive decline with impairment of social activities and daily life, which result in disabilities and limitations in the elderly (Sharma *et al*., 2013).

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From the behavioral point of view, memory deficits can be assessed in terms of their degree of impairment through the use of different psychological assessment tools. However, the physiological aspects involved in the cognitive capacity decrease of the elderly are more difficult to evaluate because they involve events that develop in the central nervous system (Libert *et al*., 2011; Abe-Higuchi *et al*., 2016). The oxidative damage generated in cellular respiration is indicated as one of the mechanisms causing biological aging. This damage can be assessed by measuring different products. Oxidative DNA damage leads to the production of 8-hydroxy-2'-deoxyguanosine (8-OHdG). This molecule is a fragment generated by the attack of reactive oxygen species on DNA. Elevated plasma levels of 8-OHdG have been found in different pathologies and chronic-degenerative diseases (Valavanidis *et al*., 2009). With regard to cognitive aging, the presence of 8-OHdG at increased plasma or urine concentrations has been linked to both mild cognitive impairment and dementia (Shao *et al*., 2008).

Gao *et al* (2010) obtained results showing that high levels of 8-OHdG in urine were correlated with low scores on cognitive tests in a sample of 45- to 75-year-old Puerto Rican adults. Data from Shi *et al*. (2012) showed that high levels of 8-OHdG were also found in the urine of individuals with vascular dementias, compared to the levels of individuals without dementia. Recently, Moslemnezhad *et al*. (2016) have demonstrated that not only 8-OHdG levels, but those of other markers of oxidative stress are altered in the plasma of patients with Alzheimer's. In addition to the cognitive aspect, Namioka *et al*. (2016) found a relationship between oxidative damage and Alzheimer's in physically fragile patients in whom plasma levels of 8-OHdG are significantly elevated. In humans, the protein Sirtuin 1 (SIRT1) is one of the most studied biological markers in the aging process (Michán *et al*., 2010; Sanchéz-Hidalgo *et al*., 2016). SIRT1 has a broad spectrum of biological activities capable of regulating cell survival, apoptosis (programmed cell death) and various aspects of energy metabolism (Radak *et al*., 2013). Research on the impact of genetic variation of SIRT1 on human health has revealed that the RS3758391 T allele is associated with better cognitive performance among individuals over 85 years of age in a population survey of a sample of 1245 subjects (Kuningas *et al*., 2007). This protein has different neuroprotective effects, such as the maintenance of genomic stability in postmitotic neurons (Radak *et al*., 2013), modulation of oxidative stress in different cell types (Salminen *et al*., 2013).

In addition, SIRT1 deficiency in microglial cells has also been implicated in cognitive decline in aging and neurodegeneration in rodents (Cho *et al*., 2015). In those animal models, it has also been shown that experimental inhibition of SIRT1 in hippocampal neurons leads to the appearance of behaviors similar to depression (Abe-Higuchi *et al*., 2016). Some authors have shown that there is a decline in levels of this protein in normal individuals as they age, a decline that is much more pronounced in individuals with cognitive impairment and may be related to the onset of early signs of Alzheimer's dementia. Recently, it has been suggested that serum levels of SIRT 1 protein can be used as markers for the early detection of Alzheimer's disease (Kumar *et al*., 2013). In order to find an explanation for these facts, several authors investigate the relationship between stressor events and physiological effects on behavior, from the biochemical point of view. Particularly with regard to oxidative stress, it is known that molecules generated by active species of oxygen are increased in individuals undergoing prolonged stress, and are also related to anxiety and depression (Hirose *et al*., 2016).

Resilience, according to Rutter (1993), can be described as the ability to adapt to stressful events, and it is usually accepted as a process. The same author also affirms that the resilience is the result of the interaction between genetic and environmental factors, which is configured in something complex, since these aspects can act as both protection and risk factors. Although there is a reasonable bibliography on the cognitive implications of stressful events, aspects such as their relation with resilience are still poorly explored in this context. Thus, in the psychosocial intervention field, resilience seeks to facilitate processes that involve the individual and his social environment, helping him overcome adversity, adapt to society and have a better quality of life (Infante, 2008), including finding ways to avoid and / or to face the stress coming from the conflicts experienced at the moment or along its life trajectory.

Thus, the idea of the cumulative effect of several risk events and their degree of adversity throughout life is defended by Pesce *et al*. (2004) as capable of generating negative effects on development. This aspect is important to be considered in this study because the studied population of the elderly there had a great chance to be exposed to this risk situation for a long time. It is known that stressful life events are considered for the great majority of people as a risk to the maintenance of health and well-being. This is also true especially for the elderly (Couto, 2007). In the process of aging, physical, psychological, and social role changes are challenges to the self, and to the maintenance of the well-being. In this sense, old age can be characterized as a promising period for investigating factors and processes of resilience and vulnerability. Couto (2007) explains the importance of studying factors that promote resilience or vulnerability. The author affirms that these aspects are important to be investigated because they can help to draw plans of care and intervention with the elderly population with the objective of promoting the development of resilience.

Therefore, it is important in the aging process to increase the resilience of the elderly, so that adaptive behavior can be maintained in old age due the unpleasant events related to physical health, well-being and to the lives of the loved ones. Knowing what factors constitute protective elements will be able to stimulate them, favoring the emergence of resilience. Studies of these transformations confirm the need to plan and implement psychosocial interventions with this population. Evidence suggests that aging is related to a dysregulated increase in immune function and stress may exacerbate this process. However not all people experience the dysfunction of this age-related function in the same way. Understanding the factors that promote or prevent resilience before stress and the decline of age-related immune function, may help older adults to age successfully (Fagundes *et al*., 2013). The field of psychoneuroimmunology seeks to understand how psychological factors such as stress and depression affect immune function. There is a good reason for this: the primary ways in which the psyche influences immune function are negative. Stress increases autonomic activity and HPA activity (hypothalamus, pituitary and adrenal) alters immune function. However, psychological factors can lessen the negative impact of stress. Likewise, the practice of healthy habits can promote better responses of the immune function and allow the reduction of changes of this same function related to stress. Therefore, different factors can be correlated in this field such as behavior, neuroendocrine and immune alterations, personality, social support network, coping strategies, affective states, life events and physical and psychosocial stressors (Biondi, 2001).

Resilience seems to positively influence longevity. Optimism and flexibility are associated with resilience in population samples of centenarian individuals. Research carried out in Sweden (Nygren *et al*., 2005) revealed higher resilience scores among the elderly population than among the younger ones. Based on these assumptions, one may think that the ability to incorporate positive emotion into daily life may be the path to resilience (Laranjeira, 2007). Depression is related to changes in practically all mental functions, but the most affected are affective-volitional ones, which involve affectivity, counting, and psychomotricity. Thus, mood or affect changes are considered to be the most important in depression, which classifies major depressive disorder as a mood disorder

(Cheniaux, 2013), which tends to cause problems in several areas of functioning including education, relationships, employment, and financial success. The cognitive functions affected are usually attention, sense perception, memory, speech and language, thought, intelligence, and imagination. Other functions that may also be affected are: appearance, attitude, alopsychic orientation, self-awareness, pragmatism, prospecting, and morbidity awareness.

Considering the age range chosen for this study, it can be stated that among mental disorders, depression is the more frequent disease of emotional suffering in the elderly, and this fact may affect the quality of their life, thus constituting a problem of public health (Bottino, Barcelos-Ferreira, & Ribeiz, 2013). In addition, depression is also being considered as a risk factor for dementia processes. Therefore, it can be a life-threatening element, especially of those who have a chronic-degenerative or incapacitating illness. Taking into account the evidence cited, this article aims to analyze the relationships between serum levels of SIRT1 and 8-OHdG with the variables resilience, depression and cognitive performance in the elderly between 60 and 75 years old, both sexes and with life independent, resident in Ivoti city, RS, Brazil.

METHODS

The present study had a transversal quantitative delineation. The research was performed in the municipality of Ivoti / RS in partnership with the Municipal Council of the Elderly of the municipality and the Department of Health and Social Assistance of the Municipality of Ivoti / RS.

Participants

A total of 144 volunteers were recruited, ranging from 60 to 79 years old, of both genders. The elderly were contacted through the existing registers in the five health centers of the municipality and invited to participate spontaneously. The participants were selected considering the exclusion criteria to present the dementia process or to be institutionalized.

Tools

The research instruments were used to evaluate the dependent variables SIRT1 and 8-OHdG, as well as the independent variables resilience, cognition and depression.

- Detection of SIRT1 - SIRT1 protein dosing was done by the competitive ELISA assay from isolated serum samples, with reading at 405nm, and detection sensitivity between 0.781 and 50 ng / ml. The SEE912Hu siren kit (Cloud-clone Corp), which uses a monoclonal antibody specific for human SIRT1 (Kumar *et al*, 2013), was used. Each kit has the capacity to test 96 individuals.16 samples included in the kit were used as controls.
- Detection of 8-OHdG - 8-hydroxy-2'-deoxyguanosine (8-OHdG) was detected in serum samples. The 8-OHdG detection kit employed was KOG-HS10E (Jaica), a competitive ELISA assay, which utilizes a monoclonal antibody that is highly specific for DNA damage, with a wavelength reading of 450 nm, with interval of standard curve ranging from 0.125 to 10 ng / ml. (Shi *et al*., 2012). Each kit has the capacity to test 96 individuals, 16 of them used as controls.
- Resilience Scale - The scale was developed by Wagnild and Young (1993) and is used to measure resilience assessed by levels of positive psychosocial adaptation to major life events (Pesce *et al*., 2005). It is composed of 24 likert-type items ranging from 1 (totally disagree) to 7 (totally agree). Scores vary from 24 to 168 and high values indicate high resilience (Pesce *et al*., 2005). This scale was adapted by Pesce *et al*. (2005) and considered relevant for Brazilian culture.
- Mini Mental State Examination (MMSE) - This is a cognitive screening test widely used in the evaluation of the elderly and was developed by Folstein *et al*. (1975) and translated by Bertolucci *et al*. (1994). It consists of several questions typically grouped into seven categories, each one designed to evaluate specific cognitive functions: orientation for time (5 points), orientation for place (5 points), record of three words (3 points), attention and calculation (5 points), recall of three words (3 points), language (8 points) and visual constructive capacity (1 point). Its application is fast, ranging from 5 to 10 minutes. The items are evaluated by a score ranging from 1 to 5 points, reaching a maximum of 30 points. Schooling was pointed out by Bertolucci *et al*. (1994), Juva *et al*. (1997), Almeida and Almeida (1999) as a determinant factor for the evaluation presenting differentiated cut-off points according to the number of years of study. The cut-off points were based on the criteria of Brucki, Nitrini, Caramelli, Bertolucci and Okamoto (2003). According to Almeida and Almeida (1999) the MMSE scores have a significant age influence.
- Geriatric Depression Scale (GDS-15) - This scale is one of the most used, mainly in the Brazilian reality. Initially composed of 100 questions, it was reduced to 30 and subsequently to only 15 questions that demonstrate sensitivity and specificity similar to full scale. The Brazilian version GDS-15 offers valid measures for the detection of major depressive episode in the elderly. The scale is scored according to the presence of depressive symptoms, with a cut-off point of 6 symptoms (normal $\leq$ 5, mild depression $\geq$ 6 and $\leq$ 10 symptoms,> 10 severe depression). It presents an easy and quick application, with questions that ask for yes or no answers according to the perception of how it felt in relation to the last two weeks preceding the evaluation (Yesavage *et al*., 1996; Almeida & Almeida, 1999).

Data collection and analysis procedure

The project under number 747.080 was approved by the Research Ethics Committee of the University and the participants of this study were contacted through the Municipal Council for the Rights of the Elderly and the Department of Health and Social Assistance of the Municipality of Ivoti. Explanatory lectures were given to the research participants and interested community members about the core concepts and objectives of the study. Participants signed a free and informed consent form (TCLE), in accordance with the norms of resolution No. 466 of December 12, 2012 of the National Health Council of the Ministry of Health that deals with research involving human beings. The study was carried out in two meetings held in the 5 health centers in the municipality where the elderly were recruited.
At the first meeting, the ICF was signed and blood collection was carried out.

At the subsequent meeting, the evaluations of resilience, depression and cognition were carried out. In all statistical tests, the level of significance was set at $\alpha = 0.05$. Numerical data are presented in the mean ± standard deviation (SD) format. The visual presentation of the results is in the SPSS v. 22.0. The variables analyzed were: resilience, depression, cognitive performance, 8-OHdG and SIRT1. For these variables, Mann Whitney's analysis was used with the factors sex and age group. In order to verify the relationship between the parameters of SIRT1 and 8-OHdG and the variables: age, sex, resilience, cognitive performance and depression, a Spearman correlation analysis was performed. Multiple stepwise linear regression analysis was performed to obtain which of the variables resilience, cognitive performance and depression are responsible for possible changes in the parameters of SIRT1 and 8-OHdG analysis in men and women aged 60 to 79 years.

RESULTS

The psychological variables of resilience, depression (GDS-15) and cognitive performance (MMSE), 8-OHdG and SIRT1 protein were not significantly different when compared to the gender variable. Regarding the variable age group divided between 60 to 69 years and 70 to 79 years of age, a significant difference was found only in the MMSE variable ($p = 0.045$). The participants of our study, in the lower age group, presented better cognitive performance (Table 1).

In the Spearman correlation analysis we identified that the SIRT1 protein is negatively related to the MMSE score in the general sample of our study (rho = -0.195; $p = 0.014$). In the sample of people aged 70 to 79 years we also found a negative correlation with the MMSE score (rho = -0.356; $p = 0.013$).
In the sample of males aged 70 to 79 years we found again a negative relation with the MMSE score (rho = -0, 685; $p = 0.007$). For multiple linear regression analysis, the SIRT1 and 8-OHdG proteins were tested as dependent variables because they represent variables that would allow the relationship of psychological variables with physiological responses to stress in the successful aging process. Consequently, SIRT1 and 8-OHdG represent variables that make it possible to mediate the understanding of the relationship between the successful aging process and the emotional strategies adopted throughout the life cycle. Initially, the following independent variables entered the multiple regression model: resilience, self and life acceptance, personal competence, cognitive performance, and depression. In the stepwise, multiple linear regression of the male group sample (Table 2), the following independent variables remained in the final model: Mental Status Mini Exam score and resilience. The determination coefficient was $R^2 = 0.356$ ($p = 0.020$).

The independent variable of the final multiple regression model showed a positive association with the SIRT1 variable. While the variable Mini Exam of the Mental State presented negative association with the variable SIRT1.

Table 1. Characterization of participants

	60 to 69 years (n=114)		70 to 79 years (n=48)		Total (n=162)	*p*
	Male (n=28)	Female (n=86)	Male (n=14)	Female (n=34)		
Sirt1 (ng/µl)	0,14	0,20	0,30	0,18	0,200	0,384*
	±0,83	±0,25	±0,35	±0,20	±0,238	0,974**
8-OHdG (ng/µl)	5,83	6,83	6,94	6,82	6,89	0, 965 *
	±9,25	±8,14	±9,80	±8,65	±8,95	0,134**
Resilience	142,96	142,39	136,18	144,86	142,51	0,974*
	±10,87	±12,94	±30,73	±14,20	±14,89	0,597**
MMSE	25,67	24,62	23,79	22,79	24,33	0,045*
	±2,35	±3,30	±4,42	±4,22	±3,58	0,082**
Depression	3,13	2,89	2,76	2,78	2,91	0,771*
	±2,38	±2,46	±2,16	±2,27	±2,36	0,450**

* Mann Whitney's U-test for the comparison between the variable age group.
** Mann Whitney U test for the comparison between the sex variable.

Table 2. Multiple linear regression analysis for the dependent variable SIRT1 in the male sample

Model	Non-stand. coefficients		Stand. coefficients	T	Sig.	Collinearity statistics	
	B	Stand. error	Beta			Tol.	VIF
(Constante)	,828	,245		3,378	,002		
MMSE	-,051	,013	-,797	-3,997	,000	,559	1,789
Resilience	,226	,092	,490	2,460	,020	,559	1,789

Table 3. Multiple linear regression analysis for the group from 70 to 79 years

Model	Non Standardized Coefficients		Standard. Coef.		Sig.	Collinearity statistics	
	B	Erro Padrão	Beta			Tol.	VIF
(Constant)	,135	,043		3,157	,003		
MMSE	-,163	,070	,355	2,340	,025	1,000	1,000

Table 4. Analysis of multiple linear regression for female and male group in the age range of 70 to 79 years

Sex	Model	Non Standardized coefficients		Stand. coeffs.	t	Sig.	Collinearity statistics	
		B	Standard Error	Beta			Tol.	VIF
Male	(Constant)	,109	,095		1,149	,280		
	MMSE	-,485	,158	,716	3,075	,013	1,000	1,000
Female	(Constant)	,135	,013		10,529	,000		
	GDS	,763	,069	,904	11,007	,000	1,000	1,000

Demonstrating that elevation of SIRT1 protein is related to impaired cognitive performance and improved resilience. In the stepwise multiple linear regression of the 70-79 year old group of our sample, we identified only the mini mental status variable test (Table 3). The determination coefficient was R^2 = 0.126 (p = 0.025). The independent variable of the final multiple linear regression model Mini Mental State Examination (MMSE) showed a negative association with the variable SIRT1. Demonstrating that elevation of SIRT1 protein is related to increased cognitive deficit in older age groups.

Table 5 - Multiple linear regression analysis for female group from 70 to 79 years

Sexo	Model	Non-Standardized Coefficients		Stand. Coeffs.	T	Sig.	Collinearity statistics	
		B	Stand. Error	Beta			Toleran.	VIF
Female	(Constant)	,844	,251		3,367	,002		
	Resilience	-,235	,086	-,466	-2,737	,011	1,000	1,000

Table 6. Multiple linear regression analysis of the 8-OHdG independent variable

Model	Non-Standardized Coefficients		Stand. Coeffs	t	Sig.	Collinearity statistics	
	B	Stand. Error	Beta			Tolerance	VIF
(Constante)	25,287	7,598		3,328	,001		
Personal Competence	-3,047	1,255	-,237	-2,427	,017	1,000	1,000

In the stepwise, multiple linear regression of the male group and in the female group of 70 to 79 years old of our sample, we identified the variables cognitive performance and depression, respectively (Table 4). The coefficient of determination was R^2 = 0.512 (p = 0.013) for the male group and R^2 = 0.818 (p = 0.000) for the female group. The independent variable of the final multiple linear regression model mini mental state test showed a negative association with the variable SIRT1. Demonstrating that the SIRT1 protein elevation is related to the increase in cognitive deficit in older age groups in elderly men. Older women presented the variable depression as an independent variable in the regression model demonstrating the association between the increase in SIRT1 and the increase in the symptoms of depression. The female group of 70 to 79 years also presented a regression model with the resilience variable (Table 5). The determination coefficient was R2 = 0.217 (p = 0.011).

The independent variable of the final multiple regression model showed a negative association with the SIRT1 variable. Demonstrating that elevation of SIRT1 protein is related to decreased resilience capacity. In the analysis of 8-OHdG the group of 60 to 69 years (Table 6) presented a regression model with the personal competence variable (resilience). The determination coefficient was R^2 = 0.056 (p = 0.017). The independent variable of the final multiple linear regression model 8-OHdG showed a negative association with the resilience variable. Demonstrating that the decrease of 8-OHdG is related to the increase in the perception of personal competence (resilience) in people between the age of 60 and 69 years.

DISCUSSION

Even for purely physiological aspects, differences in the effects of SIRT1 and 8-OHdG between genders are still poorly studied. As far as we know, the present study is the first to evaluate the effects of SIRT1 and 8-OHdG, simultaneously, on depression and resilience, as well as human cognition during aging. With advancing age, cognitive processes can undergo environmental, psychosocial, and physiological influences. Establishing the relationships between these factors is a complex task. Over the last decade, a number of genetic and biochemical markers have been employed for this purpose. The SIRT1 protein is one of them and is characterized by being a master regulator of the expression of several genes for stress response, as well as energy metabolism, two groups of factors that determine longevity. In order to evaluate the effects of different variants of this gene in humans, Kuningas *et al*. (2007) genotyped five single nucleotide polymorphisms (SNPs) in a sample of 1245 elderly individuals over 85 years old. Although data on the effect of these variants on longevity were inconclusive, one of them, the rs378391 T allele, was found in individuals with better cognitive performance, being positively correlated with the MMSE score. Later studies have pointed SIRT1 as essential for learning, memory and synaptic plasticity in animal models (Michán *et al*., 2010). SIRT1 protein has also been implicated in mediating behaviors similar to depression and anxiety in animal models, suggesting that their reduction would contribute to the increase in the manifestation of depressive symptoms induced by stress (Abe-Higuchi *et al*., 2016). Additionally, it has been shown, experimentally, that increased protein expression in rodents was able to induce cognitive enhancement through neurotrophic and proteostatic mechanisms (Corpas *et al*., 2016). Given the impossibility of measuring in vivo the levels of this protein in the central nervous system in humans, the measurement of serum concentrations of SIRT1 was used by Kumar *et al*. (2013) as a non-invasive alternative. These authors demonstrated a correlation between low serum levels of SIRT1 and a low score in the mini-mental, as a possible predictor of Alzheimer's development. However, in the present study, no gender differences in serum levels of this protein were identified. The data in this article, however, point in the opposite direction. Considering the overall outcome, there was an inverse correlation between cognitive performance and serum SIRT1 levels in men and women between the ages of 70 and 79 but not in the 60-69 age range for both sexes.

It is possible that the environmental and genetic factors contributed to this discrepancy. The sample studied by Kumar *et al*. (2013) was composed of Indian elderly, suggesting that ethnic differences could contribute to the great disparity described for SIRT1 levels, whose maximum value was sixteen times higher than that obtained in our sample. In addition, a number of SIRT1 activator molecules, such as curcumin, are present in the daily diet of Indian elderly, a fact that does not occur in the subjects of our study. It could contribute to the elevated serum concentrations of SIRT1 in the indian sample and, perhaps, to the absence of significant differences between the sexes in the study of these authors

(Sun *et al*., 2014). One possibility is that, in our sample, increasing concentrations of this protein is a consequence and not a cause of cognitive deficit. In this case, elevation of SIRT1 concentrations would be a response to physiological factors involved in cognitive impairment, similar to the increased activity of this protein in disorders unrelated to cognition, as in certain types of tumors. In the literature, the expression of SIRT1 can be increased in response to physiological stresses, such as active oxygen species or pro-inflammatory agents, which reinforces this possibility (Liu *et al*., 2015; Huang *et al*., 2013). While cognitive performance declined in both sexes, resilience and depression presented different results in men and women in the sample regarding to the increase in SIRT1. In men, the correlation between SIRT1 and resilience was direct and in women, specifically in the 70-79 age group, it was inverse. In addition, depression was directly associated with SIRT1 levels in women and was no association in men. Although the literature lacks studies on behavioral differences between the sexes related to SIRT1 in animal models, they have already been reported, suggesting that the activity of this protein in female subjects would be influenced by estrogen levels at different ages (Rao *et al*., 2013). The results of 8-OHdG were more specific, demonstrating that there was no relationship between the levels of this molecule with cognitive performance or depression. However, the resilience variable presented a negative association with 8-OHdG in the age group of 60 to 69 years, suggesting that the exposure to stressful events throughout life could affect both physiological and behavioral resilience responses. These data corroborate the hypothesis of Rutter (1993), suggesting that resilience is a result of the interaction between genetic and environmental factors, which is complex, since these aspects can act as both protection and risk factors.

Conclusion

Serum levels of SIRT1 in the elderly of both sexes presented an inverse correlation with the MMSE score, between the ages of 70 and 79 years, but not at younger ages, suggesting an effect of age on the regulation of this protein. Since SIRT1 is considered vital for normal cognitive function, this data suggests that the elevation of serum SIRT1 levels correlated with a low score in MMSE, could be explained as a physiological response to the progression of cognitive deficit.
Unlike cognition, resilience and depression were strongly influenced by sex. Elevated SIRT1 levels reduced scores on the resilience scale of the elderly between 70 and 79 years, while depression, as measured by the GDS scale, increased. The increase in the serum level of 8-OHdG was associated in the age group of 60 to 69 years with the increase of the index of the competence factor of the person of the resilience. The overall data suggest that SIRT1 increases with age in the 70-79 age range, but has different effects between the sexes, possibly influenced by the drop in estrogen levels following. However, the regulatory mechanisms involved are poorly understood and additional studies, which also involve genetic analyzes of this population, could help to clarify this topic.

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