COGNITIVE RESERVE OF PATIENTS WITH CHRONIC CEREBRAL ISCHEMIA

Fokin VF ✉, Ponomareva NV, Shabalina AA, Konovalov RN, Medvedev RB, Boravova AI, Lagoda OV, Krotenkova MV, Tanashyan MM

Research Center of Neurology, Moscow, Russia

Cognitive reserve (CR) is characterized by the ability to engage neural networks for adaptive reorganization of brain functions in response to damage or stress. This study aimed to identify the structural and functional organization of neural networks in patients with chronic cerebral ischemia (CCI) having different CR. The study involved 137 women aged 50–85 years suffering from CCI without diabetes. The average duration of CCI was 10.1 ± 0.7 years. CCI patients were divided into two groups: with secondary (SE) and higher (HE) education. Salivary cortisol levels were measured before and after cognitive load, along with the differences in brain connectivity organization based on fMRI data in two patient groups. Connectivity patterns were primarily found in the auditory areas, different in two groups after applying multiple comparison correction (FDR) and were responsive to cortisol levels. Patients with greater CR developed CCI later, showed significantly more positive connectivity values, had lower baseline cortisol levels, and displayed larger shifts in cortisol levels during cognitive load.

Keywords: cognitive reserve, chronic cerebral ischemia, higher and secondary education, resting fMRI, connectivity, cortisol, cognitive load

Author contribution: Fokin VF — manuscript writing; Ponomareva NV — study design; Shabalina AA — biochemical testing, determining salivary cortisol levels; Konovalov RN — design of neuroimaging tests; Medvedev RB — Doppler tests; Boravova AI — psychophysiological tests; Lagoda OV — clinical tests; Krotenkova MV — neuroimaging test management; Tanashyan MM — clinical test management, general study design.

Compliance with ethical standards: the study was approved by the Ethics Committee of the Research Center of Neurology (protocol No. 5-6/22 dated 1 June 2022). The informed consent was submitted by all study participants.

✉ **Correspondence should be addressed:** Vitaly F. Fokin
Volokolamskoye shosse, 80, Moscow, 125367, Russia; fvf@mail.ru

Received: 28.11.2024 **Accepted:** 08.01.2025 **Published online:** 31.01.2025

DOI: 10.24075/brsmu.2025.002

КОГНИТИВНЫЙ РЕЗЕРВ БОЛЬНЫХ ХРОНИЧЕСКОЙ ИШЕМИЕЙ МОЗГА

В. Ф. Фокин ✉, Н. В. Пономарева, А. А. Шабалина, Р. Н. Коновалов, Р. Б. Медведев, А. И. Боравова, О. В. Лагода, М. В. Кротенкова, М. М. Танашян

Научный центр неврологии, Москва, Россия

Когнитивный резерв (КР) характеризуется способностью активировать нейронные сети для адаптивной реорганизации функций мозга в ответ на повреждение или стресс. Целью работы было выявление структурно-функциональной организации нейросетей у больных хронической ишемией мозга (ХИМ) с различным КР. В исследовании участвовали 137 женщин в возрасте 50–85 лет больных ХИМ без диабета. Средняя давность заболевания ХИМ — 10,1 ± 0,7 года. Больные ХИМ были разделены на две группы: со средним (СО) и с высшим (ВО) образованием. Определяли содержание кортизола в слюне до и после когнитивной нагрузки, а также различие коннективной организации мозга по данным фМРТ в двух группах больных. Найдены коннективности преимущественно в слуховых областях, различные в двух группах, с учетом поправки на множественность сравнений (FDR), и чувствительные к уровню кортизола. Больные с более высоким КР позже заболевали ХИМ, имели достоверно более положительные значения коннективностей, более низкий уровень фонового кортизола и более высокий сдвиг кортизола при когнитивной нагрузке.

Ключевые слова: когнитивный резерв, хроническая ишемия мозга, высшее образование, среднее образование, фМРТ покоя, коннективность, кортизол, когнитивная нагрузка

Вклад авторов: В. Ф. Фокин — написание статьи; Н. В. Пономарева — дизайн исследования; А. А. Шабалина — биохимические исследования, определение кортизола в слюне; Р. Н. Коновалов — дизайн нейровизуалиционных исследований; Р. Б. Медведев — допплерогафические исследования; А. И. Боравова — психофизиологические исследования; О. В. Лагода — клинические исследования; М. В. Кротенкова — руководство нейровизуалиционными исследованиями; М. М. Танашян — руководство клиническими исследованиями, общий дизайн работы.

Соблюдение этических стандартов: исследование одобрено локальным этическим комитетом Научного центра неврологии (протокол № 5-6/22 от 1 июня 2022 г.). Все участники обследований подписали добровольное информированное согласие.

✉ **Для корреспонденции:** Виталий Федорович Фокин
Волоколамское шоссе, д. 80, г. Москва, 125367, Россия; fvf@mail.ru

Статья получена: 28.11.2024 **Статья принята к печати:** 08.01.2025 **Опубликована онлайн:** 31.01.2025

DOI: 10.24075/vrgmu.2025.002

Cognitive reserve (CR) is a concept describing the brain's ability to adapt to damage or aging. CR is characterized by the capability of engaging neural networks and ensuring adaptive reorganization of brain functions in response to damage or stress [1]. The concept of CR is widely used when describing aging, as well as neurodegenerative and vascular disorders of the brain.

There are two oppositely directed factors playing a key role in the CR organization: education and the effects of stress, which are often replaced by a more measurable trait, stress hormone cortisol levels. Let us consider carefully these three characteristics.

The studies describing the effects of person's education on his/her body are divided into two large groups: the effects of social benefits associated with pursuing higher education (HE) and alterations of brain's structural and functional organization occurring under the influence of education. The period of cognitive training associated with pursuing HE can be considered as longer, than that associated with pursuing secondary education (SE). HE is often finished at a relatively young age characterized by high brain plasticity, so there is an opportunity to optimally shape brain networks. The larger accumulated CR also manifesting itself in attitude to stress caused by cognitive stress represents one of the major benefits for individuals with HE.

The course of stress is different in men and women, so it is feasible to consider it separately. This paper is focused on the responses associated with cognitive stress in women with HE and SE suffering from chronic cerebral ischemia (CCI). Women with HE have potentially improved stress regulation mechanisms. This can be due to the dynamic changes in cortisol levels [2]. In women with HE, there is possibility of more intense activation of the prefrontal cortex (PFC) playing an important role in executive functions and emotional regulation [3]. HE is likely to result in stronger PFC cortex activation during stress, thereby contributing to better cognitive control and emotional regulation. This is especially true for interconnections between PFC and cyngulate gyrus. Furthermore, HE is associated with enlargement of the hippocampus playing a role in regulation of memory and responses to stress, possibly ensuring a protective effect of education on hippocampal integrity [4].

One can see various patterns of activation of the amygdala involved in developing responses to fear and threat. HE can result in the less prominent and better controlled activation of the amygdala during stress [5].

Women with lower socioeconomic status that is often associated with little education have elevated basal cortisol levels, even when there seem to be no severe stressors [6]. Reduced hippocampal volume under conditions of chronic stress can negatively affect its functioning, which results in deterioration of memory and impaired stress regulation [7], as well as to reduction of CR.

In individuals with inadequate education, the increased amygdala reactivity and chronic stress can sensitize the amygdala, thereby contributing to enhanced fear response. Furthermore, PFC is not always able to regulate responses of the amygdala, which results in the less effective emotional regulation [8].

Studies of the neuronal correlates of cognitive load in women with different levels of education are still fairly limited, and the results of different studies are not always consistent. Higher cognitive load require larger cerebral energy resources, which results in the increased neuronal activity. This is suggested by the functional magnetic resonance imaging (fMRI) studies, where the increase in BOLD signal (Blood Oxygen Level Dependent) is associated with activation in parietal lobes and PFC. The increased activation in parietal lobes is associated with spatial processing, attention, and working memory, and their activity increases with increasing cognitive problems [9].

METHODS

The study involved 137 women aged 50–85 years suffering from CCI without diabetes. The average duration of CCI was 10.1±0.7 years. CCI patients were divided into two groups: with SE and HE. The main etiological causes of CCI are as follows: atherosclerosis, hypertension (including hypertensive heart disease), venous insufficiency, diabetic angiopathy, vasculitis of various etiology, etc. Inclusion criteria: initial manifestations and subcompensated CCI; no need for permanent care from others in patients' daily life [10]. Non-inclusion criteria: dementia severity score 1 or more (Clinical Dementia Rating) [11]; history of acute cerebrovascular accident, traumatic brain injury, severe heart or renal failure, uncompensated thyroid dysfunction. The diagnosis of CCI was further verified by duplex scan and follow-up MRI. All the patients were right-handed. The patients' body height and body weight were measured to determine body mass index (BMI). BMI = body weight/body height^2. Two age characteristics were taken into account: patient's age at the time of recording and age at first referral to a medical institution due to CCI symptoms. The first referral was usually associated with memory and concentration problems accompanying arterial hypertension, as well as with cerebrovascular accidents. The second trait was age at the time of experimental assessment. It was assumed that patients with different levels of education reached this stage at different age. Both groups of women were mainly knowledge workers, while women with SE were mainly accountants or nursing staff.

Resting state fMRI

The subjects (25 CCI patients) underwent T2* weighted resting state fMRI of the brain in order to record BOLD signal in the Magnetom Verio magnetic resonance imaging scanner (Siemens, Germany) with the magnetic field strength of 3.0 Tesla. The subjects were offered to follow the instructions: to relax as much as possible, lay still with the eyes closed (to avoid stimulation of visual sensory system), not to think about anything in particular. MRI data were processed using the SPM12 software in the MATLAB computing environment. The CONN-18b application on the SPM-12 platform was used to assess connectivity. Connectivity was assessed in various neural networks of the brain. We compared connectivity in two groups of CCI patients with different levels of education. Significance of differences in these groups was assessed based on the standardized regression coefficient adjusted for multiple comparisons (FDR, False Discovery Rate) in CONN-18b.

The MAGNETOM Verio magnetic resonance imaging unit (Siemens, Germany) had the magnetic field strength of 3.0 Tesla. Functional scans were acquired in the resting state using the T2* weighted EPI sequence: TR = 1500 ms, TE = 30 ms, flip angle 70°, slice thickness 2 mm, FOV = 190 mm, FoV phase 100.0%.

Cognitive tests

Patients were assessed using the previously reported correction test, verbal fluency test, Luria's verbal working memory test, MoCA test [12]. Furthermore, we recorded blood pressure, calculated pulse pressure (difference between systolic and diastolic blood pressure) and heart rate.

Biochemical tests

The patients' salivary cortisol levels were determined using the Abbott i2000 ARCHITECT immunochemiluminescence analyzer (Abbott Laboratories, Illinois, USA) using the reagent kit of the same brand.

Saliva samples were collected in accordance with the previously reported protocol [13]. The patients did not drink alcohol for a week, tea or coffee for 1 h before saliva collection, rinsed their mouth with water 10 min before this. Saliva collection was accomplished through spitting into a test tube with the volume of at least 1.5 mL. Saliva samples contaminated with blood were excluded from the study. For that the enzyme immunoassay kit was used to determine contamination of saliva with blood [13].

Statistical processing

Analysis of the data obtained was performed using the Statistica-12 software package (Dell, USA). The Kolmogorov–Smirnov test

Table 1. Demographic data of women with SE and HE suffering from CCI and significance of differences between the values of these groups

	CCI Women	BMI	Average age at the time of assessment	Initial presentation
SE	*n* = 72	28.3 ± 0.7	65.0 ± 0.9	51.3 ± 1.8
HE	*n* = 65	27.7 ± 0.6	70.2 ± 0.8	58.2 ± 1.8
p	0.48	0.55	0.00003	0.0077

Note: SE — secondary education, HE — higher education, *p* — significance of differences; the first value is the mean, the second value is the standard error. BMI — body mass index; Average age at the time of assessment — average age of patients at the time of experimental data recording; Initial presentation — average age of the patient's first referral to the medical institution due to the objectively confirmed CCI symptoms.

was used to test the distribution for normality. We calculated mean values, standard errors, conducted one-way analysis of variance and correlation analysis. To analyze neural networks, Student's t-test was calculated, and adjustment for multiple comparisons was applied – FDR (False Discovery Rate).

Assessment procedure

Saliva was first collected at least 2 h after the meal; initially, we performed background recording of slow electrical activity (for no more than 5 min), then, with the 1–2 min break, the patients performed three cognitive tests: Kirchner' correction test (3 min), verbal fluency test (phonemic variant) (4–5 min), Luria's verbal working memory test (5–7 min). Saliva was collected again immediately after performing tests, within 1–2 min. The MoCa test was performed after the end of the experiments and saliva collection.

RESULTS

In CCI patients, contingency between the level of education and age characteristics is significantly manifested in women. Table 1 provides demographic data showing the role of education in the dynamics of abnormal vascular aging (CCI).

There is a clearly visible effect of HE on the women's age characteristics: women with HE seek medical care for CCI later (Table 1). Initial presentation to the medical institution of individuals with SE took place about 7 years earlier compared to patients with HE. Since there are literature data on the impact of continued education on stress, let us consider the effects of education on the stress mechanisms, specifically on cortisol, the stress hormone (Table 2).

In women with HE, baseline cortisol levels were about 14 nmol/L lower, and responsiveness to cognitive load was about 3.5–5 times higher (Table 2). There are no significant differences in cortisol values after cognitive load in two groups. This largely explains different cortisol shift values reported for both groups. It seems that there is some maximum possible cortisol level associated with cognitive load, and the difference in cortisol shift values is explained by different baseline cortisol levels reported for both groups. We have revealed a significant correlation between baseline cortisol levels and relative cortisol reactivity: $r = 0.41$; $n = 88$; $p = 0.00008$.

The cortisol level shift associated with cognitive load is related to the age of first referral to the medical institution due to the emergence of CCI symptoms in patients with HE (Fig. 1).

The greater the cortisol reactivity, the later the patient seeks medical help due to the emergence of CCI symptoms. It should be noted that patients with almost the same disease severity were selected in the hospital for assessment. Individuals with HE had lower baseline cortisol levels, than women with SE (Table 1), while the patients' age had no significant effect on cortisol levels ($p = 0.14$). Under cognitive load, cortisol levels of individuals with HE and SE were almost the same: on average 63.0 ± 3.4 nmol/L ($n = 83$).

What are the differences in organization of neural networks based on fMRI data in patients with different levels of education? Let us consider the differences in indicators of connectivities connecting brain regions in individuals with HE and SE (Fig. 2).

Predominance of positive connectivity differences showing that contingency of some brain structures in patients with HE is higher, than in patients with SE, can be seen (Fig. 2). These differences relate mainly to the temporal regions of both hemispheres and hippocampus, as well as to some regions of the cerebellum and cerebellar vermis.

Let us consider statistical characteristics of the difference in connectivities significant taking into account multiple comparisons and different in both groups of patients (Table 3). The analysis of these connectivities shows, which connections predominate in patients with HE and SE.

It should be noted that positive connections predominate in individuals with HE (Table 3). The only negative connectivity linking the Heschl's gyrus with the cerebellar vermis is non-significant considering multiple comparisons (p-FDR > 0.5). This connectivity is provided in Table 3, since the p-FDR value exceeds significant by less than 0.008.

Connectivities between the above regions can be digitized and presented as vectors, where a regression coefficient would

Table 2. Effects of education on cortisol levels in women suffering from CCI with higher and secondary education

	n	F	*p*	SE	HE
Baseline cortisol, nmol/L	93	6.256	0.014	62.2 ± 3.4 (52)	48.0 ± 4.7 (41)
Cortisol after cognitive load, nmol/L	83	0.206	0.651	64.4 ± 4.4 (47)	61.3 ± 5.3 (36)
Cortisol shift after cognitive load, nmol/L	83	8.597	0.004	3.4 ± 2.6 (47)	14.0 ± 2.2 (36)
Relative cortisol shift relative to baseline cortisol	83	19.666	0.00002	0.08 ± 0.04 (47)	0.4 ± 0.07 (36)

Note: *n* — number of surveyed individuals, F — Fisher's exact test, *p* — significance of differences between the values of two groups; in brackets the number of individuals surveyed; other abbreviations are the same, as in Table 1.

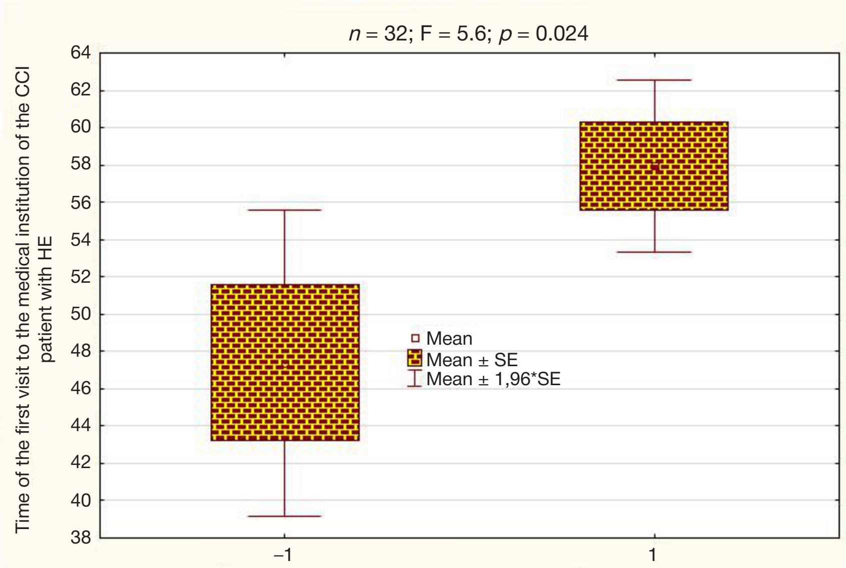

Fig. 1. Value of the cortisol shift associated with cognitive load is related to the time of initial presentation to the medical institution in patients with HE. –1 — average cortisol shift is close to zero (0.02 ± 2.4 nmol/L); 1 — average cortisol shift is 20.09 ± 2.1 nmol/L. On the top there are statistical characteristics of differences in the age of first visit to the medical institution vs. cortisol shift

be correlated to each connectivity of each patient. These connectivities show significant differences in both groups based on the F-test varying between 17.5 and 27.4 with the significance levels between 0.00035 and 0.00003.

Some connectivities are related to cortisol regulation (Table 4).

Connectivities that are positive by sign are negatively correlated to baseline cortisol levels and positively correlated with relative cortisol reactivity; negative connectivity (HGr-Ver10) is negatively correlated to relative cortisol reactivity.

Thus, certain connectivities are significantly different in individuals with different levels of education and are associated with regulation of cortisol levels. The contribution of the PPr-pSTGl, COr-PTl, and HGr-Ver10 connectivities to ensuring cognitive reserve is likely to be associated with their connections with the auditory-speech system.

DISCUSSION

Our studies have revealed a later incidence of CCI in women with HE. It is likely that direct impact of education has a significant effect on CR. CR of women with HE combined with such factors, as social status and a more healthy lifestyle, contribute to stress reduction and, therefore, to the later CCI onset. This is also confirmed by lower baseline cortisol levels

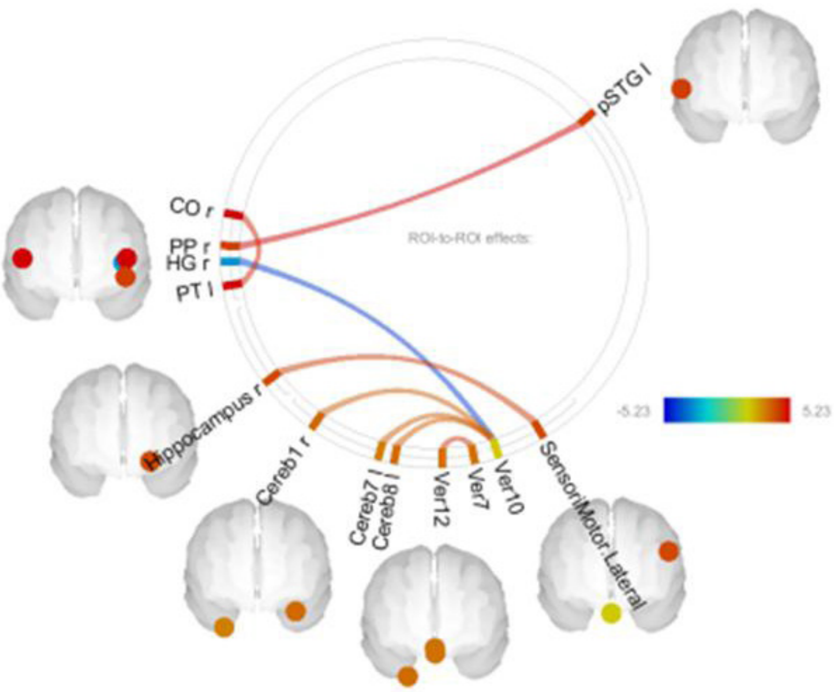

Fig. 2. Connectivity showing significant differences in patients with HE and SE. *Red* lines are positive, these correspond to higher connectivity values in patients with HE. *Blue* lines are negative, these correspond to higher connectivity values in patients with SE. Significance was calculated considering multiple comparisons (p-FDR < 0.05). On the right there is a color chart of differences based on the t-test. CO — central operculum cortex, PP — planum polare (part of superior temporal gyrus), HG — Heschl's gyrus, PT — planum temporale, Hippocampus — hippocampus, SensorMotor.Lateral — sensorimotor lateral neural network, STG — superior temporal gyrus, Cereb — cerebellum, Ver — cerebellar vermis, numbers after Cereb and Ver are areas of the cerebellum and vermis, *p* – posterior, *r* — right hemisphere, l — left hemisphere

Table 3. Connectivities that are significantly different in the groups of patients with HE and SE and their statistical characteristics

Коннективности	*beta*	T (25)	*p-unc*	*p-FDR*
PP r-pSTG l	0.29	5.23	0.000026	0.004331
Hippocampus-SensoriMotor.Lateral	0.28	4.36	0.000229	0.037552
HG r-Ver 10	–0.19	–4.19	0.000353	0.057909
COr-PTl	0.36	4.69	0.000101	0.016558
Ver7-Ver12	0.23	4.56	0.000138	0.022645

Note: *beta* — average regression coefficient, T — T-test, *p-unc* — uncorrected significance level, *p-FDR* — significance level considering multiple comparisons. Number of patients — 25 individuals.

in patients with HE and increased cortisol responsiveness to cognitive load. High cortisol reactivity in such individuals supports a more effective energy supply of cognitive functions and their successful realization, especially when the mental load is relatively brief. The fact of higher brain connectivity in women with HE and the relationship between these connectivities and cognitive functions seems to be important.

According to our data, women with HE develop chronic cerebral ischemia (CCI) later, which is suggested by their later referral to medical institutions (on average by 7 years) and the older age of the beginning of assessment, given they have the same disease stage corresponding to stage 1 or 2 dyscirculatory encephalopathy. The fact that CCI patients with HE age slower is confirmed by higher connectivity of the brain neural networks, which is generally considered to be the sign of the better functioning and younger brain [14].

Modern literature describes differences in aging of women with HE and SE. These differences relate to biological age and external manifestations of age-related changes. Undoubtedly, several factors, including the level of education, contribute to slowing down the aging processes [15]. HE is often correlated to higher socioeconomic status, which results in better access to the resources affecting health and aging. This includes access to high-quality healthcare, proper diet and healthy habits. Well-educated women can be more prone to maintaining healthy lifestyle, including regular physical exercise, smoking cessation, and body weight control. All of them also know more about the health risks and preventive measures.

HE is associated with the larger CR, i.e. the brain's ability to cope with damage and maintain normal functioning [1]. This can result in the later onset or slower progression of the age-related cognitive decline. Women with HE develop CCI at older age and show slower disease progression, which is also true for Alzheimer's disease and the development of other dementia types [16].

The relationship between education and cortisol levels suggesting lower baseline cortisol levels in individuals with HE is also worth attention. The issue of connectivities that are different in individuals with different levels of education and sensitive to cortisol levels suggests that there is a principal relationship between two major CR factors.

Functional connectivity between certain brain regions, such as posterior parietal region (PPr), posterior superior temporal gyrus (pSTG), corticomotor output region (COr), parietal cortex (PTl), and the cerebellar vermis (HGr-Ver10), play an important role in auditory processing, speech and cognitive functions in general. Neuroimaging studies have shown that the characteristics of these connectivities are often different in patients with various disorders of auditory processing, such as verbal and auditory load. These connectivities are also correlated to cortisol levels, especially in response to cognitive load [17–18].

Based on the structural and physiological organization of these brain regions, it can be assumed that the PPr-pSTG connectivity being part of the auditory association system contributes to integration of auditory information and understanding of language [19]. The COr-PTl connection is considered to be involved in synthesis of speech and sensorimotor integration essential for speech functions [20]. The HGr-Ver10 connectivity connecting primary auditory cortex with the cerebellar vermis is considered to be basic for auditory-motor regulation, which contributes to implementation of the tasks requiring coordination of auditory stimuli and motor responses under normal and abnormal conditions [21]. Thus, the role of these connections in construction and organization of CR becomes more evident.

CONCLUSION

HE of women is highly likely to ensure a number of extra benefits. This is often associated with the higher material wealth, awareness of healthy lifestyle, lower adherence to harmful habits, and other factors. All the above, along with lower cortisol levels in individuals with HE, contribute to higher CR and longer health preservation. This is also confirmed by higher connectivity values associated with lower cortisol levels in individuals with HE.

Table 4. Correlation coefficients (r) and significance levels (p) for connectivities and cortisol characteristics

n = 25	PPr-pSTGl	COr-PTl	HGr-Ver10
Cortisol, baseline, *r*	–0.437	–0.418	0.2981
p	0.029	0.038	0.148
Relative cortisol shift, *r*	0.517	0.485	–0.498
p	0.008	0.014	0.011

Note: *n* — number of patients. PP — right planum polare, pSTGl — posterior part of the left superior temporal gyrus; COr — right central operculum cortex, PTl — left planum temporale; HGr — right Heschl's gyrus, Ver10 — Vermis 10.

References

1. Stern Y. What is cognitive reserve? Theory and findings. Journal of the International Neuropsychological Society. 2002; 8 (3): 450–58. Available from: https://doi.org/10.1017/S1355617702814268.
2. Schuurmans IK, Hoepel SJW, Cecil CAM, Hillegers MHJ, Ikram MA, Luik AI. The Association of Life Stress with Subsequent Brain and Cognitive Reserve in Middle-Aged Women. J Alzheimers Dis. 2023; 93 (1): 97–106. DOI: 10.3233/JAD-220923. PMID: 36938734; PMCID: PMC10200172.
3. Ochsner KN, Gross JJ. The cognitive control of emotion. Trends in Cognitive Sciences. 2005; 9 (5): 242–9. Available from: https://doi.org/10.1016/j.tics.2005.03.005.
4. Tang X, Varma VR, Miller MI, Carlson MC. Education is associated with sub-regions of the hippocampus and the amygdala vulnerable to neuropathologies of Alzheimer's disease. Brain Struct Funct. 2017; 222 (3): 1469–79. DOI: 10.1007/s00429-016-1287-9. Epub 2016 Aug 17. PMID: 27535407; PMCID: PMC5850930.
5. Phelps EA. Emotion and cognition: insights from studies of the human amygdala. Annu Rev Psychol. 2006; 57: 27–53. DOI: 10.1146/annurev.psych.56.091103.070234. PMID: 16318588.
6. Dowd JB, Simanek AM, Aiello AE. Socio-economic status, cortisol and allostatic load: a review of the literature. Int J Epidemiol. 2009; 38 (5): 1297–309. DOI: 10.1093/ije/dyp277. Epub 2009 Aug 31. PMID: 19720725; PMCID: PMC2755130.
7. Wingenfeld K, Wolf OT. Stress, memory, and the hippocampus. Front Neurol Neurosci. 2014; 34: 109–20. DOI: 10.1159/000356423. Epub 2014 Apr 16. PMID: 24777135.
8. Davidson RJ, Jackson DC, Kalin NH. Emotion, plasticity, context, and regulation: perspectives from affective neuroscience. Psychol Bull. 2000; 126 (6): 890–909. DOI: 10.1037/0033-2909.126.6.890. PMID: 11107881.
9. Culham JC, Kanwisher NG. Neuroimaging of cognitive functions in human parietal cortex. Curr Opin Neurobiol. 2001; 11 (2): 157–63. DOI: 10.1016/s0959-4388(00)00191-4. PMID: 11301234.
10. Tanashyan MM, Maksimova MYu, Domashenko MA. Discirkuljatornaja jencefalopatija. Putevoditel' vrachebnyh naznachenij. 2015; 2: 1–25.
11. Morris JC. Clinical dementia rating: a reliable and valid diagnostic and staging measure for dementia of the Alzheimer type. Int Psychogeriatric. 1997; (9 Suppl 1): 173–76.
12. Fokin VF, Ponomareva NV, Konovalov RN, Krotenkova MV, Medvedev RB, Lagoda OV, Tanashyan MM. Vlijanie urovnja obrazovanija na funkcional'nuju organizaciju mozga bol'nyh hronicheskoj cerebral'noj ishemiej. Annaly klinicheskoj i jeksperimental'noj nevrologii. 2021; 15 (2): 35–41. DOI: 10.25692/ACEN.2021.2.5.
13. Fokin VF, Shabalina AA, Ponomareva NV, Medvedev RB, Lagoda OV, Tanashyan MM. Kortizol, citokiny i vegetativnye izmenenija pri kognitivnoj nagruzke u bol'nyh hronicheskoj ishemiej mozga. Patologicheskaja fiziologija i jeksperimental'naja terapija. 2023; 67 (3): 51–57. DOI: 10.25557/0031-2991.2023.03.51-57.
14. Cansino S. Brain connectivity changes associated with episodic recollection decline in aging: A review of fMRI studies. Front Aging Neurosci. 2022; 14: 1012870. DOI: 10.3389/fnagi.2022.1012870. PMID: 36389073; PMCID: PMC9640923.
15. Seblova D, Berggren R, Lövdén M. Education and age-related decline in cognitive performance: Systematic review and meta-analysis of longitudinal cohort studies. Ageing Res Rev. 2020; 58: 101005. DOI: 10.1016/j.arr.2019.101005. Epub 2019 Dec 24. PMID: 31881366.
16. Zahodne LB, Stern Y, Manly JJ. Differing effects of education on cognitive decline in diverse elders with low versus high educational attainment. Neuropsychology. 2015; 29 (4): 649–57. DOI: 10.1037/neu0000141. Epub 2014 Sep 15. PMID: 25222199; PMCID: PMC4362867.
17. Rivera-Bonet CN, Birn RM, Ladd CO, Meyerand ME, Abercrombie HC. Cortisol effects on brain functional connectivity during emotion processing in women with depression. J Affect Disord. 2021; 287: 247–54. DOI: 10.1016/j.jad.2021.03.034. Epub 2021 Mar 17. PMID: 33799044; PMCID: PMC8128282.
18. Jentsch VL, Merz CJ, Wolf OT. Restoring emotional stability: Cortisol effects on the neural network of cognitive emotion regulation. Behav Brain Res. 2019; 18 (374): 111880. DOI: 10.1016/j.bbr.2019.03.049. Epub 2019 Apr 1. PMID: 30946860.
19. Hickok G, Poeppel D. The cortical organization of speech processing. Nature Reviews Neuroscience. 2007; 8 (5): 393–402. Available from: https://doi.org/10.1038/nrn2113.
20. Heald SL, Nusbaum HC. Speech perception as an active cognitive process. Front Syst Neurosci. 2014; 8: 35. DOI: 10.3389/fnsys.2014.00035. PMID: 24672438; PMCID: PMC3956139.
21. Wang Z, Wang Y, Sweeney JA, Gong Q, Lui S, Mosconi MW. Resting-State Brain Network Dysfunctions Associated With Visuomotor Impairments in Autism Spectrum Disorder. Front Integr Neurosci. 2019; 13: 17. DOI: 10.3389/fnint.2019.00017. PMID: 31213995; PMCID: PMC6554427.

Литература

1. Stern Y. What is cognitive reserve? Theory and findings. Journal of the International Neuropsychological Society. 2002; 8 (3): 450–58. Available from: https://doi.org/10.1017/S1355617702814268.
2. Schuurmans IK, Hoepel SJW, Cecil CAM, Hillegers MHJ, Ikram MA, Luik AI. The Association of Life Stress with Subsequent Brain and Cognitive Reserve in Middle-Aged Women. J Alzheimers Dis. 2023; 93 (1): 97–106. DOI: 10.3233/JAD-220923. PMID: 36938734; PMCID: PMC10200172.
3. Ochsner KN, Gross JJ. The cognitive control of emotion. Trends in Cognitive Sciences. 2005; 9 (5): 242–9. Available from: https://doi.org/10.1016/j.tics.2005.03.005.
4. Tang X, Varma VR, Miller MI, Carlson MC. Education is associated with sub-regions of the hippocampus and the amygdala vulnerable to neuropathologies of Alzheimer's disease. Brain Struct Funct. 2017; 222 (3): 1469–79. DOI: 10.1007/s00429-016-1287-9. Epub 2016 Aug 17. PMID: 27535407; PMCID: PMC5850930.
5. Phelps EA. Emotion and cognition: insights from studies of the human amygdala. Annu Rev Psychol. 2006; 57: 27–53. DOI: 10.1146/annurev.psych.56.091103.070234. PMID: 16318588.
6. Dowd JB, Simanek AM, Aiello AE. Socio-economic status, cortisol and allostatic load: a review of the literature. Int J Epidemiol. 2009; 38 (5): 1297–309. DOI: 10.1093/ije/dyp277. Epub 2009 Aug 31. PMID: 19720725; PMCID: PMC2755130.
7. Wingenfeld K, Wolf OT. Stress, memory, and the hippocampus. Front Neurol Neurosci. 2014; 34: 109–20. DOI: 10.1159/000356423. Epub 2014 Apr 16. PMID: 24777135.
8. Davidson RJ, Jackson DC, Kalin NH. Emotion, plasticity, context, and regulation: perspectives from affective neuroscience. Psychol Bull. 2000; 126 (6): 890–909. DOI: 10.1037/0033-2909.126.6.890. PMID: 11107881.
9. Culham JC, Kanwisher NG. Neuroimaging of cognitive functions in human parietal cortex. Curr Opin Neurobiol. 2001; 11 (2): 157–63. DOI: 10.1016/s0959-4388(00)00191-4. PMID: 11301234.
10. Танашян М. М., Максимова М. Ю., Домашенко М. А. Дисциркуляторная энцефалопатия. Путеводитель врачебных назначений. 2015; 2: 1–25.
11. Morris JC. Clinical dementia rating: a reliable and valid diagnostic and staging measure for dementia of the Alzheimer type. Int Psychogeriatric. 1997; (9 Suppl 1): 173–76.
12. Фокин В. Ф., Пономарева Н. В., Коновалов Р. Н., Кротенкова М. В., Медведев Р. Б., Лагода О. В., Танашян М. М. Влияние уровня образования на функциональную организацию мозга больных хронической церебральной ишемией. Анналы клинической и экспериментальной неврологии. 2021; 15 (2): 35–41. DOI: 10.25692/ACEN.2021.2.5
13. Фокин В. Ф., Шабалина А. А., Пономарева Н. В., Медведев Р. Б., Лагода О. В., Танашян М. М. Кортизол, цитокины и вегетативные изменения при когнитивной нагрузке у больных хронической ишемией мозга. Патологическая физиология и

экспериментальная терапия. 2023; 67 (3): 51–57. DOI: 10.25557/0031-2991.2023.03.51-57.
14. Cansino S. Brain connectivity changes associated with episodic recollection decline in aging: A review of fMRI studies. Front Aging Neurosci. 2022; 14: 1012870. DOI: 10.3389/fnagi.2022.1012870. PMID: 36389073; PMCID: PMC9640923.
15. Seblova D, Berggren R, Lövdén M. Education and age-related decline in cognitive performance: Systematic review and meta-analysis of longitudinal cohort studies. Ageing Res Rev. 2020; 58: 101005. DOI: 10.1016/j.arr.2019.101005. Epub 2019 Dec 24. PMID: 31881366.
16. Zahodne LB, Stern Y, Manly JJ. Differing effects of education on cognitive decline in diverse elders with low versus high educational attainment. Neuropsychology. 2015; 29 (4): 649–57. DOI: 10.1037/neu0000141. Epub 2014 Sep 15. PMID: 25222199; PMCID: PMC4362867.
17. Rivera-Bonet CN, Birn RM, Ladd CO, Meyerand ME, Abercrombie HC. Cortisol effects on brain functional connectivity during emotion processing in women with depression. J Affect Disord. 2021; 287: 247–54. DOI: 10.1016/j.jad.2021.03.034. Epub 2021 Mar 17. PMID: 33799044; PMCID: PMC8128282.
18. Jentsch VL, Merz CJ, Wolf OT. Restoring emotional stability: Cortisol effects on the neural network of cognitive emotion regulation. Behav Brain Res. 2019; 18 (374): 111880. DOI: 10.1016/j.bbr.2019.03.049. Epub 2019 Apr 1. PMID: 30946860.
19. Hickok G, Poeppel D. The cortical organization of speech processing. Nature Reviews Neuroscience. 2007; 8 (5): 393–402. Available from: https://doi.org/10.1038/nrn2113.
20. Heald SL, Nusbaum HC. Speech perception as an active cognitive process. Front Syst Neurosci. 2014; 8: 35. DOI: 10.3389/fnsys.2014.00035. PMID: 24672438; PMCID: PMC3956139.
21. Wang Z, Wang Y, Sweeney JA, Gong Q, Lui S, Mosconi MW. Resting-State Brain Network Dysfunctions Associated With Visuomotor Impairments in Autism Spectrum Disorder. Front Integr Neurosci. 2019; 13: 17. DOI: 10.3389/fnint.2019.00017. PMID: 31213995; PMCID: PMC6554427.