

Behavioral evaluation of central auditory processing in climacteric women

Avaliação comportamental do processamento auditivo central em mulheres no climatério

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ABSTRACT

Purpose: To compare the central auditory abilities of climacteric women, with and without hormone replacement therapy. **Methods:** Observational study, performed with climacteric women with and without hormone replacement therapy. Sound localization tests were performed in five directions; Sequential Verbal Memory Test; Sequential Memory Test for Nonverbal Sounds; Duration Pattern Test; Random Gap Detection Test; Masking Level Difference; Dichotic Digit Test and Speech With White Noise Test and the questionnaire “Informal Fatigue Assessment” was applied. **Results:** The differences pointed out revealed the biased difference that occurs due to higher average performance in the group with TH compared to the group without TH for TMSnV. In the TLS, TMSN, RGDT and MLD tests, the group with HT presented quantitatively better results. **Conclusion:** Climacteric women, with and without hormone therapy, have central auditory processing disorder involving the auditory skills of sound localization, simple and complex temporal ordering, background figure, temporal resolution and binaural interaction. However, women in the hormone therapy group performed better in simple temporal ordering.

Keywords: Hearing; Auditory perception; Auditory tests; Climacteric; Memory; Attention

RESUMO

Objetivo: Comparar as habilidades auditivas centrais de mulheres no climatério, com e sem terapia de reposição hormonal. **Métodos:** Estudo observacional, realizado com mulheres no climatério, divididas em dois grupos, segundo o uso ou não de terapia hormonal. Foram realizados os testes de Localização Sonora em cinco direções; Memória Sequencial para Sons Verbais e Não Verbais; Padrão de Duração; Random Gap Detection Test (RGDT); Masking Level Difference (MLD); Dicótico de Dígitos; Fala Com Ruído Branco, e aplicado o Questionário Avaliação Informal de Fadiga. **Resultados:** Houve diferença tendenciosa de melhor desempenho médio no grupo com terapia hormonal, em comparação ao grupo sem terapia para o teste de Memória para Sons Não Verbais. Nos testes de Localização Sonora, Memória para Sons Verbais, RGDT e MLD, o grupo com terapia hormonal apresentou resultados quantitativamente melhores. O grupo com terapia hormonal demonstrou maior porcentagem de mulheres com alto nível de fadiga. **Conclusão:** Mulheres no climatério, com e sem terapia hormonal, apresentam transtorno de processamento auditivo central envolvendo as habilidades auditivas de localização sonora, ordenação temporal simples e complexa, figura-fundo, resolução temporal e interação binaural. No entanto, as mulheres do grupo com terapia hormonal apresentam melhor desempenho em ordenação temporal simples.

Palavras-chave: Audição; Percepção auditiva; Testes auditivos; Climatério; Memória; Atenção

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INTRODUCTION

Menopause is the period in women's lives between the end of their reproductive phase and senescence. It is considered a syndrome with variable symptoms affecting the body as a whole^(1,2). One such change is the decreased production of estrogen, which is the main female reproductive hormone and influences other systems, including the nervous system.

Women often report cognitive problems during menopause, which studies suggest arise more frequently in the transition to menopause and after menopause. Estrogens modulate neurogenesis and synaptic plasticity by interacting with neurotransmitter systems and maintaining cognitive function and brain health. Based on these assumptions, studies have also found relationships between cognitive complaints and menopausal symptoms. They list the latter along with hormonal fluctuations as contributing factors to memory decline, as they can interrupt sleep and compromise activities of daily living, which in turn can affect memory^(3,4).

Furthermore, changes in hormonal levels are often related to symptoms of mood swings, such as anxiety, depression, and irritability, likely resulting from decreased estrogen levels. Such changes may also be associated with deficits in memory, attention, and information processing speed, which are important for central auditory processing – i.e., the series of processes involved in the detection, analysis, and interpretation of sounds⁽⁵⁻⁷⁾.

Central auditory processing (CAP) corresponds to the auditory skills underlying the activities of the central auditory nervous system to understand sounds efficiently. CAP disorders (CAPD) have been defined as changes specifically in auditory processing, which may be associated with difficulties in hearing or understanding speech, language development, and learning^(6,7). To understand the speech signal in noisy environments, both individuals with normal hearing thresholds and those with some degree of hearing loss must activate their attention, memory, and cognitive resources responsible for processing and interpreting auditory information. The term “listening effort” is defined as the amount of cognitive resources required to recognize acoustic signals, especially speech⁽⁷⁾.

Healthcare for menopausal women is an ongoing challenge for health professionals. Hormone replacement therapy (HRT), generally aiming to restore estrogen levels, is one of the options that provide immediate relief from the symptoms caused by the syndrome⁽⁸⁾.

Female hormones affect the auditory system, and women's hearing fluctuates throughout the menstrual cycle. A study has reported that hearing sensitivity improved during the late follicular phase and decreased during the luteal phase, demonstrating the effect of female sex hormones – although the specific effects of estradiol and progesterone fluctuations in the central auditory system remain unclear. On the other hand, no such fluctuations in men during the same period have been reported. As for menopause, hearing sensitivity has been found to decrease rapidly as early as its onset⁽⁹⁾.

Given the effects of estrogen on memory, attention, and information processing speed, menopausal women may be more susceptible to CAPD complaints as estrogen hormone production decreases, which is closely related to verbal information processing. CAPD can increase listening effort, as women at this

stage of life may not have satisfactory conditions for interpreting sounds, placing greater demands on other cognitive resources, such as memory and attention⁽⁸⁾.

Studies have examined the effects of estrogen on postmenopausal women in HRT and found they had improved pure-tone hearing thresholds, reduced latencies, and increased amplitudes in brainstem auditory response examination (ABR)⁽¹⁰⁾.

Thus, HRT not only reduces menopause symptoms but also has a beneficial effect on women's CAP – which must be assessed along with the listening effort to prove the auditory effects before and after HRT.

No studies have been found with behavioral CAP assessment in menopausal women, which highlights the originality of the present research. Even though restrictive measures taken during the COVID-19 pandemic hampered data collection, this study brings relevant results and opens the way for further research.

Hence, this research aimed to compare the central auditory skills of menopausal women with and without HRT.

METHODS

This cross-sectional study comprised two groups of menopausal women, one of them having and the other not having HRT. The sample was selected at the Menopause Outpatient Center of the University Hospital 2 – São Paulo Hospital, of the Federal University of São Paulo (HU2 – HSP/UNIFESP). The behavioral CAP assessment was carried out at the UNIFESP Clinical Audiology Outpatient Center. The study was approved by the institution's Research Ethics Committee under number 31453120.9.0000.5505.

The sample selection included women aged 45 to 59 years; right-handed; nonsmokers; diagnosed with surgical or nonsurgical pre-menopause or menopause; having normal audiological, pap smear, and mammography examination results; and being on HRT for at least 3 months or having no contraindication to HRT. All participants signed an informed consent form.

It must be pointed out that data collection was negatively impacted by the COVID-19 pandemic. The outpatient clinics did not operate normally during isolation, and the flow of patients remained low even after activities resumed. The time for data collection was limited, and many potential patients did not attend the assessment even after several calls. Thus, 15 women were invited to participate in the research, whereas three of them were excluded from the sample due to issues such as hearing loss and nonattendance to the examinations.

Thus, the sample comprised 12 women – six in the non-HRT group (control group) and six in the HRT group (study group) –, aged 45 to 58 years. All women in both groups had no hearing sensitivity complaints.

Hormonal replacement in the HRT group was carried out with Suprelle (1 mg of estradiol valerate and 0.5 mg of norethisterone acetate) or Sandrena Gel (1 mg or 0.5 mg of estradiol).

The assessments were carried out in one session, lasting approximately 2 hours with rest intervals.

After recruitment, all patients were submitted to a medical history survey and otoscopy. They also filled out the Informal Fatigue Assessment Questionnaire⁽¹¹⁾, whose 11 questions approach overall fatigue and are answered on a 4-point scale. Its minimum total score is 0, indicating a lower level of fatigue, and its maximum score is 33 points, indicating a higher level

of fatigue; the maximum typical fatigue score is 14.83 points. Therefore, subjects who score above this value indicate that they are more fatigued than others.

Then they underwent a behavioral CAP assessment with the following tests: Five-direction Sound Localization Test (SLT), Sequential Memory Test for Verbal Sounds (SMTV), Sequential Memory Test for Nonverbal Sounds (SMTNV), Duration Pattern Test (DPT), Random Gap Detection Test (RGDT), Masking Level Difference, (MLD), Dichotic Digit Test (DDT), and Speech by White Noise Test (SWN).

After collection, the behavioral CAP assessment results were classified as normal or abnormal, according to normal standards⁽¹²⁻¹⁴⁾ (Chart 1).

Hearing skills were classified as normal or abnormal, depending on the test(s) in which they performed below the normal standards and their overall assessment performance. Hearing skills classified as abnormal were indicative of CAPD, following the recommendation of the Brazilian Academy of Audiology⁽¹²⁻¹⁴⁾ (Chart 1).

Then, the data were organized in a spreadsheet and sent to a statistician for analyses, which were performed in SPSS (IBM), version 19, and Excel 2013.

Descriptive statistics with summary measures of position and variability were used to analyze numerical data and quantitative variables. Inferential statistics with Student's t-test for independent samples compared numerical data. The descriptive statistics of the qualitative (categorical) variables were presented with simple and double-entry tabulations, referring to the relevant frequencies and percentages inherent to the object of study. Nonparametric statistical techniques were used to compare categorical data.

The discrepancy between the statistical hypothesis and the observed data was verified with statistical significance analysis, considering a measure of evidence, the probability of type I error (α) of 0.05, meaning a 5% rejection region.

RESULTS

The sample had 12 women – six in the non-HRT group (control group) and six in the HRT group (study group) –, aged 45 to 58 years, with no hearing complaints. The HRT group had a higher mean chronological age (52 years and 2 months) than the non-HRT group (50 years and 8 months).

The educational attainment of the study and control groups was partially matched (greater than 83%). The most frequent degree was that of high school graduates.

None of the women in the study group (with HRT) had been exposed to noise throughout their lives. However, they had comorbidities such as anxiety, psychological and/or psychiatric support, thyroid problems, lupus, bone diseases, kidney diseases, and high blood pressure.

Neither of the groups in the sample had hearing sensitivity complaints (Figure 1).

The results shown in Table 1 revealed the trend toward a difference due to better mean SMTNV test performance in the HRT group than the non-HRT group. In the SLT, SMTNV, SMTV, RGDT, and MLD tests, the HRT group had quantitatively better results, but with no statistical differences.

Table 2 demonstrates that the non-HRT group had a higher mean number of correct answers in the right ear (RE) SWN than the HRT group. Moreover, according to the analysis, the non-HRT group had better DPT and DDT results in both the RE and left ear (LE).

The qualitative analysis of the tests verified that the HRT group performed better in SMTV, RGDT, and MLD, with a higher normal result index (Table 3).

On the other hand, the non-HRT group was qualitatively better in the DDT in the RE and LE, with a higher percentage of normal results.

Chart 1. Analysis criteria for the central auditory processing behavioral tests used in the research

Test	Hearing Skill	Physiological Mechanism	Reference Criteria
Five-direction Sound Localization Test (SLT)	Localization	Discriminating the direction of the sound source	Identifying at least four out of the five directions.
Sequential Memory Test for Verbal Sounds (SMTV)	Temporal ordering	Discriminating sequential verbal sounds	Identifying at least three out of the four sequences.
Sequential Memory Test for Nonverbal Sounds (SMTNV)	Temporal ordering	Discriminating sequential nonverbal sounds	Identifying at least two out of the three sequences.
Duration Pattern Test (DPT)	Temporal ordering	Discriminating temporal patterns	Above 12 years old, $\geq 83\%$ correct answers
Random Gap Detection Test (RGDT)	Temporal resolution	Discriminating interstimulus pauses	Identifying intervals ≥ 10 ms
Masking Level Difference (MLD)	Binaural interaction	Identifying sounds in the presence of noise	≥ 10 dB
Dichotic Digits Test (DDT)	Figure-ground	Discriminating verbal sounds in dichotic hearing	Above 11 years old: $> 95\%$ correct answers
Speech by White Noise Test (SWN)	Auditory closure	Discriminating physically distorted sounds	$\geq 72\%$ correct answers; SRPI – SRPIWN $< 20\%$

Subtitle: \geq = higher than or equal to; \leq = lower than or equal to; $>$ = higher than; $<$ = lower than; SRPI = speech recognition percentage index; SRPIWN = speech recognition percentage index by white noise

Table 1. Descriptive statistics of quantitative performance in central auditory processing behavioral tests and comparative statistics between groups

Groups		N	Mean	Median	SD	Min	Max	95% CI		p-value ¹
								Lower limit	Higher limit	
SLT	Non-HRT	6	63.33%	60.00%	15.06%	40.00%	80.00%	53.33%	73.33%	0.541
	HRT	6	70.00%	70.00%	20.98%	40.00%	100.00%	53.42%	83.33%	
SMTV	Non-HRT	6	55.53%	66.60%	45.54%	0.00%	100.00%	22.20%	88.87%	0.155
	HRT	6	88.88%	100.00%	27.23%	33.30%	100.00%	66.65%	100.00%	
SMTNV	Non-HRT	6	72.17%	66.60%	13.64%	66.60%	100.00%	66.60%	83.30%	0.092**
	HRT	6	88.87%	100.00%	17.25%	66.60%	100.00%	77.73%	100.00%	
SWN RE	Non-HRT	6	95.33%	96.00%	3.01%	92.00%	100.00%	93.33%	97.33%	0.043*
	HRT	6	88.00%	90.00%	7.16%	76.00%	96.00%	82.67%	92.67%	
SWN LE	Non-HRT	6	92.00%	92.00%	5.66%	84.00%	100.00%	88.00%	96.00%	>0.999
	HRT	6	92.00%	92.00%	6.69%	80.00%	100.00%	86.67%	96.65%	
DPT	Non-HRT	6	60.34%	71.44%	27.23%	26.00%	89.91%	41.15%	79.30%	0.740
	HRT	6	55.50%	52.28%	21.55%	29.97%	83.25%	39.96%	71.04%	
RGDT (ms)	Non-HRT	6	13.54	12.50	7.29	5.00	22.50	8.50	18.92	0.911
	HRT	6	12.96	11.25	10.12	2.75	27.50	6.33	20.42	
DDT RE	Non-HRT	6	89.17%	90.00%	10.68%	72.50%	100.00%	80.84%	96.67%	0.207
	HRT	6	77.92%	76.25%	17.42%	50.00%	100.00%	65.42%	90.00%	
DDT LE	Non-HRT	6	84.58%	87.50%	15.44%	62.50%	100.00%	72.50%	95.83%	0.239
	HRT	6	73.33%	72.50%	15.71%	50.00%	92.50%	61.67%	84.17%	
MLD (dB)	Non-HRT	6	6.00	7.00	4.20	0.0	10.0	3.00	9.00	0.811
	HRT	6	5.33	6.00	5.16	0.0	10.0	2.00	8.67	

¹Statistical test: Student's independent t-test; *Significant p-value; **Trend towards a significant p-value

Subtitle: N = Number of subjects; > = higher than; ms = milliseconds; dB = decibels; Min = Minimum; Max = Maximum; SD = standard deviation; CI = confidence interval; HRT = hormone replacement therapy; RE = right ear; LE = left ear; SLT = Sound Localization Test; SMTV = Sequential Memory Test for Verbal Sounds; SMTNV = Sequential Memory Test for Nonverbal Sounds; SWN = Speech By White Noise Test; DPT = Duration Pattern Test; RGDT = Random Gap Detection Test; DDT = Dichotic Digits Test; MLD = Masking Level Difference

Table 2. Descriptive statistics regarding the qualitative performance in the central auditory processing assessment and comparative statistics between the groups

Classification		Non-HRT		HRT		p-value ¹
		N	Freq (%)	N	Freq (%)	
SLT	Normal	3	50.0	3	50.0	0.716
	Abnormal	3	50.0	3	50.0	
SMTV	Normal	4	66.7	5	83.3	0.500
	Abnormal	2	33.3	1	16.7	
SMTNV	Normal	6	100.0	6	100.0	- x -
	Abnormal	0	0.0	0	0.0	
SWN RE	Normal	6	100.0	6	100.0	- x -
	Abnormal	0	0.0	0	0.0	
SWN LE	Normal	6	100.0	6	100.0	- x -
	Abnormal	0	0.0	0	0.0	
DPT	Normal	1	16.7	1	16.7	0.773
	Abnormal	5	83.3	5	83.3	
RGDT	Normal	2	33.3	3	50.0	0.500
	Abnormal	4	66.7	3	50.0	
DDT RE	Normal	2	33.3	1	16.7	0.500
	Abnormal	4	66.7	5	83.3	
DDT LE	Normal	2	33.3	0	0.0	0.227
	Abnormal	4	66.7	6	100.0	
MLD	Normal	2	33.3	3	50.0	0.500
	Abnormal	4	66.7	3	50.0	

¹Statistical test: extension of Fisher's Exact test

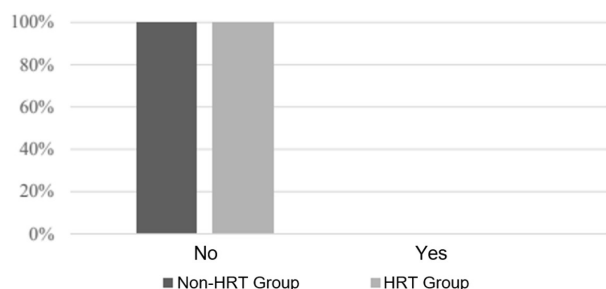
Subtitle: N = number of subjects; % = percentage; Freq = Frequency; HRT = hormone replacement therapy; RE = right ear; LE = left ear; SLT = Sound Localization Test; SMTV = Sequential Memory Test for Verbal Sounds; SMTNV = Sequential Memory Test for Nonverbal Sounds; SWN = Speech By White Noise Test; DPT = Duration Pattern Test; RGDT = Random Gap Detection Test; DDT = Dichotic Digits Test; MLD = Masking Level Difference; - x - = it was not possible to use statistics

Table 3. Descriptive statistics of qualitative performance in the questionnaire and comparative statistics between groups

Questionnaire	NON-HRT		HRT		p-value ¹
	N	Freq (%)	N	Freq (%)	
Typical fatigue level	5	83.3	4	66.7	0.505
High fatigue level	1	16.7	2	33.3	

¹Statistical test: Pearson's chi-square or extension of Fisher's Exact test

Subtittle: N = number of subjects; Freq = Frequency; HRT = hormone replacement therapy

**Figure 1.** Distribution frequency of hearing complaints per group

Subtittle: % = percentage; HRT = Hormone replacement therapy

In the other tests, the groups did not have qualitatively different results.

The mean quantitative results of the fatigue questionnaire were similar in both groups – the non-HRT group had a mean of 12.33 points, and the HRT group had a mean of 12.67 points.

The HRT group had a higher percentage of women with a high fatigue level, according to the qualitative analysis, though with no statistically significant difference.

DISCUSSION

The most frequent level of education in the characterization of the sample (which partially matched between the groups) was that of high school graduates. The sample women in either group did not have hearing sensitivity complaints (Figure 1). However, most of them reported hearing perception problems, such as difficulty understanding in a noisy environment. Their hearing thresholds were normal in the pure-tone assessment. Therefore, the reported complaints may be due to CAP-related hearing difficulties, as their results were normal in the quantitative assessments (hearing thresholds)⁽¹⁵⁾. The fact that two women in the sample recruitment process had hearing loss called attention to and demonstrated the need to include audiological assessments among the examinations of menopausal women. Both were excluded from the sample.

Estrogen and progesterone, female hormones, greatly influence the central nervous system. Estrogen production tends to gradually decrease with the menopause onset, which occurs at the mean age of 51 years and 9 months in Brazilian women. Various changes are perceived in the female body during menopause, such as hot flashes, changes in sleep, mood, fatigue, anxiety, memory difficulties, and reduced information processing speed⁽⁷⁾.

Memory changes and slow information processing during menopause occur because cellular receptors for sex hormones

are located in specific areas of the brain, such as the pituitary gland, hypothalamus, limbic system, and cerebral cortex⁽⁷⁾.

Women's cognitive performance at different stages of menopause was studied using speech processing tests, immediate and delayed verbal memory, and working memory, with the Digit Span Test. The results showed that postmenopausal women had reduced auditory information processing speed in delayed verbal memory tests. Women undergoing HRT slightly improved their working memory, speech processing, and immediate and delayed verbal memory results⁽⁵⁾.

Another study found no relationship between memory complaints reported by menopausal women and memory and attention test performance⁽⁴⁾. Moreover, increased stress levels and changes in health and sleep may also be related to changes in attention⁽¹⁶⁾.

The transition between menopause phases is accompanied by changes in cortisol levels, which may be associated with declined memory and attention. Cognitive changes in postmenopausal women over 60 years old were verified in another study using auditory processing and word list memory tests. Their results were related to Mini-Mental State Examination results, indicating a possible relationship between CAP changes (immediate and short-term memory) and later development of dementia. However, this study did not address peripheral auditory aspects that could be affected by hearing changes that occur after 50 years old – i.e., age-related hearing loss or presbycusis^(5,17).

The sample in the present study had women aged 45 to 58 years, with an older mean age in the HRT group than in the non-HRT group.

The statistical analysis showed a trend toward a difference for better SMTNV mean performance in the HRT group than in the non-HRT group. The HRT group also performed had quantitatively better SLT, SMTV, RGDT, and MLD results, though not statistically significant (Table 1). Both groups had the same result in SWN LE.

In the qualitative analysis, the HRT group performed better in SMTV, RGDT, and MLD, with a higher normal result index (Table 2), demonstrating better performance in temporal processing.

Thus, the HRT group had better CAP assessment results in general, demonstrating a possible relationship between HRT and CAP (Table 2). The test results were not statistically significant, probably due to the sample size. Hence, a study with more participants may statistically demonstrate an advantage in the HRT group.

The present study also found an advantage of the RE in the DDT test in both groups, confirming left hemisphere dominance, even in menopause years. The results of a study with dichotic tests found decreasing binaural processing with increasing age, which affects the auditory system and interhemispheric integrity. Such a decline usually occurs between 40 and 55 years old, regardless of the sex. The decline in interhemispheric

integrity is demonstrated in dichotic tests by measuring the advantage of the RE in tests with words – i.e., when the LE performs worse than the RE. The RE advantage in word tests occurs during the maturation of the auditory pathways, whereas by 9 years old, the two ears become equivalent. When dichotic or competitive stimuli are presented to both ears, the ipsilateral central auditory pathway is suppressed by the stronger contralateral pathway. Because the language-dominant hemisphere (usually the left one) is recruited for the verbal perception of auditory linguistic stimuli, information presented on the left side needs to be transferred from the right hemisphere to the left side via the posterior part of the corpus callosum, whereas stimuli presented to the RE do not require this path. Thus, an RE advantage would indicate poor interhemispheric function⁽¹⁸⁾.

Lastly, the results of the Informal Fatigue Assessment Questionnaire were analyzed to investigate the study groups' listening effort – although the questionnaire does not directly address auditory and CAP issues. The research participants had difficulties in differing listening efforts from physical and mental fatigue symptoms. The statistical quantitative and qualitative analyses revealed no statistically significant differences between the HRT and non-HRT groups. Thus, the questionnaire was not effective in discriminating the groups (Table 3).

The main limitation of the study was the difficulty in recruiting participants, especially due to the social isolation imposed by the COVID-19 pandemic. The study also had other limitations, such as not assessing the women's executive functions, despite their proven relationship with CAP. Due to the short collection period, it was not possible to evaluate the same women before and after HRT. Finally, the study did not control the type, time, or manner of medication use by the participants – it was only assured that they had been in HRT for at least 3 months. Therefore, the study results must be cautiously generalized.

Nevertheless, these results open the way for future perspectives, such as studying the same group of women before and after HRT with different types of medication, proposing hearing skills rehabilitation with acoustically controlled training after HRT, comparing neuropsychological with central auditory skills, and using specific self-assessed hearing questionnaires to subjectively characterize CAPD.

Thus, further studies in the area, especially with larger samples, are needed to better clarify the associations between cognitive domains and CAP.

CONCLUSION

Menopausal women with and without HRT in this study had CAPD involving the following hearing skills: sound localization, simple and complex temporal ordering, figure-ground, temporal resolution, and binaural interaction.

On the other hand, the women in the HRT group performed better in simple temporal ordering. They also had better quantitative results, though not statistically significant, in the sound localization, figure-ground, temporal resolution, and binaural interaction tests.

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