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Cognitive auditory training in subjects after COVID-19: an analysis of the effects of the intervention in adults

Treinamento auditivo cognitivo em sujeitos após COVID-19: uma análise dos efeitos da intervenção em adultos

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ABSTRACT

Purpose: To analyze the effectiveness of a therapeutic intervention plan through an existing cognitive auditory training program, adapted for adults, after one year of COVID-19 infection. **Methods:** 13 subjects, between 18 and 59 years old, four males and nine females participated in the study. All underwent anamnesis, visual inspection of the external acoustic meatus, pure tone audiometry, speech audiometry and acoustic immitance measurements as selection procedures. For the research, the following procedures were carried out in the evaluation and reassessment: evaluation of central auditory processing, brief neuropsychological evaluation - NEUPSILIN, Speech, Spatial and Qualities of Hearing Scale and the Cognitive Potential - P300 with speech stimulus. Cognitive auditory training was carried out in six consecutive sessions, in an open field, lasting approximately 50 minutes. In all analyses, a significance level of 5% ($p \leq 0.05$) was considered. **Results:** When comparing the variables between the periods, pre and post intervention, there was a statistically significant difference in the Dichotic Digit Test ($p = 0.009$), in the Frequency Pattern Test ($p = 0.020$) and in Speech, Spatial and Qualities of Hearing Scale ($p = 0.001$). And a tendency to significance ($p < 0.10$) in the Gap in Noise test and Total Attention. **Conclusion:** Cognitive auditory training proved to be an effective therapeutic strategy for the treatment of adults with speech comprehension and cognition complaints after COVID-19 infection.

Keywords: Hearing; COVID-19; Hearing tests; Auditory evoked potentials; Auditory training; Cognition.

RESUMO

Objetivo: analisar a eficácia de um plano de intervenção terapêutica por meio de um programa de treinamento auditivo cognitivo já existente, adaptado para adultos, após um ano de infecção por COVID-19. **Métodos:** participaram do estudo 13 sujeitos, entre 18 e 59 anos de idade, quatro do gênero masculino e nove do gênero feminino. Todos foram submetidos a um questionário, inspeção visual do meato acústico externo, audiometria tonal liminar, logoaudiometria e medidas de imitância acústica, como procedimentos de seleção. Foram realizados, na avaliação e na reavaliação, os seguintes procedimentos: avaliação do processamento auditivo central, avaliação neuropsicológica breve-NEUPSILIN, *Speech, Spatial and Qualities of Hearing Scale* e o Potencial Cognitivo - P300, com estímulo de fala. O treinamento auditivo cognitivo foi realizado em seis sessões consecutivas, em campo aberto, com duração de, aproximadamente, 50 minutos. Em todas as análises foi considerado o nível de significância de 5% ($p \leq 0,05$). **Resultados:** na comparação das variáveis entre os períodos, pré e pós-intervenção, houve diferença estatisticamente significativa no Teste Dicótico de Dígitos ($p = 0,009$), no Teste Padrão de Frequência ($p = 0,020$) e no *Speech, Spatial and Qualities of Hearing Scale* ($p = 0,001$). Houve tendência à significância ($p < 0,10$) no teste *Gap in Noise* e na Atenção Total. **Conclusão:** o treinamento auditivo cognitivo demonstrou ser uma estratégia terapêutica eficaz para o tratamento de adultos com queixas de compreensão de fala e de cognição após infecção por COVID-19.

Palavras-chave: Audição; COVID-19; Testes auditivos; Potenciais evocados auditivos; Treinamento auditivo; Cognição.

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INTRODUCTION

In December 2019, a new type of coronavirus, caused by the agent SARS-CoV-2, emerged in Wuhan, China, and quickly spread around the world, causing thousands of deaths and sequelae to survivors[1]

Since then, this viral infection has become the target of many studies, which seek to understand the side effects caused by the virus in various systems. The literature has shown its negative impacts on the central auditory nervous system (CANS), as well as on cognition[2-6].

The Covid-19 pandemic has generated social changes that have influenced the way listeners process speech, leading to modifications in language processing[7] and, consequently, in cognition.

One of the forms of treatment for the alterations found in the SNAC is auditory training, which provides plasticity and reorganization of the neural networks[8].

There are different intervention methods, such as acoustically controlled, uncontrolled, computerized, musical[8-10] and, recently[11], cognitive auditory training (CAT).

The CAT was developed to work on auditory and cognitive skills, such as attention, memory, figure-background for verbal sounds, temporal ordering and resolution, auditory closure, executive functions, and motor praxes[11]. Considering the sequelae caused by the virus in the auditory pathway and in the cognitive aspects, the CT becomes one of the treatment possibilities for subjects after infection.

There is still a lack of therapeutic treatments in subjects after COVID-19, which justifies the relevance of this study. Thus, the hypothesis is that after auditory cognitive training, subjects will perform better in the tests performed, as well as improve auditory and cognitive symptoms.

Therefore, the aim of the present study was to analyze the effectiveness of a therapeutic intervention plan by means of an existing cognitive auditory training program adapted for adults after one year of COVID-19 infection.

METHODS

This study was approved by the Ethics Committee on Human Research of the Universidade Federal de Santa Maria - CEP/UFSM, under number 56038322.10000.5346. It presents a prospective, quantitative, and longitudinal design. All procedures were carried out in a clinic-school of a public university. Only individuals who consented to voluntary participation and signed the Informed Consent Form (ICF) participated.

To compose the sample, the following criteria were considered: age between 18 and 59 years; after one year of COVID-19 proven by RT-PCR examination; both genders; no tinnitus before COVID-19; Brazilian Portuguese as mother language; absence of conductive component; alteration in at least one hearing ability; presence of complaints related to hearing abilities, or cognitive, or both, after COVID-19 infection; hearing thresholds within normality standards and/or sensorineural hearing loss of mild degree, bilaterally[12]. Subjects with evident speech, neurological and/or psychological alterations, a history of head or brain trauma, and chronic tinnitus were excluded.

The sample size calculation, performed by a specialized professional and statistics professor from a university, resulted in a sample size of n=18. The following calculation parameters were considered in the *G*Power* computer program: effect size equal to 0.3 in an upper one-sided test, with a significance level of 5% and test power of 80%.

A total of 70 individuals from the community were evaluated. They were recruited through social media and the audiology clinic of the institution. All presented the RT-PCR exam to prove the diagnosis of COVID-19. Of these, 32(45.7%) were excluded for not meeting the eligibility criteria and 25(35.7%), for not wishing to participate in the CT scan, totaling 81.4% exclusion.

Thus, the final casuistic included 13 subjects, aged between 18 and 59 years, four males and nine females (Chart 1).

No research subjects were diagnosed with peripheral hearing loss after COVID-19; they all had mild sensorineural hearing loss, pre-existing SARS- CoV-2 infection.

The main drugs/supplementation reported by the subjects in treating the infection were: vitamin D, zinc, paracetamol, azithromycin, ivermectin, prednisone, and dipyrone.

Hospitalization was necessary in only two subjects of the sample; for one of them for 30 days and for the other, 15 days. Intubation was necessary for ten days in both subjects.

As for pre-existing comorbidities, one of them reported hypertension and associated high cholesterol, and the other, only hypertension.

It is emphasized that the analysis was conducted intrasubject and the intervention thus analyzed.

To estimate the power of the collected sample, the final sample size and the same parameters of effect and significance as before were used, and the sample power was 74.7% (the recommended value would be 80% or more, for evidence and significance). The research took place from November 2021 to September 2022.

As sample selection procedures, all individuals answered a questionnaire with questions related to COVID-19 and underwent visual inspection of the external auditory meatus, tonal threshold audiometry, logoaudiometry, and acoustic immittance measurements.

a) Brief Neuropsychological Assessment Instrument - NEUPSILIN: is a cognitive assessment instrument, used in this study to assess eight neuropsychological functions: temporal-spatial orientation, focused attention, visual perception, arithmetic skills, oral and written language, verbal and visual memory, praxes, and executive functions[13] For the analyses in this research, the total sum of all skills was made in order to obtain the global cognitive development response (GCD) of each subject and, after that, the total sum of the attention and memory skills.

b) Central auditory processing evaluation: this was carried out in an acoustically treated room, with the aid of an Interacoustics AD229e two-channel audiometer and Telephonics TDH-39P type headphones. The behavioral tests were applied by means of a computer coupled to the audiometer and all of them at an intensity of 40 dBNS above the tritone average. In order to make up the assessment, we used the Dichotic Digit Test (DDT), binaural integration stage[14], *Gap In* Noise (GIN) per ear[15], Speech in Noise Test (SIN) ratio +5 dB ipsilateral[14], *Masking Level Difference (*MLD)[16] and the Pitch Pattern Sequence (PPS), Auditec® version, in binaural mode[16].

c) *Speech, Spatial and Qualities of Hearing Scale* (SSQ): the short version was used, consisting of 12 questions - which address three domains: speech hearing, spatial hearing, and hearing qualities - to measure the subjects' hearing complaints and quantify everyday listening abilities. The subjects were instructed to score from 0 - meaning that they were not capable of performing a given task - to 10, when they were perfectly capable. They were also instructed about the option called "not applicable", in case the question did not represent a daily situation[17].

d) Cognitive potential - P300, with speech stimulus: the test was performed on Smart EP equipment from Intelligent Hearing Systems. The subjects were seated in an armchair, after which the skin was cleaned with abrasive paste (NUPREP). The reference electrodes were placed on the right and left earlobes, the ground electrode was placed on the forehead in position Fpz, and the active electrode was placed in Cz. We used 300 verbal stimuli (syllables /ba/ and /di/), divided into 240 frequent /ba/ and 60 rare /di/ stimuli (80% frequent and 20% rare), one stimulus per second, applied at an intensity of 80 dB SPL. The subjects' task was to pay attention to the rare stimuli and to count them. The protocol used relied on impedance equal to or less than 3 KΩ, with a maximum number of artifacts accepted of 10% of the total stimuli, band-pass filter 1-30 HZ, 510 ms window, alternating stimulus polarity, speed 1.1/sec. For wavelet analysis and labeling, the values from a previous study conducted in 2016 were used[18]. In the present study, if the P300 was subdivided into two potentials, that is, P3a and P3b, the value of P3b was considered for pre- and post-intervention analysis[19].

e) Auditory cognitive training protocol: the subjects, after one year of proven COVID-19 infection, who had symptoms or alterations in the aforementioned tests, received the existing auditory cognitive training protocol, from 2021[11], which has auditory and cognitive stimulation tasks. Since the present study was developed for adults and the initial protocol was developed for the elderly, it was necessary to adapt the existing protocol[11] (Chart 2).

Chart 1. Description of the final casuistic

Casuistry	13 subjects
Average Age	35 years old
Average Schooling	14 years old
Genre:	
Female	9
Male	4
Peripheral Hearing:	
Hearing thresholds within normal limits	9
Mild sensorineural hearing loss pre-existing to COVID-19	4
Tinnitus after COVID-19	0
Dizziness after COVID-19	0
Speech Understanding Complaint after COVID-19	10
Memory complaint after COVID-19	11
Attention complaint after COVID-19	7
Medication after COVID-19:	
Yes	9
No	4
Medication time:	
Up to 15 days	7
More than 15 days	2
Internment:	
Yes	2
No	11
Intubation:	
Yes	2
No	11
Pre-COVID-19 associated comorbidities:	
Yes	2
No	11

Chart 2. Adaptations made to the auditory cognitive training protocol

Material and task instruction	Stimulated Skills	Adaptations
Session 1 - addition of an activity		
● **Phonemic strategy/phoneme recognition:**	Time Sorting	No modifications(11)
This stage consists of four phases:		- Activity added
1 - "I am going to introduce two sounds /p/ and /v/, tell me what is the difference between them? Which one is thin and which one is thick?"		
2 - "Next, you will hear a sequence of three sounds, after hearing them, repeat the sequence in order and write the letters corresponding to that sequence. Example: FFG - VVP".		
3 - "I will introduce two more sounds /b/ and /f/, tell me what is the difference between them? Which one is thin and which one is thick?"		
4 - "Again, you will hear a sequence of three sounds, but now two new sounds will be inserted. After hearing them repeat the sequence in order and write the letters corresponding to this sequence. Example: BPF or VFP".		
Session 3 - change in an activity		
● **Identifying the name of songs, by means of the melody - Use 10 melodies of songs known by the adult population:**	Attention and Memory	With modifications(11)
"Listen to some melodies and, from the melody, identify the tune."		- **Previous version: Ten melodies of songs known to the elderly population:** "Listen to some melodies and, from the melody, identify the song."
		- **Adaptation: Identifying the name of songs, by means of the melody - Use 10 melodies of songs known to the adult population:** "Listen to some melodies and, from the melody, identify the song."
Session 5 - changing one task and adding two		
● **Put the audio with two songs together, unknown to the adult population, played simultaneously and the lyrics of one of them:**	Auditory figure-background ability	With modifications(11)
"Listen to two concurrent songs and pay attention to only one. Along with it, you will have the lyrics of that song in hand containing words that are not part of it. Pay attention, identify and circle them.	for verbal sounds and attention	- **Previous version: Audio of two songs unknown to the elderly population, played simultaneously and the lyrics of one of them:** "Listen to two songs simultaneously, pay attention to only one, the one you have the lyrics in hand and should sing."
		- **Adaptation: Put the audio with two songs together, unknown to the adult population, played simultaneously and the lyrics of one of them:** "Listen to two songs simultaneously and pay attention to only one. Next you will have the lyrics of the song containing words that are not part of it. Pay attention, identify and circle them.
● **Memory activity with noise together: On a**	Memory	No modifications(11)
clipboard, the examiner will present the following letters: A, G, V, R, and S. All patients will receive the clipboard in the same order.		
		- Activity added
- Each letter will present a sample task to follow, and you will have one minute to accomplish each one:		
Letter A: Tell me the name of five animals that begin with the corresponding letter;		
Letter G: Tell me the name of five objects that are part of the kitchen;		
Letter V: Tell me the name of five colors; Letter R: Tell me the name of five countries;		
Letter S: Tell me the names of five professions.		
● **Competitive noise word search with people in a restaurant - 40% volume:**	Attention and Memory	No modifications(11)
"Here is a word search containing words related to the session (attention, activity, hearing, cognition, colors, strategy, speech, speech therapy, annoyance, memory, music, music, order, words, noise, session, sound, task, therapy, tinnitus). You must concentrate well and find the words you remember.		- Activity added

Chart 2. Continued...

Material and task instruction	Stimulated Skills	Adaptations
Session 6 - adding one activity and changing three		
● **Memory task with competitive noise from people in a restaurant - 20% volume:**	Memory and attention	No modifications[11]
"Write a sentence with the requested words (girl, chair, cat, medicine, and yesterday) and turn in the paper. At the end of the session, you should enunciate the sentence, without a reminder from the therapist." "Now I am going to read you a list of 14 words and you are to recognize them from among 40 other words."		- Activity added
● **Time resolution activity:**	Time resolution and memory	With modifications[11]
"Now you will hear a sequence of ten whistles, which will vary between one, two, three, and four whistles.		**- Previous version: *Gap In Noise* Track 1, 2, 3, and 4:** "Hear a squeak, and in that squeak there will be some intervals of silence; you must identify and respond each time you notice silence.
Memorize the following code: 4 whistles: MARGARIDA; 3 whistles: DOOR; 2 whistles: ELEPHANT; 1 whistle: COPO.		They may have one, two, three, or no break at all."
The applicator should show on a clipboard four alternatives with a sequence of images and ask the patient which one is correct. "After you hear the sequence of whistles, I will show you a sequence of images and I want you to tell me which of the options is the correct one."		**- Adaptation: Time Resolution Activity:** "Now you will hear a sequence of ten whistles, which will vary between one, two, three, and four whistles. Memorize the following code: 4 whistles: MARGARIDA; 3 whistles: DOOR; 2 whistles: ELEPHANT; 1 whistle: COPO. The applicator should show on a clipboard four alternatives with a sequence of images and ask the patient which one is correct. "After you hear the sequence of whistles, I will show you a sequence of images and I want you to tell me which of the options is the correct one."
● **Audio from the Musiek Duration Standard Test,** **associated with an instrumental song, volume 40%:**		With modifications[11]
"Now you will hear three sounds, some are short and some are long. After hearing the three sounds, you have to name them as short and long. Ignore the background melody. E.g. short-long-short.	Temporal Sorting	**- Previous version: Audio Test** **Pattern Duration (four sounds):** "Listen to four sounds, some are short and some are long. After listening to the four sounds, you should name as short and long. Ex.: short-short-long-short". **- Adaptation: Audio from the Musiek Standard Duration Test, associated with instrumental music, volume 40%:** "Now you will hear three sounds, some are short and some are long. After hearing the three sounds, you have to name them as short and long. Ignore the background melody. E.g. short-long-short.
● **Audio from the Musiek Frequency Pattern Test associated with an instrumental song:**	Temporal Sorting	With modifications[11]
"Now you will hear three sounds, some are thick and some are thin. After hearing the 3 sounds, you have to name them as thick and thin. Ignore the background melody. E.g.: thin-thin-thick		**- Previous version: Audio of the Frequency Pattern Test (four sounds):** "Listen to four sounds, some are coarse and some are fine. After listening to the four sounds, you should name thick and thin. E.g.: fine-thin-coarse- thin" **- Adaptation: Audio from the Musiek Frequency Pattern Test associated with an instrumental song:** "Now you will hear three sounds, some are coarse and some are fine. After hearing the three sounds, you have to name them as thick and thin. Ignore the background melody. Ex: thin-thin- thick".

All subjects who agreed to participate in the intervention attended once a week, with six consecutive sessions of approximately 50 minutes, held in the open field, with speakers attached to the computer. In addition, they were instructed that if they had any absences, they would be disconnected.

After intervention, a time of two months was waited to re-evaluate the subjects, with assessment of central auditory processing, SSQ, NEUPSILIN, and P300.

As for the reevaluation time, there is no consensus in the literature[20-22]. For this study, the time chosen was two months, based on studies that reported the presence of new neurons after six to eight weeks, from the moment an adult performs a new skill, that is, a certain amount of time is necessary for neuroplasticity to occur[23-25].

The subjects were evaluated, trained, and re-evaluated by different researchers.

First, the data were analyzed for normality using the Shapiro-Wilk test. Given the findings, non-parametric tests were selected. To calculate the difference between the right and left sides, the t-test or Wilcoxon test was used. Since no variable showed a significant difference between the sides ($p(W,T) > 0.05$), the mean measurement of the sides was obtained.

For comparison of the paired pre- and post-intervention subjects, the variables were tested according to the corresponding parametric or nonparametric test (t-test or Wilcoxon). For all analyses, a significance level of 5% ($p \leq 0.05$) was considered. The data were analyzed in R *software* and presented as figures.

RESULTS

Figures 1 and 2 show the comparison of the individuals in a paired manner. When comparing the variables between the periods, pre-and post- intervention, the difference in DDT ($p = 0.009$), PPS ($p = 0.020$), and SSQ ($p = 0.001$) was significant. The GIN and Total Attention (TA) variables were not significant, but showed a trend toward significance ($p < 0.10$).

DISCUSSION

The present study sought to meet the demands related to the auditory and cognitive complaints of adult subjects proven to be affected by COVID-19, through a therapeutic intervention proposal using an existing auditory cognitive training protocol[11] .

This therapeutic intervention model[11] was developed and applied with the goal of having an integral rehabilitation (cognition + auditory skills). According to the creators of the[11] method, rehabilitation by means of cognitive auditory training enables neuronal reorganization, by virtue of neuroplasticity, reducing in patients the complaints related to auditory and cognitive abilities. Studies show that the combination of auditory and cognitive tasks, when included in auditory training, provides a more efficient intervention[22,26].

Regarding the sample studied here, even in the face of the heterogeneity of the data (Chart 1) regarding the comorbidities present in pre-COVID-19, hospitalization, medications, and intubation, it was clear in the findings presented that the therapeutic intervention was positive for almost all of the research subjects. The two subjects who required hospitalization with intubation did not have the same benefit as the others (Figure 1), which may be justified because the most severe cases of COVID-19, which require hospitalization and intubation, may present greater sequelae after infection[27,28], making the intervention by means of CT alone not enough. Another hypothesis raised is that the SNAC of these subjects needs more time to generate neuroplasticity, considering what was exposed in a study[22], in which the authors report a time of two to six months to analyze the effects of the training.

When observing the age range item, we observed an average of middle- aged adults; the subjects with higher age were the ones who presented the least differences in the pre- and post-auditory training (Figures 1 and 2). This can happen because of the gradual aging process, in which information processing slows down, that is, the brain of older adults is slower and needs a longer period of time for neuronal reorganization to occur in an efficient way[25,26].

The need for treatment in this population is evident, and the pre- intervention findings agree with those of another study[6], which found, in its sample of 161 subjects, 81% of them with hearing complaints and 43% with memory impairment. Figure 1 shows the benefits in relation to the auditory skills assessed and also in relation to the subjects' self-perception, a benefit that was significant in the figure-background skills for verbal sounds, temporal ordering, and self-perception. Studies have reported the importance of the aforementioned skills in speech perception and have also shown improvement after auditory training[9,10], findings that agree with the present study.

Regarding the self-assessment questionnaire, it is known that it has been reported as one of the most important procedures in the rehabilitation process, being the only one capable of measuring the complaints self-reported by the subjects in their daily lives[17]. In the present study, the use of the questionnaire was extremely important, since the subjects reported significant improvement after the intervention.

In the previously mentioned study[6], the authors concluded that the degradation in speech test scores in patients after COVID-19 may occur due to central auditory processing disorder, memory impairment or changes in cognitive status in general and, therefore, the choice and relevance of the auditory-cognitive approach. Figure 2 shows an improvement in global cognitive performance, attention, memory, and in cognitive potential - P300, but without statistical significance. This data shows that the training protocol can be modified and improved, aiming to include more cognitive tasks within the intervention program.

In a study, the cognitive potential - P300, which is a cognitive auditory potential, showed considerable change, both in latency and amplitude, showing the effect of neuroplasticity after the intervention[29]. When analyzing the effectiveness of auditory training through the P300, the authors found reduced latency and increased P300 amplitude after the intervention, results that are consistent with the findings of the current study. This potential has been described as the best indicator of auditory function, being highly dependent on cognitive skills, including attention and memory[30]. Therefore, it is believed that there was no statistically significant difference in latency and amplitude of the cognitive potential - P300 in this study, due to the sample n and the great variability of the sample.

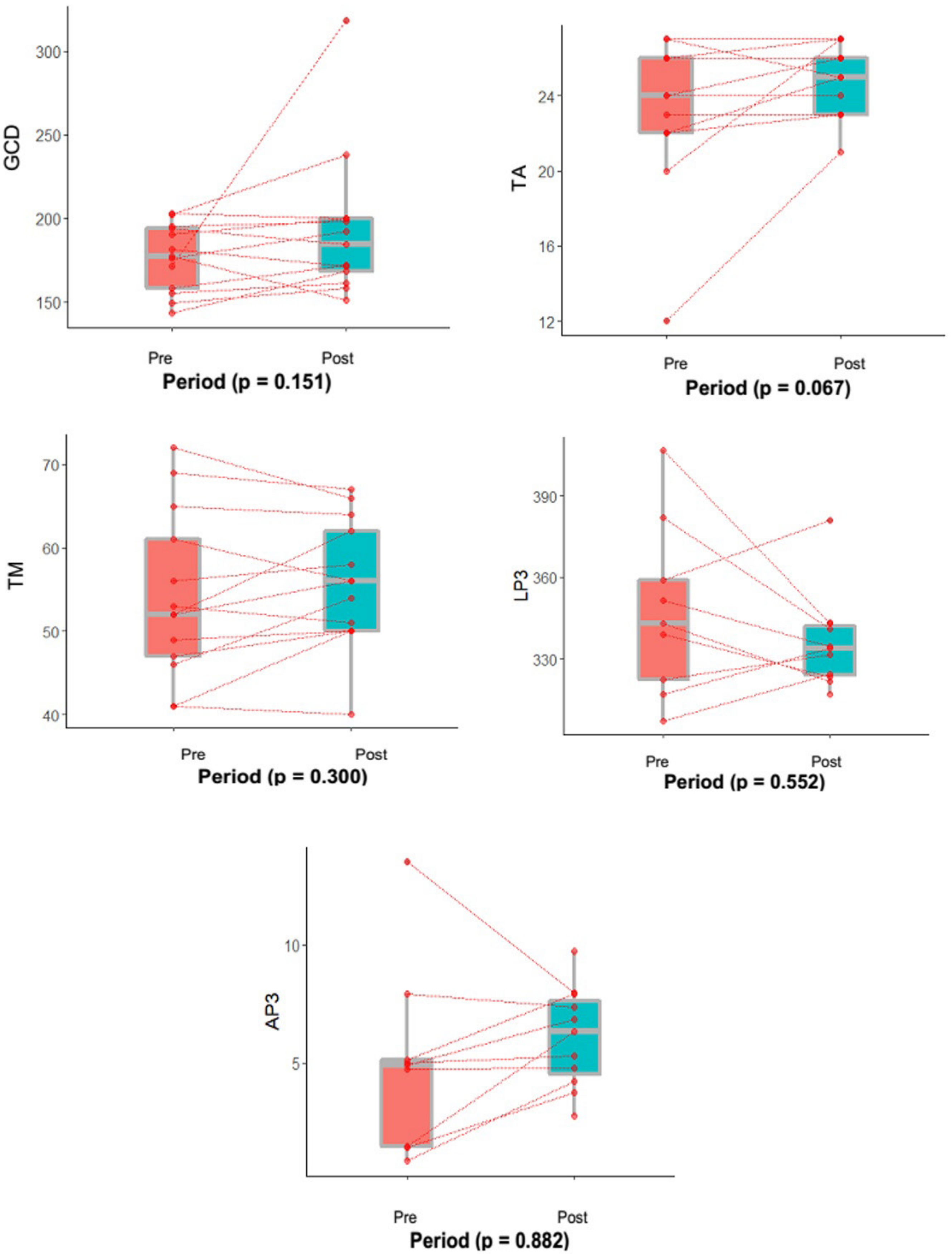

Figure 1. Comparison of pre- and post-cognitive auditory training subjects regarding auditory skills and self- assessment
Legend: DDT = Digits Dichotic Test; MLD = *Masking Level Difference;* GIN= *Gap In Noise;* SIN = Speech In Noise; PPS = Pitch Pattern Sequence; SSQ = *Speech, Spatial and Qualities of Hearing* * t-test or Wilcoxon test

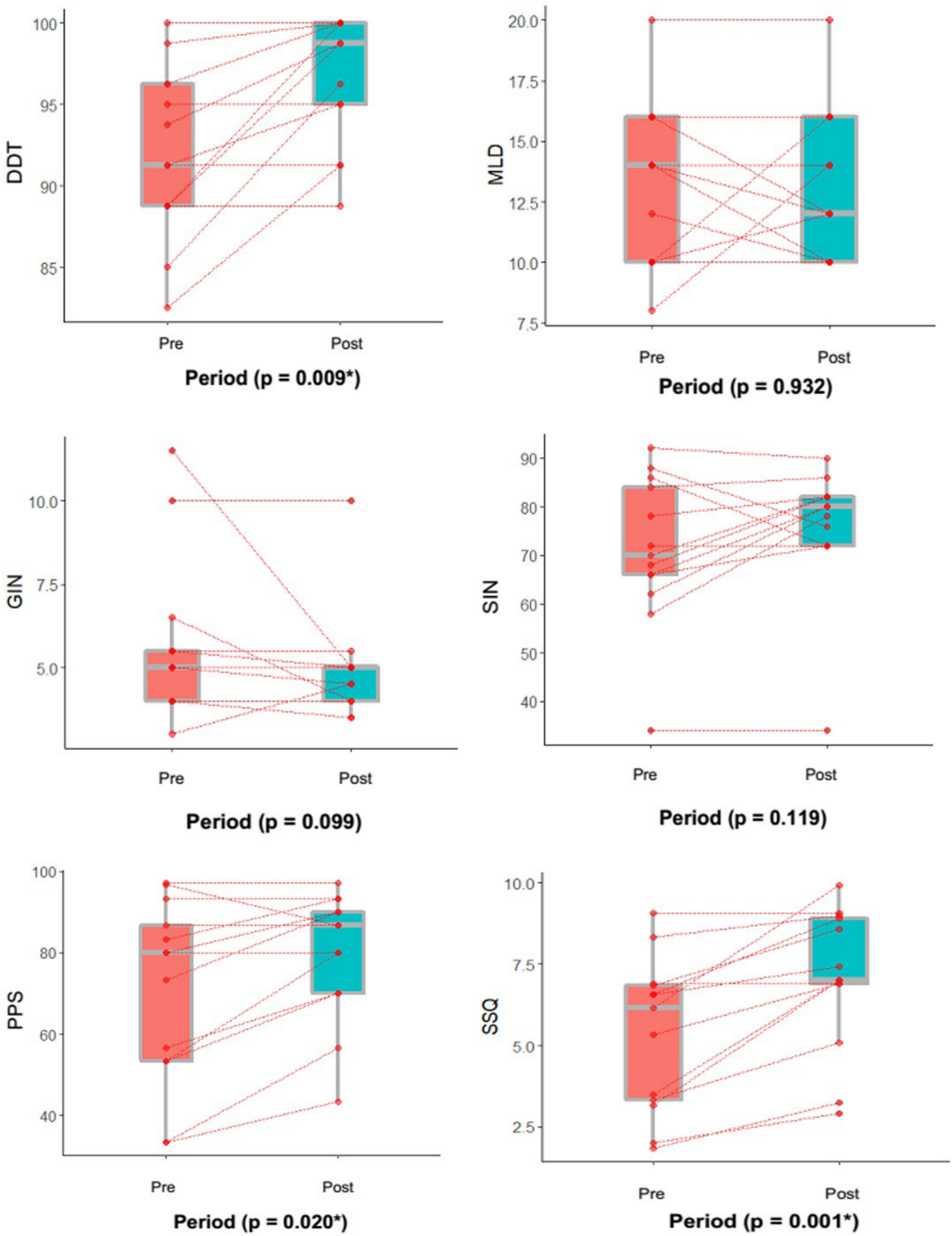

Figure 2. Comparison of pre- and post-cognitive auditory training subjects regarding global cognitive performance, total attention, total memory, and cognitive potential - P300

Legend: GCD = Global Cognitive Development; TA = Total Attention; TM = Total Memory; LP3 = P3 wave latency; AP3 = P3 wave amplitude

It is worth mentioning that two subjects who presented P3a and P3b started to have the P300 potential uniquely, this being another demonstration of the neuroplasticity evidenced after the six sessions of CT. P3a shows a neural function of the automatic process of attention and perception to the sound stimulus, and P3b, the real auditory discrimination[8]. Thus, by undoing P3a and P3b, there is a reduction of frontal lobe activation due to the optimization of neural responses in the temporoparietal region.

Even with the heterogeneity of the findings and complaints in the post- COVID-19, one thing is clear: intervention is necessary to reduce the effects of the post-COVID syndrome and to resume the quality of life of the subjects. The present study contributed to the treatment of the symptoms and improvement of the alterations found in these individuals, by means of auditory cognitive training.

One of the limitations of this study, however, was the sample n and the absence of a placebo group. Therefore, for future studies, interventions in randomized clinical trials on a larger sample size are suggested.

CONCLUSION

Cognitive auditory training has been shown to be an effective therapeutic strategy for the treatment of speech comprehension and cognition complaints after COVID-19 infection.

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