CENTRAL AUDITORY PROCESSING IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Ana Paula Bruner,* Emilia Inoue Sato,** Liliane Desgualdo Pereira***

Abstract

Systemic Lupus Erythematosus (SLE) patients can also present neuropsychiatric disorders, such as impaired memory and attention. Central auditory processing depends on a great number of skills controlled by the central nervous system.

Objective: To characterize the performance of SLE patients, with and without neuropsychiatric disorders (NP), in central auditory processing tests.

Patients and Methods: A prospective controlled study of Dichotic Speech and Temporal Processing Tests was carried out at a tertiary teaching Institution. Three groups were formed with 20 individuals each, totalizing sixty women with age varying from 18 to 48 years: Group I – SLE patients without neuropsychiatric disorders; Group II – SLE patients with neuropsychiatric disorders as well; and Group III - age and gender matched healthy controls.

Results: Dichotic Speech Test showed similar results for patients in Group I and for healthy controls; however, most of the patients in Group II presented impaired performance with great variability of response. SLE patients (Groups I and II) presented a significantly lower performance in Temporal Processing tests than controls.

Conclusion: SLE patients especially those with neuropsychiatric disorders presented impaired central auditory processing, which may contribute to the memory and attention impairment.

Keywords: Audiometry; Audiology; Central Nervous System Diseases; Lupus Erythematosus.

*Audiology Division Otolaryngology Department, Santa Casa School of Medicine of São Paulo
**Full Professor Rheumatology Division, Department of Medicine, Federal University of São Paulo
***Full Professor Speech Pathology and Audiology Department, Federal University of São Paulo

Introduction

Neuropsychiatric (NP) disorders are frequent in patients with Systemic Lupus Erythematosus (SLE)[1-3] and may result from a number of different pathogenic mechanisms and events occurring in the central and peripheral nervous systems.[4] A number of disorders have been reported associated to SLE, from mild mental dysfunctions to seizures, psychosis, headaches, depression, cognitive dysfunction and anxiety disorders.[5-9] Attention span disorders, impaired processing of short and long term memory, and verbal and visual-spatial information have also been associated to SLE.[10]

Central Auditory Processing is a complex analysis performed by the auditory system from the outer ear to the interpretation of the auditory information by structures in the central nervous system (CNS) and in the brain. The following processes and mechanisms are involved: selective attention, sound detection, sensation and localization, discrimination of isolated and sequential sounds, as well as speech recognition, comprehension and memory. All these processes present both neurophysiologic and functional correspondents.[11-13]

Temporal processing is one of the functions performed by the auditory system. It involves a number of temporal skills such as resolution, masking, integration and ordering, which allow a listener to hear acoustic variations in a certain time interval.[12-14] These skills are essential for the processing of the sounds of speech.[14-16] Temporal processing tests offer a comprehension of the way in which acoustic events occurring over time are perceived by the listener and how his/her work memory functions. The primary auditory cortex and the association cortex are involved in gap-detection tasks during auditory stimulation, where the same group of neurons is activated before and after a silent interval.[17,18] Thus, the temporal resolution skill depends on the integrity of central neurological structures, especially the auditory cortex.

Auditory processing impairment results from

functional abnormalities in one or more of these auditory processes, and may be caused by neurological problems associated to demyelination, brain atrophy, focal brain lesions, and others.[13] Patients with others systemic diseases and altered cognitive and psycho-emotional functions may also present central auditory processing impairment.[19]

Many studies have shown the association between poor central auditory processing and central nervous system abnormality in various diseases.[13,18,19] However, auditory processing evaluation is limited in SLE. Auditory processing disorders could impair the cognitive-communicative and/or language related functions in lupus patients.

The aim of the study was to evaluate the central auditory processing skills in SLE patients, with and without neuropsychiatric disorders, using dichotic listening and temporal processing tests.

Patients and Methods

A total of 40 adult women with SLE, according to ACR classification criteria[20] from a tertiary Rheumatology out-patient clinic and twenty healthy volunteers were studied. The participants were subdivided into three groups: 20 SLE patients without NP involvement (Group I), 20 SLE patients with NP involvement (Group II), and 20 age-matched healthy women with no systemic disease, auditory or neurological impairment (Group III). Patients' age ranged from 18 to 48 years. All participants were literate and signed a post informed consent form approved by the Institutional Ethics Committee.

Group I included patients without neuropsychiatric feature. Patients with memory or attention impairment or any other cognitive impairment complaints were excluded. Group II NP manifestations were: lupus headache (10%), panic syndrome (10%), strokes (15%), anxiety disorder (15%), major depression (30%), psychosis (40%) and/or seizures (65%). Seventy-five percent of patients presented more than one manifestation.

All the participants had normal[21] hearing thresholds and normal mobility of the tympanic- ossicular system assessed by tonal threshold audiometry, speech reception testing, percentage index of speech recognition, and acoustic immitance. None of the participants presented mechanical or neurosensorial hearing loss, which could interfere with the tests interpretation.

Auditory processing was evaluated through three specific tests performed in the following order: Binaural integration task of the Dichotic Digit Test (DDT) Portuguese version[22] for assessment of recognition of overlapped verbal sounds in dichotic hearing (different auditory stimuli presented to each ear simultaneously) and hearing capability of binaural integration; Random Gap Detection Test – RGDT (Auditec, Saint Louis, MO)[23] for identification and quantification of the subject's resolution capacity; Pure tone Duration Pattern Test (DPT)[24,25] to assess sound discrimination abilities related to duration and temporal ordering and is also known as temporal processing. Responses were expressed in percentages of correct answers for the DDT and DPT, and in milliseconds (ms) for the RGDT.

The DDT was comprised of 80 words presented in pairs, a different pair of digits in each ear presented at the same time (dichotic hearing). There were 20 pairs of dissyllabic words (digits) which were randomly repeated twice in each ear.

In RGDT the subject was expected to identify the presence of two short consecutive sounds; the gap detection was expressed as the shortest interval (in milliseconds) of detection of both sounds. The test includes stimuli at four frequencies (0,5k, 1k, 2k, 4kHz), presented to both ears at the same time.

In DPT the subject was expected to identify a series of three sounds by verbalizing if the sound was short or long (V_DPT) or by imitating or humming the sound (H_DPT). Stimuli were presented separately to the right and left ears.

Hearing tests were performed at 50dBNS in a sound treated booth using TDH-49 supra-aural headphones (*Telephonics,* Denmark*)*. A two channel *Orbiter-Madsen* 922 audiometer *(GN Otometrics,* Denmark*)* calibrated according to ANSI S 3:6 – 1989 guidelines was used. The audiometer was connected to a CD recorder/player (*Panasonic Inc.*, USA) for digital recording of the tests.

Statistical analysis: Descriptive analysis was performed using mean and 95% of confidence interval. Patients in Groups I and II were compared to the control (Group III). In DDT, V_DPT and H_DPT tests responses were considered abnormal when the average number of correct answers was below the minimum average of the control group. RGDT interpretation was performed by averaging the gap detection threshold for all tonal stimuli (0,5k, 1k, 2k, 4kHz). The results were considered abnormal

when they exceeded the maximum threshold observed in the control group. The correlation between results and duration of the disease was carried out using Spearman's correlation test (r). Inferential analysis of auditory processing tests was based on the results obtained from each ear for DDT and DPT, or the frequency tested in RGDT. The comparison of abnormal results in Group I and Group II was performed using Tukey test. Fisher's exact test was used to compare the results obtained in each separate ear in the SLE patients who responded below the average of the control group.[26] P value ≤ 0,05 was considered significant.

Results

The mean disease duration of Group I and II was 7.7±4.71 years and 7.9±5.19 years, respectively. The mean age of group I, II and III was 29± 4.64, 31±7.82 and 32±8.47 years, respectively.

Dichotic Digit Test (DDT)

Group I and III presented similar responses on DDT. However, most Group II patients had poor DDT responses with great variability. The mean percentage of correct responses on DDT of Group I, II and III was respectively 99% (CI 98.17–99.83%), 93.4% (CI 90.3–96.5%) and 99.6% (CI 99.2–100.0%); p=0.027 for right ear, and 98.6% (CI 97.65–99.35%), 91.5% (CI 88.8–94.92%) and 99.4% (CI 98.91–99.89%); p=0.027 for left ear.

No significant difference on DDT results was observed in any of the three groups when comparing right and left ear (p=0.054). Groups I and III presented similar average performance on DDT (p=0.860), whereas Group II had poorer results when compared to the other two groups (p<0.001).

Random Gap Detection Test (RGDT)

RGDT results were poor in Group I and worse in Group II, whereas healthy controls presented the best responses. Only one patient of Group II presented outlier responses (Figure 1). Group III presented gap detection thresholds ≤ 10 ms on all sound frequencies of RGDT [mean 6.6 ms (CI 5.92–7.28 ms)]. Groups I and II presented a mean of 16 ms (CI 11.95–20.05 ms) and 46.1 ms (CI 31.24–60.96 ms), respectively, on all frequencies.

There was no significant difference on RGDT results obtained by different sound frequencies in any of the three groups (p=0.065). When comparing the three groups, Group III presented the best results, i.e., the lowest average gap detection thresholds on RGDT, and Group II presented the highest average gap detection thresholds on RGDT when compared to Group I and Group III (p<0.001 for all the comparisons).

Duration Pattern Test (DPT)

A significant number of Group I patients presented poor DPT results (V_DPT and H_DPT, for both right and left ear stimuli), when compared to Group III. The worst DPT responses were found in Group II (Figure 2).

A similar response on the right and left ears on DPT tests was found in Group II and III. The percentage of correct responses in V_DPT and H_DPT tests was similar for all three groups. Only Group I presented a significant difference between DPT scores in each ear, the left ear presenting a lower average response than the right ear (p<0.001). The averages of the three groups were distinct when compared two by two in each ear. A higher average of correct responses was found in Group III, followed by Group I and finally by Group II (p<0.001).

Only Group II presented a significant correlation between DDT and V_DPT results (p=0.016). No correlation was found between the performance on any of the auditory processing tests in patients from Group I and healthy controls.

There was no correlation between the performance on DDT or RGDT and the disease duration. A weak negative correlation was found between DPT responses and the disease duration in Group I (V_DPT in the right, r= -0.49; p= 0,029, and left ears, r= -0.44; p= 0,05, and H_DPT in the right ear, r= -0.60; p= 0,005, and r = -34; p= 0.144 in the left ear), suggesting that the percentage of correct answers decreases as the disease progresses in these patients (Figures 3 and 4). No correlation was observed in Group II.

Table I depicts the abnormal test results in Group I and II, using the healthy controls as reference. A great occurrence of abnormal RGDT and DPT results (both V_DPT and H_DPT) was found in both groups.

Discussion

Our study showed that SLE patients present impaired auditory processing skills, mainly those with neuropsychiatric disorders. Most abnormal results

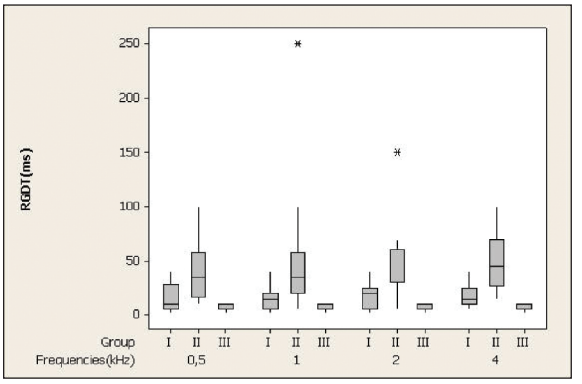

Figure 1. Box-plots for RGDT results by sound frequency (Hz) of groups I, II and III.
RGDT Random Gap Detection Test; *Group I*: patients with systemic lupus erythematosus and no neuropsychiatric involvement; *Group II:* patients with systemic lupus erythematosus and neuropsychiatric involvement; *Group III:* control group. * aberrant responses.
Confidence intervals (averaging the gap detection for all stimuli) Group I: 11.95 – 20.05 ms, Group II: 31.24 – – 60.96 ms, Group III: 5.92 – 7.28 ms.

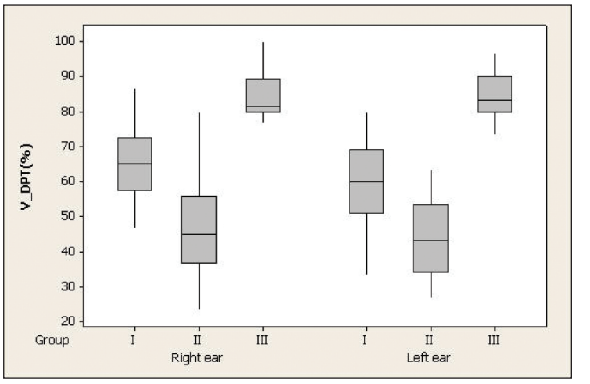

Figure 2. Box-plots for V_DPT results of groups I, II and III for the right and left ear.
V_DPT Duration Pattern Test by verbalizing; *Group I*: patients with systemic lupus erythematosus and no neuropsychiatric involvement; *Group II:* patients with systemic lupus erythematosus and neuropsychiatric involvement; *Group III:* control group;
Confidence intervals for right ear Group I: 60.4 – – 68.6%, Group II: 40.3 – 52.3%, Group III: 81.4 – 87.6%; and for left ear Group I: 53,3 – 63.7%, Group II: 39.4 – – 49.6%, Group III: 81.5 – 87.5%.

were found in tests of temporal processing.

The studied sample was comprised solely of females, which is in accordance with the prevalence of SLE in this gender.[27] The neuropsychiatric symptoms associated to SLE varied greatly and were similar to those previously reported in literature.[1,28,29]

SLE patients with NP disorders had poorer DDT responses with greatest standard deviation, when compared to the other two groups. The same alteration was also observed in patients with epilepsy in another study.[30] No significant differences were found between the responses of the right and left ears in any of the groups, differently from what was reported by Kimura.[31] This difference may be explained by the characteristics of the verbal stimuli used in the test. Although both the English and the Portuguese language versions use representations of numbers, in the former language the words were monosyllables and in Portuguese, the words were disyllables.

Concerning RGDT, only Group III presented results similar to or better than those found in currently available normative data.[23,32,33] It is expected that normal individuals respond correctly to 70% or more of the stimuli in DPT.[24] In the current study none of the SLE patients presented a percentage of correct responses as high as the healthy controls. SLE patients with NP involvement presented the worst responses (for both V_DPT and H_DPT, regardless of the tested ear).

Temporal processing involves the right and left hemispheres. The right hemisphere recognizes the whole and provides ordering and the *corpus callosum* transfers the information to the left hemisphere which will label it linguistically after sequencing the message, regardless of the ear tested.[34,35] Thus, in SLE patients with *corpus callosum* involvement, DPT would become a valuable tool by differentiating verbal and humming responses.[2,36]

The normal interval for detection and ordering of two distinct acoustic stimuli is at least 20 ms.[17] In the current study, SLE patients with NP involvement presented a higher interval, suggesting that the relatively short duration of the acoustic stimuli in DPT was insufficient to allow ordering of the distinct sounds by these patients.

SLE patients with NP involvement presented the greatest variability of responses in all the tests and were characterized as the most heterogeneous group. This finding may be related to structural neurological deficits, since performance variability has been suggested as a predictive factor of neurological impairment.[37] However, a number of patients in Group II did not present neurological disorders likely to cause structural neurological sequelae. It is also important to note that the current study did not consider the possibility of perma-

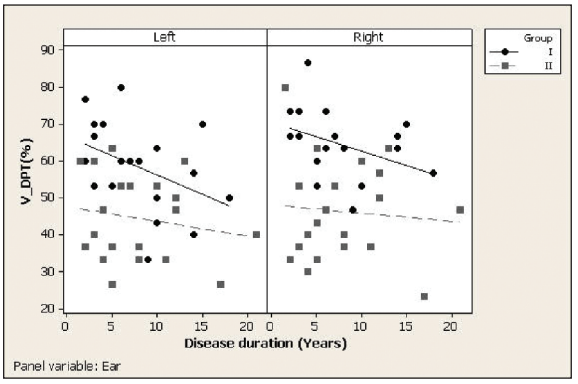

Figure 3. Box-plots for V_DPT and duration of the disease of Groups I and II for the right and left ear. *V_DPT* Duration Pattern Test by verbalizing; *Group I*: patients with systemic lupus erythematosus and no neuropsychiatric involvement; *Group II:* patients with systemic lupus erythematosus and neuropsychiatric involvement.

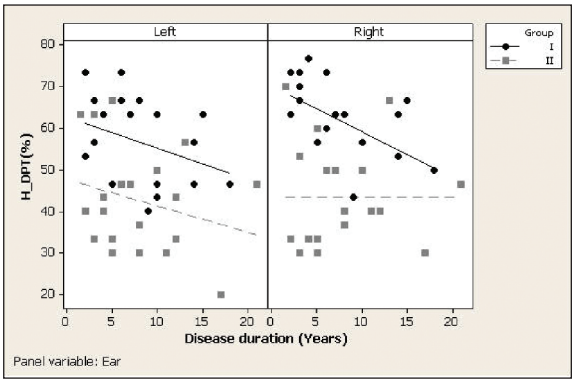

Figure 4. Box-plots for H_DPT and disease duration of Groups I and II for the right and left ear. *H_DPT* Duration Pattern Test by humming; *Group I*: patients with systemic lupus erythematosus and no neuropsychiatric involvement.

nent neurological damage as a variable in the evaluation of auditory processing, since both anatomical and functional abnormalities of the CNS may be involved in abnormal central auditory processing.[38]

The disease duration did not seem to interfere in the test results of Group II patients. This finding may be explained by the great variability of responses and neuropsychiatric symptoms presented by these patients. Patients without NP involvement were not influenced by the duration of the disease in DDT and RGDT, but presented worse responses in V_DPT in both ears and H_DPT in the right ear as the duration of the disease increased. It has been reported that performance in these tests may be intrinsically correlated to the work memory, and the current study agrees with previous reports.[39] Other studies of specific neuropsychiatric disorders have also not found a correlation between the duration of the disease and attention deficits[40] or cognitive/psychological impairment[41] in SLE patients.

Patients in Group I and healthy controls showed no correlation of the performance between specific auditory processing tests. This is comprehensible, considering that each test involves distinct physiological mechanisms. However, SLE patients with NP involvement presented significantly lower performance on DDT and DPT, suggesting

Tabela I. Percentage of SLE patients with responses below those of the reference group (healthy controls).

		Responses below the reference (Control Group III)		
Test	**Ear**	**Group I n = 20**	**Group II n = 20**	**p**
DDT	Right	15 %	65 %	0.003*
	Left	10 %	70 %	0.002*
average RGDT	–	65 %	100 %	0.008*
V_DPT	Right	95 %	95 %	1.000
	Left	90 %	100 %	0.487
H_DPT	Right	95 %	100 %	1.000
	Left	90 %	100 %	0.487

DDT Dichotic Digit Test; *RGDT* Random Gap Detection Test; *V_DPT* Duration Pattern Test by verbalizing; *H_DPT* Duration Pattern Test by humming; *Group I*: patients with systemic lupus erythematosus and no neuropsychiatric involvement; *Group II:* patients with systemic lupus erythematosus and neuropsychiatric involvement; * significant p values (<0,05).

these tests are highly sensitive to CNS disorders.[23,30,41-43] The majority of SLE patients without NP involvement performed well on DDT, unlike patients with SLE with NP disorders who presented a higher and significant percentage of poor responses, once again showing that these individuals present greater difficulty in recognizing familiar linguistic sounds in dichotic hearing.

As to RGDT, the results showed a significant impairment in temporal resolution, especially in patients with NP involvement, which adds to the difficulty in acoustic perception of speech sounds.

Most SLE patients and all those with NP involvement responded poorly to DPT for stimuli presented to at least one of the two tested ears. A couple of possible reasons may explain why SLE patients without NP involvement also presented poor DPT responses: a higher demand of attention capabilities[40] or the presence of mild undetectable CNS dysfunctions most likely associated to microvascular abnormalities or anti-CNS neuron autoantibodies.[4,8,28,44,45] These discrete abnormalities may still be asymptomatic and clinically undetectable,[1,10] but could determine the poorer responses. Temporal processing and Dichotic digit results have shown to be very sensitive at detecting neuromorphological lesions such as cranial trauma, epileptic seizures, etc.[24,46,47 48] Tests that assess temporal resolution have been found to be more sensitive to cortical than to brain stem lesion.[47]

Conclusions

Auditory processing tests contributed to the identification of abnormal physiological auditory mechanisms in SLE patients. The current findings suggest SLE may be associated to difficulties in central auditory processing, impairing dichotic listening and temporal processing, especially in patients with neuropsychiatric involvement.

Correspondence to
Ms. Ana Paula Bruner
Departamento de Fonoaudiologia UNIFESP.
Rua Botucatu, 802, São Paulo,
SP, Brazil / CEP: 04023-900.
Phone/Fax: +55-11-5576-4531
E-mail: ana_bruner@yahoo.com.br

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References

1. Cotton F, Bouffard-Vercelli J, Hermier M, et al. Apport de lÍRM cérébrale dans une série de 58 cas de malade lupique avec ou sans manifestations neuropsychiatriques. [MRI of central nervous system in a serie of 58 systemic lupus erythematosus patients with or without overt neuropsychiatric manifestations]. Rev Med Interne 2004; 25: 8-15.
2. Appenzeller S, Rondina JM, Li LM, Costallat LTL, Cendes F. Cerebral and corpus callosum atrophy in systemic lupus erythematosus. Arthritis Rheum 2005; 52:2783-2789.
3. Shimojima Y, Matsuda M, Gono T, Ishii W, Ikeda S. Relationship between clinical factors and neuropsychiatric manifestations in systemic lupus erythematosus. Clin Rheumatol 2005; 24:469-475.
4. Sanna G, Bertolaccini ML, Mathieu A. Central nervous system lupus: a clinical approach to therapy. Lupus 2003; 12:935-942.
5. Appenzeller S, Kobayashi E, Costallat LTL, et al. Magnetic resonance imaging in the evaluation of patients with aseptic meningoencephalitis and connective tissue disorders. Arq Neuropsiquiatr 2000; 58:45-51.
6. Koseda-Dragan M, Hebanowski M, Badzio-Jagiello H, et al. New diagnostic criteria for the neuropsychiatric form of systemic lupus erythematosus. Psychiatr Pol 2000; 34:993-1005.
7. Weiner SM, Otte A, Schumacher M, et al. Diagnosis and monitoring of central nervous system involvement in systemic lupus erythematosus: value of F-18 fluorodeoxyglucose PET. Ann Rheum Dis 2000; 59:377-385.
8. Csépány T, Bereczki D, Kollár J, Sikula J, Kiss E, Csiba L. MRI findings in central nervous system systemic lupus erythematosus are associated with immunoserological parameters and hypertension. J Neurol 2003; 250:1348-1354.
9. Takahashi T, Kokubun Y, Okuhata Y, Sawada S, Mizutani T. A central nervous system lupus showing peculiar findings on cranial magnetic resonance imaging (MRI). Rinsho Shinkeigaku 2003; 43:409--416.
10. Sabaddini MG, Manfredi AA, Bozzolo E, et al. Central nervous system involvement in systemic lupus erythematosus patients without overt neuropsychiatric manifestations. Lupus 1999; 8:11-9.
11. Phillips DP. Central auditory processing: a view from auditory neuroscience. Am J Otol 1995; 16:338-352.
12. American Speech-Language-Hearing Association (ASHA). Central auditory processing: current status of research and implications for clinical practice. Am J Audiol 1996; 5:41-54.

13. Chermak GD. Deciphering auditory processing disorders in children. Otolaryngol Clin North Am 2002; 35:733-749.
14. Phillips SL, Gordon-Salant S, Fitzgibbons PJ, Yeni-Komshian G. Frequency and temporal resolution in elderly listeners with good and poor word recognition. J Speech Lang Hear Res 2000; 43:217-228.
15. Emmanuel DC. The auditory processing battery: survey of common practices. J Am Acad Audiol 2002;13:93-117.
16. Purcell DW, John SM, Schneider BA, Picton TW. Human temporal auditory acuity as assessed by envelope responses. J Acoust Soc Am 2004;116:3581--3593.
17. Bellis TJ. Mechanisms of selected auditory and related processes. In: Bellis TJ. Assesment and management of central auditory processing disorders in the educational setting: from science to practice. 2nd ed. New York: Delmar Learning, 2003: 51-102.
18. Sulakhe N, Elias LJ, Lejbak L. Hemispheric asymmetries for gap detection depends on noise type. Brain Cogn 2003; 53:372-375.
19. Musiek FE, Baran JA, Pinheiro ML. Neuroaudiology: case studies. San Diego: Singular Publishing Group; 1994: 279p.
20. The 1997 Update of the 1982 American College of Rheumatology Revised Criteria for Classification of Systemic Lupus Erythematosus, 1997. http://www.rheumatology.org/publications/classification/SLE/1997UpdateOf1982RevisedCriteriaClassificationSLE.asp
21. Davis, H. Abnormal hearing and deafness. In: Davis H, Silverman SR, ed. Hearing and deafness. New York: Holt, Rinehart and Winston, 1970: 83-139.
22. Pereira LD, Schochat E. Processamento auditivo central: manual de avaliação. São Paulo: Lovise; 1997: 147-149.
23. Keith RW. Random gap detection test. Auditec of Saint Louis. Missouri: 2000.
24. Musiek FE, Baran JA, Pinheiro ML. Duration pattern recognition in normal subjects and patients with cerebral and cochlear lesions. Audiology 1990; 29:304-313.
25. Musiek FE. Frequency (pitch) and duration pattern tests. J Am Acad Audiol 1994; 5:265-268.
26. Fisher LD, Van Belle G, ed. Biostatistics: A methodology for the health sciences. 1993. New York: John Wiley & Sons Inc, 1993: 858p.
27. Vilar MJP, Sato EI. Estimating the incidence of systemic lupus erythematosus in a tropical region (Natal, Brazil). Lupus 2002;11:528-532.
28. Bluestein HG. Neuropsychiatric manifestations of systemic lupus erythematosus. N Engl J Med 1987; 317:309-311.
29. Miguel EC, Pereira RM, Pereira CA, et al. Psychiatric manifestations of systemic lupus erythematosus: clinical features, symptoms and signs of central nervous system activity in 43 patients. Medicine (Baltimore) 1994;73:224-232.
30. Kimura D. A note on cerebral dominance in hearing. Acta Otolaryngol 1963; 56:617-618.
31. Kimura D. Left-right differences in the perception of melodies. Q J Exp Psychol 1964; 16:355-358.
32. Snell KB. Age-related changes in temporal gap detection. J Acoust Soc Am 1997; 101:2214-2220.
33. Schneider BA, Pichora-Fuller MK. Age-Related Changes in Temporal Processing: Implications for Speech Perception. Semin Hear 2001; 22: 227-240.
34. Musiek FE, Pinheiro ML, Wilson DH. Auditory pattern perception in 'split brain' patients. Arch Otolaryngol 1980; 106:610-612.
35. Musiek FE, Pinheiro ML. Frequency patterns in cochlear, brainstem and cerebral lesions. Audiology 1987; 26:79-88.
36. Appenzeller S, Faria A, Marini R, Costallat LT, Cendes F. Focal transient lesions of the corpus callosum in systemic lupus erythematosus. Clin Rheumatol 2006; 25:568-571.
37. Paulus MP, Geyer MA, Braff DL. Use of methods from chaos theory to quantify a fundamental dysfunction in the behavioral organization of schizophrenic patients. Am J Psychiatry 1996; 153:714--717.
38. Gladman DD, Goldsmith CH, Urowitz MB, et al. The systemic lupus international collaborating clinics/American College of Rheumatology (SLICC/ACR) damage index for systemic lupus erythematosus international comparison. J Rheumatol 2000; 27:373-376.
39. Schucard JL, Parrish J, Shucard DW, McCabe DC, Benedict RH, Ambrus J. Working memory and processing speed deficits in systemic lupus erythematosus as measured by the paced auditory serial addition test. J Int Neuropsychol Soc 2004; 10:35-45.
40. Kerr EN. Attentional capacity in patients with systemic lupus erythematosus. Diss Abstr Int [B] 1996; 56:5771.
41. Kozora E, Thompson LL, West SG, Kotzin BL. Analysis of cognitive and psychological deficits in systemic lupus erythematosus patients without overt central nervous system disease. Arthritis Rheum 1996; 39:2035-2045.
42. Strouse AL, Hall JW. Test-retest reliability of a dichotic test for assessing central auditory function in Alzheimer's disease. Audiology 1995; 34:85-90.
43. Olivares-García MR, Peñaloza-López YR, García-Pedroza F, et al. Identificación de la lateralidad auditiva mediante una prueba dicótica nueva con dígitos en español, y de la lateralidad corporal y orientación espacial en niños con dislexia y en controles. [Identification of auditory laterality by means of a new dichotic digit test in Spanish, and body laterality and spatial orientation in children with dyslexia and in controls]. Rev Neurol 2005; 41:198-205.

44. Futrell N, Schultz LR, Millikan C. Central nervous system disease in patients with systemic lupus erythematosus. Neurology 1992; 42:1649-1657.
45. Muñoz-Málaga A, Anglada JC, Paez M, Girón JM, Barrera A. Psicosis como manifestación de lupus eritematoso sistémico: valor de prueba de la banda lúpica frente a los anticuerpos antirribosomales. [Psychosis as the initial manifestation of systemic lupus erythematous: the role of lupus band test and antiribosomal antibodies.] Rev Neurol. 1999; 28:779-781.
46. Shinn JB. Temporal processing and temporal patterning tests. In: Musiek FE, Chermak GD. Handbook of (central) auditory processing disorder: auditory neuroscience and diagnosis. San Diego: Plural Publishing, 2007: 231-256.
47. Musiek FE, Shinn J, Jirsa R, Bamiou D, Baran JA, Zaidan E. The GIN® (Gaps-in-Noise) Test performance in subjects with confirmed central auditory nervous system involvement. Ear Hear 2005;26:608-618.
48. Musiek FE, Wilson DH. SSW and dichotic digit results pré- and post-commissurectomy: a case report. J Speech Hear Disord 1979;44:528-533.

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