Aud Vestib Res (2019);28(4):221-227.

RESEARCH ARTICLE

Dichotic listening processing in patients with multiple sclerosis

Mahsa Habibi[1], Saeid Farahani[1*], Nematollah Rouhbakhsh[1], Farzaneh Zamiri Abdollahi[1], Shohreh Jalaie[2]

[1]- Department of Audiology, School of Rehabilitation, Tehran University of Medical Sciences, Tehran, Iran

[2]- Biostatistics, School of Rehabilitation, Tehran University of Medical Sciences, Tehran, Iran

Received: 12 Jan 2019, Revised: 11 Mar 2019, Accepted: 8 Apr 2019, Published: 15 Oct 2019

Abstract

Background and Aim: Dichotic listening disorders occur secondary to interhemispheric transfer dysfunction. Central processing tests such as staggered spondaic words (SSW) and dichotic digits test (DDT) are recommended for the evaluation of dichotic listening in patients with multiple sclerosis (MS). The present study aimed to evaluate dichotic listening in subjects with MS by SSW and DDT.

Methods: This cross-sectional study was conducted on 45 patients with MS, including 20 males (mean ± SD age: 35.95 ± 5.73 y) and 25 females (mean ± SD age: 37.40 ± 6.1 y) and their data were collected by the Persian version of SSW (P-SSW) and DDT. The results compared to 45 normal subjects age- and gender-matched as the control group.

Results: In patients with MS, P-SSW quantitative and qualitative errors (except for Sm2 and reversals), errors were significantly more than the control group ($p \leq 0.001$). Right and left ear scores in DDT for the patients with MS were significantly lower, and right ear advantage was significantly higher than that in the control group ($p \leq 0.001$). The results also showed a significant correlation between the test of P-SSW and DDT in the left ear.

Conclusion: The present study showed that patients with MS have lower performance in dichotic listening and binaural processing than normal peers. Identification of binaural processing deficit in patients with MS may lead to early rehabilitation and improving their function by facilitating auditory processing.

Keywords: Speech perception; auditory processing; dichotic listening; multiple sclerosis; binaural hearing

Citation: Habibi M, Farahani S, Rouhbakhsh N, Zamiri Abdollahi F, Jalaie S. Dichotic listening processing in patients with multiple sclerosis. Aud Vestib Res. 2019;28(4):221-227.

[*] **Corresponding author:** Department of Audiology, School of Rehabilitation, Tehran University of Medical Sciences, Piche-Shemiran, Enghelab Ave., Tehran, 1148965141, Iran. Tel: 009821-77530636, E-mail: s_farahani@tums.ac.ir

Introduction

Jean Charcot first identified multiple sclerosis (MS) in 1860 [1]. MS is an inflammatory autoimmune disease which affects the central nervous system [2]. MS is a demyelinating disease. Myeline accelerate electrical flow along the neurons so that demyelination can change essential central functions [1]. This disease leads to the improper transmission of the electrical impulses in the central nervous system (CNS) or stop them entirely and consequently various manifestations, including tiresome, speech disorders, and visual defects can be developed [3]. In this disease, T cells that typically play a protective role in the body, attack the CNS, and destroy myelin sheath [4]. MS has an unknown etiology, but it appears that a combination of genetic vulnerabilities and non-genetic factors such as viruses, metabolism disorders, or even environmental factors contribute to changing the immune system so that it attacks CNS [5]. MS is mostly seen at the age of 20–40 years [6], and due to hormonal and immune factors, females have 2−3 times more involved than males [7].

MS can compromise auditory centers and consequently affects central auditory processing (CAP). The central auditory nervous system (CANS) is a complex network in which neural information of ears are analyzed, and the processed data are transmitted to the auditory cortex and other centers in the brain [8].

Auditory processing disorder (APD) is a deficit in one or more central auditory behaviors. The most common manifestation of APD is a poor auditory function in the presence of competing signals and or understanding degraded signals [9]. Nowadays, several models and test batteries have been introduced for central auditory evaluations [9]. In almost all of the models and test batteries, dichotic listening assessment is incorporated. In dichotic listening, two different stimuli are presented to the left and right ears simultaneously. This auditory function has a significant contribution in challenging listening situations such as hearing in noise. Dichotic speech tests are sensitive to brainstem, cortex, and corpus callosum disorders [10]. Clinical dichotic tests include dichotic digit test (DDT), competing sentence test (CST), dichotic consonant-vowel test (DCV) [11], and staggered spondee word (SSW) test [12]. Based on the SSW results, there are 4 pathologic central auditory categories; decoding (DEC), integration (INT), organization (ORG), and tolerance-fading memory (TFM). DEC disorder is a phonemic-level disorder which affects phonemic detection, recognition, manipulation, and memorization. DEC disorder is attributed to left posterior temporal dysfunction. TFM dysfunction leads to poor speech perception in challenging situations, and there is a poor short-term memory. Any impairment in the anterior temporal region, including hippocampus and amygdala as well as frontal lobe makes TFM category more probable. ORG is an error in ordering and sequencing. In this category, reversals happen. The ORG errors originate from post-central and pre-central gyri and also anterior areas of the temporal lobe. INT is a deficit of integrating auditory information with visual and other non-verbal aspects of speech. It is originated from corpus callosum and angular gyrus dysfunction [13].

Dichotic listening and corpus callosum involvement have been reported in patients with MS [14,15]. The patientsalso have difficulty in temporal resolution processing, which is indicative of CANS involvement and consequently APD [16]. All auditory processing disorders that are reported in patients with MS can cause difficulty in speech perception in noisy environments, segregating the desired signal from competing signals, and processing of fast signals. These difficulties can result in auditory fatigue and low quality of life [17].

Few studieshave used SSW as a test for dichotic listening in patients with MS. Besides, SSW and DDT have yielded contradictory results in some studies. Therefore there are no conclusive results about dichotic processing in this group. This study aimed to evaluate dichotic processing in patients with MS by using P-SSW and DDT and compare the results with healthy subjects.

Methods

This cross-sectional study was conducted on 45 patients (20 males and 25 females) with MS in the age range of 25 to 45 years (mean ± SD age: 36.76 ± 5.87 y) and 45 healthy subjects (20 males and 25 females) as control group in the same age range (mean ± SD age: 37.53 ± 6.02 y). Individuals with the confirmed diagnosis were selected. This confirmation was based on a medical record, neurologist diagnosis, and MRI examination. The duration of the disease was between 4 to 10 years (mean ± SD duration: 2.14 ± 7.2 y). The subjects were selected from the members of the MS Association of Iran through convenient sampling method. The age and gender-matched control group consisted of people living in Tehran without a history of neurological or auditory problems. All individuals were monolingual Persian speakers and right-handed (determined via Edinburgh Questionnaire). Initially, the research process was explained to the samples, and written consent was obtained from them. This research was approved by the Ethics Committee of Tehran University of Medical Sciences (Code No. IR.TUMS. FNM REC 1397.171).The participants were volunteers, and they could leave the study at any time they wanted. The inclusion criteria for both groups were as follows:normal otoscopy,the type A tympanogram and presence of ipsilateral reflex via immittance audiometry test, normal pure tone thresholds (≤ 25 dB HL) at octave frequencies from250 Hz to 8000 Hz, and speech recognition score ≥ 90% [18]. In addition, there was no history of hearing loss, seizure, depression, and head trauma in both groups. In all subjects, the central auditory processing tests, including Persian staggered spondaic words (P-SSW) test [13] as well as two-paired DDT [19] were conducted via Pavilion dm4 dual-channel CD playerand Phillips calibrated headphones.

P-SSW consists of 40 items, and each item consists of 4 single-syllable words that form a compound word [13]. The firstsyllable of the first word (right non-competing; RNC) and the second syllable of the second word (left non-competing; LNC)are presented as non-competing to the right and left ear, respectively and the second syllable of the first word (right competing; RC) and the first syllable of the second word (left competing; LC) are presented simultaneously to the right and left ear, respectively [20]. Items are presented at the 50 dB SL re: three-frequency pure tone average (500, 1000, 2000 Hz). The subject is asked to repeat both syllables of each word odd items start from the right ear, and even items start from the left ear. So 20 items start from the right ear (right ear first; REF), and 20 item start from the left ear(left ear first; LEF). The P-SSW test has quantitative and qualitative analysis [21]. The quantitative scores include the errors of each mode (RNC, RC, LC, LNC) and the total errors of these 4 modes (total). Qualitative scores include bias responses (ear and order effect) and descriptive indicators. The ear effect is obtained by comparing the total errors when items start from the right ear (total errors in the REF) and the total errors when items start from the left ear (the total errors in LEF). The order effect is one of the bias responses,which is referred to the total errors happening at the beginning and end of the items regardless of the ear. Descriptive indicators included the specific rhythms of the responding to the stimuli , delay (X), too much delay (XX), quiet rehearsal (QR), smush 2 (Sm2), intrusive word (IW), back to back (BTB), quick response (Q), smush (Sm), twister tongue (TW), and preservation (P) [13].

To perform DDT, two pairs of monosyllabic digits from 1 to 10 except for number 4, which is two syllabic in Persian are used. The test is performed at 50 dB SLre: speech reception threshold (SRT). Four numbers are presented simultaneously (two to each ear), and subjects must repeat all numbers regardless of the order of the presentation ear or the presentation number (free recall method).Twenty pairs of numbers (40) to each ear are presented (each digit has 5% score). The total score for both ears and each ear is recorded [19,21]. The ear advantage is calculated by subtracting the left ear score from the right ear score. A positive score indicates a right ear advantage (REA), and the negative score represents the left ear advantage (LEA) [22].

In this study, SPSS 21 was used to analyze the data. Mann-Whitney nonparametric test was used for comparing the results between two groups and two genders. The Pearson correlation was used for the evaluation of the relationship between the two test results. The significance level in this study was set at 0.05.

Results

In the P-SSW test, 16 (35%) out of 45 patients with MS had normal results, and 29 (46%) showed abnormalities. In Table 1, the quantitative errors of the P-SSW test are shown fortwo groups. As it is seen, the mean ± SD number of errors in the MS group (8.67 ± 10.51) was higher than that in the control group (1.07 ±

Table 1. Mean and standard deviation of staggered spondaic words test in the control and multiple sclerosis groups

	MS (n = 45)		Control (n = 45)	
	Mean	**SD**	**Mean**	**SD**
RNC	1.22	3.35	0	0
RC	1.62	4.36	0.09	0.28
LC	4.07	3.94	0.78	1.04
LNC	1.76	2.36	0.2	0.5
Total	8.67	10.57	1.07	1.51

MS; multiple sclerosis, RNC; Right non competing, RC; right competing, LC; left competing, LNC; left non competing

1.51), a statistically significant difference confirmed by the Mann-Whitney test($p < 0.001$).
Table 2 shows the qualitative errorsof the SSW test. The rates of qualitative eerrors in the P and BTB categories are higher in the MS group than those in the control group. This difference is statistically significant according to the Mann-Whitney test ($p \leq 0.001$), while in the Sm2 and reversal categories, this difference was not significant. It should be noted that other SSW test errors (X, QR, IW, Q, Sm, TTW, XX) were not observed in any groups.
In terms of ear effect, 9 out of 45 patients with MS had High/Low (H/L) status and 31 cases had Low/High (L/H) status, while in the control group, 18 out of 45 cases had H/L and 1 had L/H. Also in order effect, H/L status was observed in 30 and L/H in 10 subjects with MS, but in the control group H/L status was seen in one subject, and L/H was seen in 19 subjects. The Chi-square test was used for comparing ear and order effects between two groups, which was proven to be significant ($p < 0.001$). In an examination of the total-ear-condition (TEC) approach (consisted of 3 points:total, ear, and condition) in the P-SSW test, the patients with MS were normal to mild, indicating brain lesions without the involvement of the auditory cortex. These patients are considered as patients with mild APD [13]. The mean ± SD error values of the patients with MS in 4 general categories of APD, including decoding, tolerance fading memory, integration, and organization were 6.76 ± 9.69, 5.84 ± 6.6, 3.76 ± 4.36, and 2.84 ± 5.362, respectively and in the control group, they were 0.84 ± 1.38, 1.42 ± 1.87, 0.6 ± 1.05, and 1.87 ± 1.61, respectively. There was a significant difference between the two groups with regard to general categorization based on the Mann-Whitney test ($p \leq 0.001$). The mean and standard deviation of right and left ear correct responses and ear advantage of the DDT in the MS and control groups are summarized in Table 3. Also, the percentage of correct responses in the right and left ear of the patients with MS were lower than those in the control group, and in terms of the right ear advantage score, the scores of the patients with MS were higher than those in the control group, and the difference between the two groups was significant($p \leq 0.001$).
The Pearson test showed no significant relationship between right ear errors in P-SSW test and right ear score in the DDT with a correlation coefficient of -0.19 ($p = 0.05$). However, there was a significant correlation between left ear errors in P-SSW test and left ear score in DDT with a correlation coefficient of -0.49 ($p < 0.001$).

Discussion

The present study aimedto evaluate dichotic processing by using P-SSW and DDT in 45 patients with MS (25 females and 20 males) in comparison with 45 healthy subjects (25 females and 20 males) as the control group. The age range of the subjects was 25 to 45 years. In the present study, the mean values of the qualitative and quantitative errors in the P-SSW and DDT scores for the right and left ears and right ear advantage (REA) were investigated. The results showed a significant difference between the two groups in both tests. The P-SSW qualitative and quantitative errors were higher in the MS group than those in the control group. There were only a few qualitative errors in the MS group, which can be attributable to the small sample size. The most common deficit in P-SSW was DEC that is

Table 2. Mean and standard deviationof staggered spondaic words test in control and multiple sclerosis groups

	MS (n = 45)		Control (n = 45)		
	Mean	**SD**	**Mean**	**SD**	**p**
Smash 2	0.04	0.29	0	0	0.31
Perservation	1.53	1.35	0.42	0.75	0.00
Back to back	1.16	1.31	0.33	0.67	0.00
Reversal	3.02	5.28	1.2	1.45	0.27

MS; multiple sclerosis

indicative of left posterior temporal lobe involvement [13].

DDT score for the right and left ear in the MS group was lower, and REA was higher than that in the control group. The findings showed that higher REA in the MS group was due to a significant reduction in the left ear scores. As patients had a verbal response to DDT and left hemisphere is dominant for speech, it seems that the difference between the two groups is due to corpus callosum impairment [23]. Corpus callosum is rich with myeline and demyelinating disorders can easily affect this structure and impair neural conduction velocity. This can lead to increased right ear advantage ordecreased left ear advantage [24]. Interhemispheric conduction deficit leads to better recognition for the right ear in patients with MS, and this improvement might be due to the elimination of central competition between two hemispheres [23]. Another factor is the severity and the location of the atrophy in the corpus callosum. When there is extensive atrophy in the posterior region of the corpus callosum, left ear advantage is suppressed considerably, and this can indicate that most of the auditory information is transmitted via posterior part of the corpus callosum [23]. In general, the results of the present study is representative of dichotic listening involvement in patients with MS. Dichotic listening disorder can cause speech perception difficulties, especially in noisy environments.

On the contrary, Lindeboom showed that right ear score increased in the patients with MS. He studied 24 patients with MS via DDT with free recall and directed attention method, and the results showed an increase in right ear score and decreased in the left ear in comparison to control group which is indicative of the interhemispheric disorder. He explained that reduction of the interference from the left ear caused higher right ear score. The present study failed to show such a result, and this might be due to little corpus callosum involvement in the present study [25].The findings of the present study are in line with Gadea et alresults. They studied 13 patients with MS via dichotic consonant-vowel test. They had progressive demyelination in the posterior part of corpus callosum (isthmus and splenium) and showed increased right ear advantage over time. The results were due to a significant increase in right ear score and a slight decrease in the left ear score. It was shown that the volume of the posterior part of the corpus callosum in patients with relapsing-remitting MS reduces and its dysfunction increases for short periods [26]. Berlow et al. studied 28 patients with MS and 26 normal subjects via DDT and MRI. They investigated the effects of the degenerative neural process on dichotic listening patients with MS and reported the lower volume of grey matter and corpus callosum compared to the control group. In DDT, there was no significant difference between the two groups, which might be due to different DDT task in their study. They did not

Table 3. Mean and standard deviation of dichotic digit test in control and multiple sclerosis groups

	MS (n = 45)		Control (n = 45)		
	Mean	SD	Mean	SD	p
Right ear	87.35%	8.09	93.94%	5.18	0.00
Left ear	56.11%	23.29	87.00%	8.24	0.00
Ear advantage	0.33%	0.23	0.07%	0.10	0.00

MS; multiple sclerosis

use the verbal expression for responding to stimuli. In patients with MS, corpus callosum status was highly correlated to DDT score. MRI showed several significant differences between brain tissue of two groups that can explain the problems in dichotic listening. The mean volume of grey matter in patients with MS was significantly less than that in the control group.

In contrast, there was no significant change in the volume of the white matter between the two groups. Corpus callosum dimensions showed a considerable reduction. In addition, white matter tissue had abnormal histology. This finding confirms that MS is not restricted to white matter lesions, but white matter, grey matter, and the whole brain. It is worth noting that MRI investigations have shown a strong relationship between DDT score and grey matter volume, white matter lesions, and cerebrospinal fluid volume [27].

Lewis et al. conducted a study on 26 patients with MS and 27 healthy subjects. They suggested that SSW was one of the best screening tests among all APD screening tests proposed for these patients. This test is a dichotic test which needs interhemispheric transmission through the corpus callosum. Corpus callosum has a high density of myeline, so it is logical to see the dichotic listening difficulty in these patients, which is secondary to corpus callosum lesions. In this study, the authors showed that DDT was not a proper test for identifying APD in patients with MS. Thisconclusion might be due to the low sample size in their study [28].

El-Zarea studied APD in patients with relapsing-remitting MS and similar to the present study, they reported that these patients had poorer performance in DDT compared to normal subjects. They did not show any significant inter-ear difference in patients with MS.This finding might be attributable to their sample that confined to the patients with relapsing-remitting MS and excluded other types of MS (cited in 14).

The most important limitations of the study were small sample size and lack of access to the recent MRI of the patients. As the MS plaques change their position in time, recent MRI can show the position and severity of plaques. Comparing the results of the central auditory tests with MRI enables us to achieve a more accurate interpretation of the test results based on the lesion location within CANS.

Conclusion

Based on the present study, patients with MS have lower performance in dichotic listening and binaural processing tasks than age-matched healthy subjects. These functional disorders can affect their auditory performance. As this disease manifests a variable nature, routine periodic auditory assessments are recommended. SSW and DDT appear to be suitable central tests for identifying the binaural hearing disorder in these patients. The early detection of any binaural hearing disorder in patients with MS may lead to early rehabilitation services, which in turn improves their quality of life.

Acknowledgments

This paper is extracted from Dissertation of M. Habibi's MSc. at Tehran University of Medical Sciences.The authors would like to express their gratitude to Mr. Hooshmand, head of Iran MS Society, and Dr. Moosavi, head of the research team of Iran MS Society. We thank all participants in the study.

Conflict of interest

The authors declared no conflicts of interest.

References

1. Katz J, Smith PS. The staggered spondaic word test. a ten-minute look at the central nervous system through the ears. Ann N Y Acad Sci. 1991;620:233-51.
2. Matas CG, de Andrade Matas SL, de Oliveira CRS, Gonçalves IC. Auditory evoked potentials and multiple sclerosis. Arq. Neuro-Psiquiatr. 2010;68(4):528-34. doi: 10.1590/S0004-282X2010000400010
3. Calabresi PA. Diagnosis and management of multiple sclerosis. Am Fam Physician. 2004;70(10):1935-44.
4. Lewis MS, Lilly DJ, Hutter M, Bourdette DN, Saunders J, Fausti SA. Some effects of multiple sclerosis on speech perception in noise: Preliminary findings. J Rehabil Res Dev. 2006;43(1):91-8.
5. Graham J. Managing multiple sclerosis naturally: a self-help guide to living with ms. Vermont: Healing Arts Press. 2010.
6. Goldenberg MM. Multiple sclerosis review. P T. 2012;37(3):175-84.
7. McCabe MP. Mood and self-esteem of persons with multiple sclerosis following an exacerbation. J Psychosom Res. 2005;59(3):161-6. doi: 10.1016/j.jpsychores.2005.04.010
8. O'Connor P. Multiple sclerosis: everything you need to know. Revised edition. New York: Firefly Books (U.S) Inc. 2005.
9. Bellis TJ. Assessment and management of central auditory processing disorder, in the educational setting: from science to practice. 2nd ed. San Diego: Singular publishing group; 2011.
10. Rawool VW. Temporal processing in the auditory system. In: Geffner D, Ross-Swain D, editors. Auditory processing disorders: Assessment, management, and treatment. San Diego: Plural Publishing, Inc; 2007. p. 117-37.
11. Geffner D, Ross-Swain D. Auditory processing disorders: assessment, management and treatment. 2nd ed. San Diego: Plural Publishing; 2012.
12. Berlin CI, Lowe-Bell SS, Jannetta PJ, Kline DG. Central auditory deficits after temporal lobectomy. Arch Otolaryngol. 1972;96(1):4-10.
13. Katz J. The use of staggered spondaic words for assessing the integrity of the central auditory nervous-system. J Aud Res.1962;2:327-37.
14. Negin E, Barootiyan SS. Staggered Spondaic Word Test. (Central) auditory processing assessments: Buffalo Auditory Processing Model. Tehran: Setayesh Hasty; 1396. p. 88-123.
15. El-Zarea GA, Shalaby AA, Hussin HM, Mohammad A. Evaluation of central auditory processing in egyptian multiple sclerosis patients. Egypt J Hosp Med. 2018; 71(7);3667-75.
16. Peñaloza López YR, Orozco Peña XD, Pérez Ruiz SJ. Multiple sclerosis: multiple sclerosis: left advantage for auditory laterality in dichotic tests of central auditory processing and relationship of psychoacoustic tests with the multiple sclerosis disability scale-EDSS. Acta Otorrinolaringol Esp. 2018;69(6):325-30. doi: 10.1016/j.otorri.2017.11.003
17. Valadbeigi A, Rouhbakhsh N, Mohammadkhani G, Jalaie S, Musiek FE, Jalilvand Karimi L. [Comparison the duration patterns sequence test (DPST)between multiple sclerosis and normal participants]. Journal of Modern Rehabilitation. 2012;5(4):35-41. Persian.
18. Atcherson SR, Nagaraj NK, Kennett SE, Levisee M. Overview of central auditory processing deficits in older adults. Semin Hear. 2015;36(3):150-61. doi: 10.1055/s-0035-1555118
19. McArdlw R, Hnath-Chisolm Th.Speech Audiometry. In: Katz J, Chasin M, English K, Hood L, Tillery KL. Handbook of Clinical Audiology. 6th ed. Philadelphia: Lippincott Williams & Wilkins; 2009. p. 61-77.
20. Shahmir B, Hajiabolhassan F, Mohammadkhani G, Tahaei AA, Jalaie S. Development and evaluation of the reliability of Persian version of double dichotic digit test in girls aged 7 to 11 years. Aud Vestib Res, 2015; 24(3):164-70.
21. Rezapour M, Zamiri Abdollahi F, Delphie M, Lotft Y, Bakhshi E. Normalization and reliability evaluation of persian version of two-pair dichotic digits in 8 to 12-year-old children. Iranian Rehabilitation Journal. 2016;14(2):115-20.
22. Moncrieff DW. Dichotic listening in children: age-related changes in direction and magnitude of ear advantage. Brain Cogn. 2011;76(2):316-22. doi: 10.1016/j.bandc.2011.03.013
23. Musiek FE, Cheek DE. Dichotic paradigms and multiple sclerosis. Canadian Hearing Report, 2015:**10**;7-13.
24. Mustillo P. Auditory deficits in multiple sclerosis: a review. Audiology. 1984;23(2):145-64.
25. Lindeboom J, ter Horst R. Interhemispheric disconnection effects in multiple sclerosis. J Neurol Neurosurg Psychiatry. 1988;51(11):1445-7.
26. Gadea M, Marti-Bonmatí L, Arana E, Espert R, Salvador A, Casanova B. Corpus callosum function in verbal dichotic listening: inferences from a longitudinal follow-up of relapsing-remitting multiple sclerosis patients. Brain Lang. 2009;110(2):101-5. doi: 10.1016/j.bandl.2009.03.006
27. Berlow YA, Pollaro J, Krisky C, Grinstead J, Snodgrass M, Kohout K, et al. Magnetic resonance imaging correlates of dichotic listening performance in multiple sclerosis. Semin Hear. 2012;33(03):283-94. doi: 10.1055/s-0032-1315727
28. Lewis MS, Wilmington D, Hutter M, McMillan G, Casiana L, Fitzpatrick M, et al. Preliminary identification of central auditory processing screening tests for individuals with multiple sclerosis. Semin Hear 2012;33(03):261-73. doi: 10.1055/s-0032-1315725