Eur J Appl Physiol (2002) 87: 469–473
DOI 10.1007/s00421-002-0652-y

ORIGINAL ARTICLE

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Handedness and language cerebral lateralization

Accepted: 20 April 2002 / Published online: 5 July 2002

Abstract Repetitive transcranial magnetic stimulation (rTMS) induces lateralized speech arrest consistent with cerebral dominance for language. Studies of language cerebral dominance in differently handed healthy subjects have been limited. Using a focal magnetic coil, we examined the degree of consistency between handedness as evaluated by the Stanley Coren Score and hemispheric dominance for language as determined by rTMS in 25 right- and 25 left-handed medical students. They were categorized according to the score into 24 strongly right-handed, 1 moderately right-handed, 19 strongly left-handed, 3 moderately left-handed and 3 ambidextrous (equally-handed). In the strongly right-handed subjects, left-sided language cerebral dominance was recorded in 87.5% of the subjects, and bilateral cerebral representation in 8.2%, and right-sided language cerebral dominance in 4.2%. In the strongly left-handed subjects, 73.7% had left-side language cerebral dominance, 15.8% had bilateral cerebral representation and 10.5% had right-side cerebral language dominance. In mixed handed subjects (moderately right, left and ambidextrous), bilateral cerebral representation was observed in 57% and left-side cerebral language dominance in 43%. There were 27 subjects who developed speech arrest at 140% of motor threshold, the others developed speech arrest at lower intensities. Speech lateralized to the left-side cerebral dominance in strongly right- and left-handed subjects, but bilateral cerebral representation was frequent in mixed handedness and right-sided cerebral dominance rarely occurred.

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Keywords Repetitive transcranial magnetic stimulation · Speech centre · Right-, left- and mixed-handed subjects

Introduction

Handedness is the best known and most studied human asymmetry. It has long been known that speech function is primarily localized in the left hemisphere of right-handed individuals. However, lateralization of language is not as well defined in left-handed people as it is in their right-handed counterparts (Geschwind and Galaburda 1985). Satz (1980) has reviewed the literature on aphasia in left-handed people and has concluded that speech is bilaterally represented in many of them. The intracarotid amobarbital test (IAT) defines cerebral dominance for language. However, it is an invasive procedure, the patients need hospitalization, and the test carries the same risks as does cerebral angiography. It is used usually in pathological states and therefore, knowledge concerning the variability of language dominance is heavily biased towards pathological states in which, among other problems, there is high likelihood of functional hemisphere re-organization (Rasmussen and Milner 1977). Recently, repetitive transcranial magnetic stimulation (rTMS) has been used to determine the lateralization of the motor speech area (Pascual-Leone et al. 1991; Jennum et al. 1994; Michelucci et al. 1994). A high concordance with IAT was found in two of these studies (Pascual-Leone et al. 1991; Jennum et al. 1994). Nevertheless, rTMS studies of cerebral lateralization in normal left- and mixed-handed people are still scarce. Moreover, knowledge concerning the exact incidence of right hemisphere language dominance in healthy right-, left- and mixed-handed people would be important for functional neurophysiological studies.

The present study was designed to examine the degree of consistency between handedness as evaluated by the Stanley Coren Inventory Score (Claus et al. 1992) and hemispheric dominance for language as determined by rTMS.

Methods

Subjects

A group of 50 male medical student volunteers (25 right- handed and 25 left-handed, self-reported as to which hand was preferred for writing) participated in this study. The mean (SD) age of the subjects studied was 22.7 (1.85) years (range 19–26 years). Students were classified according to the Stanley Coren Handedness Inventory (Claus et al. 1992) as strongly right-handed (24 students), moderately right-handed (1 student), strongly left-handed (19 students), moderately left-handed (3 students) and ambidextrous (3 students).

A complete personal and family history was taken of each student, concerning age and college class. All subjects were given a full neurological examination to exclude neurologic, psychiatric, any relevant medical disease and other exclusion criteria for the rTMS test (e.g. seizure, the wearing of a biomedical device). The goal of this study was explained to the participants and written consent to participate was obtained. The Ethics Committee of Assiut University approved the experiment procedure.

Procedure

Each subject was submitted to rTMS to determine the side of cerebral dominance for speech. The rTMS was performed using Dantec Keypoint (Copenhagen, Denmark) with a magnetic stimulator (MagLite) figure-of-eight coil. The subject motor thresholds were determined using single TMS pulses. An electromyogram was recorded from the right abductor pollicis brevis muscle. The representation of the right hand in the left primary motor area was located by moving the coil until maximal amplitude motor evoked potentials (MEP) were produced. Once the optimal position was located, the motor threshold was determined by decreasing the stimulation intensity (expressed as a percentage of maximal output) and continuing single pulse stimulation. Motor threshold was defined as the intensity required to produce MEP of at least 50 μV amplitude in five of ten consecutive stimulation trials (Flitman et al. 1998). Estimation was made while stimulating over the same scalp position at a rate of 2 Hz. Preliminary speech testing was performed in the seated position, using an initial stimulator output at 100% of motor threshold and a repetition rate of 3 Hz. The coil was oriented so that the induced electric fields were aligned horizontally. The subjects were instructed to count upward while the coil was moved across the frontotemporal region on the left and then on the right hemisphere. If speech arrest was not obtained the stimulus intensity was increased sequentially by 10% up to 150% of motor threshold and the process repeated. We used intensities above the motor threshold because low intensities could have been insufficient to inhibit speech as recorded by Claus et al. (1993). The coil was applied to the marked centre point and energized for 1–5 s after the subject had begun counting. The time of stimulation was 5–10 s. Complete speech arrest was defined as the absence of any structural or recognizable language and not necessarily the cessation of the sound (Epstein et al. 1996). Stimulation was stopped as soon as total speech arrest was observed. An observer noted whether the subjects pulled their heads away from the coil when it was energized and rated speech interruption. Experimenters recorded any side-effects during or after rTMS. Evaluation of the speech area was performed blind without knowing the handedness.

Results

Subjects were divided into three groups strongly right-, strongly left- and mixed-handed. The strongly right-handed group included 24 male volunteers; their mean age was 23 (1.4) years with handedness score 35 (1.3). The strongly left-handed group included 19 volunteers; their mean age was 23(1.6) years with handedness score 13 (1.5). The mixed-handed group (moderately right-, left-handed and ambidextrous) included 7 volunteers; their mean age was 23 (0.6) years, with handedness score illustrated in Table 1.

Pattern of language dominance

The dominant hemisphere for language in the three handed groups was determined by the side of the cerebral hemisphere that showed speech arrest during rTMS while the subject was counting. Total speech arrest was frequent, but some volunteers continued to generate repetitive meaningless noises. Rhythmic ipsilateral facial contractions were noted during stimulation in all subjects.

Table 2 shows the pattern of cerebral dominance for language in three handedness groups. The majority of strongly right-handed subjects showed left-sided cerebral dominance (87.5%); rTMS over the right hemisphere did not lead to speech arrest at any stimulation positions in any of those subjects. The rTMS procedure at these positions induced dysarthria, while the remainder of the strongly right-handed subjects showed bilateral-cerebral dominance (8.4%) and right-cerebral dominance (4.2%). Strongly left-handed subjects had 73.7% of left-sided cerebral dominance, 15.8% of bilateral-cerebral representation and 10.5% for right-sided cerebral dominance. Bilateral-cerebral representation was the main type seen in mixed-handed subjects (57%) followed by left-sided cerebral dominance in 43%.

As regards to the different intensities of rTMS at which complete speech arrest had occurred, most of subjects (27 subjects) developed speech arrest at 140% of motor threshold. The others developed speech arrest at 120% (17 subjects), at 110% (3 subjects) and at 150% of motor threshold (3 subjects). In 29 subjects, the first

Table 1. Mean (SD) participants' demographic information

	Strongly right-handed (*n* = 24)	Strongly left-handed (*n* = 19)	Mixed-handed (*n* = 7)		
			Moderately right-handed (*n* = 1)	Moderately left-handed (*n* = 3)	Ambidextrous (*n* = 3)
Age (years)	23.40 (1.41)	22.60 (1.60)	23.0	22.0 (1.00)	23.30 (0.57)
Handedness score (Stanley Coren score)	35.28 (1.30)	13.23 (1.51)	29	17.0 (1.73)	24.00

Table 2. Relationship of handedness to language cerebral dominance as determined by repetitive transcranial magnetic stimulation

Handedness	Score	Subjects ($n=50$)		Left-side cerebral dominance		Right-side cerebral dominance		Bilateral-cerebral representation	
		number	%	number	%	number	%	number	%
Strongly right-handed	33–36	24	48	21	87.5	1	4.2	2	8.4
Mixed right-handed	29–32	1	2	0	0	0	0	1	100
Strongly left-handed	12–15	19	38	14	73.7	2	10.5	3	15.8
Mixed left-handed	16–19	3	6	1	33.3	0	0	2	66.7
Ambidextrous	24	3	6	2	66.6	0	0	1	33.3

reaction to speech arrest was laughing, which was attributed to surprise at their inability to count. A small amount of discomfort was observed in many subjects due to contraction of the oral-facial musculature especially when high intensity rTMS (140%–150%) was administered. There were 6 subjects who pulled their heads away from the coil when it was energized and rated speech interruption. This effect was ascribed to frustration caused by the inability to speak, rather than to discomfort from stimulation. We never observed crying or any side-effect such as headache, confusion or convulsion.

Discussion

The present study was carried out to clarify the pattern of language cerebral dominance, in different handedness groups. In the present study, we used the most recent handedness inventory test (Claus et al. 1992), for the determination of handedness which included 12 questions, and for each question 3 possible answers: right, left or mixed handed.

The use of IAT for the lateralization of cerebral speech dominance was first described by Wada (1949) and thus is often referred to as the "Wada test".The IAT has been widely used in preoperative evaluation before neurosurgery near the language areas (Wada and Rasmussen 1960). The IAT is performed after an angiography catheter has been inserted in the artery. Injection of sodium amobarbital is intended to anaesthetize the arterial territories of one hemisphere for several minutes, allowing an examiner to assess the language and memory capabilities of the other hemisphere in isolation (Fields and Tröster 1998). In practice, the IAT is hampered by significant risks, costs and potential pitfalls. Problems include normal and pathological variations in the territories perfused by the internal carotid artery, overflow of the drug into other vascular territories even during careful injection, and wide variation in the effects of the same dose among different patients (Epstein 1999). Interpretation of the results is complicated by the brief time available for testing and by simultaneous behavioural changes including hemiparesis, mood changes, and somnolence from the administration of intravenous barbiturate. Repeat testing is difficult and seldom performed (Epstein 1999).

The production of *temporary lesions* that would supplement or replace the IAT was one of the earliest goals for TMS in cognitive testing. Determination of the different patterns of cerebral dominance for language in this study was done by rTMS, a new noninvasive technique previously validated by direct comparison with the IAT procedure (Pascual-Leone et al. 1991; Jennum et al. 1994) and functional magnetic imaging (fMRI) (Pujol et al. 1999). In the present study the right and left-handed subjects had a high percentage of left-sided cerebral dominance for language. Nevertheless, bilateral cerebral representation, and right-sided cerebral dominance occurred in a significant proportion of our normal left- and right-handed subjects. The arrest of speech observed during rTMS suggested that rTMS interfered with language processing in the dominant hemisphere.

The dysarthria observed during rTMS of the other hemisphere (non-dominant hemisphere) was due to contraction of the facial and laryngeal muscles. In general terms, the incidence of the three types of cerebral dominance in right-handed subjects obtained in this study agree well with data from the Wada test literature (Rasmusseen and Milner 1977; Rey et al. 1988; Loring et al. 1990; Jennum et al. 1994; Risse et al. 1997). Jennum et al. (1994) used rTMS in 18 right-handed patients and recorded the same results as obtained by IAT, whereas all 6 of the subjects of Pascual-Leone et al. (1991) developed speech arrest when rTMS was applied to left-hemisphere (left-sided cerebral dominance). Pujol et al. (1999), Springer et al. (1999) and Knecht et al. (2000) used fMRI in determination of cerebral dominance in right-handed subjects and their results were similar to the pattern of cerebral dominance observed in our right-handed subjects. Knech et al. (2000) reported right hemisphere dominance in 75% of 188 right-handed subjects. Previous estimates of "atypical" right hemisphere language dominance were either based on the results from the IAT in patients evaluated for resective neurosurgery or on the occurrence of "crossed aphasia" i.e. aphasia after right hemisphere lesions. In patients with epilepsy submitted to the IAT test the number of the right handers with right hemisphere language dominance was 4% in a large series (Rasmussen and Milner

1977). By evaluation of stroke patients with crossed aphasia, the incidence of right hemisphere language dominance in right-handers has been inferred to be between 1% and 2% in the majority of series (Gloning et al. 1969; Borod et al. 1985; Kertesz 1985). In a single recent study on 880 stroke patients it was reported, in passing, that 9% of right-handed aphasics had right-side hemispheric lesions (Pedersen et al. 1995). These data suggested a low incidence of right hemisphere language dominance in the right-handed individuals.

Few authors have studied language cerebral dominance in left-handed subjects. In accordance with those of other investigators (Satz 1980; Seglowitz and Bryden 1983), our results showed that left-handed subjects had more atypical presentations for cerebral dominance than did right-handers, but in both groups the majority showed left sided cerebral dominance. Satz (1980) reviewed the literature on aphasia in left-handed people and concluded that speech is bilaterally represented in many left-handers. The same conclusion was reached by Segalowitz and Bryden (1983) by evaluating the relationship between aphasia and handedness. Recently Knecht et al. (2000) studied the relationship between handedness and language dominance in 326 healthy subjects using functional transcranial Doppler sonography and found that the incidence of right-hemisphere language dominance increases linearly with the degree of left-handedness, from 4% in strong right-handed to 27% in strong left-handed people.

The larger incidence of left-cerebral dominance in right-handed people than in the left-handed may explain why the asymmetry in the size of language areas toward the left-hemisphere was more prominent for the majority of right-handed people compared to the majority of the left-handed. (Geschwind and Galaburda 1985).

To the authors' knowledge, the pattern of cerebral dominance has never been investigated in subjects who use both hands, *mixed-handers*, as a separate group. In this study, the pattern of cerebral dominance in *mixed-handers* was 57% for bilateral representation and 43% for left-side cerebral dominance. The possible explanations for the bilaterality of speech as detected by speech arrest on stimulation of either right or left hemispheres in left-handed and mixed-handed subjects may be due to bilateral distributions of the speech functions, indicating that speech is mediated by, and dependent upon, both hemispheres. In support of this assumption is the fact that speech disorder differs in certain aspects between left- and right-handed patients. The IAP studies (Rasmussen and Milner 1977; Mateer and Dodrill 1983; Strauss and Wada 1983; Rey et al. 1988; Loring et al. 1990; Risse et al. 1997) evaluated language lateralization of ambidextrous patients and concluded that the proportion of left-hemisphere language dominance among them range from approximately 48%–75%.

In the present study, all 50 subjects successfully underwent 3 Hz rTMS over both frontotemporal regions and experienced speech arrest on at least one side. We observed neither crying nor any major side effects for rTMS, a fact that was possibly due to the reduced frequency of stimulation used in this study. It was also possible that the emotional responses (laughing) observed in some subjects, were due in part to the effects of lateral frontal rTMS on mood (George et al. 1995).

As in all studies that have used rTMS in localization of language hemispheric dominance, our results showed that there were different repetitive transcranial stimulation intensities at which speech arrest occurred. Most of our subjects (27 subjects) developed speech arrest at 140% of motor threshold with a frequency rate 3 Hz. The others developed speech arrest at 120% of motor threshold (17 subjects), at 110% of motor threshold (3 subjects), or at 150% of motor threshold (3 subjects) at the same frequency rate. So there was a clear association between speech arrest and stimulus intensity. A similar figure was presented in the study of Jennum et al. (1994).

Therefore rTMS rates down to 3 Hz are highly effective at blocking speech output, and the resulting discomfort is substantially less than that at higher frequencies of stimulation. This is contrary to the expectation of other authors (Michelucci et al. 1994; Jennum et al. 1994). The earliest magnetic study demonstrated total speech arrest at 8 Hz in 3 subjects, but most patients have been stimulated at higher frequencies of 16–30 Hz (Pascual-Leone et al. 1991; Jennum et al. 1994). However, Epstein et al. (1996) found that speech arrest could be obtained with a rTMS repetition rate as low as 2 Hz, an intensity of 150% motor threshold or less, and pulse trains of no more than 5 s. It is noteworthy to point out here that the safety of the stimulation at 3 Hz observed in this study should allow a more wide-spread use of magnetic speech localization in clinical and research applications. The present findings in healthy subjects indicate that even under natural conditions the association between handedness and language dominance is not an absolute one. We suggest that right hemisphere language dominance is not a pathological but a natural phenomenon. Finally, we would like to emphasize that our assessment of cerebral language lateralization is not comprehensive. Our results may, however, contribute to establishing useful procedures for language lateralization using rTMS.

References

Borod JC, Carber M, Naeser M, Goodglass H (1985) Left-handed and right-handed aphasics with left hemisphere lesions compared on non verbal performance measures. Cortex 21:81–90

Claus D, Weis M, Treig T, Lang C, Eichhorn KF, Coren S (1992) The left-hander syndrome. The causes and consequences of left-handedness, 1st edn. Free Press, New York, pp 43–44

Claus D, Weis M, Treig T, Lang C, Eichhorn KF, Sembach O (1993) Influence of repetitive magnetic stimuli on verbal comprehension. J Neurol 240:149–150

Epstein CM (1999) Language and TMS/rTMS. In: Paulus W, Hallet M, Rossini PM, Rothwell JC (eds) Transcranial magnetic stimulation. Electroencephalogr Clin Neurophysiol [Suppl] 51:325–333

Epstein C, Lah JK, Meador K, Weissman JD, Gaitan LE, Dihenia B (1996) Optimum stimulus parameters for lateralized suppression of speech with magnetic brain stimulation. Neurology, 47:1590–1593

Fields JA, Tröster AI (1998) The sodium amytal (Wada) test: procedural and intertative considerations. In: Stemmer B, Whitaker H (eds) Handbook of neurolinguistics. Academic Press, New York, pp 189–203

Flitman SS, Grafman J, Wassermann EM, Cooper V, O'Grady J, Pascual-Leone A, Hallett M (1998) Linguistic processing during repetitive transcranial magnetic stimulation. Neurology 50:175–181

George MS, Wassermann EN, Williams WA, Callahan A, Ketter TA, Basser P, Hallett M, Post RM (1995) Daily repetitive transcranial magnetic stimulation (rTMS) improve mood in depression. Neuroreport 6:1853–1856

Geschwind N, Galaburda M (1985) Cerebral lateralization, biological mechanisms, associations, and pathology. I. A. Hypothesis and a program for research. Arch Neurol 42:428–459

Gloning I, Gloning K, Haub G, Quatember R (1969) Comparison of verbal behavior in right-handed and non right-handed patients with anatomically verified lesion of one hemisphere. Cortex 5:43–52

Jennum P, Friberg L, Fuglsang-Frederiksen A (1994) Speech localization using repetitive transcranial magnetic stimulation. Neurology 44:269–273

Kertesz A (1985) Aphasia. In: Vinken PJ, Bruyn GW, Klawans HL (eds) Handbook of clinical neurology, vol 45. Elsevier, Amsterdam, pp 287–331

Knecht S, Drager B, Deppe M, Bobe L, Lohmann H, Floel A, Ringelstein B, Henningsen H (2000) Handedness and hemispheric language dominance in healthy humans. Brain 123:2512–2518

Loring W, Meador J, Lee P, Murro M, Smith R, Flanigin F, Gallagher W (1990) Cerebral language lateralization: evidence from intracarotid amobarbital testing. Neuropsychologia 28:831–838

Mateer A, Dodrill C (1983) Neuropsychological and linguistic correlates of atypical language lateralization: evidence from sodium amytal studies. Hum Neurobiol 2:135–142

Michelucci R, Valzania F, Passarelli D (1994) Rapid-rate transcranial magnetic stimulation and hemispheric language dominance: usefulness and safety in epilepsy. Neurology 44:1697–1700

Pascual-Leone A, Gates R, Dhuna A (1991) Induction of speech arrest and counting errors with rapid-rate transcranial magnetic stimulation. Neurology 41:697–702

Pedersen PM, Jorgensen HS, Nakayama H, Raaschou HO, Olsen TS (1995) Aphasia in acute stroke: incidence determinants, and recovery. Ann Neurol 38:659–666

Pujol S, Deus J, Losilla J, Capdevila A (1999) Cerebral lateralization of language in normal left-handed people studied by functional MRI. Neurology 52:1038–1043

Rasmussen T, Milner B (1977) The role of early left-brain injury in determining lateralization of cerebral speech functions. Ann NY Acad Sci 299:355–369

Rey M, Dellatolas J, Bancaud J, Talairach J (1988) Hemispheric lateralization of motor and speech functions after early brain lesion: study of 73 epileptic patient with intracarotid amytal test. Neuropsychologia 26:167–172

Risse L, Gates R, Fangman C (1997) A reconsideration of bilateral language representation based on the intracarotid amobarbital procedure. Brain Cogn 33:118–132

Satz P (1980) Incidence of aphasia in left-handers: a test of some hypothetical models of cerebral organization. In: Herron J (ed) Neuropsychology of left-handedness. Academic Press, New York, pp 55–69

Segalowitz J, Bryden P (1983) Individual differences in hemispheric representation of language. In: Segalowitz J (ed) Language functions and brain organization, 1st edn. Academic Press, New York, p 341

Springer A, Binder R, Hammeke A, Swanon J, Frot A, Bellgowan F, Brewer C, Perry M, Morris L, Muller M (1999) Language dominance in neurologically normal and epilepsy subjects. Brain 122:2033–2046

Strauss E, Wada J (1983) Lateral preferences and cerebral speech dominance. Cortex 19:165–169

Wada J (1949) A new method for determination of the side of cerebral speech dominance. A preliminary report on the intracarotid injection of sodium amytal in man. Med Biol 14:221–222

Wada J, Rasmussen T (1960) Intracarotid injection of sodium amytal for the lateralization of cerebral speech dominance. J Neurosurg 17:266–282