ELSEVIER

Neuroscience Letters 267 (1999) 89–92

Neuroscience Letters

Thalamic asymmetry is related to acoustic signal complexity

Cynthia King*, Trent Nicol, Therese McGee, Nina Kraus

Northwestern University, Auditory Neuroscience Laboratory, Frances Searle Building, 2299 North Campus Drive, Evanston, IL 60208, USA

Received 26 January 1999; received in revised form 18 March 1999; accepted 25 March 1999

Abstract

Hemispheric asymmetries in response to speech sounds are well documented. However, it is not known if these asymmetries reflect only cortical hemispheric specialization to language or whether they also reflect pre-conscious encoding of signals at lower levels of the auditory pathway. This study examined differences in neural representations of signals with acoustic properties inherent to speech in the left versus right side of the thalamus. Specifically, 2000 Hz tone bursts, clicks and synthesized forms of the phoneme /da/ were presented to anesthetized guinea pigs. Evoked responses were recorded simultaneously from aggregate cell groups in the left and right medial geniculate bodies. Results showed an asymmetric response to complex auditory stimuli between the left versus right auditory thalamus, but not to the simple tonal signal. Moreover, asymmetries differed in male versus female animals. © 1999 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Medial geniculate body; Guinea pig; Phoneme; Click; Tone burst; Neurophysiologic representation; Hemispheric asymmetry; Thalamus

In humans, the specialized role of the left hemisphere in speech perception is well documented [3,13,14,21,23]. There is also evidence across different species of anatomical and physiological asymmetries between the left and right side of the brain at cortical as well as sub-cortical levels [4,12,25]. However, little is known about right versus left asymmetries in the physiologic representation of the acoustic structure of sound, especially acoustically complex signals. Physiologic data from human subjects indicate that a left-side specialization exists to encode speech at an elemental acoustical level [10,22,27]. The extent to which these asymmetric responses occur pre-consciously and at sub-cortical levels of the auditory pathway is unknown. Our aim was to determine whether there was a right-side versus left-side difference in the representation of acoustic signals in the auditory thalamus in the guinea pig and whether this difference varied with different types of acoustic stimuli, including both speech and non-speech signals[1]. Also of interest was whether sex differences were evident in neurophysiologic responses. Behavioral differences between males and females in different species have been noted in auditory perception of tonal information [3,11], but little is known about gender specific perception of more complex auditory signals and the underlying neurophysiology. In this study, we were motivated by the expectation that this work could provide a basic biological link between normal representation of speech-like sounds and abnormal speech-sound perception and lateralization seen in certain clinical populations [7,9,17–19,24].

Subjects were 12 pigmented guinea pigs (six males, six females), each weighing between 300–400 g. Animals were anesthetized with ketamine hydrochloride and xylazine (dosage by weight) and maintained with additional injections, typically given every hour. High impedance (500 kΩ) recording electrodes were placed within the left and right medial geniculate bodies (MGB). Recording locations were approximately 4.8 mm rostral to the interaural line, 4.0 mm

* Corresponding author. Tel.: +1-847-491-2465; fax: +1-847-491-2523.

E-mail address: cdking@nwu.edu (C. King)

[1] Why use human speech signals for guinea pigs instead of other sounds such as a species-specific communication call? Left hemisphere dominance in response to species-specific communication calls has been documented in mice [8], but it is not known if this is a result of basic encoding differences in stimuli or if the dominance is due to some meaningful interpretation of the signal. In this experiment, an acoustically complex signal is presented to an anesthetized guinea pig and responses to this signal are recorded at a pre-conscious level. The stimulus does not need to be meaningful to the guinea pig, but it must have complex acoustic properties (as do guinea pig communication calls) in order to provide insight into processing of the elemental acoustics of complex auditory signals that is common among many animals, including humans.

PII: S0304-3940(99)00336-5

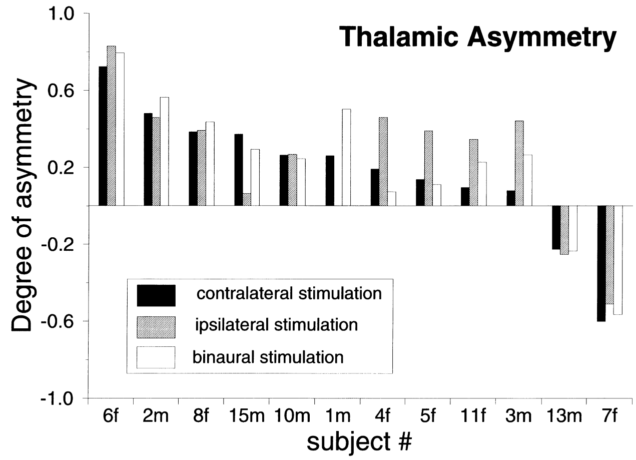

Fig. 1. Amplitude of onset responses were asymmetric at the level of the auditory thalamus. Degree and direction of asymmetry was determined for each animal by subtracting the right MGB onset amplitude from the left MGB onset amplitude and dividing by the sum of those two values [(L − R)/(L + R)]. Onset responses showed larger amplitudes for the left side compared with the right side in 10 of 12 animals, indicating a left-side dominance. The remaining two animals showed larger onset amplitudes for the right versus left, indicating a right-side dominance. These data represent an average of all three stimulus conditions. (Note: animal #1 did not show any asymmetry for the ipsilateral condition).

lateral to the sagittal suture and 7.2 mm ventral to the surface of the brain. Following each experiment, recording locations were marked with electrolytic lesions (35 μA for 10 s). Brains were cut in 17-μm sections and stained with Luxol Fast Blue and Cresyl Violet to show cell bodies as well as fiber pathways. For each animal, left and right MGB recording locations were required to be within 500 μm of each other, within the same subdivision of the nucleus, and approximately 0.5 mm from the edge of that subdivision in order to be included in the study. (Note that by using a 500 kΩ electrode, the recording region was approximately 1 mm^3 in area). Recordings were from the ventral subdivision of the MGB in nine animals and from the caudomedial subdivision in three animals.

All stimuli were presented to the right ear, left ear and binaurally at 85 dB SPL. Signals were delivered through hollow earbars in a stereotaxic device using ER-3 insert earphones. The 2000 Hz tone burst and the /da/ were 100 ms in duration. The tone burst had a 5 ms rise/fall (Blackman ramp). The /da/ was a five-formant synthetic speech syllable produced with a Klatt cascade-parallel formant synthesizer. The click was 100 μs in duration (rarefaction). All stimuli were presented at a rate of 1.7/s with 1000 repetitions per stimulus for each animal. The recording window was 200 ms post-stimulus with a 75 ms pre-stimulus baseline. Responses were low-pass filtered at 500 Hz and high-pass filtered at 0.05 Hz.

In order to be certain that the same physical stimulus was delivered to both ears and that hearing was the same between ears, the following procedures were employed. First, ABRs were recorded to click stimuli from the posterior midline of the scalp in all animals. In order to be included in the data set, it was necessary that each animal's responses be present down to 10 dB HL and symmetric between ears. Second, prior to any data collection, the signals were delivered through each transducer and calibrated using a B&K sound level meter with an insert earphone coupler. Halfway through the experimental series, the earphone transducers were switched so that half the animals received right ear stimulation with the right transducer and half the animals received right ear stimulation with the left transducer.

Responses were recorded simultaneously from the left and right MGB to 2000 Hz tone bursts, clicks, and synthesized syllables (/da/). Onset responses showed larger amplitudes for the left side compared with the right side in 10 of 12 animals (two-tailed binomial test, $P < 0.038$). The remaining two animals showed larger onset amplitudes for the right versus left. A measure of asymmetry was determined for each animal, regardless of side of dominance. Degree of asymmetry was computed by subtracting the right MGB onset amplitude from the left MGB onset amplitude and dividing by the sum of those two values [(L−R)/(L+R)]. Thus, completely symmetric responses would have a value of zero and asymmetric responses would be positive for left side dominance and negative for right side dominance. Fig. 1 shows that the degree of asymmetry varied across the animals, but all animals showed a large degree of

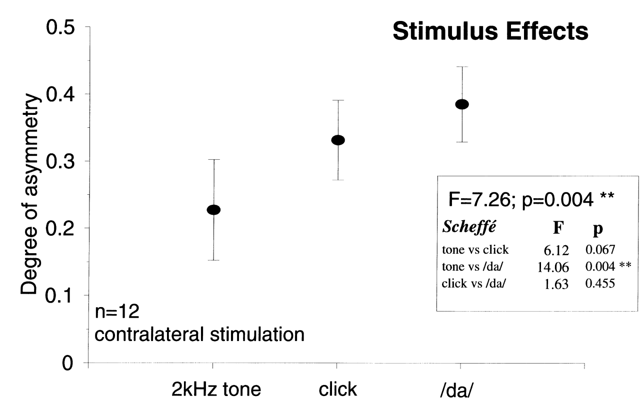

Fig. 2. Degree of asymmetry varied for different acoustic stimuli. Degree of asymmetry for each acoustic stimulus (2 kHz tone, click, and /da/) was determined by subtracting the non-dominant (or smaller) MGB onset amplitude from the dominant MGB onset amplitude and dividing by the sum of those two values [(d − nd)/(d + nd)]. This procedure allowed the inclusion of the two right-side dominant animals in the statistical analysis. A 1 × 3 repeated measures ANOVA revealed a significant stimulus effect ($F = 7.26$, $P = 0.004$). Post-hoc tests using paired Scheffé comparisons revealed that the 2 kHz tone was significantly different from the /da/ ($P < 0.01$). Although only the experimental condition using contralateral stimulation is shown, the pattern of results, where the responses to /da/ stimuli show a greater asymmetry than the responses to the 2 kHz tones and the clicks, is the same for the ipsilateral and binaural conditions.

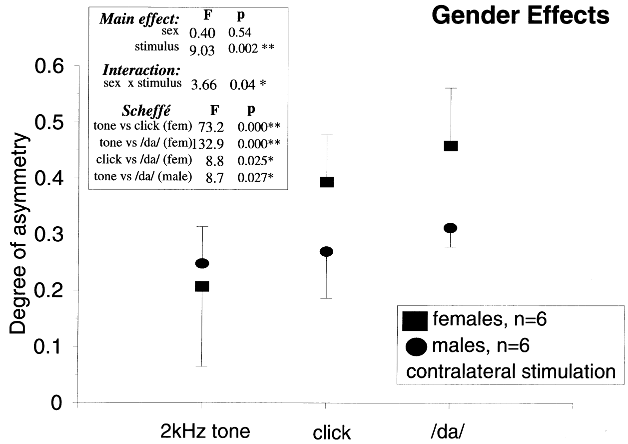

Fig. 3. The pattern of asymmetry across different acoustic stimuli was different for males and females. A 2×3 split-plot ANOVA (comparing sex×stimulus) revealed a significant effect for the stimuli ($F = 9.03$, $P = 0.002$) and a significant interaction ($P = 0.04$). Follow-up testing using Scheffé comparisons revealed that the 2 kHz tone was significantly different from the click and the /da/ ($P < 0.01$) and that the click was significantly different from the /da/ ($P < 0.05$) for the females. For the males, only the tone was significantly different from the /da/ ($P < 0.05$). Although only the experimental condition using contralateral stimulation is shown, the pattern of results, where females show a more asymmetric response to /da/ than the males, is the same for the ipsilateral and binaural conditions.

asymmetry in at least one of the stimulus presentations (contralateral, ipsilateral or binaural).

The degree of asymmetry or dominance was found to be stimulus dependent (Fig. 2). The responses to the 2000 Hz tone burst showed the least degree of asymmetry while the responses to /da/ showed the greatest degree of asymmetry. Responses to the click fell somewhere in between. However, while the onset amplitudes to the tone burst were significantly different from those elicited by the click and the /da/, the click and /da/ onset responses were not significantly different from each other. These findings indicate that the more complex the acoustic signal, the greater the asymmetry. In turn, those asymmetries may be evolutionary precursors to asymmetric language processing in humans.

Although both males and females showed hemispheric asymmetries, these asymmetries were significantly greater in female animals (Fig. 3). Males and females displayed approximately the same degree of asymmetry to the tone burst. However, females showed larger onset amplitude asymmetries than the males to both the click and /da/ stimuli.

To our knowledge, these findings are the first to demonstrate a lateralized dominance for the neurophysiologic encoding of the elemental acoustics of speech in the auditory thalamus in an anesthetized animal model. Consequently, hemispheric asymmetries to speech sounds must reflect, at least in part, pre-conscious differences in the encoding of the basic acoustic structure of complex auditory signals. The larger amplitude responses recorded in the dominant (mainly left) medial geniculate nucleus may be a result of a greater number of neuronal firings and/or better neural synchrony to the stimulus onset. This hemispheric asymmetry likely underlies perception of complex acoustic signals in normal listeners and may provide insight into the biological bases for symmetry abnormalities seen in children with learning problems [7,16].

The degree of asymmetry reflected in the neurophysiology, and possibly the behavioral perception, of an auditory signal is dependent on the acoustic structure of that signal. The relationship between the responses to the tone burst, click and speech signals indicates that there is a gradient in the degree of asymmetric lateralization across stimuli, with the tone burst eliciting the greatest similarity between left-right responses (i.e. showing the least asymmetry) and the speech syllable eliciting the greatest difference (i.e. showing the most asymmetry). It appears that these acoustically simple stimuli are processed differently from more complex signals like those inherent in speech. This pattern is consistent with known perceptual deficits observed in patients with cortical lesions who lose their ability to understand speech but retain their ability to discriminate simple stimuli [1,20].

Meaningful interpretation of the sex differences noted in this study are difficult in light of the conflicting findings published to date [5,26]. However, what we do know is that the incidence of learning and attentional problems is much higher in boys than girls [2,15]. In addition, the pattern of hemispheric asymmetry reflected in behavioral perception is disrupted in children with learning problems [6,16,19]. The possibility of a link between sex differences noted in the physiology and reported differences in learning/attentional problems is worth further examination.

In conclusion, an asymmetric neural code exists between the left and right sides of the auditory thalamus in guinea pigs. This asymmetry is greater for complex speech-like signals than for tones. Furthermore, the pattern of asymmetry is different for males and females. These findings provide evidence that the left side of the brain, traditionally associated with language processing, codes the acoustic structure of complex auditory signals differently from the right side of the brain. It can be hypothesized that impaired populations may have abnormalities in the basic neurophysiologic representation of acoustically complex signals, even at subcortical levels of the auditory pathway, which result in perceptual language deficits.

This work was supported by NIH-NIDCD-DC01510. Special thanks to Roxanne Edge for her histological expertise and Dawn Koch, Ph.D. for editorial comments.

[1] Auerbach, S.H., Allard, T., Naeser, M., Alexander, M.P. and Albert, M.L., Pure word deafness. Analysis of a case with bilateral lesions and a defect at the prephonemic level. Brain, 105 (1982) 271–300.

[2] Barkley, R.A., Attention-Deficit Hyperactivity Disorder: A Handbook for Diagnosis and Treatment, Guilford Press, New York, 1990.

[3] Cohen, H., Levy, J.J. and McShane, D., Hemispheric specialization for speech and non-verbal stimuli in Chinese and French Canadian subjects. Neuropsychologia, 27 (1989) 241–245.

[4] Cynx, J., Williams, H. and Nottebohm, F., Hemispheric differences in avian song discrimination. Proc. Natl. Acad. Sci. USA, 89 (1992) 1372–1375.

[5] Davidson, R.J., Schwartz, E., Pugash, E. and Bromfield, E., Sex differences in patterns of EEG asymmetry. Biol. Psychol., 4 (1976) 119–138.

[6] Dalby, J.T. and Gibson, D., Functional cerebral lateralization in subtypes of disabled readers. Brain Lang., 14 (1981) 34–48.

[7] Dawson, G., Finley, C., Phillips, S. and Lewy, A., A comparison of hemispheric asymmetries in speech-related brain potentials of autistic and dysphasic children. Brain Lang., 37 (1989) 26–41.

[8] Ehret, G., Left hemisphere advantage in the mouse brain for recognizing ultrasonic communication calls. Nature, 325 (1987) 249–251.

[9] Elliott, L.L. and Hammer, M., Longitudinal changes in auditory discrimination in normal children and children with language-learning problems. J. Speech. Hear. Disord., 53 (1988) 467–474.

[10] Elmo, T., Hemispheric asymmetry of auditory evoked potentials to comparisons within and across phonetic categories. Scand. J. Psychol., 28 (1987) 251–266.

[11] Fitch, R.H., Brown, C.P., O'Connor, K. and Tallal, P., Functional lateralization for auditory temporal processing in male and female rats. Behav. Neurosci., 107 (1993) 844–850.

[12] Gannon, P.J., Holloway, R.L., Broadfield, D.C. and Braun, A.R., Asymmetry of chimpanzee planum temporale: humanlike pattern of Wernicke's brain language area homolog. Science, 279 (1998) 220–222.

[13] Gazzaniga, M.S., Right hemisphere language following brain bisection. A 20-year perspective. Am. Psychol., 38 (1983) 525–537.

[14] Geschwind, N., Language and the brain. Sci. Am., 226 (1972) 76–83.

[15] Hallahan, D.P., Kauffman, J.M. and Lloyd, J.W., Introduction to Learning Disabilities, Allyn and Bacon, Boston, MA, 1996.

[16] Harel, S. and Nachson, I., Dichotic listening to temporal tonal stimuli by good and poor readers. Percept. Mot. Skills, 84 (1997) 467–473.

[17] Kraus, N., McGee, T.J., Carrell, T.D., Zecker, S.G., Nicol, T.G. and Koch, D.B., Auditory neurophysiologic responses and discrimination deficits in children with learning problems. Science, 273 (1996) 971–973.

[18] Merzenich, M.M., Jenkins, W.M., Johnston, P., Schreiner, C., Miller, S.L. and Tallal, P., Temporal processing deficits of language-learning impaired children ameliorated by training. Science, 271 (1996) 77–81.

[19] Obrzut, J.E., Hynd, G.W. and Zellner, R.D., Attentional deficit in learning-disabled children: evidence from visual half-field asymmetries. Brain Cogn., 2 (1983) 89–101.

[20] Phillips, D.P. and Farmer, M.E., Acquired word deafness, and the temporal grain of sound representation in the primary auditory cortex. Behav. Brain Res., 40 (1990) 85–94.

[21] Schwartz, J. and Tallal, P., Rate of acoustic change may underlie hemispheric specialization for speech perception. Science, 207 (1980) 1380–1381.

[22] Sharma, A., Kraus, N., Carrell, T. and Thompson, C., Neurophysiologic bases of pitch and place of articulation perception: a case study. J. Acoust. Soc. Am., 95 (1994) 3011.

[23] Studdert-Kennedy, M. and Shankweiler, D., Hemispheric specialization for speech perception. J. Acoust. Soc. Am., 48 (1970) 579–594.

[24] Tallal, P., Miller, S.L., Bedi, G., Byma, G., Wang, X., Nagarajan, S.S., Schreiner, C., Jenkins, W.M. and Merzenich, M.M., Language comprehension in language-learning impaired children improved with acoustically modified speech. Science, 271 (1996) 81–84.

[25] Williams, H., Crane, L.A., Hale, T.K., Esposito, M.A. and Nottebohm, F., Right-side dominance for song control in the zebra finch. J. Neurobiol., 23 (1992) 1006–1020.

[26] Wogan, M., Kaplan, C., Moore, S. and Epro, R., Lateralized differences associated with semantically varied auditory material. Int. J. Neurosci., 14 (1981) 163–167.

[27] Zatorre, R.J., Evans, A.C., Meyer, E. and Gjedde, A., Lateralization of phonetic and pitch discrimination in speech processing. Science, 256 (1992) 846–849.