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# Diffusion tensor imaging depicting damage to the arcuate fasciculus in patients with conduction aphasia: a study of the Wernicke–Geschwind model

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**Objectives:** In contrast with disorders of comprehension and spontaneous expression, conduction aphasia is characterized by poor repetition, which is a hallmark of the syndrome. There are many theories on the repetition impairment of conduction aphasia. The disconnection theory suggests that a damaged in the arcuate fasciculus, which connects Broca's and Wernicke's area, is the cause of conduction aphasia. In this study, we examined the disconnection theory.

**Methods:** We enrolled ten individuals with conduction aphasia and ten volunteers, and analysed their arcuate fasciculus using diffusion tensor imaging (DTI) and obtained fractional anisotropy (FA) values. Then, the results of the left hemisphere were compared with those of the right hemisphere, and the results of the conduction aphasia cases were compared with those of the volunteers.

**Results:** There were significant differences in the FA values between the left and right hemispheres of volunteers and conduction cases. In volunteers, there was an increase in fiber in the left hemisphere compared with the right hemisphere, whereas there was an increase in fiber in the right hemisphere compared with the left hemisphere in conduction aphasia patients. The results of diffusion tensor tractography suggested that the configuration of the arcuate fasciculus was different between conduction aphasia patients and volunteers, suggesting that there was damage to the arcuate fasciculus of conduction aphasia cases.

**Conclusions:** The damage seen in the arcuate fasciculus of conduction aphasia cases in this study supports the Wernicke–Geschwind disconnection theory. A disconnection between Broca's area and Wernicke's area is likely to be one mechanism of conduction aphasia repetition impairment.

**Keywords:** Conduction aphasia, diffusion tensor imaging, arcuate fasciculus, Wernicke–Geschwind model

## Introduction

Conduction aphasia is characterized by severely impaired repetition, fluent verbal output consisting of mostly literal paraphasic errors, and spelling errors; however, comprehension, reading and naming are well preserved. Patients typically produce many paraphasias when trying to repeat, and they may be able to reproduce short utterances, although they are unable to repeat polysyllabic words or syntactically complex utterances. Aphasics have difficulty repeating even high probability sentences, whereas the ability to repeat numbers is typically much better than the ability to repeat words.

There are many mechanisms of conduction aphasia, such as Wernicke–Geschwind's theory of

disconnection, Storch–Goldstein's theory of central aphasia, the defect pattern of auditory-speech shorten memory and the bidirectional pattern. The theory of brain disconnection (Wernicke–Geschwind model) suggests that conduction aphasia results from arcuate fasciculus lesions that disconnect receptive-language regions from expressive-language regions<sup>1</sup>. The arcuate fasciculus is a white matter tract that runs from Wernicke's area in the posterior superior temporal gyrus, arches around the Sylvian fissure and runs anteriorly from the inferior parietal lobe to the inferior frontal lobe of Broca's region<sup>2</sup>. Wernicke postulated that a lesion of the arcuate fasciculus would produce a deficit in repetition, or 'conduction aphasia.'

Anisotropic water diffusion in neural fibers, such as nerve or white matter in the spinal cord or brain, is the basis for the use of diffusion tensor imaging (DTI) to track fiber pathways. Water diffusion is

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sensitive to the underlying tissue microstructure, providing a unique method of assessing the orientation and integrity of these neural fibers, which may be useful in understanding a number of neurological disorders.

Diffusion tensor magnetic resonance imaging (DT-MRI) is a relatively new imaging technique based on measuring water diffusivity in brain tissue, and it provides excellent characterization of white matter<sup>3</sup>. The utility of DT-MRI can be extended using the directional information in the diffusion tensor to generate fiber tracts, allowing direct visualization of the anatomy of known white matter pathways with excellent correspondence to conventional dissection<sup>4,5</sup>. Based on DTI and the characteristics of conduction aphasics, we studied one of the proposed mechanisms of conduction aphasia to prove Wernicke–Geschwind’s theory of disconnection, and we attempted to verify the repetition impediment of conduction aphasia.

## Methods

Ten individuals with conduction aphasia were selected from the inpatients of the Department of Neurology, Beijing Tiantan Hospital, from February 2006 to October 2008. They were diagnosed with cerebral infarction by computed tomography or magnetic resonance imaging (MRI), and all ten patients were male, aged  $43.1 \pm 2.05$  years old. We also selected ten healthy volunteers, male, aged  $42.7 \pm 1.89$  years old, for the control group. All the subjects gave informed consent.

First, we assessed the handedness of all subjects using methods established by the Neurology Department of Peking University First Hospital. Then, a DTI examination was conducted in Tiantan hospital, and imaging data were acquired on Siemens Signal 3.0 Tesla LX MRI systems. We performed a virtual dissection of the left hemisphere arcuate fasciculus using approaches with three regions of interest (ROIs). Guided by color fiber orientation maps, we defined the ROIs. The fractional anisotropy (FA) volumes were re-sliced in axial, coronal and sagittal planes and displayed in conjunction with tractography, producing approximate neuroanatomical locations of the tract reconstructions (scanning parameters: slice=36, layer thickness=3.5, layer distance=0, FOV=230 × 230 mm, TR=6000 ms, TE=103 ms, fat sat=154 × 192, phase partial Fourier 6/8, different directors=12,  $b=0/1000$  s/mm<sup>2</sup>, bandwidth=1086, EPI factor=154).

We measured the FA and analysed the configuration of the arcuate fasciculus; then we compared the

results of the left hemisphere with those of the right hemisphere. Finally, we compared the results of conduction aphasia patients with those of volunteers.

## Results

### Evaluation of handedness

All subjects were right-handed. Case 4 had crossed aphasia, which is caused by a lesion located in the right hemisphere.

### DTI analysis of healthy volunteers and conduction aphasics

We measured the FA of the arcuate fasciculus and compared the values with those of the mirror side. Table 1 shows that the left-side FA values of volunteers were greater than those of the mirror side, suggesting there are more normally functioning fibers in the left arcuate fasciculus than in the right. On the other hand, the left-side FA values of conduction aphasics were smaller than those of the mirror side, indicating damage in the arcuate fasciculus of conduction aphasics.

### Analysis of the configuration of the arcuate fasciculus

There was no difference in the configuration of the arcuate fasciculus between the left and right hemispheres of volunteers, while the configuration of the arcuate fasciculus was significantly different between the left and right hemispheres of conduction aphasia patients.

### Healthy volunteer’s DTI analysis

The DTI of a right-handed, 32-year-old male with a bachelor’s degree showed that the FA values of the left arcuate fasciculus and the right mirror side were 0.441 and 0.4118, respectively, that is, there were more normally functioning fibers in the left arcuate fasciculus compared with that of the right side (Figure 1A), and the configuration of the arcuate fasciculus was not different between the left and right hemispheres (Figure 1B).

### Conduction aphasia case analysis

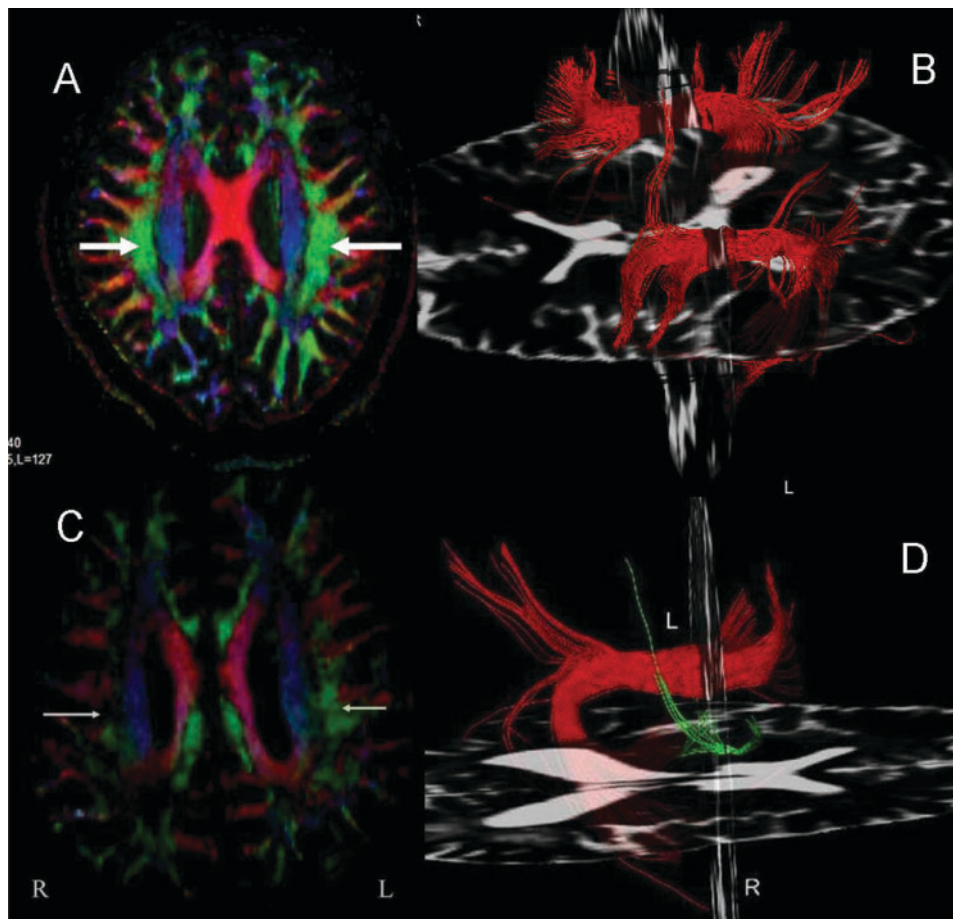
One patient in the study was a 50-year-old male, who was admitted to the hospital with ‘4 days slurred speech’ and ‘cerebral infarction’. He had coronary heart disease for the last 5 years and a long history of smoking and drinking alcohol. He was right-handed and was diagnosed with conduction aphasia using the Western aphasia battery test.

The arcuate fasciculus FA values of the right and left mirror side were 0.3123 and 0.358, respectively. Thus, the arcuate fasciculus of this conduction aphasic was damaged (Figure 1C), and the configuration of the arcuate fasciculus was badly damaged (Figure 1D).

**Table 1 Comparison of arcuate fasciculus FA values between left and right hemispheres**

Group	Left (mean ± SD)	Right (mean ± SD)	<i>p</i>
Volunteer group	0.7012 ± 0.0896	0.4776 ± 0.0531	<0.05
Conduction aphasia group	0.3488 ± 0.0795	0.4805 ± 0.0621	<0.05
<i>p</i>	<0.05	>0.05	

Table 1 shows that in volunteers, the FA values of the left arcuate fasciculus were greater than those of the mirror side, indicating that there were more normally functioning fibers in the left arcuate fasciculus compared with the mirror side. In conduction aphasics, the FA values of the left arcuate fasciculus were smaller than those of the right areas, and the left arcuate fasciculus was damaged.



**Figure 1** Arcuate fasciculus of one volunteer and one conduction aphasia patient. A and B are color-fiber orientation maps. Red represents left and right orientations, green represents forward and behind orientations and blue represents ascending and descending orientations. The arrowhead denotes the left and right arcuate fasciculus. From A, we saw that there were no significant differences in the FA values between the left and right hemispheres of volunteers, while there were statistically significant differences in conduction aphasia cases (B, the patient's lesion was located in the right hemisphere, called crossed aphasia); C shows that the configuration of the arcuate fasciculus was not different between the left and right hemispheres of volunteers, while the configuration of the arcuate fasciculus was significantly different between the left and right hemispheres of conduction aphasia patients (D); the right arcuate fasciculus was badly damaged

## Discussion

The post-stroke cerebral lesion is the basis for exploring the pathogenesis of conduction aphasia. Researchers suggest that there are two pathological anatomic origins of conduction aphasia: one is the left supramarginal gyrus and the arcuate fasciculus, and the other is the insular lobe connected with cortex and underlying white matter. One study<sup>6</sup> reported a multiple sclerosis patient with large white matter lesions subjacent to the left supramarginal gyrus and a symptom pattern consistent with the diagnosis of conduction aphasia. Another study<sup>7</sup> reported a case of conduction aphasia because of a small infarction in the left parietal lobe and concluded that lesions in the pathway connecting Broca's area and Wernicke's area can cause conduction aphasia. But Bartha and Benke<sup>8</sup> reported that most conduction aphasia was associated with damage to the arcuate fasciculus, and in our study, the arcuate fasciculus was involved in all of the conduction aphasia cases.

The theory of disconnection, first pointed out by Wernicke, is the principal explanation of conduction aphasia. Wernicke suggested that there was a storage location of speech stamps, found by Broca, in the posterior part of the inferior frontal gyrus of the left cerebral hemisphere. Wernicke also suggested that there were hearing speech stamps in the posterior part of the superior temporal gyrus, and the interruption of the connection between these two areas may induce conduction aphasia. Geschwind thought that there was a direct pathway connecting the two language areas, a connection of hearing memory stamps and kinetic phonation stamps. Moreover, there was an indirect pathway, a net complex of sensory stamps about substance conception, which contacted the listening comprehension region and the speech-formative region. They posited that the critical lesion in conduction aphasia is in the dominant hemisphere's arcuate fasciculus, which was thought to be responsible for the functional relationship between speech production (in the

frontal and anterior parietal lobes) and speech perception (in the temporal lobe). Although patients with conduction aphasia have been identified, it is still unclear whether their symptoms are because of white matter dysfunction, cortical dysfunction or a combination of both. One study<sup>9</sup> reported three conduction aphasia cases and pointed out that there are two routes for the speech production process. One is located between Broca's and Wernicke's areas; the other one is located between speech input and output, which adjusts the transition between speech understanding, semantics and phonetics

Clinical and physiological evidence from subjects with conduction aphasia usually supports the concept of disconnection. In these studies<sup>1,10–12</sup>, disruption of the arcuate fasciculus is obligate with variable involvement of adjacent regions of suprasylvian or subsylvian cortex. Circumscribed lesions of the arcuate fasciculus that spared overlying cortex have been offered as evidence of disconnection. Weisman *et al.*<sup>13</sup> reported an aphasia induced by a lesion of the thalamus, without cortical effect caused by stroke and with no change in cortical blood flow. The study suggested that the connection interruption between temporal and frontal lobe might result from a lesion of the spinothalamic tract induced by stroke.

Diffusion tensor imaging, which assesses myelination *in vivo*, is based on the characteristic of myelin sheaths and cell membranes of white matter tracts that restrict the movement of water molecules. As a result, water molecules move faster parallel to the major axis of nerve fibers rather than perpendicular to them. This characteristic, which is referred to as anisotropic diffusion and is measured by FA, is determined by several factors including the thickness of the myelin sheath and of the axons as well as the organization of the fibers and properties of the intracellular and extracellular spaces around the axon. FA ranges from 0 to 1, where 0 represents maximal isotropic diffusion and 1 represents maximal anisotropic diffusion, that is, movement parallel to the major axis of a white matter tract. Areas with high FA such as the corpus callosum appear bright, whereas tissue with low FA appears darker on FA maps derived from DTI<sup>14</sup>. One study<sup>15</sup> suggested that DTI technology can replicate the actual arcuate fasciculus and fiber monitor connections among language centers. Recently Yamada *et al.*<sup>16</sup> reported an MR tractography depicting damage to the left hemisphere arcuate fasciculus in association with presumed conduction aphasia in a patient who had sustained left hemisphere stroke.

In our study, the FA values of the left arcuate fasciculus of volunteers were greater than those of the right side. Thus, there was a tendency for there to be more functional fibers in the left arcuate fasciculus compared with the mirror side, which is in agreement with a study by Nucifora *et al.*<sup>17</sup>. We

also demonstrated a significant left-dominant asymmetry, which may provide the foundation for future functional and structural studies. On the other hand, there were fewer functional fibers in the left arcuate fasciculus of conduction aphasics compared with the mirror side. Thus, the number of normal, connected fibers between Broca's area and Wernicke's area was decreased in conduction aphasics, supporting Wernicke–Geschwind's disconnection theory.

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