

# Anatomical evidence of an indirect pathway for word repetition

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## Study objective and summary result

This study aimed to describe the anatomic correlates of word repetition deficits in patients with primary progressive aphasia (PPA), and it obtained evidence that such deficits result from damage to a pathway that indirectly connects Wernicke and Broca regions.

## What is known and what this paper adds

Word repetition deficits have traditionally been attributed to disruption of the arcuate fasciculus, a direct connection between Wernicke and Broca regions. This investigation provides evidence that disruption of an indirect connection relaying in the parietal lobe can also produce such deficits.

## Participants and setting

The investigators recruited 30 patients with PPA (53% female; mean age,  $64.27 \pm 8.51$  years) and 22 age- and sex-matched healthy controls (45% female; mean age,  $62.68 \pm 6.14$  years) through the Northwestern University Feinberg School of Medicine (Chicago, IL).

## Design, size, and duration

The participants completed a word repetition subtest within the revised Western Aphasia Battery. They also underwent MRI with diffusion-weighted imaging (DWI) and T1-weighted magnetization-prepared rapid gradient-echo (MPRAGE) imaging sequences. The DWI scans were used for tractography analyses of direct and indirect pathways between Wernicke and Broca regions. The MPRAGE images were used for cortical morphometry assessments of 8 perisylvian language areas.

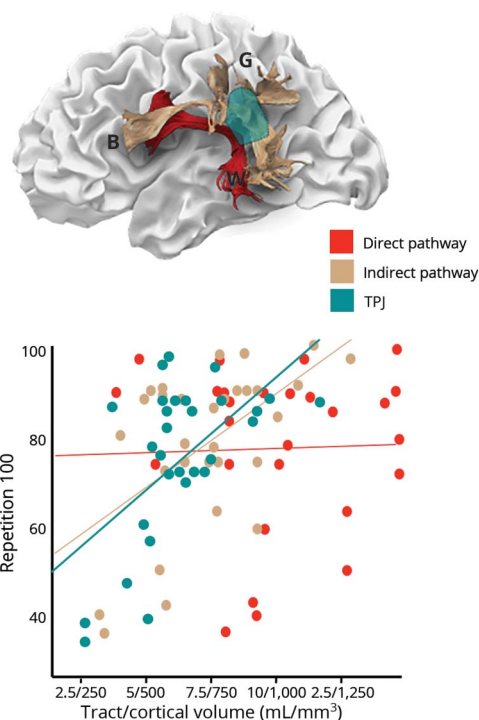
## Primary outcome measures

The primary outcomes were the volumes of direct and indirect connections between Wernicke and Broca regions.

## Main results and the role of chance

Relative to the healthy controls, the patients with PPA had word repetition deficits ( $p < 0.001$ ), which were more severe in patients with greater volume reduction of the indirect pathway ( $r = 0.55$ ,  $p < 0.005$ ) and the temporo-parietal junction ( $r = 0.6$ ,  $p < 0.001$ ).

**Figure** Correlations between repetition scores, white matter volumes of the direct ( $r = 0.020$ ,  $p = 0.917$ ) and indirect pathways ( $r = 0.545$ ,  $p < 0.005$ ) and the cortical volume of the temporo-parietal junction (TPJ) ( $r = 0.598$ ,  $p < 0.001$ )



## Bias, confounding, and other reasons for caution

The present study's sample size was too small to permit subgroup analyses for different variants of PPA.

## Generalizability to other populations

The present study's single-center nature may limit the generalizability of the results.

## Study funding/potential competing interests

This study was funded by the Wellcome Trust and the NIH. The authors report no competing interests. Go to [Neurology.org/N](http://Neurology.org/N) for full disclosures.

A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The corresponding author(s) of the full-length article and the journal editors edited and approved the final version.

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