

# Neural consequences of symptomatic convergence insufficiency: A small sample study

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## Abstract

**Introduction:** Convergence insufficiency (CI) is an oculomotor abnormality characterised by exophoria and inadequate convergence when focusing on nearby objects. CI has been shown to cause symptoms when reading. However, the downstream consequences on brain structure have yet to be investigated. Here, we investigated the neural consequences of symptomatic CI, focusing on the left arcuate fasciculus, a bundle of white matter fibres which supports reading ability and has been associated with reading deficits.

**Methods:** We compared the arcuate fasciculus microstructure of participants with symptomatic CI versus normal binocular vision (NBV). Six CI participants and seven NBV controls were included in the analysis. All participants were scanned with 3T magnetic resonance imaging (MRI), and anatomical and diffusion-weighted images were acquired. Diffusion-weighted images were processed with TRACULA to identify the arcuate fasciculus in each participant and compute volume and radial diffusivity (RD).

**Results:** Compared with NBV controls, those with symptomatic CI had significantly smaller arcuate fasciculi bilaterally (left:  $t = -3.21$ ,  $p = 0.008$ ; right:  $t = -3.29$ ,  $p = 0.007$ ), and lower RD in the left ( $t = -2.66$ ,  $p = 0.02$ ), but not the right ( $t = -0.81$ ,  $p = 0.44$ , false discovery rate (FDR)-corrected  $p > 0.05$ ) arcuate fasciculus. Those with higher levels of reading symptoms had smaller arcuate fasciculi ( $r = -0.74$ ,  $p = 0.004$ ) with lower RD ( $r = -0.61$ ,  $p = 0.03$ ).

**Conclusions:** These findings suggest that symptomatic CI may lead to microstructural changes in the arcuate fasciculus. Since it is highly unlikely that abnormalities in the arcuate fasciculus are the cause of the neuromuscular deficits in the eyes, we argue that these changes may be a potential neuroplastic consequence of disruptions in sustained reading.

## KEYWORDS

convergence insufficiency, diffusion tensor imaging, reading, symptoms

## INTRODUCTION

Convergence insufficiency (CI) is a common binocular vision anomaly with a prevalence between 2.25% and 17.0%.<sup>1–5</sup> CI is characterised by exophoria when focusing on nearby objects,

a receded near point of convergence and insufficient positive fusional vergence.<sup>6</sup> Because the eyes do not converge adequately, CI often results in symptoms during reading and other near work, such as frequent loss of place while reading, blurred vision, double vision, eyestrain, headache, difficulty

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concentrating, reading slowly and trouble remembering what was read.<sup>7–11</sup> Additionally, an association between convergence demand and performance on neuropsychological cognitive tests has been reported.<sup>12,13</sup>

Furthermore, children with CI are frequently reported to have trouble completing schoolwork, avoid reading and appear inattentive or distracted when reading compared with children with normal binocular vision (NBV).<sup>14–16</sup> Moreover, following successful therapy for CI, their parents report a decrease in these behaviours - specifically, reduced difficulties in completing schoolwork, avoidance of reading and inattentiveness or distractibility during reading activities, etc. and less concern about their child's school performance.<sup>16</sup> While some studies have reported a relationship between reading ability and CI,<sup>17</sup> exophoria at near<sup>18–20</sup> and/or vergence ability,<sup>19,21,22</sup> results have been mixed.<sup>23–26</sup>

Brain activation patterns observed during convergence tasks in individuals with CI suggest the engagement of 'top-down processing', a cognitive mechanism where the brain's higher level functions guide lower level processes, often requiring conscious attention or effort.<sup>27</sup> However, the potential effects on the brain's structure and function resulting from CI, particularly in areas involved in reading, have not been fully explored. Diffusion-weighted imaging, a magnetic resonance imaging (MRI) modality that measures water diffusion, allows analysis of white matter microstructure. Because diffusion of water across axons (as opposed to along axons) is restricted by cytoskeletal elements, cell membranes and the fatty structure of myelin, diffusion-weighted imaging analysis allows identification of major white matter tracts, measurement of their volume and assessment of properties such as radial diffusivity, a measure of myelination.<sup>28,29</sup> Using this MRI modality, researchers have probed the relationship between white matter microstructure, for example in the arcuate fasciculus, with various aspects of cognition such as reading.<sup>30–32</sup> The arcuate fasciculus is a bundle of white matter fibres which supports reading ability by connecting language regions in the frontal cortex with visual regions in the inferior temporal cortex, most typically in the left hemisphere, which is corroborated by the left hemispheric dominance of cortical language and reading areas.<sup>33</sup> Thus, the purpose of this paper was to compare white matter volume and organisation in the left arcuate fasciculus, as measured by diffusion-weighted imaging, between participants with symptomatic CI and NBV (controls). Furthermore, we sought to uncover a more detailed understanding of the downstream effects of CI in the brain, which may lead to the development of more precise therapeutic interventions for children and young adults, in order to prevent or reduce such downstream neural consequences.

## METHODS

### Participants

The current study followed the tenets of the Declaration of Helsinki and was approved by the Ohio State University Biomedical Institutional Review Board. Participants

### Key points

- Compared to those with normal binocular vision, subjects with symptomatic convergence insufficiency had significantly smaller arcuate fasciculus volumes, a bundle of white matter fibres which supports reading ability and has been associated with reading deficits.
- Compared to those with normal binocular vision, subjects with symptomatic convergence insufficiency had significantly lower radial diffusivity of the arcuate fasciculus in the left hemisphere (which shows dominance in language-related brain areas), but not in the right hemisphere.
- Smaller left arcuate fasciculus volume and radial diffusivity were significantly correlated with higher reading-related symptoms.

provided written informed consent and completed comprehensive screenings for safety prior to any MRI scans. Participants completed an eligibility eye examination (performed by a trained optometrist), a symptom survey and a series of anatomical MRI scans.

Participants, aged 18–30 years, had no history of brain injury or neurological disease, no systemic diseases known to affect accommodation, vergence or ocular motility and were not taking medication known to affect accommodation, vergence or ocular motility. Participants had no amblyopia, strabismus, vertical phoria  $>1\Delta$ , manifest or latent nystagmus, history of refractive surgery or vergence therapy. All participants were required to have undergone a cycloplegic refraction within the past 3 months and be wearing any required correction for significant refractive error (without a near addition or base-in prism). All participants had best-corrected visual acuity of 6/7.5 or better in each eye at distance and near. Additionally, those with CI met the criteria for symptomatic CI as defined by the convergence insufficiency treatment trial (CITT).<sup>34,35</sup> Specifically, inclusion criteria for those with CI included exophoria at least  $4\Delta$  greater at near than at distance, a receded near point of convergence ( $\geq 6$  cm break), insufficient positive fusional convergence (i.e., failing Sheard's criterion<sup>36</sup> or  $<15\Delta$  base-out blur or break), Convergence Insufficiency Symptom Survey (CISS) score  $\geq 21$  and accommodative amplitude  $\geq 5$  D. Inclusion criteria for NBV participants included distance and near heterophoria between  $2\Delta$  esophoria and  $6\Delta$  exophoria with  $\leq 6\Delta$  difference between distance and near, adequate near point of convergence ( $<6$  cm break), negative fusional vergence at near  $>7\Delta$  break/ $5\Delta$  recovery, positive fusional vergence at near  $>10\Delta$  break/ $7\Delta$  recovery, age-normal accommodative amplitude (greater than  $15 - 0.25 \times$  age as measured by push-up testing in the right eye) and random dot stereoacuity of 500" or better.<sup>8,9</sup>

## Eligibility eye examination

Eligibility testing included evaluation of symptoms, prism alternate cover testing at distance and near, near point of convergence and positive fusional vergence range following the CITT protocol<sup>35</sup> and briefly summarised here. Participants were queried about symptoms using the CISS before and after vision testing with the mean value used as the symptom score.<sup>9</sup> The CISS is a commonly used inventory comprising 15 questions that rate symptom level on a scale ranging from 0 (best) to 60 (worst). Participants fixated a 6/9 vertical column of letters (Gulden Ophthalmics, [guldenophthalmics.com](http://guldenophthalmics.com)) for near testing. A near point rule (Gulden Ophthalmics) was used for testing the near point of convergence and amplitude of accommodation. Near point of convergence (break; mean of 3 measures to the nearest half centimetre) was determined as the point when the participant reported the target split into two or the examiner observed an eye turn. Positive fusional vergence ranges (blur, break and recovery) were measured with a prism bar (mean of three measures). Accommodative amplitude was determined using the push-up method in the right eye as the point when the participant reported first sustained blur.

## MRI scan parameters

All MRI scans were performed in the same Siemens 3.0-T Prisma MRI (MR software version 12, with a 20-channel array head coil; Siemens Medical Systems, [siemens-healthineers.com](http://siemens-healthineers.com)). After a reference sequence, high-resolution anatomical images were acquired using MPRAGE (Magnetisation-Prepared Rapid Gradient-Echo) T<sub>1</sub>-weighted MRI (TR/TE=1950/4.44 ms, flip angle=12°, matrix size=72×72, voxel resolution=1.0 mm<sup>3</sup>); a technique that provides detailed images of the brain's structure. A diffusion-weighted image (DWI) series (voxel resolution=2.0 mm<sup>3</sup>, 64 gradient directions, *b*-value=900 s/mm<sup>2</sup>) was also acquired for each participant. During these sequences, participants remained still and relaxed with their eyes closed.

## Image preprocessing

We used Freesurfer version 7.2.0 ([surfer.nmr.mgh.harvard.edu/](http://surfer.nmr.mgh.harvard.edu/))<sup>37–39</sup> to perform image pre-processing. Surface models were reconstructed from each participant's MPRAGE T<sub>1</sub>-weighted images using the Freesurfer recon-all pipeline. This includes a series of preprocessing steps, including motion correction, skull stripping, intensity normalisation, bias field correction, spatial normalisation, tissue segmentation and surface reconstruction. Quality control was performed by visual inspection of the intermediate and final output files to ensure accurate segmentation and surface reconstruction. Any errors or inaccuracies were manually

corrected using the tools provided in Freesurfer. The resulting cortical and subcortical surfaces were used for subsequent analyses.

## TRActs constrained by underlying anatomy (TRACULA)

The T<sub>1</sub>-weighted MRI images were first preprocessed using the standard Freesurfer pipeline as described in the previous section. Then, the diffusion MRI data were registered to the MPRAGE T<sub>1</sub>-weighted MRI using a linear transformation. Next, TRACULA used a multi-atlas segmentation approach to automatically segment the major white matter tracts.<sup>40</sup> This involved co-registering a set of atlases to the participant's T<sub>1</sub>-weighted images and using the warped atlas segmentations to create a probabilistic atlas of waypoints, start and end points for each tract in each participant's native diffusion space. TRACULA then applied a method (FSL's *probtrackx*) to estimate the pathways of brain connections based on each participant's own DWI data, allowing for the reconstruction of the major white matter tracts based on the fibre orientation probability of each voxel (i.e., probabilistic tractography). The mapping of the tract was initiated from the grey matter–white matter interface and propagated along a specific direction based on the diffusion tensor model, until it reached the next grey matter region. The output of TRACULA included a set of 42 major white matter tracts, each represented as a set of streamlines in 3D space. In this study, we configured TRACULA to reconstruct bilateral arcuate fasciculi, which connect several language-related brain regions. Finally, TRACULA computed average tensor parameters over each pathway.

## Statistical analysis

A two-sample *t*-test was used to examine the intergroup differences (CI and NBV) across tracts of interest. Our hypothesis was that the population with vision problems when reading up close (CI participants) may have disrupted reading experience, which might affect the development of their brain's arcuate fasciculus compared to those without vision problems (NBV participants). Pearson correlation was used to assess the relationship between the TRACULA results of the left arcuate fasciculus and reading-related symptoms, as well as clinical measures. We predicted that the volume of the left arcuate fasciculus was associated with reading-related symptoms, consistent with the results observed in non-ocular reading-related disorders.<sup>41</sup> Additionally, we predicted that diffusivity was also associated with reading-related symptoms, potentially leading to weakened white matter connectivity in the left hemisphere regions supporting reading symptoms reported by CI participants.<sup>33,41</sup>

## RESULTS

Eight participants had CI and seven were NBV controls. Of the CI group, two were excluded; one for incomplete MRI scanning and another for poor scan quality due to excessive movement, leaving six participants with CI and seven with NBV in the final analysis. The average age of the participants was 26.7 years (25.5 years for those with CI; 27.7 years for those with NBV). Characteristics of participants with CI and NBV are shown in Table 1 and CISS scores in Figure 1a.

Because the symptoms associated with CI disrupt sustained reading, we hypothesised that NBV participants should have better organised and larger arcuate fasciculi, due to greater and/or better quality lifetime experience with reading. We focused specifically on the left and right arcuate fasciculus (Figure 1b), as this has been found to play a critical role in reading ability by connecting language regions in the frontal cortex with visual regions in the inferior temporal cortex. To test this hypothesis, we compared the volume and radial diffusivity (RD, a measure of myelination<sup>28,29</sup>) of the left and right arcuate fasciculus between participants with CI and NBV (Figure 2a). The arcuate fasciculus volumes were significantly larger in NBV participants than those with CI in both the left (NBV:  $2394.4 \pm 466.8$ ; CI:  $1698.3 \pm 154.6$ ;  $t(12) = -3.21$ ,  $p = 0.008$ ) and right hemispheres (NBV:  $2063.4 \pm 351.5$ ; CI:  $1519.8 \pm 132.8$ ;  $t(12) = -3.29$ ,  $p = 0.007$ ), with the false discovery rate (FDR)-corrected  $p$ -value remaining significant at  $p < 0.05$ . Additionally, we observed that NBV participants had significantly higher radial diffusivity than CI participants in the left hemisphere (NBV:  $56.86 \pm 2.66 \times 10^{-5}$ ; CI:  $52.64 \pm 2.57 \times 10^{-5}$ ;  $t(12) = -2.66$ ,  $p = 0.02$ , FDR-corrected  $p < 0.05$ , Figure 2b). However, there was no significant difference in radial diffusivity of the arcuate fasciculus between the two groups in the right hemisphere (NBV:  $56.90 \pm 1.99 \times 10^{-5}$ ; CI:  $54.63 \pm 6.52 \times 10^{-5}$ ;  $t(12) = -0.81$ ,  $p = 0.44$ , FDR-corrected  $p > 0.05$ ).

Given the significant intergroup differences found above, in both the left arcuate fasciculus volume and radial diffusivity, and considering the left hemispheric dominance of language-related brain areas, the subsequent investigation focused on the relationship between volume/radial diffusivity and reading-related symptoms in the left

arcuate fasciculus. Notably, we found a significant negative correlation between left arcuate fasciculus volume and reading-related symptoms as measured by the CISS ( $r = -0.74$ ,  $p < 0.004$ , Figure 3a). Additionally, a significant negative correlation was observed between left arcuate fasciculus radial diffusivity and reading-related symptoms as measured by the CISS ( $r = -0.61$ ,  $p < 0.03$ , Figure 3b). In other words, across the entire data set, participants with higher levels of reading-related symptoms had smaller left arcuate fasciculi with lower radial diffusivity. Figure 3c displays an example participant from each group, demonstrating the lower left arcuate fasciculus volume and radial diffusivity in participants with symptomatic CI versus NBV.

The relationships between clinical measures and arcuate fasciculus microstructure are listed in Table 2. We found that a higher (better) positive fusional vergence blur point was significantly associated with a larger volume of the left arcuate fasciculus ( $r = 0.80$ ,  $p < 0.001$ ). Similarly, a closer (better) near point of convergence was also significantly correlated with an increased volume of the left arcuate fasciculus ( $r = -0.67$ ,  $p = 0.01$ ). Furthermore, the radial diffusivity in the left arcuate fasciculus showed a significant association with the near point of convergence ( $r = -0.68$ ,  $p = 0.01$ ).

## DISCUSSION

This investigation revealed a relationship between symptomatic CI, reading-related symptoms as measured by the CISS and arcuate fasciculus microstructure. Specifically, we found that individuals with symptomatic CI, who had significantly higher levels of reading-related symptoms due to their impaired convergence, exhibited significantly smaller arcuate fasciculi that also had lower RD, a measure of fibre myelination.<sup>28,42</sup> We further observed that this was not a simple group effect, but rather highlighted individual differences in reading-related symptoms and arcuate fasciculus integrity. Across the entire sample, individuals with fewer reading-related symptoms had larger arcuate fasciculi and higher RD. Furthermore, clinical measures showed a significant correlation with arcuate microstructure. These findings highlight the impact that vision disorders such as CI can have downstream on the brain. Interestingly, the RD difference between the two groups was only significant in the left hemisphere, which is consistent with the left hemisphere lateralisation of language. These results are consistent with reports relating arcuate microstructure (arcuate volume and RD) with reading.<sup>29,32,33,41,43-46</sup>

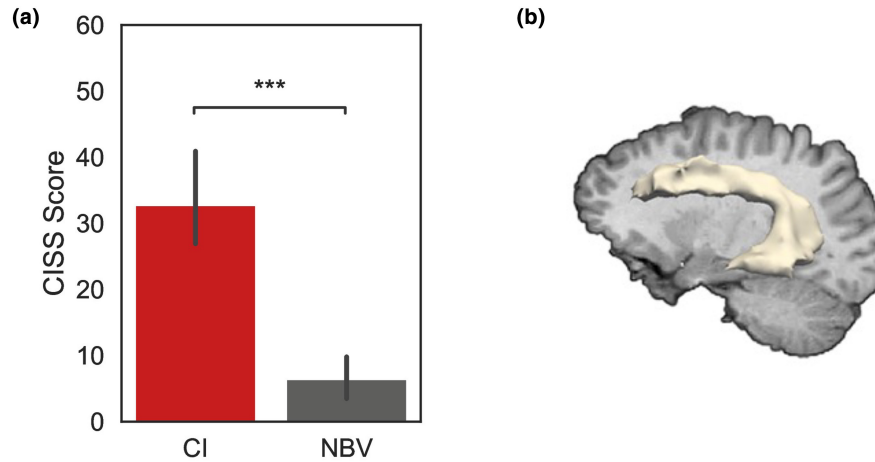
To our knowledge, there are no prior reports investigating the arcuate microstructure in individuals with CI. Prior studies on the association between reading and convergence and/or CI have shown mixed results. Cohen reported that the level of reading-related symptoms correlated with convergence amplitude and was associated with longer completion time on a test of reading comprehension, but was not associated with the reading comprehension test

**TABLE 1** Mean (standard deviation) symptom level, heterophoria and convergence measures (positive fusional vergence and near point of convergence) in participants with convergence insufficiency (CI) and normal binocular vision (NBV).

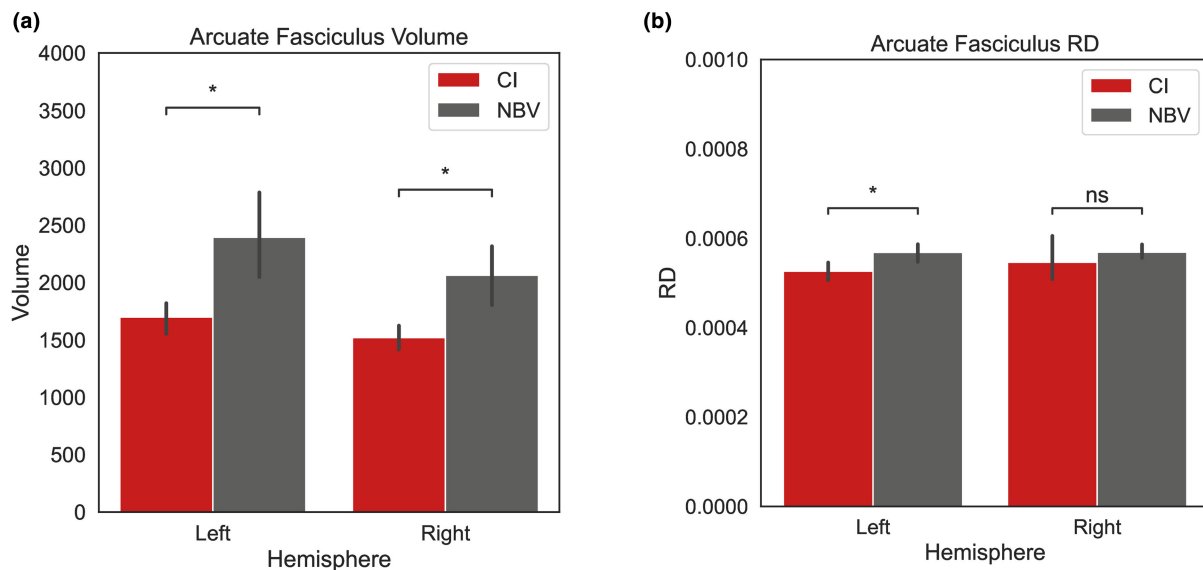
	CI	NBV
Symptom level	32.8 (9.2)	6.4 (4.3)
Exophoria ( $\Delta$ )	9.3 (4.3)	2.9 (1.6)
Positive fusional vergence blur ( $\Delta$ ) <sup>a</sup>	13.7 (1.5)	23.0 (10.3)
Positive fusional vergence break ( $\Delta$ )	18.7 (6.4)	40.0 (9.1)
Positive fusional vergence/exophoria	1.8 (0.9)	9.0 (3.2)
Near point of convergence (cm)	8.0 (1.6)	3.2 (1.0)

<sup>a</sup>Break value if no blur was reported.





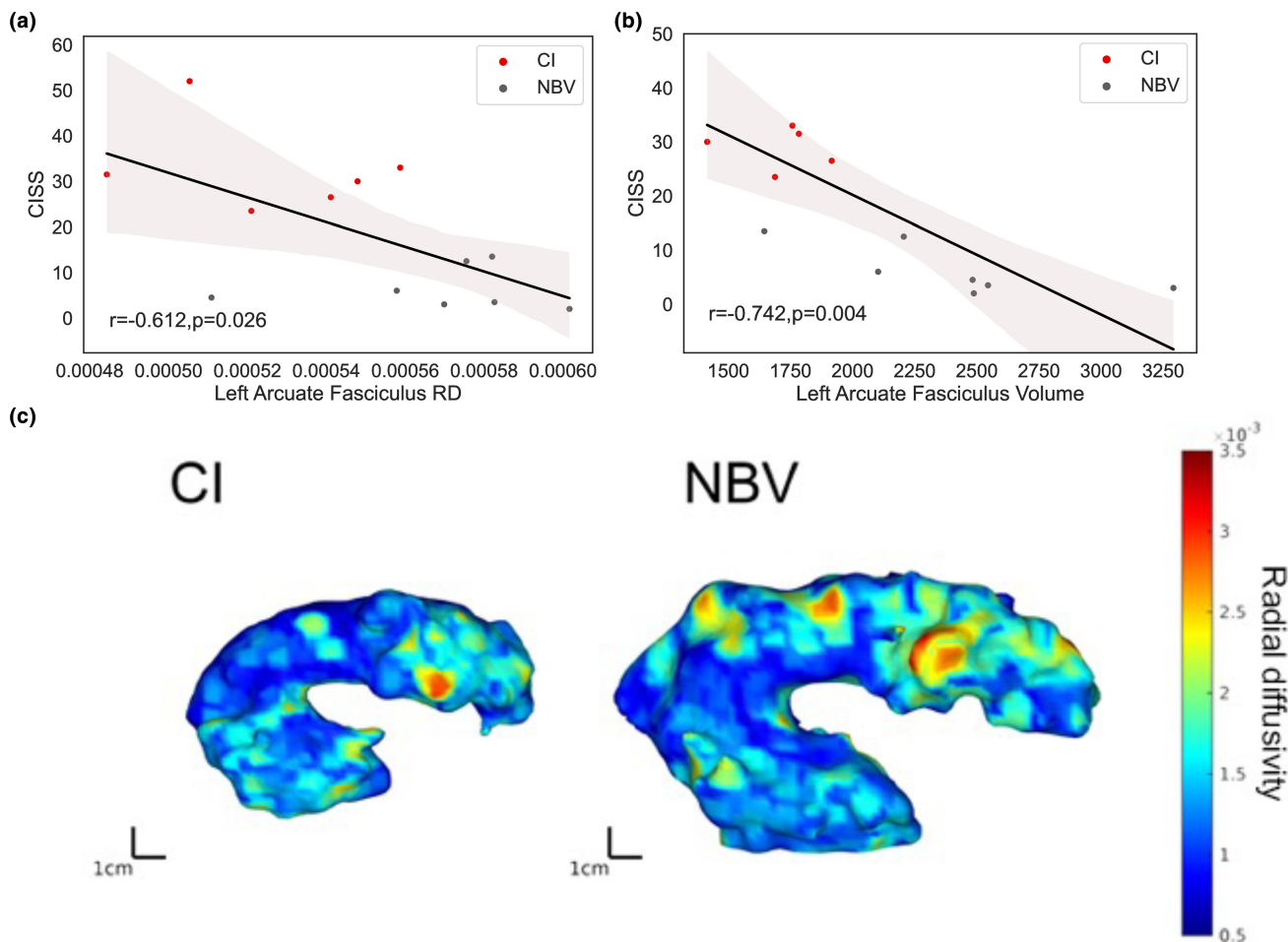
**FIGURE 1** (a) Mean symptom level (Convergence Insufficiency Symptom Survey [CISS] scores) for participants with convergence insufficiency (CI) and normal binocular vision (NBV) (CI:  $33.3 \pm 10.2$ , NBV:  $6.3 \pm 4.8$ ). (b) An example arcuate fasciculus from a healthy young adult. This fibre bundle encompasses critical circuitry for reading by connecting frontal language regions with inferior temporal visual regions. \*\*\* $p \leq 0.001$ .



**FIGURE 2** Arcuate fasciculus (a) volume (mm<sup>3</sup>) and (b) radial diffusivity (RD) (mm/s) for each hemisphere and group. Participants with convergence insufficiency (CI) had significantly smaller arcuate fasciculi in both hemispheres; further, the left arcuate fasciculi of CI patients had lower RD than normal binocular vision (NBV) controls. ns, corrected  $p > 0.05$ . \*Corrected  $p \leq 0.05$ .

score.<sup>25</sup> Two studies reported improvements in reading-related symptoms and standardised reading test performance after treatment for symptomatic CI but did not include a control group.<sup>17,20</sup> A randomised clinical trial of the effect of 16 weeks of vergence accommodative therapy on reading in 9- to 14-year-old children with symptomatic CI showed no significant differences between children assigned to real versus placebo therapy on standardised reading tests.<sup>26</sup> However, it is possible that a more intensive treatment combined with educational intervention could be needed to improve standardised reading performance significantly. For example, Keller and Just reported changes in the white matter microstructure after approximately 100h of remedial instruction in 8- to 10-year-old children.<sup>29</sup>

In contrast to conditions such as dyslexia, where alterations in the arcuate fasciculus may potentially be a cause or a consequence of the disorder (due to greatly reduced reading time),<sup>31</sup> the relationship with CI presents a different scenario. It is extremely unlikely that the microstructural abnormalities in the arcuate fasciculus are the *cause* of the ocular symptoms or the reduced convergence ability associated with CI, as the arcuate fasciculus is not directly involved in the control of vergence. Instead, these microstructural changes may be a secondary effect of CI, likely resulting from a reduction in reading activities. Visual and somatic disturbances characteristic of CI (e.g., frequent loss of place, blurred vision, double vision, eyestrain and headache) likely lead to disruptions in sustained reading and/or reduced engagement with reading. Over time, this



**FIGURE 3** (a) Greater left arcuate fasciculus volume was significantly associated with fewer reading-related symptoms. (b) Greater left arcuate fasciculus radial diffusivity was also significantly associated with fewer reading-related symptoms. In both a and b, black lines represent the best fits and the red shadow represents the 95% confidence intervals. (c) Example of the left arcuate for a convergence insufficiency (CI) participant and a normal binocular vision (NBV) participant. CI participants had smaller arcuate fasciculi with lower radial diffusivity (represented by the heatmap). CISS, Convergence Insufficiency Symptom Survey.

**TABLE 2** Correlation between clinical measures and left arcuate fasciculus across convergence insufficiency (CI) and normal binocular vision (NBV) participants.

	Left arcuate fasciculus volume	Left arcuate fasciculus RD
Positive fusional vergence blur ( $\Delta$ )	$r = 0.80$ $p < 0.001^*$	$r = 0.33$ $p = 0.26$
Positive fusional vergence/exophoria	$r = 0.58$ $p = 0.04$	$r = 0.36$ $p = 0.23$
Near point of convergence (cm)	$r = -0.67$ $p = 0.01^*$	$r = -0.68$ $p = 0.01^*$

Abbreviation: RD, radial diffusivity.

\*Corrected  $p \leq 0.05$ .

diminished reading experience could curtail the neuroplastic changes in the brain that would otherwise occur with typical reading exposure. Specifically, we suggest that the observed differences in the arcuate fasciculi might be

a consequence of experience-driven neuroplasticity; for individuals with NBV, years of exposure to reading may lead to neuroplastic changes in the arcuate fasciculi (i.e., larger volume and higher RD), while individuals with CI may experience poorer quality reading and not undergo the same degree of change. This hypothesis is consistent with the understanding that the brain adapts based on experiences and behaviours,<sup>47</sup> and underscores the influence of visual disorders like CI on brain structure and function, especially in areas involved in reading. Moreover, this reduction in reading could be part of a broader pattern of avoidance of near-work activities, which includes but is not limited to reading. This overall reduction in near-work exposure could potentially lead to the observed changes and represents an area ripe for future investigation to understand fully the downstream effects of CI on neuroplasticity. There is evidence that the associated symptoms and convergence measures improve to normal levels after CI therapy.<sup>15,16,34,48,49</sup> Furthermore, changes in functional activity in the brain have been reported after CI therapy.<sup>27,50,51</sup>

Investigating how therapeutic interventions may drive broader neuroplastic changes offers a promising avenue for a more comprehensive understanding of CI's impact and the potential for recovery.

While the present study has provided insights into the structural interplay between the arcuate fasciculus, CI, clinical measures of convergence and reading-related symptoms, a limitation is the small sample size; larger studies are needed to investigate this question further. In addition, standardised testing of reading was not performed. Moving forward, it is essential to delve deeper into the multiple facets that shape reading abilities. This skill extends beyond structural relationships to include functional elements such as the decoding of phonological information and the comprehension of semantic content.<sup>52</sup> Future investigations should take a comprehensive approach to the various aspects of reading, assessing multiple reading skills including phonological awareness, reading speed, comprehension and word knowledge, to name a few, and relate them to microstructural and functional differences observed in the brains of individuals with CI. Furthermore, it will be important to include surveys of current and lifelong reading time. Accounting for the amount of reading time experienced, whether in development or in adulthood, will allow for stronger inferences into the nature of these findings. Future studies should also investigate whether the differences in arcuate fasciculus microstructure occur in children with symptomatic CI and should look into the development of treatment approaches to counterbalance these changes in the arcuate fasciculus.<sup>53</sup> Furthermore, CI therapies may benefit from individual brain data, opening the door to adaptive medicine in this specific domain. Such investigations would not only broaden our understanding of how the brain's plasticity responds to interventions but also potentially provide practical solutions for improving the reading abilities of those affected by CI.

This investigation revealed significantly smaller arcuate fasciculi (a brain region that supports reading ability) with lower radial diffusivity (a measure of fibre myelination) in adults with symptomatic CI as compared to adults with NBV. Smaller arcuate fasciculi with lower radial diffusivity were associated with higher levels of reading-related symptoms as measured by the CISS. These findings highlight the impact that symptomatic CI can have downstream on the brain and may suggest the need for early treatment of symptomatic CI in children.

## AUTHOR CONTRIBUTIONS

**Yuxuan Zeng:** Conceptualization (equal); formal analysis (equal); methodology (equal); visualization (equal); writing – original draft (equal); writing – review and editing (equal). **Tamara S. Oechslin:** Data curation (equal); writing – review and editing (equal). **Douglas E. Widmer:** Data curation (equal); writing – review and editing (equal). **Marjean T. Kulp:** Conceptualization (equal); data curation (equal); supervision (equal); writing – original draft (equal);

writing – review and editing (equal). **Nicklaus Fogt:** Conceptualization (equal); data curation (equal); writing – review and editing (equal). **Andrew Toole:** Data curation (equal); writing – review and editing (equal). **Steven Manning:** Data curation (equal); writing – review and editing (equal). **David E. Osher:** Conceptualization (equal); formal analysis (equal); methodology (equal); supervision (equal); visualization (equal); writing – original draft (equal); writing – review and editing (equal).

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## CONFLICT OF INTEREST STATEMENT

None.

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