Received: 8 February 2023 | Revised: 31 March 2023 | Accepted: 18 April 2023

DOI: 10.1002/hbm.26325

WILEY

RESEARCH ARTICLE

Deficits in naming pictures of objects are associated with glioma infiltration of the inferior longitudinal fasciculus: A study with diffusion MRI tractography, volumetric MRI, and neuropsychology

Costanza Papagno[1,2] | Riccardo Pascuzzo[3] | Camilla Ferrante[4] | Alessandra Casarotti[5] | Marco Riva[5,6] | Luigi Antelmi[3] | Antonio Gennari[3] | Giulia Mattavelli[7,8] | Alberto Bizzi[3]

[1]CIMeC (Center for Mind/Brain Sciences), University of Trento, Rovereto, Italy

[2]CISmed (Center for Medical Sciences), University of Trento, Trento, Italy

[3]Neuroradiology Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy

[4]Department of Psychology, University of Milano-Bicocca, Milan, Italy

[5]Department of Neurosurgery, IRCCS Humanitas Research Hospital, Milan, Italy

[6]Department of Biomedical Sciences, Humanitas University, Milan, Italy

[7]ICoN Center, Scuola Universitaria Superiore IUSS, Pavia, Italy

[8]Istituti Clinici Scientifici Maugeri IRCCS, Cognitive Neuroscience Laboratory of Pavia Institute, Pavia, Italy

Correspondence
Costanza Papagno, CIMeC (Center for Mind/Brain Sciences), University of Trento, Via Matteo del Ben 5/b, 38068 Rovereto, Italy.
Email: costanza.papagno@unitn.it

Funding information
Ministero della Salute

Abstract

It has been suggested that the inferior longitudinal fasciculus (ILF) may play an important role in several aspects of language processing such as visual object recognition, visual memory, lexical retrieval, reading, and specifically, in naming visual stimuli. In particular, the ILF appears to convey visual information from the occipital lobe to the anterior temporal lobe (ATL). However, direct evidence proving the essential role of the ILF in language and semantics remains limited and controversial. The first aim of this study was to prove that patients with a brain glioma damaging the left ILF would be selectively impaired in picture naming of objects; the second aim was to prove that patients with glioma infiltrating the ATL would not be impaired due to functional reorganization of the lexical retrieval network elicited by the tumor. We evaluated 48 right-handed patients with neuropsychological testing and magnetic resonance imaging (MRI) before and after surgery for resection of a glioma infiltrating aspects of the left temporal, occipital, and/or parietal lobes; diffusion tensor imaging (DTI) was acquired preoperatively in all patients. Damage to the ILF, inferior frontal occipital fasciculus (IFOF), uncinate fasciculus (UF), arcuate fasciculus (AF), and associated cortical regions was assessed by means of preoperative tractography and pre-/postoperative MRI volumetry. The association of fascicles damage with patients' performance in picture naming and three additional cognitive tasks, namely, verbal fluency (two verbal non-visual tasks) and the Trail Making Test (a visual attentional task), was evaluated. Nine patients were impaired in the naming test before surgery. ILF damage was demonstrated with tractography in six (67%) of these patients. The odds of having an ILF damage was 6.35 (95% CI: 1.27–34.92) times higher among patients with naming deficit than among those without it. The ILF was the only fascicle to be significantly associated with naming deficit when all the fascicles were considered

together, achieving an adjusted odds ratio of 15.73 (95% CI: 2.30–178.16, $p = .010$). Tumor infiltration of temporal and occipital cortices did not contribute to increase the odd of having a naming deficit. ILF damage was found to be selectively associated with picture naming deficit and not with lexical retrieval assessed by means of verbal fluency. Early after surgery, 29 patients were impaired in naming objects. The association of naming deficit with percentage of ILF resection (assessed by 3D-MRI) was confirmed (beta $= -56.78 \pm 20.34$, $p = .008$) through a robust multiple linear regression model; no significant association was found with damage of IFOF, UF or AF. Crucially, postoperative neuropsychological evaluation showed that naming scores of patients with tumor infiltration of the anterior temporal cortex were not significantly associated with the percentage of ILF damage (rho $= .180$, $p > .999$), while such association was significant in patients without ATL infiltration (rho $= -.556$, $p = .004$). The ILF is selectively involved in picture naming of objects; however, the naming deficits are less severe in patients with glioma infiltration of the ATL probably due to release of an alternative route that may involve the posterior segment of the AF. The left ILF, connecting the extrastriatal visual cortex to the anterior region of the temporal lobe, is crucial for lexical retrieval on visual stimulus, such as in picture naming. However, when the ATL is also damaged, an alternative route is released and the performance improves.

KEYWORDS
anterior temporal lobe, glioma, inferior longitudinal fasciculus, optic aphasia, picture naming

1 | INTRODUCTION

The inferior longitudinal fasciculus (ILF) is connecting the occipital extrastriatal visual cortex with the anterior aspect of the temporal lobe (ATL) (i.e., pole, anterior middle, and inferior temporal gyri), the hippocampus and parahippocampal gyrus (Catani & Thiebaut de Schotten, 2008) and it is one of three associative white matter tracts that constitute the ventral language pathway. The other two tracts are the uncinate fasciculus (UF) connecting the temporal pole with the orbitofrontal cortex and the inferior fronto-occipital fasciculus (IFOF) connecting the occipital cortex with the orbitofrontal cortex through the temporal stem (Hickok & Poeppel, 2004). More precisely, the occipital projections of the ILF originate in the ventral surface of the posterior lingual and fusiform gyri, and medial regions of the precuneus. The ILF runs ventrally along the main axis of the temporal lobe, laterally to the IFOF, adjacent to the subcortical white matter of the middle and inferior temporal cortices.

The hypothetical function of the ILF is to transfer visual information (Catani, 2003) from posterior temporal and occipital lateral cortices to the anterior temporal semantic storage areas and to allow for visual object recognition (Catani & Mesulam, 2008), visual emotion and face processing (Philippi et al., 2009), reading words (Epelbaum et al., 2008), and visual memory (Ross, 2008). Given the semantic role of the ventrolateral anterior temporal areas (Mion et al., 2010), the ILF might be an essential structure for fast interactions between the ATL and information processes rooted in the occipital and parietal regions, and, consequently, for naming objects. If this hypothesis were true, all tasks requiring lexical retrieval on visual stimuli would be impaired after ILF disconnection, while spontaneous speech or verbal fluency would be preserved. Similarly, visual tasks, such as the Trail Making Test, not requiring a verbal answer, would remain intact.

There are several sources of evidence concerning the role of the ILF, as, for example, studies with diffusion tensor imaging (DTI) tractography in patients with semantic dementia (Agosta et al., 2010; Catani & Mesulam, 2008; Mummery et al., 2000) and studies exploring language recovery after stroke (Blom-Smink et al., 2020; McKinnon et al., 2017) (see Herbet et al., 2018, for a review). Additional anatomical evidence comes from postmortem studies (Déjérine & Déjérine-Klumpke, 1895; Tusa & Ungerleider, 1985; Martino et al. 2011) and further DTI Tractography studies (Martino et al., 2010, 2013; Sarubbo et al., 2013; Zigiotto et al., 2022).

In contrast, in an intraoperative monitoring (IOM) study about 12 brain glioma patients undergoing partial resection of the ILF, Mandonnet et al. (2007) showed that all four patients who had suffered severe naming impairment immediately after surgery, completely recovered after rapid, intensive, and specific speech therapy. Moreover, these same patients had not produced naming errors during IOM with direct electrical stimulation of the ILF. Therefore, at that time, the authors concluded that the ILF was not indispensable for language since its function could be compensated during IOM and after resection. More recently, however, the same group (Herbet et al., 2019) in an IOM study on 11 patients showed that stimulation

of the anterior-to-middle part of the left ILF systematically induced anomia during a picture naming task, but only when the cortex of the ATL was spared by the tumor. This result not only supported the role of the ILF in lexical retrieval but also showed that the ILF was not essential when the damage involved the ATL, likely due to the release of an alternative route. Similarly, in an IOM study, Papagno et al. (2011) found that in a group of low-grade glioma patients, alternative domain-specific cortical networks for living and non-living semantic categories, reflecting the reorganization of cortical regions driven by the subcortical fibers of those networks.

Given all the above considerations, we could argue that in the case of the ILF, the lexical deficit depends on a specific disconnection between extrastriatal visual areas and lexical representations stored in the temporal lobe. In other words, ILF damage might produce a clinical picture like optic aphasia, a rare and debated syndrome in which patients are unable to name visually presented objects but they can mimic their use or name them on tactile or verbal presentation. In glioma patients with ILF damage, we should expect, therefore, a deficit in naming pictures or real objects, but not in verbal fluency, naming by description or spontaneous speech.

With the aims to clarify the role of the ILF in naming objects, we evaluated the extent of presurgical anatomic damage of the four main fascicles involved in language (ILF, UF, IFOF, and AF) with preoperative DTI tractography and the extent of surgical resection of the four fascicles with postoperative magnetic resonance imaging (MRI) volumetry in 48 patients with a glioma infiltrating the left temporal lobe. Then, we evaluated the association of presurgical and postoperative performances on four neuropsychological tasks with the extent of damage of each fascicle. In particular, the first aim of this study was to investigate whether glioma patients with left ILF damage would be selectively impaired in picture naming of objects, but not on verbal fluency, in which lexical retrieval is not required from visual stimuli, nor in a task requiring visual detection of stimuli (Trail Making Test; TMT) that does not imply lexical retrieval. In fact, it is well known that for example in optic aphasia single letters (as those presented in TMT B) are recognized and a letter-by-letter reading can occur, while patients cannot retrieve the name of visually presented objects (Kwon & Lee, 2006; Marsh & Hillis, 2005). The second aim was to investigate whether patients with tumor infiltration of the ATL do not show naming deficits nor deterioration of naming performance after ILF resection at surgery. According to Herbet et al. (2019)'s results, no effect of ILF resection on lexical retrieval of visual stimuli would be expected when the ATL is infiltrated by gliomas.

2 | MATERIALS AND METHODS

2.1 | Participants

We retrospectively investigated a continuous series of 48 right-handed patients (31 males and 17 females) undergoing the first resection of a glioma infiltrating the left temporal lobe and the adjacent perisylvian regions. They were part of a larger cohort of patients recruited at Humanitas Research Hospital, Rozzano (Milan, Italy) between April 2012 and November 2015, as previously reported (Figini et al., 2018); patients with the following criteria were excluded from the present study: non-native Italian speakers, left-handed patients, and patients with right hemisphere or recurrent tumors (not at first surgery).

The mean age of the 48 patients was 46.9 years (standard deviation, *SD*, 15.4; *range* 22–74) and the mean educational level 12.5 (*SD* 3.8; *range* 5–23) (see Tables 1 and 2). Handedness was evaluated by means of the Edinburgh Handedness Inventory (Oldfield, 1971). Fourteen subjects were diagnosed with IDH-mutant 1p/19q-codeleted oligodendroglioma, 11 with IDH-mutant astrocytoma, and 23 with IDH-wildtype glioblastoma according to the World Health Organization (WHO) central nervous system tumor classification of 2021.

Written informed consent was obtained from all participants. The study was conducted in accordance with the Declaration of Helsinki, with the approval of the local ethics committee (IRB-1299).

2.2 | Neuropsychological assessment

All 48 patients were submitted to a neuropsychological evaluation at three time points: (i) presurgical (within a week before surgery); (ii) early postoperative (in the 2 weeks after surgery); (iii) later postoperative (3 months after surgery). Here, we report only the pre- and early postsurgery evaluations. The following tests were administered to the patients: language, memory, apraxia, and executive functions as described by Papagno et al. (2012).

Specifically, we used a 48-stimuli naming test including 24 from living (6 animals, 6 birds, 6 fruits, and 6 vegetables) and 24 from non-living (6 furniture, 6 kitchen items, 6 tools, and 6 clothing pieces) categories, controlled for several variables (visual complexity, visual familiarity, name agreement, frequency, and age of acquisition). One point was assigned for each correct response. This task is part of a standardized battery for the assessment of semantic memory disorders (Catricalà et al., 2013). The cut-off score for this test is 41.99, as assessed on 106 healthy participants (see Capitani & Laiacona, 1997, for statistical procedure).

Patients also performed, as part of the entire battery, verbal fluency on phonemic, and semantic cue and the Trail Making Task A and B. Unfortunately, only a limited number of patients ($n = 10$) also performed a naming by description task.

2.3 | MR imaging and DTI acquisition

Brain MRI including DTI was acquired at 3.0 Tesla (Siemens Verio, Erlangen Germany), reducing head movements with foam pillows and laces. The conventional MRI protocol for morphological characterization of lesions included axial T2-weighted TSE sequence (TR/TE 3000/ 85 ms; field of view [FOV], 230 mm; 22 slices; section thickness, 5/1-mm gap; matrix, 512 × 512; SENSE factor, 1.5); axial 3D-FLAIR sequence (TR/TE 10000/110 ms; FOV, 230 mm;

TABLE 1 Demographical and clinical data of the 48 patients with left glioma.

			Molecular marker status			WHO tumor classification			
ID	Sex	Age	IDH mutation	1p/19q codeletion	Hystopathology grade	2016	2021	ILF status	Tumor location (left hemisphere)
1	M	42	Mut	Cod	II	IDH-mut 1p/19q-cod oligodendroglioma	IDH-mut 1p/19q-cod oligodendroglioma	Normal	hippocampus, lingula
2	M	66	Mut	Cod	II	IDH-mut 1p/19q-cod oligodendroglioma	IDH-mut 1p/19q-cod oligodendroglioma	Normal	insula, T-stem, T pole
3	M	44	Mut	Cod	II	IDH-mut 1p/19q-cod oligodendroglioma	IDH-mut 1p/19q-cod oligodendroglioma	Interrupted	T-Insula
4	F	29	Mut	Cod	II	IDH-mut 1p/19q-cod oligodendroglioma	IDH-mut 1p/19q-cod oligodendroglioma	Normal	genu CC, Fr
5	F	58	Mut	Cod	II	IDH-mut 1p/19q-cod oligodendroglioma	IDH-mut 1p/19q-cod oligodendroglioma	Normal	hippocampus
6	M	36	Mut	Cod	II	IDH-mut 1p/19q-cod oligodendroglioma	IDH-mut 1p/19q-cod oligodendroglioma	Infiltrated	insula, STG, MTG
7	F	37	Mut	Cod	II	IDH-mut 1p/19q-cod oligodendroglioma	IDH-mut 1p/19q-cod oligodendroglioma	Interrupted	T pole
8	F	23	Mut	Cod	II	IDH-mut 1p/19q-cod oligodendroglioma	IDH-mut 1p/19q-cod oligodendroglioma	Interrupted	hippocampus, O
9	M	54	Mut	Cod	II	IDH-mut 1p/19q-cod oligodendroglioma	IDH-mut 1p/19q-cod oligodendroglioma	Interrupted	insula, T
10	F	42	Mut	Cod	II	IDH-mut 1p/19q-cod oligodendroglioma	IDH-mut 1p/19q-cod oligodendroglioma	Normal	anterior SFG
11	M	42	Mut	Cod	II	IDH-mut 1p/19q-cod oligodendroglioma	IDH-mut 1p/19q-cod oligodendroglioma	Infiltrated	Fr-T-Insular
12	M	36	Mut	Cod	III	IDH-mut 1p/19q-cod anaplastic oligodendroglioma	IDH-mut 1p/19q-cod oligodendroglioma	Interrupted	insula, STG, SMG
13	F	30	Mut	Cod	III	IDH-mut 1p/19q-cod anaplastic oligodendroglioma	IDH-mut 1p/19q-cod oligodendroglioma	Dislocated	insula, T-stem
14	F	40	NA	NA	II	Oligodendroglioma, NOS[a]	Oligodendroglioma, NOS	Normal	insula
15	F	36	Mut	Uncod	II	IDH-mut diffuse astrocytoma	IDH-mut astrocytoma	Interrupted	T
16	M	31	Mut	Uncod	II	IDH-mut diffuse astrocytoma	IDH-mut astrocytoma	Normal	paracentral lobule
17	F	42	Mut	Uncod	II	IDH-mut diffuse astrocytoma	IDH-mut astrocytoma	Infiltrated	insula, STG
18	M	30	Mut	Uncod	II	IDH-mut diffuse astrocytoma	IDH-mut astrocytoma	Normal	anterior OFC
19	M	40	Mut	Uncod	II	IDH-mut diffuse astrocytoma	IDH-mut astrocytoma	Normal	insula, T anterior
20	M	52	Mut	Uncod	II	IDH-mut diffuse astrocytoma	IDH-mut astrocytoma	Normal	Fr-T-insular
21	M	24	Mut	Uncod	II	IDH-mut diffuse astrocytoma	IDH-mut astrocytoma	Normal	insula, STG
22	F	57	Mut	Uncod	II	IDH-mut diffuse astrocytoma	IDH-mut astrocytoma	Normal	OFC, insula, CC
23	F	25	Mut	Uncod	II	IDH-mut diffuse astrocytoma	IDH-mut astrocytoma	Normal	Angular gyrus, supramarginal gyrus
24	F	25	Mut	Uncod	III	IDH-mut diffuse astrocytoma	IDH-mut astrocytoma	Normal	VPCG (BA6)
25	F	72	Mut	Uncod	IV	IDH-mut GBM	IDH-mut astrocytoma	Dislocated	Fr
26	M	70	Wt	Uncod	II	IDH-wt diffuse astrocytoma	IDH-wt molGBM	Normal	T pole
27	M	29	Wt	Uncod	II	IDH-wt diffuse astrocytoma	IDH-wt molGBM	Normal	hippocampus, insula, CC
28	M	39	Wt	Uncod	III	IDH-wt anaplastic astrocytoma	IDH-wt molGBM	Interrupted	IFOF, ILF, hippocampus, thalamus
29	M	46	Wt	Uncod	III	IDH-wt anaplastic astrocytoma	IDH-wt molGBM	Dislocated	hippocampus, lingula, thalamus
30	F	47	Wt	Uncod	III	IDH-wt anaplastic astrocytoma	IDH-wt molGBM	Normal	hippocampus, insula, thalamus, T
31	M	51	Wt	Uncod	III	IDH-wt anaplastic astrocytoma	IDH-wt molGBM	Dislocated	fusiform gyrus, ITG
32	M	66	Wt	NA	IV	IDH-wt GBM	IDH-wt histGBM	Normal	Posterior STG

TABLE 1 (Continued)

ID	Sex	Age	Molecular marker status: IDH mutation	Molecular marker status: 1p/19q codeletion	Hystopathology grade	WHO tumor classification: 2016	WHO tumor classification: 2021	ILF status	Tumor location (left hemisphere)
33	M	73	Wt	NA	IV	IDH-wt GBM	IDH-wt histGBM	Dislocated	lingula, hippocamous, splenium
34	M	66	Wt	NA	IV	IDH-wt GBM	IDH-wt histGBM	Normal	insula, IFG (BA44, BA6)
35	M	40	Wt	NA	IV	IDH-wt GBM	IDH-wt histGBM	Normal	T pole
36	M	74	Wt	NA	IV	IDH-wt GBM	IDH-wt histGBM	Normal	hippocampus, T pole, splenium
37	F	22	Wt	NA	IV	IDH-wt GBM	IDH-wt histGBM	Interrupted	STG
38	M	68	Wt	NA	IV	IDH-wt GBM	IDH-wt histGBM	Interrupted	T-O WM
39	M	57	Wt	NA	IV	IDH-wt GBM	IDH-wt histGBM	Dislocated	hippocampus, IFOF, AF
40	M	46	Wt	NA	IV	IDH-wt GBM	IDH-wt histGBM	Dislocated	parahippocampus, STG
41	M	44	Wt	NA	IV	IDH-wt GBM	IDH-wt histGBM	Normal	Fr pole, prefrontal
42	F	51	Wt	NA	IV	IDH-wt GBM	IDH-wt histGBM	Normal	insula
43	M	53	Wt	NA	IV	IDH-wt GBM	IDH-wt histGBM	Normal	STG, STS
44	M	73	Wt	NA	IV	IDH-wt GBM	IDH-wt histGBM	Interrupted	IFG, ITG
45	M	40	Wt	NA	IV	IDH-wt GBM	IDH-wt histGBM	Dislocated	fusiform gyrus
46	M	74	Wt	NA	IV	IDH-wt GBM	IDH-wt histGBM	Interrupted	anterior T
47	M	47	Wt	NA	IV	IDH-wt GBM	IDH-wt histGBM	Normal	T pole, insula
48	F	61	Wt	NA	IV	IDH-wt GBM	IDH-wt histGBM	Infiltrated	deep WM, splenium

Abbreviations: AF, arcuate fasciculus; CC, corpus callosum; Cod, codeleted; F, female; Fr, frontal; GBM, glioblastoma; histGBM, histological diagnosis of glioblastoma; IFG, inferior frontal gyrus; IFOF, inferior frontal occipital fasciculus; ILF, inferior longitudinal fasciculus; ITG, inferior temporal gyrus; M, male; molGBM, molecular diagnosis of glioblastoma; MTG, middle temporal gyrus; Mut, mutant; NA, not available; NOS, not otherwise specified; O, occipital; OFC, orbitofrontal cortex; SFG, superior frontal gyrus; STG, superior temporal gyrus; STS, superior temporal sulcus; T, temporal; Uncod, uncodeleted; VPCG, ventral precentral gyrus; WM, white matter; Wt, wildtype.

[a]Histological examination confirmed the diagnosis of oligodendroglioma; however, molecular analyses of IDH-mutation and 1p/19q-codeletion status were not available.

TABLE 2 Neuropsychological tests of the 48 patients with left glioma.

ID	Picture naming score n. v. > 41.48	Verbal fluency		TMT – A n.v. < 93	TMT – B n.v. < 282	TMT B-A n.v. < 187
		Semantic (n.v. ≥ 25)	Phonemic (n.v. ≥ 17)			
1	46.59	34.00	27.00	26.00	57.00	31.00
2	43.41	42.00	29.00	29.00	95.00	66.00
3	**39.38**	36.00	29.00	30.00	119.00	89.00
4	45.97	38.00	24.00	37.00	142.00	105.00
5	47.21	29.00	28.00	24.00	67.00	43.00
6	48	47.00	23.00	23.00	79.00	56.00
7	46.18	43.00	28.00	27.00	82.00	55.00
8	**36.77**	25.00	**15.00**	62.00	234.00	172.00
9	46.79	49.00	33.00	25.00	28.00	3.00
10	46.38	37.00	40.00	24.00	89.00	65.00
11	46.38	67.00	45.00	25.00	81.00	56.00
12	**38.18**	25.00	19.00	44.00	179.00	135.00
13	45.97	36.00	21.00	60.00	183.00	123.00
14	48	47.00	43.00	36.00	123.00	87.00
15	46.18	27.00	26.00	61.00	189.00	128.00
16	48	62.00	41.00	37.00	124.00	87.00
17	46.38	44.00	38.00	24.00	74.00	50.00
18	45.97	38.00	22.00	35.00	104.00	69.00
19	46.38	40.00	29.00	41.00	102.00	61.00
20	**40.79**	33.00	26.00	31.00	96.00	65.00
21	44.77	40.00	39.00	21.00	89.00	68.00
22	48	34.00	**11.00**	36.00	142.00	106.00
23	48	37.00	20.00	71.00	169.00	98.00
24	44.77	40.00	**14.00**	39.00	137.00	98.00
25	45.62	51.00	62.00	26.00	40.00	14.00
26	46.62	34.00	21.00	45.00	65.00	20.00
27	43.97	35.00	30.00	37.00	127.00	90.00
28	46.38	34.00	23.00	28.00	97.00	69.00
29	42.59	**24.00**	27.00	52.00	188.00	136.00
30	48	**19.00**	20.00	53.00	163.00	110.00
31	**8.79**	**7.00**	**7.00**	29.00	113.00	84.00
32	44.41	42.00	26.00	15.00	38.00	23.00
33	46.82	33.00	29.00	61.00	152.00	91.00
34	48	50.00	**16.00**	16.00	26.00	10.00
35	48	53.00	25.00	30.00	125.00	95.00
36	**40.82**	**23.00**	27.00	21.00	91.00	70.00
37	43.77	**22.00**	32.00	**113.00**	**315.00**	**202.00**
38	**22.62**	**19.00**	**15.00**	30.00	164.00	134.00
39	46	30.00	20.00	37.00	142.00	105.00
40	48	43.00	**13.00**	45.00	162.00	117.00
41	48	52.00	19.00	29.00	96.00	67.00
42	46.79	49.00	45.00	12.00	23.00	11.00
43	43	**24.00**	26.00	84.00	230.00	146.00
44	**24.82**	**22.00**	**10.00**	37.00	68.00	31.00

TABLE 2 (Continued)

ID	Picture naming score n. v. > 41.48	Verbal fluency		TMT – A n.v. < 93	TMT – B n.v. < 282	TMT B-A n.v. < 187
		Semantic (n.v. ≥ 25)	Phonemic (n.v. ≥ 17)			
45	48	33.00	45.00	45.00	115.00	70.00
46	47.82	55.00	34.00	45.00	61.00	16.00
47	48	53.00	44.00	22.00	70.00	48.00
48	**40.21**	25.00	**10.00**	NA	NA	NA

Note: Pathological scores are depicted in bold.
Abbreviations: NA, not available; n.v., normal value; TMT, Trail Making Test.

120 slices; section thickness, 1.5/0-mm gap; matrix, 224 × 256; SENSE factor 2); and postcontrast T1-weighted inversion recovery sequence (TR/TE 2000/10 ms; FOV, 230 mm; 22 slices; section thickness, 5/1-mm gap; matrix, 400 × 512; SENSE factor, 1.5). The following DTI parameters were used: TE = 96 ms, TR = 15 s, eight $b = 0$, and 60 diffusion volumes (b values: 2000 s/mm^2) with 40 diffusion gradient directions; 64 axial sections with *Field of View* of 256 × 256 mm^2 and isotropic resolution of 2.0 × 2.0 × 2.0 mm^3 were acquired. The total acquisition time of the DTI sequence was about 20 min.

Preprocessing with eddy current and movement distortion corrections were applied by means of ExploreDTI software. The diffusion tensor was calculated with nonlinear RESTORE algorithm (*Robust Estimation of Tensors by Outlier Rejection*) in ExploreDTI. White matter tracts were reconstructed using Trackvis (http://www.trackvis.org). The following thresholds for the reconstruction of the streamlines were applied: tracking angle <45° and FA >0.10. The following fasciculi were reconstructed using a deterministic approach with two regions of interest (ROI) (Catani & Thiebaut de Schotten, 2008): ILF, IFOF, UF, and three segments of the arcuate fasciculus (AF). Delineation of ROIs was performed in all patients by the same neuroradiologist (AG, 3 years of experience) within 1 week interval time; the position of all ROIs was confirmed by a neuroradiologist (AB, 18 years of experience); both were blinded with respect to all patients' clinical data. Three ROIs were manually delineated to track the three ventral fascicles: a first ROI was delineated in the occipital lobe white matter on coronal slice positioned at the level of the splenium of the corpus callosum; a second ROI for tracking the ILF was placed in the white matter of the anterior aspect of the left temporal lobe; a second ROI for tracking the IFOF was delineated in the temporal stem and in the anterior aspect of the extreme capsule. Tracking of the UF was achieved connecting the ROI in the temporal stem with that in the left ATL white matter.

The three segments of the AF were reconstructed separately according to Catani et al. (2005). To track the long (direct) segment that connects Wernicke with Broca areas, two ROIs were delineated in the subcortical white matter adjacent to *pars triangularis*, *pars opercularis* of the inferior frontal gyrus and Broadman Area 6 (Broca area) and adjacent to the posterior third of the middle and superior temporal gyrus (Wernicke area). A third ROI was delineated in the subcortical white matter of the inferior parietal lobule (Geschwind's territory) and connected with Broca and Wernicke areas to track the anterior and posterior indirect segments of the AF, respectively.

A qualitative assessment of the integrity of the six white matter tracts was performed independently by two neuroradiologists (AB and AG, 18 and 3 years of experience in white matter tractography, respectively) blind to neuropsychological test results and intraoperative findings. The tracts were classified as normal, dislocated, infiltrated, and interrupted; it was noted when a tract was coursing through edematous areas. Normal and dislocated tracts were considered together as intact, while infiltrated and interrupted tracts were considered pathological. In addition, we examined the integrity of the ILF separately considering three parts of the ILF, namely, the anterior, middle, and posterior third. A consensus was reached between the two neuroradiologists after review of the tractography results in each patient. We did not perform FA tract-specific measurements because it may not be a reliable quantitative measure, especially so when the tracts are infiltrated by gliomas. The increase in extracellular water in edematous tissue leads to increased MD and decreased FA, introducing a bias in the measurement that is not related to tracts integrity (Pasternak et al., 2009).

2.4 | Tumor lesion and ILF resection overlay mapping

Analysis of the extent of tumor lesion was performed on preoperative 3D-MRI. The analysis of extent of resection of the four fascicles was performed on postoperative 3D-MRI acquired the day of the postoperative neuropsychological testing. Individual tumor lesion and tract resection mapping were performed by independent judges (RP, GM, and AB), who manually traced a volume of interest (VOI) delineating the tumor location (on preoperative T1 axial slices) and the surgical cavity (on postoperative T1 axial slices) with the MRIcron software (www.mricro.com/mricron). The VOI delineated on preoperative MRIs considered signal changes in T2 or FLAIR sequences when necessary to define tumor boundaries. The VOI delineated on postsurgery MRIs included the surgical cavity, namely, the brain tissue removed by surgical procedure; residual tumor, if present, was not included. All VOIs

were then smoothed in the three planes (FWHM = 4 mm) and inspected by two neuroradiologists (AB and AG, 18 and 3 years of experience, respectively) to ensure that tumor and surgery boundaries were correctly defined on pre- and postsurgery MRI, respectively. Lastly, patients' MRIs and lesion maps were normalized to an MNI T1 template in SPM8 (Statistical Parametric Mapping; Ashburner & Friston, 1999): the estimate and write option was used on high-resolution T1 images computing the warp that best registers the source image to match the standard template, then the estimated parameters for warping were applied to VOIs (Campanella et al., 2018; Mattavelli et al., 2019; Pisoni et al., 2019). The normalized lesions were used to create overlap images and to compute the percentage of postsurgery resection for each fascicle and cortical area based on a normative atlas of white matter connections (Catani & Thiebaut de Schotten, 2008, Thiebaut de Schotten et al., 2011) and on the Harvard–Oxford cortical structural atlas (Makris et al., 2006), respectively.

2.5 | Statistical analyses

Individual associations between naming deficits with damage to fascicles and cortical occipito-temporal regions were evaluated by computing odds ratios, with 95% confidence intervals, through conditional maximum likelihood estimate. Sensitivity and specificity values (with 95% confidence intervals computed with Clopper–Pearson method) were also calculated for each fascicle and cortical area.

A multiple logistic regression model (Model 1—"Association of naming deficit with fascicles' damage before surgery") was used to investigate the combined effect of fascicles' damage (regressors) in the naming deficit, considered as a dichotomous response. This model captures and quantifies the relationship between the response and each regressor, adjusted for all other regressors, estimating the probability of having a deficit in the naming test based on the damage to the fascicles. A likelihood ratio test was used to determine the joint effect of including the three segments of the AF and, separately, the tumor infiltration of cortical regions as additional regressors in the previous model.

Fisher's test was used to assess associations between the integrity of the ATL and a naming disruption in patients with ILF damage.

The scores obtained in the four neuropsychological tests (i.e., naming, semantic verbal fluency, phonemic verbal fluency, and Trail Making Test) were compared between the two groups of patients with and without ILF damage in an integrated analysis employing a second multiple logistic regression model (Model 2—"Association of ILF damage with neuropsychological tests before surgery"), with the groups being the dependent variable (or response) and the scores of the four tests being the regressors. This model estimated the probability of having damage in the ILF based on the scores of the four neuropsychological tests.

A robust multiple linear regression model (Model 3—"Association of naming performance with fascicles' damage after surgery") was used to study the association between the postoperative scores of the naming test and the percentage of lesions in the fascicles, taking into account the presence of possible outliers in the lesion data. Subgroup analysis was performed using Pearson's coefficient, adjusted with Bonferroni correction. Finally, longitudinal comparisons of naming test performance among the preoperative and the two postoperative evaluations were conducted using Wilcoxon signed-rank tests, adjusted with Bonferroni correction.

Analyses were performed with R software (version 4.1.2), package "exact2×2" (Fay, 2010) was used for running Fisher's test, and package "robustbase" for the robust multiple linear regression model. The significance threshold was set at .05.

3 | RESULTS

Hereinafter, we report the pre- and postoperative results. We begin with the preoperative performances in the naming test, and then, we show how they are associated to tumor infiltration of fascicles and cortical regions (considered individually and together). Then, we focus on the association between ILF damage with ATL involvement and on their combined effect on naming deficit before surgery. Additionally, we show that tumor infiltration of ILF was not associated with the preoperative scores obtained in the other tasks. Finally, we present the results on the evolution in time of the naming test performances, and the association of postoperative naming test scores with extent of ILF resection.

3.1 | Naming test performance before surgery

Patients were assigned to two groups based on the object picture naming test score before surgery. Nine patients with a score <41 in the test were assigned to the impaired group (mean age 53.6 years, *SD* = 17.3 with a range of 23–74 years; mean educational level: 11.3 years, SD = 3.6 with a range of 8–17 years), the remaining 39 patients with a normal performance (mean age: 45.3 years, *SD* = 14.8 with a range of 22–74 years; mean educational level: 12.8, *SD* = 3.9 years with a range of 5–23 years) were assigned to the unimpaired group. The impaired patients' mean score was 32.49 (SD 11.26, range 8.79–40.82), while the mean score of patients without naming deficits was 46.39 (SD 1.56, range 42.59–48). The nine impaired patients had IDH-wildtype glioblastoma in five cases, IDH-mutant 1p/19q-codeleted oligodendroglioma in three cases, and IDH-mutant astrocytoma in one case. No statistical difference between the glioma subtype distribution of the two groups was found ($p = .7939$, Fisher test).

3.2 | Effect of damage to individual fascicles and cortical regions on preoperative naming deficit

Damage of the ILF was associated with a deficit in the naming test, with an odds ratio of 6.35 (95% CI 1.27–34.92). Damage of the

TABLE 3 Sensitivity, specificity and odds ratio of impaired fascicles and cortical areas in patients with and without a deficit in the naming test before surgery.

	Sensitivity		Specificity		
	% (95% CI)	n/N	% (95% CI)	n/N	Odds ratio (95% CI)
Fascicles					
ILF	67 (30–93)	6/9	77 (61–89)	30/39	6.35 (1.27–34.92)
ILF anterior third	22 (3–60)	2/9	77 (61–89)	30/39	0.95 (0.12–5.45)
ILF middle third	44 (14–79)	4/9	87 (73–96)	34/39	5.18 (1.00–30.20)
ILF posterior third	33 (7–70)	3/9	97 (87–100)	38/39	17.16 (1.63–502.06)
IFOF	33 (7–70)	3/9	62 (45–77)	24/39	0.80 (0.15–3.90)
UF	33 (7–70)	3/9	59 (42–74)	23/39	0.72 (0.14–3.51)
AF anterior	0 (0–34)	0/9	92 (79–98)	36/39	0.00 (0.00–7.72)
AF long	11 (0–48)	1/9	87 (73–96)	34/39	0.85 (0.03–9.08)
AF posterior	33 (7–70)	3/9	97 (87–100)	38/39	17.16 (1.63–502.06)
Grey matter					
ATL	22 (3–60)	2/9	74 (58–87)	29/39	0.83 (0.11–4.82)
Fusiform gyrus	22 (3–60)	2/9	95 (83–99)	37/39	5.03 (0.48–53.54)
ITG	33 (7–70)	3/9	92 (79–98)	36/39	5.69 (0.85–39.00)
MTG	0 (0–34)	0/9	90 (76–97)	35/39	0.00 (0.00–5.05)
Hippocampus	22 (3–60)	2/9	77 (61–89)	30/39	0.95 (0.12–5.45)
Insula	33 (7–70)	3/9	62 (45–77)	24/39	0.80 (0.15–3.90)
STG	22 (3–60)	2/9	69 (52–83)	27/39	0.65 (0.09–4.11)
Occipital lobe	11 (0–48)	1/9	90 (76–97)	35/39	1.09 (0.04–9.65)

Abbreviations: AF, Arcuate Fasciculus; ATL, Anterior temporal lobe; IFOF, Inferior Fronto-Occipital Fasciculus; ILF, Inferior Longitudinal Fasciculus; ITG, inferior temporal gyrus; MTG, middle temporal gyrus; STG, superior temporal gyrus; UF, uncinate Fasciculus.

posterior and mid-third, but not of the anterior third of the ILF, and of the posterior segment of the AF (AFp), were also associated with a naming deficit, as shown in Table 3. No other fascicles and none of the cortical regions (Table 3) were individually associated with naming performance.

The ILF was damaged in six patients out of nine with a naming deficit: three with IDH-wildtype glioblastomas and three with IDH-mutant 1p/19q-codeleted oligodendrogliomas (Table 4). In four out of these six patients, the lesion concerned the middle third of the fascicle (plus the posterior third in three patients), while in the other two patients, only the anterior third was damaged. In the remaining three patients, the ILF was dislocated in one and intact in two.

In the group with normal naming test scores, the ILF was not damaged in 30 out of 39 (77%) patients: it was intact in 23 and dislocated in seven patients. In the nine patients with no naming deficits despite ILF damage (Table 5), the ILF was infiltrated in three patients and interrupted in six. Notably, in all nine patients with preserved naming performance the ILF damage was localized in its anterior third and, in four of them, it was associated with tumor infiltration of the ATL. All nine patients did not have AF damage.

No significant difference ($p = .622$, Fisher test) was found when comparing glioma subtype distribution of the nine patients with ILF damage and normal naming test performance against that of the six patients with ILF damage and a naming deficit.

3.3 | Combined effect of fascicles and cortical damage on preoperative naming deficit

Among the fascicles, only damage to the ILF showed a significant association with a deficit in the naming test (adjusted odds ratio = 15.726 [95% CI: 2.303–178.157], $p = .0105$) when adjusting for the effects of all the fascicles together (namely, AF, UF, IFOF, and ILF) in Model 1, as reported in Table 6. Interestingly, the additional inclusion of damage to the AF posterior, anterior, and long segments in Model 1 was not significant (likelihood ratio test, $p = .2883$), further confirming that the ILF was the only fascicle to be strongly associated with a deficit in the naming test. Likewise, the inclusion of gray matter regions (see Table 3) as additional regressors in Model 1 was not significant (likelihood ratio test, $p = .2201$).

As supplementary analysis, in order to independently evaluate the specific effect of each of the three thirds of the ILF on the naming deficit, we examined three different versions of Model 1 which included the anterior, mid, and posterior third of the ILF, respectively, as regressor in place of the whole ILF. We found that all three versions of Model 1 were not significantly different from the null model (i.e., a model with no regressors), thus showing that the individual thirds of the ILF were not significantly associated with naming deficit when adjusting for the other fascicles (likelihood ratio tests for Model 1 with anterior third of ILF: $p = .8266$; for Model 1 with mid third of ILF: $p = .1879$; for Model 1 with posterior third of ILF: $p = .1175$).

TABLE 4 Fascicles status in the nine patients with naming deficit.

		ILF					AF		
ID	WHO 2021 classification	Anterior third	Mid third	Posterior third	IFOF	UF	Anterior	Long	Posterior
Without infiltration of the ATL									
8	IDH-mutant 1p/19q-cod oligodendroglioma	Normal	interrupted	interrupted	dislocated	normal	normal	normal	interrupted
38	IDH-wt GBM	Normal	interrupted	interrupted	infiltrated	normal	normal	interrupted	interrupted
48	IDH-wt GBM	Normal	infiltrated	infiltrated	infiltrated	normal	normal	normal	normal
43	IDH-wt GBM	Normal	interrupted	normal	normal	normal	normal	normal	normal
12	IDH-mutant 1p/19q-cod oligodendroglioma	Interrupted	normal	normal	dislocated	normal	normal	normal	normal
20	IDH-mutant Astrocytoma	Normal	normal	normal	interrupted	interrupted	normal	normal	normal
31	IDH-wt GBM	Normal	dislocated	normal	dislocated	normal	normal	normal	normal
With infiltration of the ATL									
3	IDH-mutant 1p/19q-cod oligodendroglioma	Interrupted	normal	normal	normal	interrupted	normal	normal	interrupted
36	IDH-wt GBM	Normal	normal	normal	dislocated	interrupted	normal	normal	normal

Note: Only interrupted and infiltrated fascicles were considered "damaged".
Abbreviations: AF, Arcuate Fasciculus; ATL, anterior temporal lobe; cod, codeleted; GBM, glioblastoma; IFOF, Inferior Fronto-Occipital Fasciculus; ILF, Inferior Longitudinal Fasciculus; UF, Uncinate Fasciculus; wt, wildtype.

TABLE 5 Fascicles status in the nine patients with normal naming test scores despite ILF damage.

		ILF					AF		
ID	WHO 2021 classification	Anterior third	Mid third	Posterior third	IFOF	UF	Anterior	Long	Posterior
Without infiltration of the ATL									
37	IDH-wt GBM	interrupted	interrupted	interrupted	normal	interrupted	normal	normal	normal
11	IDH-mutant 1p/19q-cod oligodendroglioma	infiltrated	infiltrated	normal	infiltrated	normal	normal	normal	normal
6	IDH-mutant 1p/19q-cod oligodendroglioma	infiltrated	infiltrated	normal	interrupted	interrupted	dislocated	dislocated	normal
28	IDH-wt GBM	interrupted	interrupted	normal	interrupted	interrupted	normal	normal	normal
17	IDH-mutant astrocytoma	infiltrated	normal	normal	infiltrated	infiltrated	normal	normal	normal
With infiltration of the ATL									
15	IDH-mutant astrocytoma	interrupted	normal	normal	interrupted	interrupted	dislocated	dislocated	dislocated
7	IDH-mutant 1p/19q-cod oligodendroglioma	interrupted	normal	normal	infiltrated	interrupted	normal	normal	normal
9	IDH-mutant 1p/19q-cod oligodendroglioma	interrupted	normal	normal	interrupted	interrupted	normal	normal	normal
46	IDH-wt GBM	interrupted	interrupted	normal	interrupted	interrupted	normal	normal	normal

Note: Only interrupted and infiltrated fascicles were considered "damaged".
Abbreviations: AF, Arcuate Fasciculus; ATL, anterior temporal lobe; cod, codeleted; GBM, glioblastoma; IFOF, Inferior Fronto-Occipital Fasciculus; ILF, Inferior Longitudinal Fasciculus; UF, Uncinate Fasciculus; wt, wildtype.

3.4 | Preoperative association of ILF damage with ATL involvement.

A total of 15 patients had a preoperative damage in the ILF caused by the tumor. Six of them had a deficit in the picture naming test, whereas nine patients did not. The MRI and the DTI tractograms of two patients with ILF damage are illustrated in Figures 1 and 2, respectively. The first patient presented with naming deficits and the MRI showed tumor sparing of the ATL. The second patient presented without naming deficits and the MRI showed tumor infiltration of the ATL.

TABLE 6 Model 1 results showing the association of preoperative naming deficit with fascicles' damage adjusted for the other tests.

Fascicle	Coefficient estimate (SE)	Adjusted odds ratio (95% CI)	z-score	*p*-value
ILF	2.755 (1.077)	15.726 (2.303–178.157)	2.558	.0105*
IFOF	−1.146 (1.117)	0.318 (0.029–2.610)	−1.026	.3051
UF	−0.695 (1.030)	0.499 (0.058–3.662)	−0.674	.5001
AF	0.759 (0.996)	2.137 (0.271–15.517)	0.762	.4459
Model intercept	−2.182 (0.716)	0.113 (0.021–0.386)	−3.047	.0023*

Note: Significant values are indicated with an asterisk in the last column. This model (Model 1) is globally significant ($p = .0446$) as estimated by a likelihood ratio test for comparing this model against the model without regressors. Confidence intervals (CI) are computed through profile-likelihood method.
Abbreviations: AF, Arcuate Fasciculus; IFOF, Inferior Fronto-Occipital Fasciculus; ILF, Inferior Longitudinal Fasciculus; SE, Standard Error; UF, Uncinate Fasciculus.

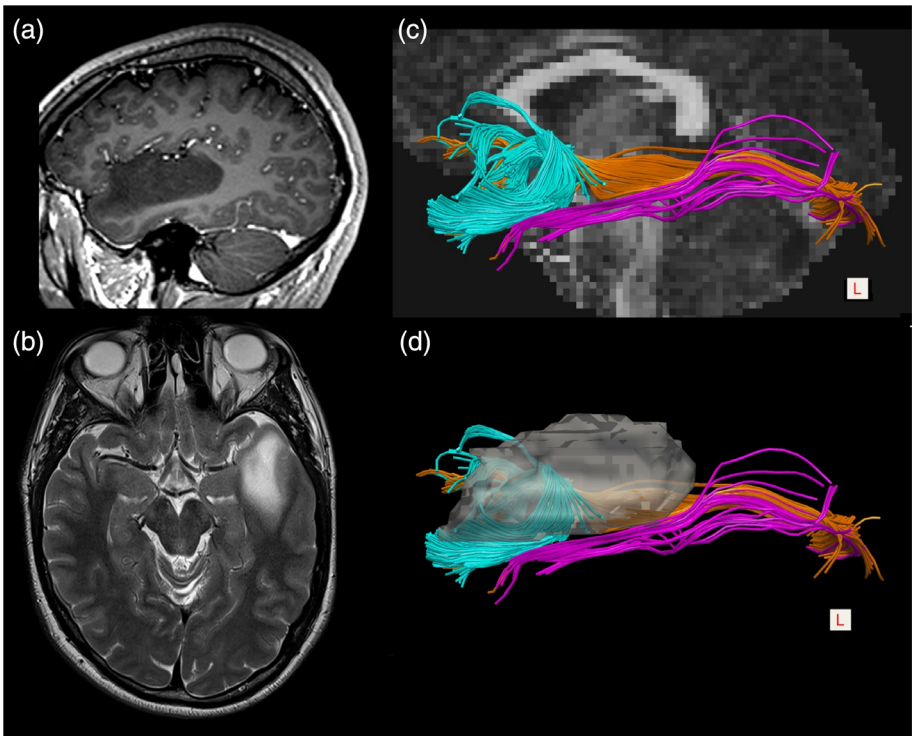

FIGURE 1 36-year-old male with oligodendroglioma IDH-mutant, 1p/19q codeleted. Before surgery the patient is presenting with naming deficit and partial interruption of the left ILF. Sagittal postcontrast T1WI (a) and axial T2WI (b) show the non-enhancing mass infiltrating the left superior and middle temporal gyri and the adjacent deep white matter. The tumor spares the anterior ventral aspect of the temporal lobe (ATL). Left lateral view of the tractograms of the three fascicles of the ventral language pathway tracked with DTI deterministic tractography were overlaid on a sagittal fractional anisotropy (FA) map (c) and displayed in relation to the mass (d). The ILF (streamlines in violet) is thinner than normal due to partial interruption by the infiltrating mass; the IFOF (orange) and UF (cyan) are within normal limits.

In 10 out of the 15 patients with ILF damage, infiltration spared the ATL, whereas in five patients (three with IDH-mutant 1p/19q-codeleted oligodendroglioma, one with IDH-wildtype glioblastoma, and one with IDH-mutant astrocytoma), infiltration also involved the ATL. In the former subgroup, picture naming was impaired in 5 out of 10 patients (50%), while in the latter subgroup only 1 out of 5 (20%) had a pathological score. There was no significant difference ($p = .58$) between the two groups although these results should be interpreted with caution due to the very small sample size. In addition, a difference in tumor overlap between the two subgroups was noted on lesion maps. In the subgroup of six patients with naming deficit the lesion map showed that the maximal overlap occurred in the ILF ($n = 5$), with relative sparing of the ATL (Figure 3a). In contrast, in the subgroup of nine patients without naming deficit, the maximal tumor overlap occurred in the ATL ($n = 9$) (Figure 3b).

3.5 | Potential alternative routes when the ILF is damaged

The finding of nine patients without naming deficits among the 15 patients with ILF damage raised the question about the existence of possible alternative routes that may substitute the ILF to carry the visual input to the temporal brain area where lexical representations are stored. We divided patients with ILF damage in two subgroups: with and without ATL infiltration. In the subgroup of five patients with ATL infiltration, the AFp was intact in all four who did not have a naming deficit, while it was infiltrated in the only one patient with a naming deficit. Interestingly, the IFOF and UF were both infiltrated by the tumor in the four patients without the deficit.

Similarly, in the subgroup of 10 patients with sparing of the ATL, the AFp was intact in all five patients without naming deficit,

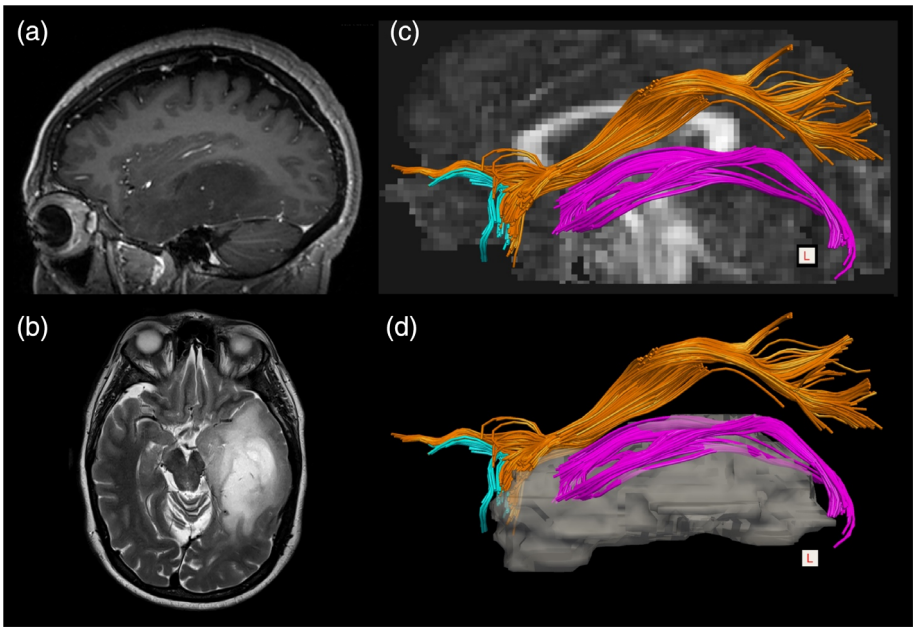

FIGURE 2 36-year-old female with oligodendroglioma, IDH-mutant, 1p/19q codeleted. Before surgery the patient is presenting without naming deficit and partial interruption of the left ILF, especially in its anterior third aspect. Sagittal postcontrast T1WI (a) and axial T2WI (b) show the non-enhancing mass infiltrating the left ventral and mesial aspect of the left temporal lobe and the adjacent deep white matter. The tumor is infiltrating the anterior ventral aspect of the temporal lobe (ATL). Left lateral view of the tractograms of the three fascicles of the ventral language pathway tracked with DTI deterministic tractography, were overlaid on a sagittal fractional anisotropy (FA) map (c) and displayed in relation to the mass (d). Note the interruption of the anterior third of the ILF (streamlines in violet) and dorsolateral dislocation of the middle and posterior thirds of the ILF by the infiltrating mass. The temporal arm of the UF (cyan) is also interrupted; the posterior half of the IFOF (orange) is dorsally dislocated by the mass.

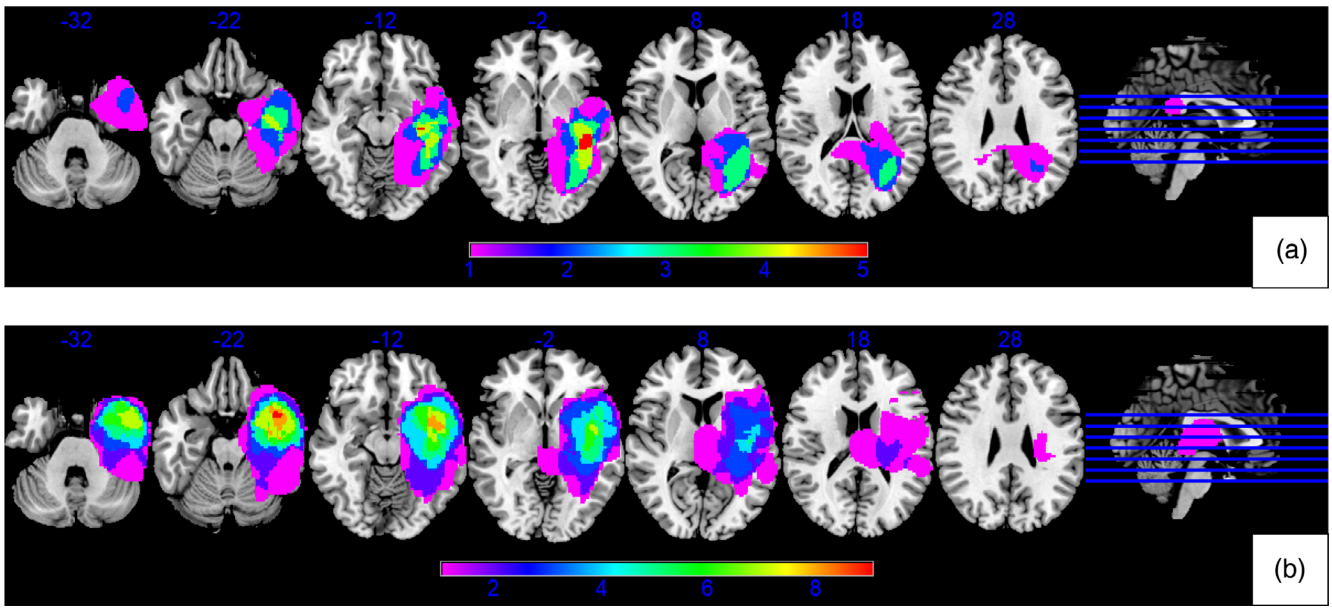

FIGURE 3 Lesion overlap maps of 15 patients with preoperative ILF damage, separated in two subgroups according to the presence (A, $n = 6$) or absence (B, $n = 9$) of a deficit in the naming test. Maps are overlaid on a T1-template in MNI space $1 \times 1 \times 1$ mm^3. MNI coordinates of each transverse section (z-axis) and a sagittal slice for visualization are reported. Color scales indicate the number of patients with a lesion in that voxel.

while it was infiltrated in 2 of 5 patients with a naming deficit. The IFOF and UF were both infiltrated by the tumor in the four of the five patients without the deficit. These data suggest that the AFp is the main candidate to substitute the ILF to carry visual stimuli to the ATL or to the area that is replacing it when it is infiltrated by the glioma.

TABLE 7 Model 2 results showing the association of ILF damage with each neuropsychological test before surgery, adjusted for the other tests.

Neuropsychological test	Coefficient estimate (SE)	Adjusted odds ratio (95% CI)	z-score	*p*-value
Object naming	0.316 (0.146)	1.372 (1.098–1.928)	2.166	.0303*
Phonemic fluency	0.001 (0.040)	1.001 (0.925–1.086)	0.027	.9787
Semantic fluency	−0.070 (0.048)	0.932 (0.841–1.021)	−1.465	.1429
TMT	−0.007 (0.010)	0.993 (0.972–1.013)	−0.703	.4822
Model intercept	−10.022 (6.201)	4×10^{-5} (3×10^{-11}-0.404)	−1.616	.1061

Note: Significant values are indicated with an asterisk in the last column. This model (Model 2) is globally significant ($p = .0348$) as estimated by a likelihood ratio test for comparing this model against the model without regressors. Confidence intervals (CI) are computed through profile-likelihood method.
Abbreviations: ILF, Inferior Longitudinal Fascicle; TMT, Trail Making Test; SE, Standard Error.

3.6 | Preoperative association of ILF damage with other neuropsychological tasks

The association of preoperative ILF damage with naming deficit was selective.

Patients with ILF damage performed significantly worse than those without ILF damage only in the naming test (odds ratio 1.372 [95% CI 1.098–1.928], $p = .0303$), as indicated by Model 2 (Table 7). In contrast, the performance did not statistically differ for verbal fluency on phonemic and semantic cue and for the Trail Making Test (all $p > .05$). In detail, the 15 patients with ILF damage had a mean score of 36.0 (SD 14.3, range 19–67) in semantic verbal fluency, 25.3 (SD 10.3, range 10–45) in phonemic verbal fluency, and 85.4 (SD 59.8, range 3–202) at the Trail Making Test; the 33 patients without ILF damage had a mean score of 37.6 (SD 11.2, range 7–62) in semantic verbal fluency, 27.8 (SD 11.7, range 7–62) in phonemic verbal fluency, and 75.1 (SD 35.9, range 10–146) at the Trail Making Test.

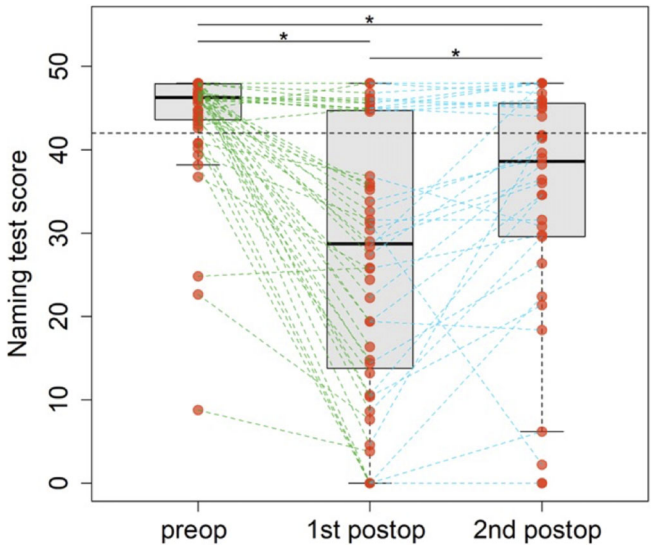

FIGURE 4 Longitudinal comparison of naming test performance among pre- and two postoperative evaluations. postoperative (1st postop, $n = 44$), and second postoperative follow-up (2nd postop, $n = 34$). Red dots represent individual patient scores. Green and blue lines connect the scores of the same patients across time points (from preop to 1st postop, and from 1st postop to 2nd postop, respectively). Horizontal black-dashed line indicates the Italian cut-off score for the naming test. The asterisks on top of the boxplots indicate significant differences between naming test scores for each pairwise comparison of the three time points (all adjusted *p*-values of the Wilcoxon signed-rank test were <0.05 after Bonferroni correction).

3.7 | Postoperative naming deficits

At early and 3 months postoperative time points, naming test scores were available in 44 and 34 patients, respectively. We observed a marked and significant decrease in performances at the early postoperative assessment with respect to the preoperative scores, with an average score of 26.8 (SD 15.8) and 43.8 (SD 7.3), respectively (adjusted $p < .001$), as illustrated in Figure 4. This sharp decrement was transitory, as the naming scores significantly increased (adjusted $p < .001$) at the 3 months follow-up, reaching an average value of 34.1 (SD 14.5), although still significantly lower than the presurgical scores (adjusted $p = .004$). In summary, in 9 patients, the naming deficit was present before and early after surgery; in 23 patients, the deficit appeared early after surgery; in 12 patients, no naming deficit was present before and after surgery. Unfortunately, naming test scores were available at the 3 months follow-up only in 21 of the 32 patients who had early postoperative deficit: the naming deficit was maintained in all but one of them.

Boxplots represent the distribution of the naming test scores at three time points: preoperative (preop, $n = 48$), first early

3.8 | Association of early postoperative naming deficit with extent of ILF resection

The extent of ILF resection (measured as percentage of the resected fascicle) was significantly associated with a deficit in the naming test ($p = .0082$), while other fascicles did not exhibit any significant association according to Model 3 (Table 8). Interestingly, this association

TABLE 8 Model 3 results showing the association between naming test scores and percentage of postoperative lesions in each fascicle, adjusted for the other fascicles.

Fascicle	Beta coefficient (standard error)	*p*-value
ILF	−56.78 (20.34)	.0082*
IFOF	−13.72 (14.80)	.3598
UF	6.88 (11.00)	.5355
AF	−33.01 (26.88)	.2272
Model intercept	41.12 (7.71)	<.0001*

Note: Coefficients and p-values were estimated through a robust linear regression model (Model 3) that included the postoperative naming test performance as dependent variable, and the percentage of postoperative lesions in each fascicle as regressor. Overall, the model was significant (robust Wald Test, $p < .0001$). Significant regressors are indicated with an asterisk in the last column.
Abbreviations: AF, Arcuate Fasciculus; IFOF, Inferior Fronto-Occipital Fasciculus; ILF, Inferior Longitudinal Fasciculus; UF, Uncinate Fasciculus.

was not observed when considering only the subgroup of patients with a preoperative ILF damage (Pearson's rho = .096, adjusted $p > .999$), but resulted significant for the subgroup without preoperative ILF infiltration (rho = −.527, adjusted $p = .012$). Similarly, the subgroup of patients with preoperative ATL infiltration did not show any association between the naming test scores and the percentage of ILF resection observed early after surgery (rho = .180, adjusted $p > .999$), whereas the subgroup of patients without ATL involvement showed significantly decreased visual naming performance as the percentage of ILF resection increased (rho = −.556, adjusted $p = .004$).

4 | DISCUSSION

This study on 48 patients with a glioma growing in the left temporal lobe showed that a deficit in picture naming was selectively associated with ILF damage before and after surgery.

The first aim of our study was, indeed, to assess whether in patients with left ILF damage, there were lexical retrieval deficits, and they were confined to visually presented stimuli. For this reason, we examined picture naming, and three additional tests, namely a visual divided attention one, not involving lexical retrieval but requiring visual identification of verbal stimuli (letters and digits), that is, the Trail Making Test, and two lexical retrieval tasks that do not involve visual stimuli, that is, verbal fluency on phonemic and semantic cues. We integrated the analysis of the effect of the left ILF damage on the four neuropsychological tests in a single multiple linear regression model, which was found to be globally significant. According to the model, the effect of the left ILF damage on picture naming of objects was selective, since the performances of verbal fluency and Trail Making Test were not affected by ILF damage. We suggest, therefore, that a disconnection of visual areas from left ATL regions in which lexical representations are stored is the most important factor for impaired picture naming of objects, preventing the subject to retrieve the appropriate lexical representation on visual input; however, the lexical representation can be accessed when it does not require processing a visual information. Notably, in our study, the ILF was the only fascicle (after adjusting for the effect of the other fascicles) to be significantly associated with lower performance on naming visual stimuli.

These results confirm our expectation based on previous studies. Indeed, in a DTI study, Agosta et al. (2010) showed that five patients with semantic dementia had significantly higher mean, parallel, and transverse diffusivities in the left ILF and UF than controls, coupled with severe impairment on the Boston Naming Test but normal performance in speech fluency (WAB). The authors suggested that in semantic dementia, the combination of cortical ATL and ILF damage, with sparing of the posterior visual cortex, produces a 'disconnection' between the degraded semantic memory store and normal visual perceptual functions.

In a retrospective study on 110 patients who underwent glioma resection, Herbet et al. (2016) provided additional evidence that the ILF is an essential component of the lexical retrieval network on the visual input. The lexical retrieval deficit was observed with picture naming; no deficits in the other lexical retrieval tasks, such as verbal fluency or naming by description, were reported.

The inability of a patient to retrieve a lexical entry in response to a visual stimulus is a clinical syndrome known as optic aphasia, a controversial syndrome that usually occurs in patients with left deep temporo-occipital lesions.

Our results suggest that the inability to name visually presented objects/pictures could be due to left ILF damage, being interpreted as a disconnection in the route connecting the structural description to the phonological output lexicon (Ratcliff & Newcombe, 1982).

A few single-case studies on optic aphasia also support the essential role of the ILF in picture naming. For example, Shinoura et al. (2010) described a 74-year-old patient with anaplastic astrocytoma examined with MRI and neuropsychology testing at 6 months interval. At the first time point, the patient did not show any deficit in object naming, with the tumor causing a disruption of the left IFOF but not of the left ILF, nor of the left superior longitudinal fascicle. 6 months later, the patient had a marked deterioration in object naming performance and DTI Tractography showed "interruption of the left ILF". Similarly, Endo et al. (1996) reported the case of a patient who fell off a cliff and had surgical evacuation of a large left acute epidural hematoma. This patient with right homonymous hemianopia named auditorily presented objects and could make semantic association tasks, while he was unable to name visually or tactually presented objects. A CT scan acquired 16 months after surgery showed a porencephalic hypodense lesion involving the left lingula, the ipsilateral optic radiations, and the occipital aspect of the IFOF and ILF; the inferior temporal and fusiform gyri were also affected. The authors concluded that the left posterior hemisphere lesions were likely preventing transmission of information from two specific sensory modalities to the common semantic memory store in the ATL, and they were responsible for optic and tactile aphasia and apraxia. In fact, multiple lesions in different anatomic regions in addition to the ILF could have caused optic aphasia in this patient.

Regarding the second aim, we found that most patients with tumor infiltration of the ATL did not present with preoperative picture naming deficits, thus confirming with a different technique (i.e. MRI and tractography) Herbet et al. (2019)'s results obtained with IOM. Overlap lesion maps in the 15 patients with ILF damage showed that overlap of gliomas was maximal in the ATL in the subgroup of patients without naming deficits. In contrast, the maximal tumor overlap occurred in the left ILF and spared the ATL in the subgroup of patients with low naming scores. In addition, we found that patients with tumor infiltration of the ATL did not have postoperative naming deficits regardless of the extent of ILF resection. Early postoperative scores in the naming test decreased as the percentage of ILF damage increased only in patients with the tumor sparing the ATL. These findings suggest, as already proposed by Papagno et al. (2011), that cortical damage may elicit a reorganization of existing networks possibly shaped by neuroplasticity phenomena. This may be particularly true for slow-growing tumors, such as IDH-mutant gliomas, which in our sample represented most of the patients with both ILF and ATL involvement. These results have important clinical implications for neurosurgery since they suggest that extensive exeresis of gliomas in the left ATL is possible without causing permanent naming deficits, thus reaching an efficient oncological outcome without damaging the functional status of the subject.

Finally, we found that the AFp appears to be the main candidate to substitute the ILF when it is damaged by glioma infiltration, either when the ATL is damaged or spared. Our data showed the AFp was not infiltrated in all patients without naming deficits despite ILF and ATL damage. This finding suggests that the brain area replacing the ATL in storing lexical representations may be located in the proximity of AFp terminations. Similarly, the finding that the AFp was not infiltrated in all five patients without naming deficit despite ILF damage suggests that terminations of the AFp may eventually carry visual stimuli to the ATL. The combined tumor infiltration of IFOF and UF in patients with naming deficits despite ILF damage indirectly further supports this vicarious role of the AFp. The AF is a large fasciculus with very distributed cortical terminations. Our results are in line with Giampiccolo and Duffau (2022) who have recently pointed out that the AFp may contribute to lexical functions with terminations that extend beyond the superior temporal gyrus and reaching the anteroventral temporal language areas in the anterior and middle aspect of the inferior temporal and fusiform gyri. Involvement of the AFp in semantic tasks during LGG resection in awake surgery (Papagno et al., 2011) and in semantic dementia (Agosta et al., 2010) is also in agreement with our results.

A few limitations should be acknowledged. The number of glioma patients with a preoperative deficit in picture naming is relatively small. Recruitment of consecutive glioma patients with different tumor histology raises the concern that IDH-wildtype glioblastomas may produce more invasive ILF damage than infiltrative IDH-mutant gliomas (Bizzi et al., 2012). Indeed, the fact that nine patients with ILF lesion were not impaired, while six were, could be associated with tumor invasiveness. However, in our cohort, we did not find a significant difference in glioma subtype or grade between the two subgroups of patients. A third limitation is that DTI tractography was not acquired after surgery because of the presence of susceptibility artifacts and time constrains. It is well known that pneumocephalus and blood products may affect accuracy of fascicles tracking in early postoperative brain tumor patients. We acknowledge that the preliminary results about a possible alternative route should be interpreted with caution due to the low number of patients with ILF damage included in this study. Another limitation was that naming by description as well as tactile naming should have been performed in all patients to verify that naming without a visual input was preserved. This would have further supported our hypothesis. However, patients underwent an already extensive neuropsychological battery that made it difficult for ethical reasons, to add further testing. Lastly, we did not retest the patients at longer time intervals from surgery to establish whether the naming deficits were long-lasting or permanent.

In future studies, the hypothesis that the disconnection of the ILF may produce a specific deficit in naming visual stimuli will have to be confirmed in a larger multi-institutional study, using comprehensive testing. Finally, if the disconnection is between visual information and lexical retrieval, any stimuli requiring this transfer should be affected, such as colors and faces.

In conclusion, we showed that a deficit in the picture naming test was associated with a selective damage of the ILF due to glioma invasion or infiltration, as estimated by DTI tractography. The naming deficit was associated also with the extent of ILF surgical resection, as estimated by MRI volumetry. In contrast, verbal fluency and visual attention tasks were preserved, indicating that ILF damage was selectively associated with lexical retrieval impairment from visual stimuli. Remarkably, we observed that decreasing picture naming performance after surgery was associated with the percentage of ILF resection only in those patients without presurgical ATL involvement, further supporting the hypothesis that adaptive functional reorganization of the lexical retrieval network is probably elicited by tumor infiltration. Our preliminary data suggest that an alternative route may run through the posterior segment of the AF.

Finally, we believe that these clinico-radiological results will have a clinical impact for the evaluation of glioma patients at presentation, preoperative counseling, surgical planning, and intraoperative neuropsychological mapping.

FUNDING INFORMATION

This work was partially supported by the Italian Ministry of Health (RC).

CONFLICT OF INTEREST STATEMENT

The authors report no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ORCID

Riccardo Pascuzzo https://orcid.org/0000-0001-6555-1784

Luigi Antelmi https://orcid.org/0000-0002-4173-5412

REFERENCES

Agosta, F., Henry, R. G., Migliaccio, R., Neuhaus, J., Miller, B. L., Dronkers, N. F., Brambati, S. M., Filippi, M., Ogar, J. M., Wilson, S. M., & Gorno-Tempini, M. L. (2010). Language networks in semantic dementia. *Brain: A Journal of Neurology*, *133*(1), 286–299. https://doi.org/10.1093/brain/awp233

Ashburner, J., & Friston, K. J. (1999). Nonlinear spatial normalization using basis functions. *Human Brain Mapping*, *7*(4), 254–266. https://doi.org/10.1002/(sici)1097-0193

Bizzi, A., Nava, S., Ferrè, F., Castelli, G., Aquino, D., Ciaraffa, F., Broggi, G., DiMeco, F., & Piacentini, S. (2012). Aphasia induced by gliomas growing in the ventrolateral frontal region: Assessment with diffusion MR tractography, functional MR imaging and neuropsychology. *Cortex*, *48*(2), 255–272. https://doi.org/10.1016/j.cortex.2011.11.015

Blom-Smink, M., Verly, M., Spielmann, K., Smits, M., Ribbers, G. M., & van de Sandt-Koenderman, M. W. M. E. (2020). Change in right inferior longitudinal fasciculus integrity is associated with naming recovery in subacute Poststroke aphasia. *Neurorehabilitation and Neural Repair*, *34*(9), 784–794. https://doi.org/10.1177/1545968320940982

Campanella, F., Del Missier, F., Shallice, T., & Skrap, M. (2018). Localizing memory functions in brain tumor patients: Anatomical hotspots over 260 patients. *World Neurosurgery*, *120*, e690–e709. https://doi.org/10.1016/j.wneu.2018.08.145

Capitani, E., & Laiacona, M. (1997). Composite neuropsychological batteries and demographic correction: standardization based on equivalent scores, with a review of published data. The Italian Group for the Neuropsychological Study of Ageing. *Journal of Clinical and Experimental Neuropsychology*, *19*, 795–809. https://doi.org/10.1080/01688639708403761

Catani, M. (2003). Occipito-temporal connections in the human brain. *Brain*, *126*(9), 2093–2107. https://doi.org/10.1093/brain/awg203

Catani, M., Jones, D. K., & ffytche, D. H. (2005). Perisylvian language networks of the human brain. *Annals of Neurology*, *57*(1), 8–16. https://doi.org/10.1002/ana.20319

Catani, M., & Mesulam, M. (2008). The arcuate fasciculus and the disconnection theme in language and aphasia: History and current state. *Cortex*, *44*(8), 953–961. https://doi.org/10.1016/j.cortex.2008.04.002

Catani, M., & Thiebaut de Schotten, M. (2008). A diffusion tensor imaging tractography atlas for virtual in vivo dissections. *Cortex*, *44*, 1105–1132. https://doi.org/10.1016/j.cortex.2008.05.004

Catricalà, E., Della Rosa, P. A., Ginex, V., Mussetti, Z., Plebani, V., & Cappa, S. F. (2013). An Italian battery for the assessment of semantic memory disorders. *Neurological Sciences*, *34*(6), 985–993. https://doi.org/10.1007/s10072-012-1181-z

Déjérine, J., & Déjérine-Klumpke, A. (1895). *Anatomie des centres nerveux*. Rueff et Cie.

De Schotten, M. T., Bizzi, A., Dell'Acqua, F., Allin, M., Walshe, M., Murray, R., … Catani, M. (2011). Atlasing location, asymmetry and inter-subject variability of white matter tracts in the human brain with MR diffusion tractography. *Neuroimage*, *54*(1), 49–59.

Endo, K., Makishita, H., Yanagisawa, N., & Sugishita, M. (1996). Modality specific naming and gesture disturbances: A case with optic aphasia, bilateral tactile aphasia, Optic Apraxia and Tactile Apraxia. *Cortex*, *32*(1), 3–28. https://doi.org/10.1016/s0010-9452(96)80014-1

Epelbaum, S., Pinel, P., Gaillard, R., Delmaire, C., Perrin, M., Dupont, S., Dehaene, S., & Cohen, L. (2008). Pure alexia as a disconnection syndrome: New diffusion imaging evidence for an old concept. *Cortex*, *44*(8), 962–974. https://doi.org/10.1016/j.cortex.2008.05.003

Fay, M. P. (2010). Confidence intervals that match Fisher's exact or Blaker's exact tests. *Biostatistics (Oxford, England)*, *11*(2), 373–374. https://doi.org/10.1093/biostatistics/kxp050

Figini, M., Riva, M., Graham, M., Castelli, G. M., Fernandes, B., Grimaldi, M., Baselli, G., Pessina, F., Bello, L., Zhang, H., & Bizzi, A. (2018). Prediction of Isocitrate dehydrogenase genotype in brain gliomas with MRI: Single-Shell versus multishell diffusion models. *Radiology*, *289*(3), 788–796. https://doi.org/10.1148/radiol.2018180054

Giampiccolo, D., & Duffau, H. (2022). Controversy over the temporal cortical terminations of the left arcuate fasciculus: A reappraisal. *Brain*, *145*(4), 1242–1256. https://doi.org/10.1093/brain/awac057

Herbet, G., Moritz-Gasser, S., Boiseau, M., Duvaux, S., Cochereau, J., & Duffau, H. (2016). Converging evidence for a cortico-subcortical network mediating lexical retrieval. *Brain*, *139*(11), 3007–3021. https://doi.org/10.1093/brain/aww220

Herbet, G., Moritz-Gasser, S., Lemaitre, A.-L., Almairac, F., & Duffau, H. (2019). Functional compensation of the left inferior longitudinal fasciculus for picture naming. *Cognitive Neuropsychology*, *36*(3–4), 140–157. https://doi.org/10.1080/02643294.2018.1477749

Herbet, G., Zemmoura, I., & Duffau, H. (2018). Functional anatomy of the inferior longitudinal fasciculus: From historical reports to current hypotheses. *Frontiers in Neuroanatomy*, *12*, 77. https://doi.org/10.3389/fnana.2018.00077

Hickok, G., & Poeppel, D. (2004). Dorsal and ventral streams: a framework for understanding aspects of the functional anatomy of language. *Cognition*, *92*(1-2), 67–99.

Kwon, M., & Lee, J. H. (2006). Optic aphasia: A case study. *Journal of Clinical Neurology*, *2*, 258–261.

Makris, N., Kaiser, J., Haselgrove, C., Seidman, L. J., Biederman, J., Boriel, D., et al. (2006). Human cerebral cortex: a system for the integration of volume- and surface-based representations. *Neuroimage*, *33*(1), 139–153.

Mandonnet, E., Nouet, A., Gatignol, P., Capelle, L., & Duffau, H. (2007). Does the left inferior longitudinal fasciculus play a role in language? A brain stimulation study. *Brain*, *130*(3), 623–629. https://doi.org/10.1093/brain/awl361

Marsh, E. B., & Hillis, A. E. (2005). Cognitive and neural mechanisms underlying reading and naming: Evidence from letter-by-letter naming and optic aphasia. *Neurocase*, *11*, 325–337.

Martino, J., Brogna, C., Robles, S. G., Vergani, F., & Duffau, H. (2010). Anatomic dissection of the inferior fronto-occipital fasciculus revisited in the lights of brain stimulation data. *Cortex*, *46*, 691–699. https://doi.org/10.1016/j.cortex.2009.07.015

Martino, J., De Witt Hamer, P. C., Vergani, F., Brogna, C., de Lucas, E. M., Vázquez-Barquero, A., … Duffau, H. (2011). Cortex-sparing fiber dissection: an improved method for the study of white matter anatomy in the human brain. *Journal of Anatomy*, *219*(4), 531–541.

Martino, J., De Witt Hamer, P. C., Berger, M. S., Lawton, M. T., Arnold, C. M., de Lucas, E. M., et al. (2013). Analysis of the subcomponents and cortical terminations of the perisylvian superior longitudinal fasciculus: a fiber dissection and DTI tractography study. *Brain Structure and Function*, *218*, 105–121. https://doi.org/10.1007/s00429-012-0386-5

Mattavelli, G., Pisoni, A., Casarotti, A., Comi, A., Sera, G., Riva, M., Bizzi, A., Rossi, M., Bello, L., & Papagno, C. (2019). Consequences of brain tumour resection on emotion recognition. *Journal of Neuropsychology*, *13*(1), 1–21. https://doi.org/10.1111/jnp.12130

McKinnon, E. T., Fridriksson, J., Glenn, G. R., Jensen, J. H., Helpern, J. A., Basilakos, A., Rorden, C., Shih, A. Y., Spampinato, M. V., & Bonilha, L. (2017). Structural plasticity of the ventral stream and aphasia recovery. *Annals of Neurology*, *82*(1), 147–151. https://doi.org/10.1002/ana.24983

Mion, M., Patterson, K., Acosta-Cabronero, J., Pengas, G., Izquierdo-Garcia, D., Hong, Y. T., Fryer, T. D., Williams, G. B., Hodges, J. R., & Nestor, P. J. (2010). What the left and right anterior fusiform gyri tell us about semantic memory. *Brain*, *133*(11), 3256–3268. https://doi.org/10.1093/brain/awq272

Mummery, C. J., Patterson, K., Price, C. J., Ashburner, J., Frackowiak, R. S. J., & Hodges, J. R. (2000). A voxel-based

morphometry study of semantic dementia: Relationship between temporal lobe atrophy and semantic memory. *Annals of Neurology*, *47*(1), 36–45. https://doi.org/10.1002/1531-8249(200001)47:1<36::aid-ana8>3.0.co;2-l

Oldfield, R. (1971). The assessment and analysis of handedness: the Edinburgh Inventory. *Neuropsychologia*, *9*, 97–113.

Papagno, C., Casarotti, A., Comi, A., Gallucci, M., Riva, M., & Bello, L. (2012). Measuring clinical outcomes in neuro-oncology. A battery to evaluate low-grade gliomas (LGG). *Journal of Neuro-Oncology*, *108*, 269–275. https://doi.org/10.1007/s11060-012-0824-5

Papagno, C., Gallucci, M., Casarotti, A., Castellano, A., Falini, A., Fava, E., Giussani, C., Carrabba, G., Bello, L., & Caramazza, A. (2011). Connectivity constraints on cortical reorganization of neural circuits involved in object naming. *NeuroImage*, *55*(3), 1306–1313. https://doi.org/10.1016/j.neuroimage.2011.01.005

Pasternak, O., Sochen, N., Gur, Y., Intrator, N., & Assaf, Y. (2009). Free water elimination and mapping from diffusion MRI. *Magnetic Resonance in Medicine*, *62*(3), 717–730. https://doi.org/10.1002/mrm.22055

Philippi, C. L., Mehta, S., Grabowski, T., Adolphs, R., & Rudrauf, D. (2009). Damage to association fiber tracts impairs recognition of the facial expression of emotion. *The Journal of Neuroscience*, *29*(48), 15089–15099. https://doi.org/10.1523/JNEUROSCI.0796-09.2009

Pisoni, A., Mattavelli, G., Casarotti, A., Comi, A., Riva, M., Bello, L., & Papagno, C. (2019). The neural correlates of auditory-verbal short-term memory: A voxel-based lesion-symptom mapping study on 103 patients after glioma removal. *Brain Structure and Function*, *224*(6), 2199–2211. https://doi.org/10.1007/s00429-019-01902-z

Ratcliff, G., & Newcombe, F. (1982). Object recognition: Some deductions from the clinical evidence. In A. W. Ellis (Ed.), *Normality and pathology in cognitive functions*. Academic Press.

Ross, E. (2008). Sensory-specific amnesia and hypoemotionality in humans and monkeys: Gateway for developing a hodology of memory. *Cortex*, *44*(8), 1010–1022. https://doi.org/10.1016/j.cortex.2008.02.002

Sarubbo, S., De Benedictis, A., Maldonado, I. L., Basso, G., & Duffau, H. (2013). Frontal terminations for the inferior fronto-occipital fascicle: anatomical dissection, DTI study and functional considerations on a multi-component bundle. *Brain Structure and Function*, *218*, 21–37.

Shinoura, N., Suzuki, Y., Tsukada, M., Yoshida, M., Yamada, R., Tabei, Y., Saito, K., Koizumi, T., & Yagi, K. (2010). Deficits in the left inferior longitudinal fasciculus results in impairments in object naming. *Neurocase*, *16*(2), 135–139. https://doi.org/10.1080/13554790903329174

Tusa, R. J., & Ungerleider, L. G. (1985). The inferior longitudinal fasciculus: a reexamination in humans and monkeys. *Annals of neurology*, *18*(5), 583–591.

Zigiotto, L., Vavassori, L., Annicchiarico, L., Corsini, F., Avesani, P., Rozzanigo, U., Sarubbo, S., & Papagno, C. (2022). Segregated circuits for phonemic and semantic fluency: A novel patient-tailored disconnection study. *NeuroImage: Clinical*, *36*, 103149.

How to cite this article: Papagno, C., Pascuzzo, R., Ferrante, C., Casarotti, A., Riva, M., Antelmi, L., Gennari, A., Mattavelli, G., & Bizzi, A. (2023). Deficits in naming pictures of objects are associated with glioma infiltration of the inferior longitudinal fasciculus: A study with diffusion MRI tractography, volumetric MRI, and neuropsychology. *Human Brain Mapping*, 1–17. https://doi.org/10.1002/hbm.26325