eAppendix 5. Generalized Linear Mixed Effect Model

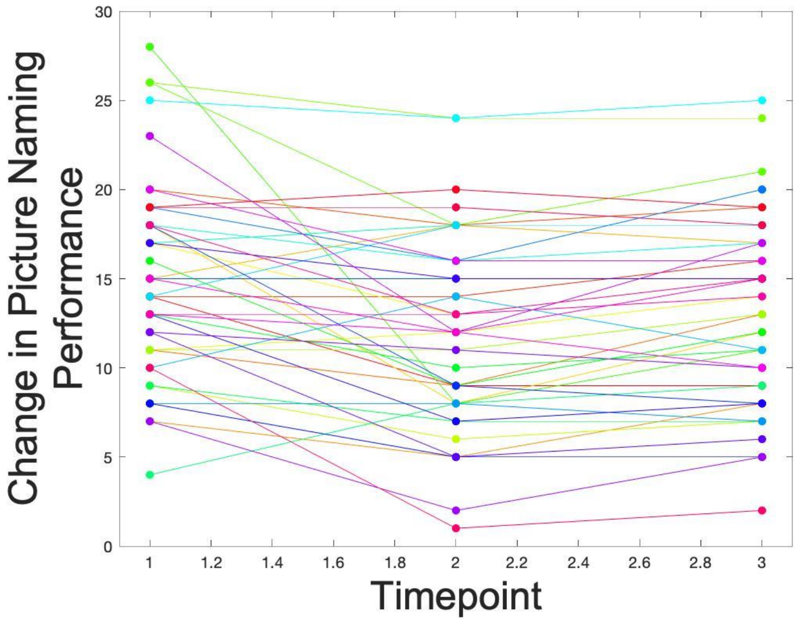
Method

A generalized linear mixed effect model was used to assess the relationship of sub-fascicle damage to RCI-determined outcome. RCI-determined outcome was used to account for outliers present and the non-linear relationship of post-surgery timepoints when looking at the change in language scores. Patients missing neuropsychology at one timepoint were included.

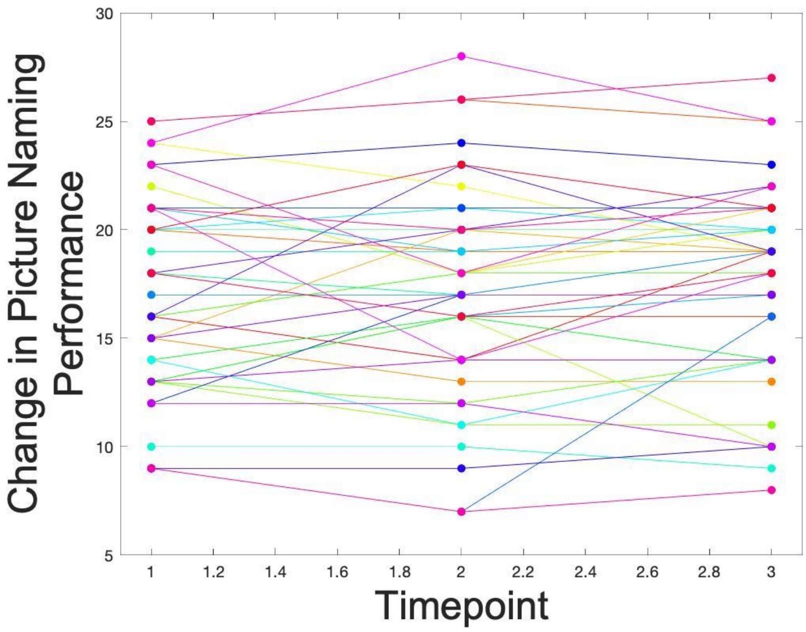
Importantly, when considering for the language-dominant resections cases with missing language data at either 3 (N=8) or 12 (N=20) months postoperatively, the resulting sample size for this all-timepoint comparison of language is significantly reduced (N=44, vs. N=57 for assessment at 3-months). For non-dominant resections, missing data at 3 (N=8) and 12 (N=17) months postoperatively reduces sample size to a similar extent for this all-timepoint comparison (N=45, vs N=54 for assessment at 3-months).

Results

Naming performance scores are shown for the language-dominant (eFigure 3) and non-dominant (eFigure 4) across the three timepoints. For the language-dominant cohort, 19 (43%) and 12 (27%) had RCI-determined significant language decline at 3- and 12-months postoperatively, respectively. For the language non-dominant cohort, 3 (7%) and 2 (4%) had RCI-determined significant language decline at 3- and 12-months postoperatively, respectively. Generalised linear mixed effect models for each of these populations (eTable 11) showed a significant contributing factor of post-operative follow-up and the IFOF-IFG sub-fasciculus in language-dominant and anterior MLF for the non-dominant resection naming change.



eFigure 3. Figure showing the different in picture naming scores preoperatively (preop), 3 months postoperatively (postop), and 12 months postop for the language dominant hemisphere. This shows the typical decline of scores at 3 months postop compared to preop and slight recovery of scores at 12 months postop.



eFigure 4. Figure showing the different in picture naming scores preoperatively (preop), 3 months postoperatively (postop), and 12 months postop for the language non-dominant hemisphere. This shows the typical decline of scores at 3 months postop compared to preop and slight recovery of scores at 12 months postop.

eTable 5. Summary of the final generalized linear mixed-effects models analysis for RCI-determined picture naming decline across both 3 and 12 months and language dominant and non-dominant resections.

Language Dominant Resection				**Language Non-dominant Resection**			
Fixed Effects	*β*	*SE*	*p-value*	*Fixed Effects*	*β*	*SE*	*p-value*
Intercept	2.133	4.046	0.598	Intercept	-2.744	1.671	0.101
Time12	-23.370	2.096	< 0.001	Time12	-0.575	1.092	0.599
Resection Volume	6.053	3.943	0.125	Resection Volume	0.043	0.636	0.946
fMRI LI	-17.598	2.223	< 0.001	fMRI LI	-0.670	0.517	0.195
IFOF-IFG	28.866	3.117	< 0.001	MLF anterior	0.812	0.350	0.020
Random Effects	*σ2*			*Random Effects*	*σ2*		
Participants				Participants			
Intercept	22175			Intercept	<0.001		

Abbreviations: fMRI LI: functional MRI lateralisation index, IFOF-IFG: inferior frontal sub-fascicle of the inferior fronto-occipital fasciculus; SE: Standard Error; Time12: RCI decline at 12 months.

Discussion

Our results show that the results from the main paper carry over when modelling sub-fascicle resection and RCI outcome across both 3- and 12-months. This translates to resection of the inferior frontal sub-fascicle of the IFOF on the language dominant hemisphere and the anterior sub-fascicle of the MLF on the language non-dominant hemisphere is likely to lead to a long-term deficit.

These results are obtained with statistical methods incorporating three time-points and thus theoretically capture the language change more comprehensively. However, the reduced sample size (N=44, vs. N=57) for dominant; N=45, vs N=54 for non-dominant) and addition of an extra parameter to account for post-operative time change (Time12) result in a model that is badly conditioned. Typically, patients who undergo temporal lobe resection have a dip in performance at 3 months, then slightly recover at 12 months (see eFigure 3, and Table 3 for group-level patterns). We have attempted to account for this by using RCI-determined outcome, however, with the reduced sample size this further leads to several events (RCI decline) that is low compared to the number of included parameters and causing class imbalance, leading to further model conditioning issues.

This recovery from 3- to 12-months postoperatively could be based on several factors that are not measured within this paper such as the preoperative plastic potential of the brain, functional connectivity of remaining cortical regions, and the health of remaining white matter connections. It is beyond the scope of this paper to investigate this; future research should aim to identify which patients recover language function and if this 12-month recovery is indicative of continued long-term recovery or even continuing improvement.