# Swallowing function in the chronic stage following stroke is associated with white matter integrity of the callosal tract between the interhemispheric S1 swallowing representation areas

M. Domin [a], G.P. Mihai [a,d], T. Platz [b,c], M. Lotze [a,*]

[a] *Functional Imaging Unit, Diagnostic Radiology and Neuroradiology, University of Greifswald, Germany*
[b] *BDH-Klinik Greifswald, Institute for Neurorehabilitation and Evidence-Based Practice, "An-Institut", University of Greifswald, Greifswald, Germany*
[c] *Neurorehabilitation Research Group, University Medical Centre, Greifswald, Germany*
[d] *AICURA Medical GmbH, Berlin, Germany*

## ARTICLE INFO

## ABSTRACT

Sensorimotor representations of swallowing in pre- and postcentral gyri of both cerebral hemispheres are interconnected by callosal tracts. We were interested in (1) the callosal location of fibers interconnecting the precentral gyri (with the primary motor cortex; M1) and the postcentral gyri (with the primary somatosensory cortex; S1) relevant for swallowing, and (2) the importance of their integrity given the challenges of swallowing compliance after recovery of dysphagia following stroke. We investigated 17 patients who had almost recovered from dysphagia in the chronic stage following stroke and age-matched and gender-matched healthy controls. We assessed their swallowing compliance, investigating swallowing of a predefined bolus in one swallowing movement in response to a 'go' signal when in a lying position. A somatotopic representation of swallowing was mapped for the pre- and postcentral gyrus, and callosal tract location between these regions was compared to results for healthy participants. We applied multi-directional diffusion-weighted imaging of the brain in patients and matched controls to calculate fractional anisotropy (FA) as a tract integrity marker for M1/S1 callosal fibers. Firstly, interconnecting callosal tract maps were well spatially separated for M1 and S1, but were overlapped for somatotopic differentiation within M1 and S1 in healthy participants' data (HCP: head/face representation; in house dataset: fMRI-swallowing representation in healthy volunteers). Secondly, the FA for both callosal tracts, connecting M1 and S1 swallowing representations, were decreased for patients when compared to healthy volunteers. Thirdly, integrity of callosal fibers interconnecting S1 swallowing representation sites was associated with effective swallowing compliance. We conclude that somatosensory interaction between hemispheres is important for effective swallowing in the case of a demanding task undertaken by stroke survivors with good swallowing outcome from dysphagia.

## 1. Introduction

An interaction of a multifocal network involved in processing swallowing in the human brain can be deduced from functional imaging studies and from impairments in swallowing following sudden brain damage. Functional representation of swallowing in healthy volunteers shows a bilateral complex pattern that includes cortical representation sites (pre- and postcentral gyrus, insula, supplementary motor area and cingulate cortex, and temporal pole), but also subcortical (dorsal brain stem, thalamus and basal ganglia) and cerebellar representation (Hamdy et al., 1999; Mosier and Bereznaya, 2001; Toogood et al., 2005; Humbert and Robbins, 2007; Malandraki et al., 2009; Teismann et al., 2009). In addition, age-related changes in swallowing representation have been reported (Malandraki et al., 2010; Windel et al., 2015). In acute stroke, aspiration, as identified with videofluoroscopy, was present in 38% of patients (Daniels et al., 1998). However, a large amount of these patients shows considerable recovery of swallowing performance after 6 months, leaving 11–13% of these patients dysphagic (Mann et al., 1999).

Actual recovery mechanisms in patient groups are difficult to evaluate because imaging is often performed in a recumbent position, which hampers swallowing for dysphagic patients in particular. In addition, an increase in functional activation in patients - when compared to HCs -

does not necessarily mean that areas with higher fMRI-activation are relevant to recovered function. This is a hotly-discussed issue in hand motor recovery following a stroke (for early contributions see Ward et al., 2003). Li et al. (2009) showed that recovery of dysphagia following a stroke is associated with cerebral activation in cortical swallowing areas compensating for increased effort or recruited areas of the intact hemisphere. Mihai et al. (2016) demonstrated increased contra-lesional S1-activation in the somatotopic swallowing representation seen in recovered dysphagia patients. In addition, they reported that increased recruitment of the non-affected hemisphere S1 swallowing representation area was associated with swallowing impairment at the time of admission (BODS).

Persisting dysphagia has a high impact on the patient's wellbeing and quality of life (Moloney and Walshe, 2018). It causes enormous healthcare costs and increases the risk of dying with pneumonia after aspirations (Marin et al., 2020). Cortical lesions associated with post-stroke dysphagia that still persist after 6 months have most frequently been reported for the insula (Daniels and Foundas, 1999; Riecker et al., 2009), the frontal operculum (Meadows, 1973), and the primary sensorimotor cortex (Daniels and Foundas, 1999). Moreover, brainstem lesions [predominantly in the dorsal part, which coordinates reflexive swallowing function (Lang, 2009)] can often lead to profound dysphagia (Vuilleumier et al., 1995). In addition, the presence of bilateral lesions is an important predictor for poor swallowing outcome after 6 months (Lee et al., 2020).

Although the widespread pattern of areas relevant to swallowing function derived from functional imaging and patient lesion data have been described extensively, there is a discrepancy in the number of studies investigating the role of structural connectivity. In particular, there are very few studies that apply modern quantification methods, such as fractional anisotrophy (FA; the most suited parameter for quantification of demyelization; see (Ding et al., 2021)) on white matter integrity in dysphagic patients following a stroke (Alvar et al., 2021). In the case of dysphagia caused by a stroke, several white matter structures might be of special interest: the corticospinal tract (CST) between the sensorimotor swallowing representation areas and the internal capsule, the callosal tracts interconnecting the sensorimotor centers between hemispheres, and the areas interconnecting the brainstem to swallowing centers. Some studies have investigated the association between the integrity of the CST and the recovery of swallowing following a stroke (Kim et al., 2016; Mihai et al., 2016). In our previous study of patients who had suffered a unilateral stroke, we reported an association between comprehensive swallowing function (swallowing compliance of a given bolus during a lying position) and CST asymmetry between the affected and unaffected hemispheres (Mihai et al., 2016). We now intended to investigate the relevance of the integrity of swallowing-related callosal fibers for partially restituted swallowing function in the same group of patients. A recent review concerning the role of white matter in the neural control of swallowing (Alvar et al., 2021) identified two studies of the corpus callosum's role in swallowing impairment, both of which used only lesion mapping, with no individual quantification of white matter fibers (Li et al., 2014; Mourão et al., 2017). In a prior characterization of somatotopic fibers interconnecting the two hemispheres via the corpus callosum, we described a method that we believe allows for more exact quantification of these fibers, at least in the case of M1 (Domin and Lotze, 2019). Astonishingly, there is no existing study that investigates intercallosal fiber tract localization for S1 swallowing connectivity. Given the special impact of somatosensory function on swallowing and its recovery (Cabib et al., 2016), we propose that somatosensory fibers should be included in addition to motor fibers, in order to test for their somatotopic relevance to recovered swallowing function. Callosal fibers interconnecting the bilateral primary motor cortices (M1) evince a strict somatotopic arrangement, with the lower and upper limb interconnecting tracts more posterior and the head/face, intermediate, and tongue/larynx interconnecting tracts more anterior (Domin and Lotze, 2019). For the recovery of motor function following a

stroke, the importance of the integrity of somatosensory function has been demonstrated repeatedly (for an overview see (Lotze et al., 2019)). This is especially true for the recovery of swallowing function following stroke-induced dysphagia, and many evidence-based treatment options are based on somatosensory stimulation techniques (Hamdy et al., 1998; Muhle et al., 2021). Increased somatosensory demand in post-stroke dysphagia results in an increase of fMRI activation magnitude of the contra-lesional S1 (Mihai et al., 2016). This underlines the importance of additional analyses of somatosensory interaction integrity for recovered swallowing function.

The questions that we investigated were as follows:

1. What is the location of the callosal tracts interconnecting the postcentral somatotopic representation of swallowing?
2. Are the diffusion-related properties of the pre- and postcentral fibers interconnecting the somatotopic representations of swallowing decreased for the patient group investigated here?
3. Is integrity of callosal fibers interconnecting pre- and postcentral swallowing representations associated with the swallowing compliance in post-stroke dysphagic patients?

## 2. Methods

### 2.1. Participants

Patients with a single ischemic cerebral infarction who had recovered from neurogenic post-stroke dysphagia were recruited from the local neurorehabilitation center (BDH-Klinik Greifswald, Germany). All patients who were severely dysphagic during the rehabilitation period (within the last 3 years prior to the study) were invited to a follow-up swallowing function assessment. All investigations on dysphagia severity were performed by a specialized speech therapist. Upon admission to the rehabilitation hospital, all patients underwent the following investigations: a clinical examination, a water-swallowing test (Daniels et al., 1997), the Bogenhausen Dysphagia Score [BODS, consisting of BODS1 and BODS2 (Schiele et al., 2015), and the swallowing impairment scale (Prosiegel et al., 2002), together with the functional communication measure [FCM, from the American Speech-Language-Hearing Association (Association, 2003)]. The clinical dysphagia assessment was complemented by videofluoroscopic dysphagia testing in a proportion of patients, using a standard clinical protocol (Bartolome and Schröter-Morasch, 2013). Whereas BODS1 is scored based on swallowing of saliva, BODS2 is scored based on the intake of food. BODS 1 and 2 are combined to arrive at a common BODS dysphagia score. The score expresses dysphagia severity thus: 2: no dysphagia, 3–4 slight dysphagia, 5–6 moderate dysphagia, 7–10: medium dysphagia, 11–14: severe dysphagia; 15–16: most severe dysphagia. The BODS was validated by Starrost and colleagues (Starrost et al., 2012). The BODS was retested in the week when the patient was discharged from the rehabilitation hospital which was in fact not more than two days apart from the MRI measurements. In addition, patients were retested on the day when fMRI measurements were taken in order to ensure that swallowing function did not deviate from the at-discharge measurement, using the clinical swallowing examination as part of the NOD, and the water-swallowing test. Risk for aspiration during swallowing in the MRI scanner should be kept as low as possible, in accordance to our ethical framework. Furthermore, a MRI cinematography sequence enabled a view of bolus transportation similar to videofluoroscopy (Mihai et al., 2014) in patients in a supine position during scanning. Patients with a single infarction were included; as a result, only unilateral and uni-temporal stroke patients were selected. Additional exclusion criteria included lack of capacity to consent due to neuropsychological, linguistic, or psychiatric disorders. Every participant provided informed, written consent. Procedures were approved by the Ethics Committee of the Medical Faculty of The University of Greifswald (registration number BB 101/08). Seventeen patients (mean age and standard deviation

56.1 ± 15.6 years, 25–72 years, 6 female; on average 59 ± 42 weeks after their stroke) were included in the study. Based on the Edinburgh Handedness Inventory [EHI; (Oldfield, 1971)] 15 subjects were right-handed and 2 were left-handed before stroke onset (Table 1). Lesion location had been provided in Table 1; lesion size was 30 ± 42 ml on average. Details on inpatient neurorehabilitative intervention have been previously described (Mihai et al., 2016).

The control group consisted of 17 healthy participants (mean age and standard deviation 54.5 ± 17.5 years, 25–72 years, 8 female), who had no history of dysphagia. The fMRI results from this data were also included in a previously published manuscript on the relationship between age differences and swallowing representation (Windel et al., 2015). We screened controls to exclude any neurological or psychiatric disease (e.g., epilepsy or a history of strokes) in order to exclude disturbances or other diseases (e.g., chronic pain, chronic medical conditions, or motor, sensory, swallowing, speech, or otolaryngologic function impairment), and checked for medication (antihypertensive indicated in ten participants). All controls were right-handed based on the EHI.

## 2.2. Testing of swallowing compliance

Swallowing compliance was measured while the patient was recumbent on the MRI table, as had been applied in our previous study (Mihai et al., 2016). Swallowing timing and task compliance was controlled by thyroid cartilage movement measurements made using a pneumatic cushion (Siemens MRI safe respiration bellows) placed around the participant's neck (Toogood et al., 2005). The pressure exerted by the thyroid cartilage on the cushion was transformed into an electrical signal measured using a biosignal recorder (Varioport-b; Becker Meditec, Karlsruhe, Germany). The total number of "effective" swallow events determined using the pneumatic cushion was then divided by the expected number (20). A compliance score of 1.0 meant that the patient swallowed the expected 20 times in one run, and any deviation from 20 swallows (for instance more than one swallowing cartilage excursion to the bolus or no swallowing response) resulted in a lower compliance score. Other deflections in the cushion signal were also counted as non-compliance; these included movements such as coughing or throat clearing. Compliance thus refers to the ability to

**Table 1**
Patient characteristics including age at MRI study, sex, time since stroke at MRI, affected hemisphere, volume of lesion in cubic centimeters, location of lesion, ASHA and SBS for dysphagia scores at admission, BODS sum of scores at admission and discharge and compliance of swallowing tested at the MRI.

| Patient | Age at MRI | Sex | Time since [weeks] | Lesion side | Lesion size (cm³) | Lesion Location | Hospital stay (weeks) | BODS Sum of scores admission | BODS Sum of scores discharge | ASHA admission | SBS admission | swallowing compliance |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 31 | M | 15 | R | 0.88 | sc: medial pons | 15 | 16 | 2 | 1 | 6 | 0.5 |
| 2 | 40 | M | 53 | R | 112.57 | c: complete arteria media | 13 | 4 | 2 | 6 | 2 | 0.6 |
| 3 | 38 | M | 54 | R | 39.54 | sc: internal capsule | 7 | 11 | 2 | 1 | 6 | 0.7 |
| 4 | 67 | M | 156 | L | 74.22 | c: fronto-parietal | 24 | 9 | 2 | 2 | 4 | 0.2 |
| 5 | 54 | M | 157 | R | 22.54 | sc: cerebell. Hem. / vermis | 6 | 11 | 2 | 1 | 6 | 0.85 |
| 6 | 70 | M | 67 | L | 62.63 | c: parietal, posterior insula | 15 | 3 | 2 | 5 | 2 | 0.35 |
| 7 | 59 | M | 75 | R | 1.82 | sc: medial pons, brainstem | 22 | 16 | 3 | 1 | 6 | 0.55 |
| 8 | 66 | M | 35 | L | 5.86 | sc: insula, putamen | 13 | 3 | 2 | 5 | 2 | – |
| 9 | 70 | M | 45 | R | 3.48 | sc: pyramidal tract | 15 | 3 | 3 | 4 | 2 | 1 |
| 10 | 70 | F | 32 | R | 14.71 | sc: temporal | 12 | 6 | 2 | 3 | 4 | 0.85 |
| 11 | 56 | M | 42 | L | 134.54 | c/sc: complete art. media | 14 | 5 | 2 | 4 | 3 | 0.35 |
| 12 | 72 | F | 4 | L | 0.07 | sc: medial brainstem | 4 | 8 | 2 | 3 | 4 | 0.9 |
| 13 | 40 | M | 22 | L | 14.11 | sc: medial cingulate | 14 | 11 | 2 | 1 | 6 | 0.85 |
| 14 | 25 | F | 87 | L | 5.82 | c: precentral gyrus | 20 | 3 | 2 | 5 | 2 | 0.85 |
| 15 | 55 | F | 49 | R | 3.4 | sc: thalamus, putamen, nucl.caud. | 8 | 3 | 2 | 5 | 2 | 1 |
| 16 | 71 | M | 41 | L | 4.52 | sc: ant. cerebell. hem. | 6 | 3 | 2 | 6 | 1 | 0.95 |
| 17 | 69 | M | 66 | R | 15.55 | c: precentral gyrus | 19 | 16 | 2 | 1 | 6 | – |

BODS: Bogenhausener Dysphagia Score (Schiele et al., 2015) quantifies the degree of dysphagia with a maximum sum of scores of 16. A discharge a score between 2 and 3 stands for "no" to "slight" dysphagia. Swallowing compliance refers to the ability to swallow in response to 20 boli as provided by perfusor intraorally; for two patients these data was missing due to pneumatic cushion signal dropout; please refer to methods for further details. Time since stroke refers to the MRI-measurement and therefore to the BODS score at discharge (provided in weeks). Hospital stay indicates the number of weeks between the BODS at admission and at discharge. R: right, L: left; M: male, F: female; c: cortical, sc: subcortical; int.: internal; cerebell. hem.: cerebellar hemisphere; art. media: aretria cerebri media; nucl. caud.: neucleus caudatus; ant.: anterior; ASHA: functional communication measure [FCM, from the American Speech-Language-Hearing Association; (ASHA 2003)]; SBS: Schluck-beeinträchtigungsskala" (SBS) based on the criteria developed by (Prosiegel, 2002).

follow the protocol of a highly demanding swallowing action in response to a perfusor. Specifically, the patient was asked to swallow 2 ml water in one bolus on a visual signal (change from blue to green light) over a period of 4 min (Mihai et al., 2014). We inserted a variance (different time onsets) for the swallowing onset signal during baseline. A higher compliance score means that the participants performed the task more accurately (swallowing a single bolus on time with an effective swallowing movement).

## 2.3. MRI data acquisition

A 3 T MRI scanner (Siemens Verio, Erlangen, Germany) with a 32-channel head coil was used to record MRI data. A structural T1-weighted anatomical image was acquired for each subject (magnetization-prepared rapid gradient echo, TR 1690 ms, TE 2.52 ms, flip angle $9°$, FoV 250 mm, voxel size $1 \times 1 \times 1 \text{ mm}^3$, parallel acquisition using a k-space based algorithm [GRAPPA] factor 2, matrix $256 \times 256$, sagittal orientation, 176 slices, ascending). In addition, a diffusion-weighted imaging (DWI) data set was measured (TR 10500 ms, TE 107 ms, flip angle $90°$, FoV 230 mm, voxel size $1.8 \times 1.8 \times 2.3 \text{ mm}^3$, matrix $128 \times 128$, 55 slices). The sequence used was the standard MDDW (multi-directional diffusion-weighted) sequence found on Siemens MRI scanners. A diffusion weighting of $b = 1000 \text{ s/mm}^2$ was applied and 64 diffusion weighting gradient directions were chosen. A reference image with no diffusion weighting ($b = 0 \text{ s/mm}^2$) was also recorded. A reverse phase encoded image was not recorded. Lesions were manually drawn by an experienced neuroscientist/neurologist [ML; using MRIcron (Rorden et al., 2007)] on structural T1-weighted images, adding the Flair-images if necessary for lesion localization, and confirmed by medical reports. A lesion overlap map of all patients included is depicted in Supplementary Fig. 1.

## 2.4. DWI preprocessing and analysis

Diffusion-weighted data and anatomical T1-weighted data were processed as described in Fig. 1. Afterwards, a quality check took place utilizing FSL's eddy QC tools (Bastiani et al., 2019). All QC-related parameters, such as subject movement, were well within required limits.

## 2.5. Tractography-based regions-of-interest

Because of the patients' MRI data being affected by stroke lesions, an individualized tractography was not advisable. Therefore, tractography-based regions-of-interest were created with the aid of a large sample consisting of young, healthy participants. The specific method is described in detail elsewhere (Domin and Lotze, 2019). In addition, the following procedure was conducted: the preprocessed diffusion-weighted data of the Human Connectome Project, comprising 1065 datasets, was used to perform probabilistic tractography. For this purpose, ROIs related to swallowing function were derived from the aforementioned fMRI study (Mihai et al., 2016) by extracting cortical BOLD activation maps depicting the motor and sensory aspects of swallowing function. These maps were separated by masking for pre- and postcentral gyri on each hemisphere, resulting in four gray matter ROIs: M1 right and left hemisphere, S1 respectively. These ROIs were projected into the white matter, by iteratively dilating and masking for white matter, until well-defined WM ROIs for the swallowing areas were created. Additionally, possible swallowing-related ROIs of the pre- and postcentral cortical areas (head/face areas) were derived from the Brainnetome Atlas [BNA; (Fan et al., 2016)] and processed similarly.
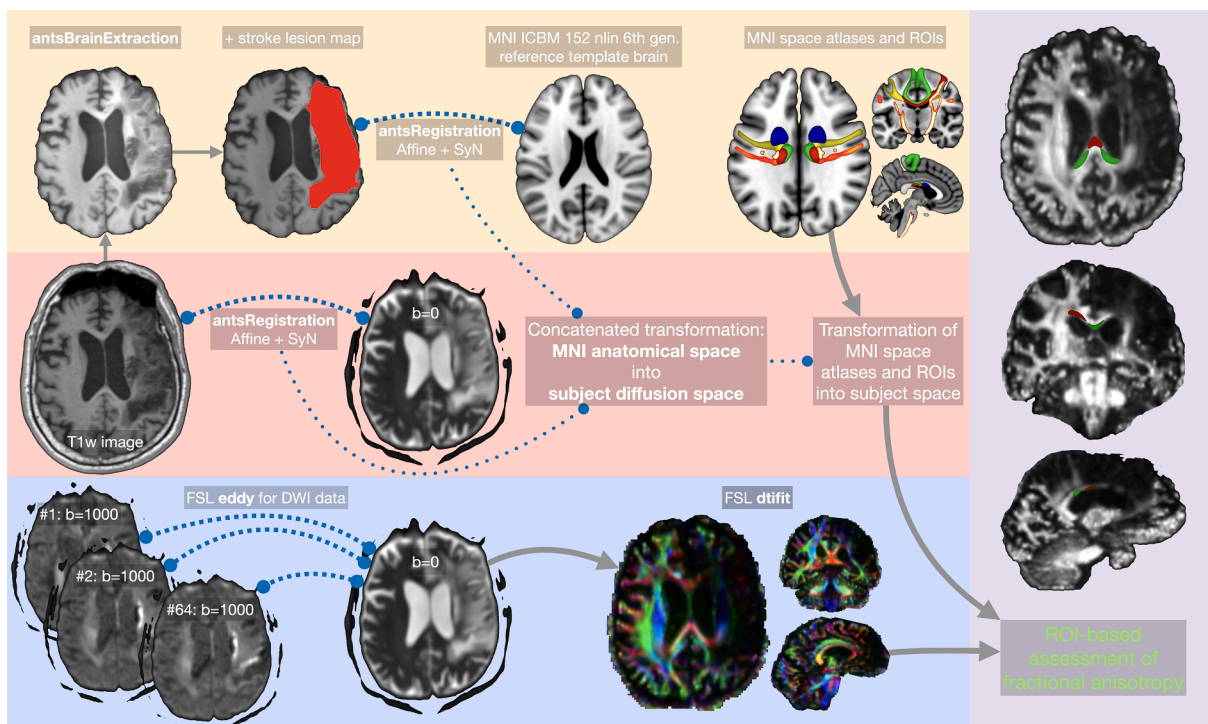


**Fig. 1.** Data processing was performed using FSL (v6.0.4, Analysis Group, FMRIB, Oxford, UK) and the Advanced Normalization Tools (ANTs, v2.3.5.dev212-g44225); (Avants et al., 2011; Tustison et al., 2009). **Upper row** (yellow): T1w images were brain extracted and (non-)linearly registered to MNI152 NLIN 6th gen. template space including the patients' lesion masks to improve registrations. **Middle row** (red): T1w images were bias field corrected, denoised and (non–) linearly registered to the DWI b0 image. A concatenated inverse transformation (MNI -> T1w -> DWI) for transformation of ROIs or atlases from MNI space into subject space was calculated. **Lower row** (blue): Eddy current-related distortions and subject movement in the DWIs were corrected (Andersson and Sotiropoulos, 2016), outlier slices were replaced (Andersson et al., 2016). The diffusion tensor and diffusion-related indices e.g., FA, were calculated. A proper diffusion tensor calculation was verified by visualizing the first eigenvector of the diffusion tensor (color-coded: x = red, y = green, z = blue) (lower row rightmost) **Right column** (pink): Transformed ROIs from MNI space into subject space were used for ROI-based assessment of fractional anisotropy.

These ROIs were inverse transformed from MNI reference space into individual subject space and used as seed ROIs for FSL probtrackx (e.g., tract M1 left to M1 right). The resulting tractograms were transformed into MNI reference space, spatially averaged, thresholded at 25%, masked by a corpus callosum mask and finally scaled to 1 (division by maximum intensity value). The tractograms were filtered by a deterministic trackable directions mask [dTDM; (Volz et al., 2018)]. The dTDM assigns the number of distinctly oriented diffusion directions to each voxel, resulting in directionality compartments. Each compartment contains a different statistical distribution of diffusion properties such as fractional anisotropy's mean and variance. Filtering by the dTDM separates these distributions and thereby improves statistical comparisons. The masked tractograms were then transformed into the space of patients as well as healthy controls and were subsequently used as ROIs for assessing callosal FA as follows: the previously created FA maps were masked by these tractograms and a weighted mean of fractional anisotropy was calculated for each masked FA map.

### 2.6. Statistical evaluation

All statistical comparisons were performed using SPSS, Version 21. As we had no hypothesis for differences between tracts, we calculated two-sample t-tests between HCs and dysphagia patients in order to compare FA values averaged over callosal tracts interconnecting M1 and S1 somatotopic representation fields separately. Pearson correlation was applied to test for relevant associations between a challenging swallowing compliance and these callosal tracts. Partial regression analysis was performed in order to control for effects of age and time elapsed since the stroke.

## 3. Results

### 3.1. Localization of callosal fibers interconnecting M1/S1 swallowing representation:

As depicted in Fig. 2, interconnecting callosal tract maps were well spatially separated for the pre- and postcentral seeds (M1 and S1) but overlapped for the Brainnetome atlas (head/face area) and the healthy swallowing representation (fMRI seeds).

### 3.2. Testing of FA-differences between participant groups

FA in both M1 and S1 swallowing representation-connecting callosal tracts was decreased for patients when compared to healthy controls. In detail, patients showed an FA of $0.65 \pm 0.079$ for postcentral and $0.63 \pm 0.092$ for precentral seeds, whereas HCs showed an FA of $0.74 \pm 0.041$ for postcentral and $0.71 \pm 0.046$ for precentral seeds. FA differences between groups for the postcentral (S1) somatotopic seeds where $t(32) = 4.09$; $p < 0.001$ and for precentral (M1) somatotopic seeds $t(32) = 3.15$; $p < 0.005$.

### 3.3. Associations between callosal FA and challenging swallowing compliance

Compliance in the 17 HCs averaged to $0.86 \pm 0.25$, whereas patients showed an average of $0.70 \pm 0.26$. In a one-sided comparison, the HCs showed slightly better swallowing compliance than patients ($t(30) = 1.75$; $p = 0.046$). The integrity of callosal fibers interconnecting S1 swallowing representation were significantly associated with swallowing compliance ($r(15) = 0.63$; $p = 0.012$; Fig. 3A). This was not the case for the M1 seeds ($r(15) = 0.093$; n.s.; Fig. 3B). This effect for the
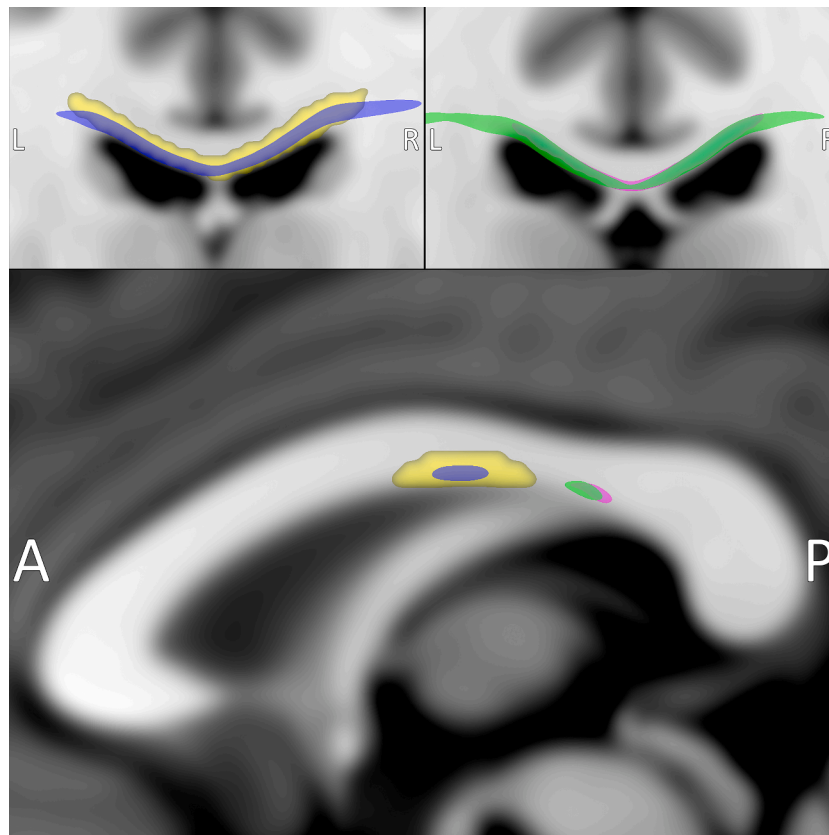


**Fig. 2.** Coronal (top; left for precentral, right for postcentral intercallosal fibers) and sagittal (bottom) slices for illustrating the location of intercallosal fibers. Yellow: precentral head/face area from the BNA; blue: precentral swallowing representation area from the healthy participants in that study. Pink postcentral head/face area from the BNA; green: postcentral swallowing representation area from the healthy participants in that study.
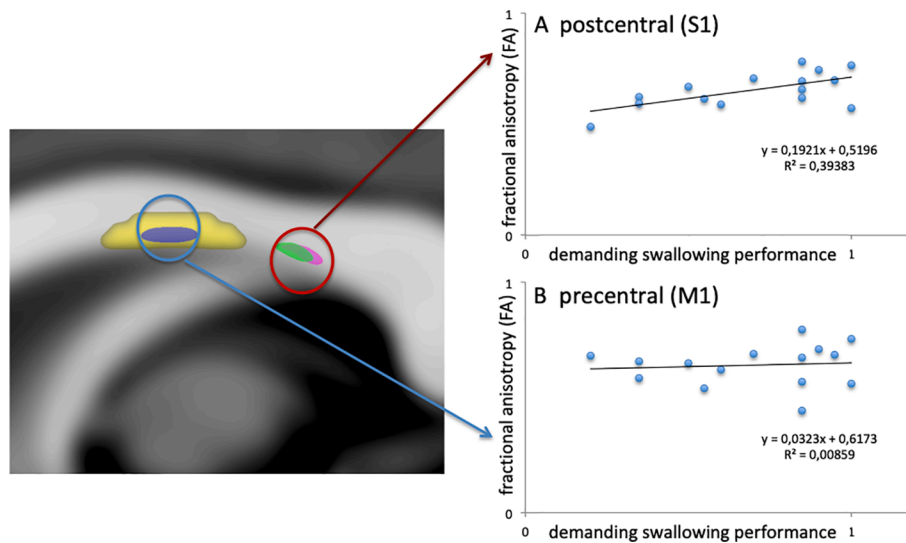
**Fig. 3.** Left part of the Figure: colored blobs indicating the precentral (yellow: BNA; blue: representation from functional study) and postcentral (pink: BNA; green: representation from functional study) ROIs for mean FA. Right side of the figure: plots of correlation analyses: S1 mean FA was positively associated with swallowing response (A; top) whereas M1 mean FA was not (B; bottom).

integrity of callosal fibers interconnecting S1 swallowing representation survived correction for age (r(12) = 0.53; p = 0.016) and for time since stroke (r(12) = 0.61; p = 0.021).

## 4. Discussion

### 4.1. Embedding our results in the current state of research

In this study, we have demonstrated that the interconnecting callosal tracts are spatially well-separated for the pre- and postcentral swallowing representations derived from generic atlas ROIs as well as from a task-related functional study. In addition, we observed a strong overlap for atlas-derived pre- and postcentral areas and their matched swallowing-related counterparts derived from healthy participants' data. This high overlap between samples is astonishing, since in this study we used the somatosensory head/face representation (Brainne-tome Atlas) for one cohort and the swallowing representation (HCs of this sample) for the other. This had to be done as there is a lack of data on somatosensory representation of the interconnecting callosal tracts involved in swallowing function itself. Prior studies investigating the role of the corpus callosum in swallowing impairment (Li et al., 2014; Mourão et al., 2017) only used lesion mapping, with no individual quantification of white matter fibers. Therefore, the elaborate approach used in this study is of great importance to the research field relating to biomarkers for dysphagia following brain damage (Alvar et al., 2021).

Secondly, FA in both callosal tracts connecting M1 and S1 swallowing representations was decreased for patients when compared to healthy controls. This was no general and unspecific white matter effect between patients and controls, since the structural integrity of the pyramidal tract of the unaffected hemisphere in these patients measured by fractional anisotropy showed no statistical difference relative to the matched hemisphere in healthy participants (Mihai et al., 2016). Therefore, the biomarker seen here was specific to the patients investigated.

Thirdly, we observed that the integrity of callosal fibres interconnecting postcentral but not precentral representation areas for swallowing function was highly associated with effective swallowing compliance during a challenging swallowing task. Interestingly, functional oropharyngeal sensory disruption interferes with the cortical control of swallowing even in HCs (Teismann et al., 2007). Integrity of somatosensory function – as processed in the postcentral gyrus – has been identified as an important modulator for swallowing recovery

(Cabib et al., 2016). In addition, promising treatment options for training dysphagic patients can be developed based on somatosensory training and stimulation techniques (Hamdy et al., 1998; Muhle et al., 2021). The particular association that we have found with challenging swallowing compliance is an indication that this task requires a precise interaction between somatosensory information processing in both hemispheres. This has been shown to be independent of age and of time elapsed since the stroke, which has been identified as specifically modulating FA [age: (Lawrenz et al., 2016); time elapsed since stroke: (Kancheva et al., 2022)].

### 4.2. Methodological advances suitable for further research perspectives

Our methods for identifying these masks were highly elaborate, as we used data from an optimal database (HCP cohort) for the process. In addition, we complemented the location of the masks with our clinically easy performable individual DTI investigations (Lotze et al., 2019; Mihai et al., 2016). The large overlap of pre- and postcentral callosal masks derived from both sources and measurement techniques offers possibilities for their broader application. Our previous publication on precentral callosal masks between somatotopic representation areas (lower and upper limbs, head/face, tongue/larynx) had already established a basis for broader application (Domin and Lotze, 2019). The postcentral seed-based transcallosal tracts investigated in this study can now be used as masks for further investigations. Further studies using our masks might have the following objectives:

(1) as a biomarker for prognostic purpose (for upper limb recovery following stroke (Stinear et al., 2012)),
(2) stratification of participants for treatment groups in intervention studies (Stinear et al., 2014),
(3) individualized selection of treatment options in order to increase outcome.

### 4.3. Limitations

Monocenter stroke studies are often hampered by low patient numbers, and this has also been the case in this study. However, recruitment via a neurorehabilitation hospital that treats high numbers of patients with dysphagia following a stroke, plus considerable funding (see Acknowledgements) enabled us to recruit this cohort of dysphagia patients who were capable of swallowing a water bolus in a recumbent

position in the MRI. Since the inclusion criteria comprised the ability to perform the comprehensive swallowing task, we did not include patients in this study who showed more severe impairments at the time of investigation. Furthermore, one patient did not improve in swallowing performance when scored with the BODS. Also, considering the quite homogeneous scoring of all patients at time of discharge from hospital (all results lying between 2 and 3) the BODS might not be sensitive enough to adequately score swallowing outcome. However, the usage of swallowing compliance might also not be optimal, as this only measures the number of swallows needed to swallow the 2 ml bolus. Therefore, it does not relevantly express the complexity of swallowing performance. In addition, we did not further validate that procedure. Future studies might also enroll patients with a less favorable outcome and use optimized performance measures at the time of the MRI scan. Additionally, this study does not include longitudinal MRI data, since the initial purpose of the dysphagia study was to investigate biomarkers for swallowing function for dysphagia following stroke, including an fMRI-investigation of swallowing in a lying position. Further studies might apply a design that allows for considerations about changes of the brain's white matter over time. In addition, our study included patients with infratentorial and suptratentorial lesions, which might have an impact on our results.

## 5. Conclusion

In this study, we have demonstrated the importance of intact transcallosal interaction in the somatotopic fibers of the postcentral gyrus for challenging swallowing compliance. Somatosensory callosal somatotopic masks can now be obtained by other researchers on GitHub (https://github.com/NitramNimod/CorpusCallosumParcellation).

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.nicl.2022.103093.

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