Cerebral activation related to shoulder apprehension in patients with glenohumeral instability: a ten years follow-up

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Background: Ten years ago, we presented evidence that shoulder apprehension is linked to reorganization in brain activation, involving areas associated with motor control, cognitive control of motor behaviour, as well as anxiety and emotional regulation.

Purpose: The present study investigates whether a decade-long follow-up after surgery is connected to the normalization of apprehension-related brain activations.

Methods: Ten patients (average age 38.6±9.7 years) who had undergone shoulder stabilisation and nine controls (average age 40.6±2.9 years) from the original study (Y0) took part in this ten-year follow-up prospective comparative study (Y10). We replicated the same experimental procedure, which included functional magnetic resonance imaging (fMRI) with videos designed to induce shoulder apprehension, and clinical assessments.

Results: In terms of task-related functional imaging, patients exhibited a complete reduction in apprehension-related brain activations at Y10 compared to Y0. In terms of functional connectivity, the differences observed in several brain networks at Y0 between patients and controls nearly completely normalized at Y10. There were no significant structural differences in brain grey matter or white matter observed between Y0 and Y10 in both patients and controls. Regarding clinical parameters, patients showed improvement at Y10 compared to Y0 across all scores.

Conclusion: In patients with shoulder apprehension, apprehension-related brain activation patterns showed near-complete normalization ten years after successful shoulder stabilisation, although subjective apprehension remained higher than in healthy controls.

What this study adds to existing knowledge: Time allows near-complete normalization after successful shoulder stabilization. For a quicker return to sports, these results support the use of a comprehensive multimodal approach. This approach includes, on one hand, shoulder 'reafferentation', which involves proprioception, mirror therapy, and even cognitive-behavioural approaches. On the other hand, it suggests implementing improved surgical stabilization techniques to reduce persistent micro-motions.

How this study might affect research, practice, or policy: This study may stimulate further research into the neurocognitive mechanisms of shoulder apprehension and encourage clinicians to integrate psychological readiness into rehabilitation and return-to-sport decision-making. It also highlights the potential for future research on incorporating cognitive-behavioral interventions into postoperative rehabilitation protocols for selected patients.

Study Design: Prospective comparative longitudinal study

Level of Evidence: Level II

Keywords: Shoulder; Functional magnetic resonance imaging (fMRI); Long-term results; Complications; PROMs; Brain; Recovery; Neurological lesion; Central nervous system.

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Introduction

Apprehension is defined as anxiety, fear, and motor resistance, and clinically elicited as fear of imminent dislocation when placing the arm in abduction and external rotation [1]. It is the most preponderant shoulder function dependent reason for inability to return to sport [2]. These aspects represent essential cognitive processes and can be investigated using functional magnetic resonance imaging (fMRI). This technique measures brain activity by detecting changes associated with blood flow, relying on the principle that cerebral blood flow increases in tandem with neuronal activity in the same region [3].

Previously, our research group utilized fMRI with visual apprehension stimulation to investigate neuronal connections and cerebral changes induced by shoulder dislocation [4]. This investigation revealed specific modifications in brain networks within the primary sensory-motor areas (related to motor resistance), dorsolateral prefrontal cortex (involved in cognitive control of motor behaviour), dorsal anterior cingulate cortex/dorsomedial prefrontal cortex, and anterior insula (associated with anxiety and emotional regulation) [4]. All of those regions are involved in the cognitive control of motor behaviour [5]. A structural alteration in white matter's integrity was also demonstrated in the left internal capsule and partially in the thalamus [6], suggesting a pathological structural plasticity due to the over-connection of the white-matter's fibres in the motor pathway. When analysing the evolution of brain activity in these areas in patients both before and one year after their stabilisation surgery, we observed that activity in the left motor and premotor cortex, somatosensory cortex, lateral occipital cortex and para-hippocampal gyrus were decreased but was still present to the result of task-related GLM analysis, indicating possible brain recovery [7]. This cerebral evolution coincided with an improvement in functional scores [7].

The purpose of the present study was to re-assess ten years after the stabilisation's surgery and describe the fMRI findings and clinical outcomes of the same cohort of patients and controls [4][7]. The hypothesis of this study was that time would finally allow normalisation of brain activations.

Materials and Methods

Study design and population

The same patients who had undergone shoulder stabilisation for a unilateral anterior glenohumeral instability, and nine age-matched controls of an initial prospective comparative study [4][6][7] were considered potentially eligible for inclusion in this ten years follow-up study. Exclusion criteria were 1) left-handed patients and controls [8][9], 2) hyperlaxity defined as more than 85 degrees of external rotation elbow against waist [10], or hyperabduction over 105 degrees [11], 3) bidirectional or multidirectional instability, 4) revision surgery, 5) new episode of dislocation since initial study, 6) major medical disorders (cancer, cardia illness), sustained head injury, 7) psychiatric or neurologic disorders, 8) alcohol or drug abuse, 9) use of psychotropics/stimulant and beta-blockers on a regular basis, 10) claustrophobia, 11) pacemaker or any other implanted electronic device.

All participants had undergone a fMRI at baseline. Only right-handed male participants were included to enhance cohort homogeneity and reduce potential sources of variability in functional imaging analyses. Recent studies have demonstrated substantial interindividual variability in functional cerebral lateralization across several cognitive domains, including body and scene perception [8][9]. Restricting the cohort to right-handed individuals was therefore intended to standardize the analysis and limit potential bias in the interpretation of functional imaging findings.

Patients underwent surgical stabilisation performed by one fellowship-trained shoulder surgeon (AL), followed by a new fMRI one year postoperatively. The control group consisted in healthy volunteers with no history of shoulder injury or glenohumeral instability.

Ethics approval and patient consent

This study was conducted in accordance with the principles of the Declaration of Helsinki in a monocentric facility after approval by the local ethic committee [CCER (Commission Cantonal d'Ethique de la Recherche) 2022-00135] and registered at ClinicalTrials.gov (identifier NCT06157788) and at Registry of all Projects in Switzerland (RAPS identifier CCER 2022-00135). Every patient enrolled provided a written informed consent for the use of their data.

Surgical Technique

In our cohort, seven patients underwent open Latarjet glenohumeral stabilisation, two patients underwent arthroscopic Bankart stabilisation and one patient underwent an arthroscopic Bankart procedure associated with a Hill-Sachs remplissage.

Primary and secondary outcomes

Primary outcomes were modifications in task-related brain activation and modifications in functional connectivity brain activation in patients ten years *vs.* baseline. The same analyses were also performed in controls for comparison to be able to disentangle potentially confounding effects related to re-testing after ten years. Secondary outcomes included

structural brain changes in grey matter and white matter. In addition, the following baseline characteristics were assessed: age, sex, shoulder side, limb dominance, and various region and condition specific or non-specific scores.

fMRI task

The paradigm was described and validated previously [4][12] and consisted of an on-off block-design with two active conditions (apprehension and control videos) and an interleaved rest condition. In the active condition, video cues were utilized (lasting 10 s) depicting everyday activities that trigger shoulder apprehension. Control videos were created to match the previous content, except for the absence of cues inducing shoulder apprehension. Following each video, a visual analog scale (VAS) appeared for a duration of 2.5 s, and participant were asked to rate the level of perceived apprehension (VAS app), using an MRI-compatible response box. The rating scale consisted of nine steps, ranging from no apprehension to high apprehension. After providing their rating, participants had a rest period during which a fixation cross was displayed visually for 17.5 s. Apprehension and control videos were shown in a pseudo-randomized fashion.

Table 1. Magnetic resonance imaging acquisition parameters at baseline (Y0) and at the 10-year follow-up (Y10), including functional MRI (fMRI), T1-weighted structural imaging, and diffusion tensor imaging (DTI). TE = echo time; TR = repetition time; EPI = echo-planar imaging.

	Y0 MRI	Y10 MRI
MRI system	3T Siemens Trio with standard 32-channel head coil	3T Siemens Prisma with standard 32-channel head coil
fMRI	Whole-brain EPI; 96 × 96 matrix; 39 slices; TR/TE = 2500/30 ms; 148 repetitions	Whole-brain EPI; 96 × 96 matrix; 39 slices; voxel size 2.3 × 2.3 × 3.3 m_m^3; TR/TE = 2500/30 ms; 148 repetitions
T1-weighted imaging	3D T1-weighted sequence; 256 × 256 matrix; 176 slices; 1 × 1 × 1 m_m^3; TR/TE = 2300/2.3 ms	3D T1-weighted sequence; 256 × 256 matrix; 176 slices; 1 × 1 × 1 m_m^3; TR/TE = 2500/2.3 ms
DTI	30 diffusion directions; b = 1000 s/m_m^2; 1 b = 0 image; 128 × 64 matrix; 2 × 2 × 2 m_m^3; TR/TE = 9000/92 ms; 1 average	30 diffusion directions; b = 1000 s/m_m^2; 1 b = 0 image; 128 × 128 × 64 matrix; 1.8 × 1.8 × 2 m_m^3; TR/TE = 9000/92 ms; 1 average

fMRI acquisition

The patient underwent functional MRI imaging at baseline and at the final follow-up. Due to the evolution of technology, the machines were not identical. Nevertheless, the settings were adjusted to be as similar as possible in order to minimize acquisition differences that could bias the analyses. To minimize acquisition-related artefacts, participants first underwent a test run in the MRI scanner. If excessive or unwanted head movements were observed, the acquisition was repeated according to the study protocol. Functional images were subsequently inspected for major motion-related or technical artefacts before analysis. Motion correction was performed during standard FSL preprocessing, and only datasets of sufficient quality were retained for further analysis. The specific acquisition characteristics at each endpoint are detailed in **Table 1**. A summary of the different modalities of functional imaging is presented in **Figure 1**.

General Linear Model Analysis of Task-Related Activation

Analysis was done as described in detail previously in the baseline study [4][6][7][12]. In short, a general linear model (GLM) analysis was done in fMRI Expert Analysis Tool (FEAT) part of FSL Version 6.0.5.1 [13]. At the first level, the contrast of apprehension and control at were calculated for each run of each participant. At the second level, both runs of each participant were combined. At the third level, a paired t-test analysis was performed to investigate group differences between baseline and follow-up. This resulted in a mixed-effects group model implementing FLAME-1 (FMRIB's Local Analysis of Mixed Effects). Then, multiple comparisons correction by threshold-free cluster enhancement (TFCE) was applied. P values < 0.05 were considered as significant [14].

TICA Analysis of Functional Connectivity

Again, analysis was done as described previously [4][6][7][12]. In short, a tensorial independent component (TICA) analysis was performed as implemented in multivariate exploratory linear decomposition into independent components (MELODIC), part of FSL software package (Version 6.0.5.1). Estimated component maps were divided by the standard deviation of the residual noise and thresholded by fitting a mixture model to the histogram of intensity values. The resulting Smodes (which are measures of the activation

strength of the component) was post hoc compared between follow-up and baseline for patient and control by implementation of 2-sample *t* tests and Bonferroni correction for multiple comparisons.

White Matter TBSS of DTI Data

Again, analysis was done as described previously described [4][6][7][12] using the standard TBSS pipeline implemented in the FSL. Age and gender were used as non-explanatory regressors. Results were corrected for multiple comparisons using TFCE [15] and p<0.05 were considered as significant.

Voxel-based morphometry analysis of Y0 images

Again, analysis was done as described previously described [4][6][7][12] using the standard FS voxel-based morphometry (VBM). Age and gender were used as non-explanatory regressors. Results were corrected for multiple comparisons using TFCE [15] and p< 0.05 were considered as significant.

Clinical assessment

All patients were assessed with six commonly used scores in the form of self-administered questionnaires. The VAS pain [16] is a widely used single-item test where a patient rates pain intensity between 0 and 10. This scale is useful for patient preoperative and postoperative monitoring and has also been correlated with patient anxiety [17]. Simple Shoulder Test (SST) consists of 12 binary "yes" or "no" questions evaluating shoulder performance in daily activities. This is a general shoulder questionnaire that is used in a broad range of shoulder conditions [18]. Subjective Shoulder Value (SSV) is a single-question test where a patient is asked to rate his overall shoulder function as a percentage of normal shoulder [19]. The Single Assessment Numeric Evaluation (SANE) instability score was assessed with the following question: "What is the overall percent value of your shoulder if a completely stable shoulder represents 100%?" [20]. Rowe score for instability is a three-item test with four choices each, measuring shoulder function, stability, and motion. The result is converted into a value between 0 and 100. This score has been specifically developed for shoulder instability [21]. An independent observer (BC) was analysing the only objective item (range of motion). Finally, Western Ontario Shoulder Instability (WOSI) is a 21-item test that is specific for shoulder instability, measuring the degree of disability in activities of daily living. The final result is also converted into a value between 0 and 100 [22]. Except for VAS pain, higher results mean higher function. The **Table 2** summarize the subjective scores.

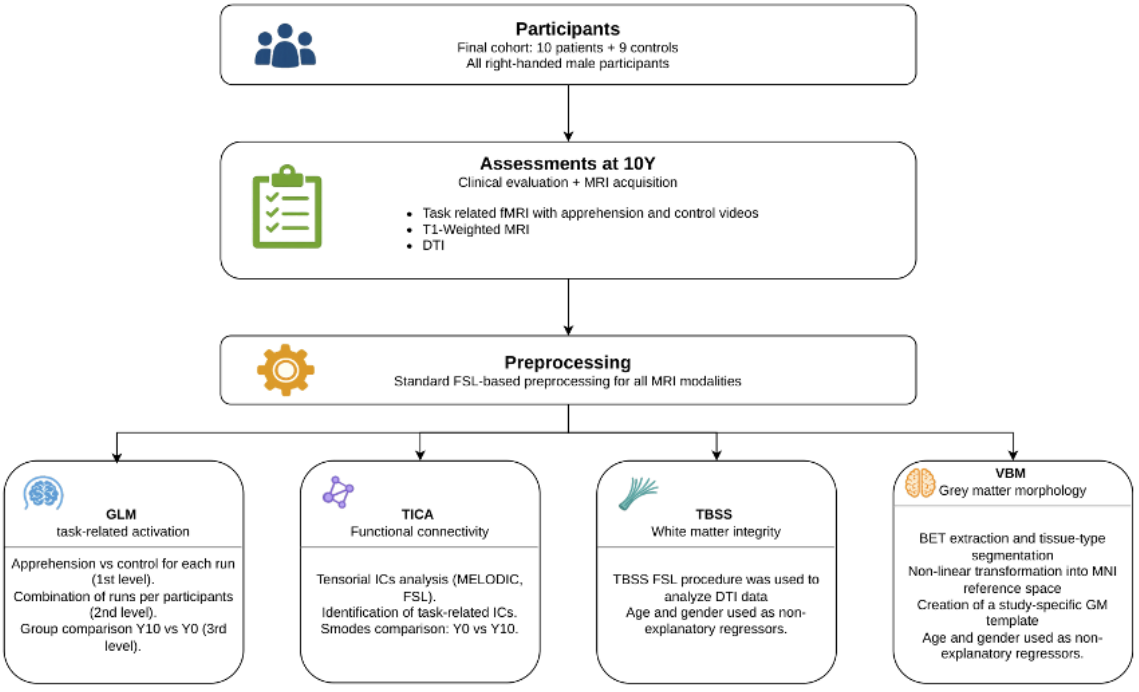


Figure 1. Overview of the neuroimaging analytic workflow. The final cohort comprised 10 patients with anterior shoulder instability and 9 healthy controls, all right-handed male participants. At the 10-year follow-up, participants underwent clinical evaluation and MRI acquisition, including task-based fMRI using apprehension and control videos, T1-weighted MRI, and diffusion tensor imaging. After standard FSL-based preprocessing, task-related activation was assessed using general linear model (GLM) analysis, functional connectivity using tensorial independent component analysis (TICA) with identification of task-related independent components (ICs), white matter integrity using tract-based spatial statistics (TBSS), and grey matter morphology using voxel-based morphometry (VBM).

Table 2. Overview of scores and their characteristics.

	Type	Items
VAS pain	Region-unspecific, condition-unspecific	1 (scale)
SST	Shoulder-specific, condition-unspecific	12 (binary: yes/no)
SSV	Shoulder-specific, condition-unspecific	1 (percentage)
SANE instability	Shoulder-specific, instability-specific	1 (percentage)
Rowe	Shoulder-specific, instability-specific	3 (4 grades each)
WOSI	Shoulder-specific, instability-specific	21 (percentage for each item)

Statistical analysis of clinical assessment

Statistical analyses were performed using R version 3.6.2 (R Foundation for Statistical Computing, Vienna, Austria). Descriptive statistics were calculated for all clinical outcomes. Continuous variables are presented as mean and standard deviation. Normality was assessed using the Shapiro–Wilk test applied to within-subject change scores for longitudinal comparisons. For comparisons between time points within the patient group, paired-samples Student t tests were used when change scores were approximately normally distributed, whereas Wilcoxon signed-rank tests were used otherwise. For between-group comparisons between patients and controls at 10-year follow-up, independent-samples Student t tests were used for normally distributed data and Mann–Whitney U tests otherwise. For each PROM comparison, effect estimates, 95% confidence intervals, appropriate effect sizes, and two-sided p values were reported. Mean differences and Cohen's d_z were reported for paired t tests; for Wilcoxon signed-rank tests, median paired differences and rank-biserial correlation coefficients were reported. All tests were two-sided, and statistical significance was set at $p < 0.05$.

Results

Demographic Data

Of the 15 patients and ten controls enrolled in the previous study (Y0), and after application of the exclusion criteria, ten patients and nine controls were included in the present follow-up study after ten years (Y10). The following flowchart describes the evolution of the different groups after application of the exclusion criteria (**Figure 2**). The mean age for patient group was 38.6±9.7 years and 40.6±2.9 years for control group.

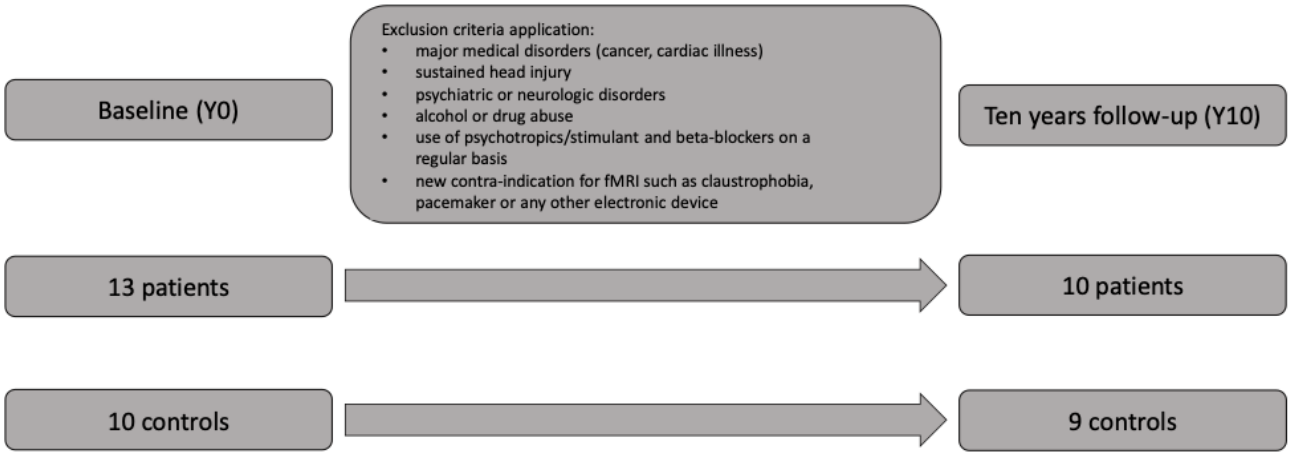


Figure 2. Flowchart of cohort selection and follow-up. Of the original baseline cohort, 13 patients with anterior shoulder instability and 10 healthy controls were assessed at Y0. After application of the predefined exclusion criteria, 10 patients and 9 controls were included in the 10-year follow-up analysis (Y10).

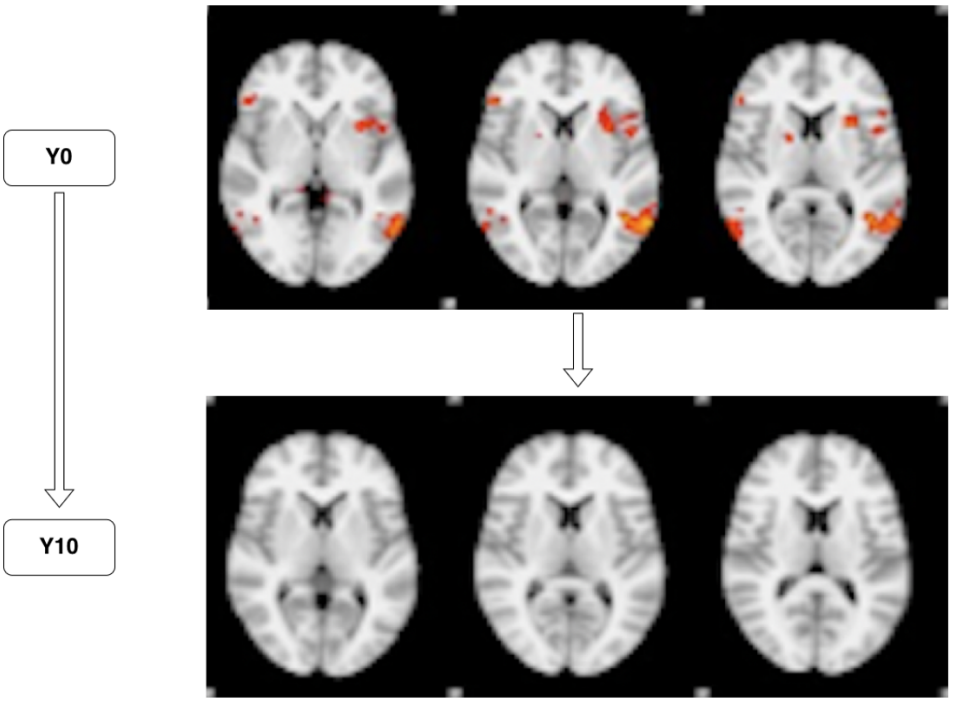


Figure 3. Simplified interpretation of longitudinal task-related GLM findings in patients. At baseline (Y0), apprehension versus control videos elicited significant task-related activation in the left motor and premotor cortex, somatosensory cortex, lateral occipital cortex, and parahippocampal gyrus. At the 10-year follow-up (Y10), no significant residual supra-threshold activation was observed for the same contrast, consistent with near-complete normalization of apprehension-related task activation patterns after surgical stabilization. Warm colours indicate significant task-related activation. Longitudinal Y0–Y10 comparisons were assessed using a paired t-test design implemented in a mixed-effects group model with FLAME1. Multiple-comparison correction was performed using threshold-free cluster enhancement (TFCE), and p values < 0.05 were considered statistically significant.

General Linear Model Analysis of Task-Related Activation

In patients, there were significant task-related activations of Y_0 *vs.* Y10 in bilateral frontal, parietal and occipital areas (**Figure 3, supplementary Table 2**). Concerning controls, minimal activations were found for both Y10 *vs.* Y_0 and Y_0 *vs.* Y10 (not shown, **supplementary Table 3 and 4**). There was no supra-threshold activation for the contrast patients *vs.* controls and controls *vs.* patients at follow-up (not shown).

TICA Analysis of Functional Connectivity

The independent component (IC) analysis revealed 9 task-related ICs with a significant (p<0.05) difference in Smodes (a unitless measure of strength of each IC) for patient Y_0 *vs.* Y10. Three ICs were attributed to higher-level cognitive networks including the default mode network (DMN), representing the neural correlate of internally-generated self-referential cognition [23], notably in the bilateral primary sensory-motor area and dorsolateral prefrontal cortex (dlPFC), bilateral dorsomedial prefrontal cortex (dmPFC), anterior insula, and dorsal anterior cingulate cortex (dACC). One IC corresponds to basic level visual network, and three ICs correspond to higher level visual/ mixed functional neuronal networks. Two ICs were corresponding to noise. The corresponding analysis of Y10 *vs.* Y0 in controls revealed only one difference in the basic level visual network (**Figure 4**, for detailed figures, see **supplemental Figures 6-15**).

VBM and TBSS Analysis

Similar to our one-year results [7], no statistical differences for patient Y_0 *vs.* Y10 were revealed concerning the voxel-based morphometry analysis of grey matter density and the tract-based spatial statistics analysis of white matter.

Functional Scores and Behavioural Data

At Y10, no patients sustained a subluxation or new episode of dislocation. Patients improved in all clinical scores at Y10 *vs.* Y_0 (see **Table 3 and Figure 5**). The level of apprehension was nevertheless significantly higher (p=0.001) between the patients *vs.* controls at Y10 (Table 3). Detailed longitudinal PROMs comparisons are presented in **Supplementary Table 1**.

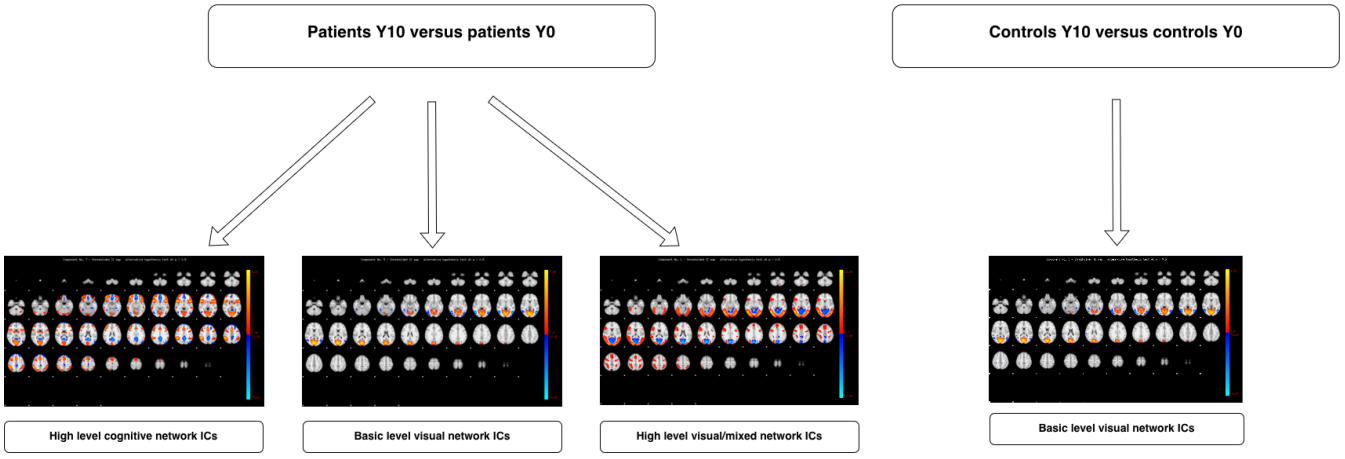


Figure 4. Simplified overview of longitudinal functional connectivity findings derived from tensorial independent component analysis (TICA). Independent components (ICs) showing significant differences in component strength (Smodes) between Y10 and Y0 are displayed for patients and controls. In patients, differences were observed across higher-level cognitive network ICs, basic visual network ICs, and higher-level visual/mixed network ICs. In controls, only one IC related to the basic visual network showed a significant longitudinal difference. Smodes were compared between follow-up and baseline using post hoc two-sample t tests with Bonferroni correction for multiple comparisons; corrected p values < 0.05 were considered statistically significant. Red indicates a positive correlation and blue a negative correlation between voxel activity and the component time course.

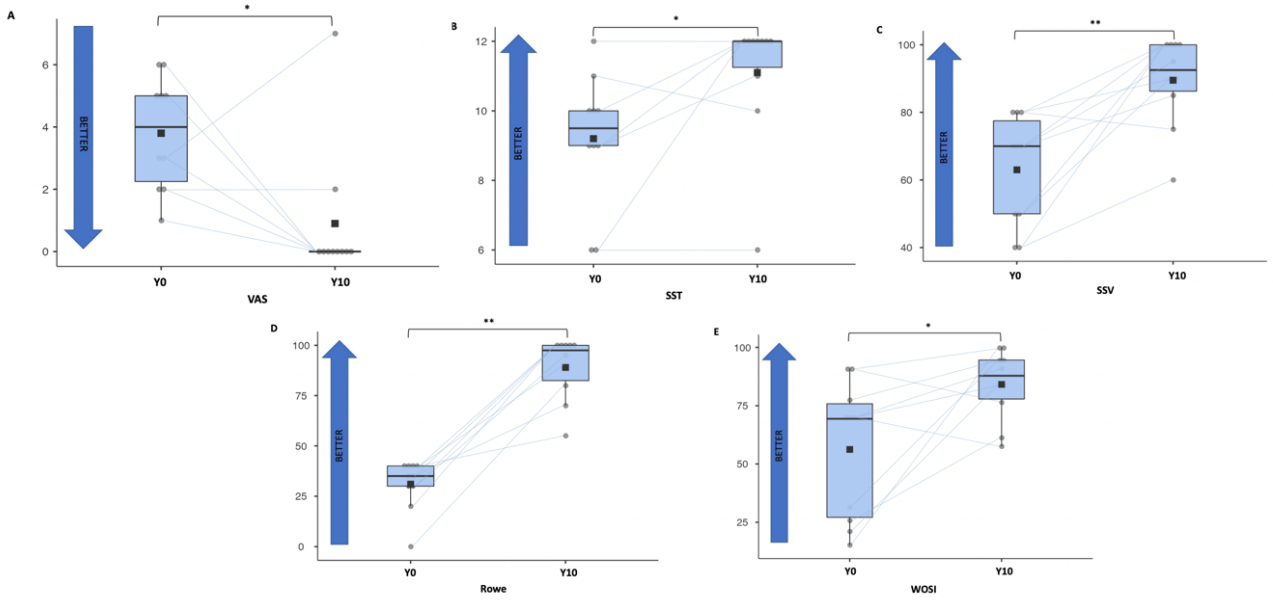


Figure 5. Longitudinal evolution of clinical outcomes in patients with anterior shoulder instability. Boxplots and individual paired trajectories illustrate changes from baseline (Y0) to the 10-year follow-up (Y10) for pain on the visual analog scale (VAS; A), the Simple Shoulder Test (SST; B), the Subjective Shoulder Value (SSV; C), the Rowe score (D), and the Western Ontario Shoulder Instability Index (WOSI; E). Arrows indicate the direction of clinical improvement. Central squares represent mean values; boxplots display the median and interquartile range, with whiskers representing the spread of observed values. *p < 0.05; **p < 0.01.

	Patients					Control			
	N (%) Mean ±SD	Median	(Min –Max)	p-value		N (%) Mean ±SD	Median	(Min –Max)	*Patients vs control* p-value
Pre-operative									
VAS pain	3.8 ±1.8	4.0	(1.0 –6.0)						
SSV	63.0 ±16.4	70.0	(40.0 –80.0)						
Rowe	31.0 ±12.6	35.0	(0.0 –40.0)						
SST	9.2 ±1.9	9.5	(6.0 –12.0)						
WOSI	56.2 ±29.6	69.4	(15.2 –91.0)						
1-year follow-up				***Y0 vs Y1***					
VAS pain	0.5 ±1.4	0.0	(0.0 –4.0)	**0.001**					
SSV	87.5 ±11.6	90.0	(70.0 –100.0)	**0.003**					
Rowe	93.8 ±13.8	100.0	(60.0 –100.0)	**<0.001**					
SST	11.3 ±1.5	12.0	(8.0 –12.0)	**0.002**					
WOSI	89.4 ±17.6	95.4	(47.1 –100.0)	**0.006**					
10-year follow-up				***Y0 vs Y10***	***Y1 vs Y10***				
VAS pain	1.0 ±2.3	0.0	(0.0 –7.0)	**0.019**	1.000	0.0 ±0.0	0.0	(0.0 –0.0)	0.146
SSV	88.3 ±13.5	90.0	(60.0 –100.0)	**0.002**	0.606	100.0 ±0.0	100.0	(100.0 –100.0)	**0.004**
Rowe	87.8 ±16.2	95.0	(55.0 –100.0)	**<0.001**	0.222	100.0 ±0.0	100.0	(100.0 –100.0)	**0.012**
SST	11.0 ±2.0	12.0	(6.0 –12.0)	**0.014**	0.773	12.0 ±0.0	12.0	(12.0 –12.0)	0.067
WOSI	82.4 ±14.8	84.8	(57.5 –99.5)	**0.026**	0.477	100.0 ±0.0	100.0	(100.0 –100.0)	**<0.001**
SANE score	86.7 ±14.1	90.0	(60.0 –100.0)			100.0 ±0.0	100.0	(100.0 –100.0)	**0.004**
Apprehension level	5.2 ±1.0	4.8	(4.2 –7.0)			3.9 ±0.2	4.0	(3.6 –4.2)	**0.001**

Table 3. Clinical scores for patients and controls for timepoints Y0, Y1 and Y10.

Discussion

The purpose of the present study was to investigate and describe the fMRI findings and clinical outcomes of the same cohort of patients who underwent successful shoulder instability surgery ten years ago, as well as controls [4][7]. This exploration aimed to shed light on the neurocognitive aspects of shoulder instability, particularly its apprehension feature. Our findings revealed a complete reduction in apprehension-related brain activations and no structural differences in grey or white matter between Y10 and Y0 in both patients and controls, thus confirming our hypothesis.

Apprehension is a complex condition with a pathogenesis that is not fully understood. However, recent studies have provided insights into certain aspects. Apprehension may be related to various factors, including joint-related issues involving persistent instability characterized by micro-motions [24], peripheral neuromuscular factors with lesions affecting proprioception [25], and central neurologic aspects involving alterations in functional brain networks induced by dislocations [4][6][7][12]. Regarding joint-related aspects, shoulder dislocation can lead to damage to soft tissues and bone structures. For instance, damage to the capsuloligamentous complex occurs in 52% [26] and the glenoid labrum is affected in 73% [27], with plastic deformation correlating with subsequent dislocation episodes [28][29][30]. Bone lesions associated with recurrent dislocation can affect the glenoid side (bony Bankart), the posterolateral humeral head (Hill-Sachs), or both [31]. These alterations result in excessive anterior translation of the humeral head, especially in flexion and abduction [24]. Even after stabilisation surgery, anterior translation of the humeral head remains close to pre-operative values [24], suggesting that the procedure prevents further dislocation but does not completely stabilize the shoulder [1].

Regarding the peripheral neuromuscular aspect, disruption of the tendinomuscular complex and peripheral nerve lesions are reported in 10% and 14% respectively [32]. However, subclinical neurologic damage may be even more prevalent. Capsuloligamentous structures surrounding the glenohumeral joint are richly innervated with proprioceptor complexes, playing a crucial role in sensing the relative position of neighbouring body parts and the effort being exerted during movement [33]. The number of dislocations correlates with the extent of damage to these structures [27], resulting in a significant reduction in proprioceptive capacity [25].

Finally, concerning the central neurologic aspect, specific reorganization was thus found in primary sensory-motor areas compatible with motor resistance, dlPFC associated with cognitive control of motor behaviour, and dACC/dmPFC and anterior insula associated with anxiety and emotional regulation, when comparing patients with instability and healthy volunteers [4]. In a subsequent study, it was also shown that white matter integrity was also modified in the left internal capsule and partially in the thalamus in patients with instability compared to healthy volunteers [6]. The internal brain capsule is a part of the pyramidal tract where motor fibres travel to and from the cortex [34][35], whose increased integrity suggesting an over-connection of white matter in the motor pathway [6]. Our group was also able to demonstrate a decreased, but still present, activation in the left pre-motor cortex one year after a stabilisation surgery, suggesting that brain was able to partially recover after this

procedure [7]. In the present study, we have demonstrated that despite the persistence of apprehension in the patient group compared to the control group (p=0.001), the patients have revealed a normalisation of activation in the previously described cerebral areas, based on task-related GLM and TICA analysis. Clinically, patients showed stability in their functional scores from assessment to one year post-operatively (Table 3). These findings support the hypothesis that, after surgical stabilisation and long-term neuromuscular recovery, apprehension-related functional brain activation patterns may progressively decrease over time.

Several studies have reported altered neural activity in musculoskeletal disorders beyond shoulder instability, including increased activation in sensorimotor, cognitive-control, and emotion-related brain regions in patients with patellar instability or after anterior cruciate ligament reconstruction [36][37][38]. Similar changes have also been described in musculoskeletal conditions primarily characterized by pain, such as chronic low back pain [39]. These findings suggest that apprehension should not be considered solely as a process related to mechanical joint instability. Rather, from a neurocognitive perspective, apprehension may share common mechanisms with painful musculoskeletal disorders, involving threat anticipation, altered sensorimotor processing, emotional regulation, and protective motor responses.

It is intriguing to observe that the normalization of activity in these brain areas coincides with a period when patients rate their apprehension higher than the control group does when assessing their emotional responses to videos depicting everyday activities that trigger shoulder apprehension. This divergence in ratings may stem from either a learning process on the part of the patients regarding these specific videos or a genuine and enduring apprehension of biomechanical origin. As previously mentioned, the stabilisation surgery employed during that period, while reducing the occurrence of dislocation, did not address the anterior translation of the humeral head that occurs in cases of anterior glenohumeral instability [24]. It is noteworthy that the right frontal pole no longer showed hyperactivity during the presentation of apprehension-inducing videos at the final follow-up. In our previous work, this region was interpreted as being involved in the rapid evaluation of the observed shoulder movement and in the decision as to whether the movement could be safely performed or should be associated with pain or threat-related sensations [4]. The absence of significant residual activation at Y10 may therefore suggest that, after surgical stabilisation and long-term recovery, patients no longer engaged the same threat-evaluation network when exposed to the visual triggers. However, this neuroimaging normalization contrasted with persistently higher subjective apprehension scores compared with controls. This dissociation may reflect several non-exclusive mechanisms, including habituation to the video paradigm, motor learning, reduced threat appraisal, emotional memory of previous dislocations, residual biomechanical sensations, or altered patient expectations regarding shoulder safety.

The present findings also have potential clinical implications for postoperative rehabilitation and return-to-sport decision-making. They suggest that shoulder apprehension should not be considered solely as a consequence of residual mechanical instability, but also as a complex neurocognitive process involving threat anticipation, fear of reinjury, emotional regulation, altered confidence, and protective motor responses. This distinction is clinically important because persistent apprehension may remain present despite successful surgical stabilisation and satisfactory conventional functional scores [2].

In patients with shoulder instability, psychological factors appear to be particularly relevant for return to sport. In a recent systematic review, Gibbs et al. have reported that, among athletes who failed to return to sport after shoulder stabilisation, 85.1% cited psychological reasons, including fear of reinjury in 42.8%, lack of confidence in the shoulder in 12.8%, and anxiety in 12.5% [40]. These findings suggest that rehabilitation protocols focused exclusively on range of motion, strength recovery, and neuromuscular reconditioning may not fully address all determinants of recovery. Return-to-sport assessment may therefore benefit from integrating subjective apprehension, psychological readiness, confidence during vulnerable positions, graded exposure to apprehension-provoking movements, and sport-specific neuromotor control.

Although orthopaedic literature on targeted neurocognitive interventions for shoulder apprehension remains limited, extensive evidence from psychology and neuroscience has shown that cognitive-behavioral and neurocognitive interventions can modulate neuroplasticity in anxiety-related disorders and post-traumatic stress disorder [41][42][43]. Such interventions have been associated with reduced hyperactivation in fear- and threat-processing networks. In this context, developing combined rehabilitation strategies that integrate neuromotor reconditioning with cognitive-behavioral approaches may represent a promising direction for selected patients with persistent apprehension. Future studies should aim to identify early postoperative clinical, psychological, or neuroimaging markers that may help determine which patients could benefit from such targeted rehabilitation protocols.

Limitations

This study has several limitations. First, the small sample size limited the statistical power to detect small or moderate longitudinal effects and reduced the precision of effect estimates. Although small cohorts were common in neuroimaging studies conducted during the period in which the original cohort was established, with a median sample size of 12 in highly cited experimental fMRI studies published between 1990 and 2012, small samples remain vulnerable to unstable effect estimates and limited reproducibility [44][45]. Accordingly, the present findings should be interpreted as exploratory and hypothesis-generating.

Second, repeated exposure to the same visual paradigm and the 10-year interval between assessments may have introduced habituation, retesting, or age-related effects. However, the inclusion of the same control group at both time points allowed these potential confounders to be partially addressed. Only one functional connectivity network, related to basic visual processing, differed between Y0 and Y10 in controls, whereas no changes were observed in higher-level cognitive networks. In addition, only minimal task-related activation changes were observed in controls. These findings support, but do not prove, that the longitudinal changes observed in patients were more likely related to apprehension-associated processes than to retesting or aging alone.

Third, the cohort was restricted to right-handed male participants. This selection was intended to reduce heterogeneity related to sex and cerebral functional lateralization, as left-handed individuals may exhibit greater interindividual variability in cerebral asymmetry across several cognitive domains [8][9]. However, this criterion limits the generalizability of the findings to female patients and left-handed individuals with anterior shoulder instability.

Fourth, An additional limitation is that MRI examinations at baseline and at 10-year follow-up were performed on different 3T Siemens platforms. Although acquisition parameters were harmonized as closely as possible and the same 32-channel head coil was used, scanner-related differences in signal-to-noise ratio, image contrast, or diffusion measurements cannot be completely excluded.

Finally, standardized radiographic follow-up was not performed at 10 years. Therefore, we were unable to assess post-instability arthropathy, degenerative changes, graft-related findings, or other structural shoulder abnormalities that could potentially contribute to persistent subjective apprehension. Radiographs were not obtained solely for research purposes because there was no clinical indication for imaging at the time of follow-up. In accordance with ethical principles aiming to minimize unnecessary exposure to ionizing radiation, additional radiographic examinations were not performed. Although this decision limited the structural interpretation of the long-term clinical and neuroimaging findings, it was considered appropriate in this clinically stable cohort.

Conclusion

In patients with shoulder apprehension, apprehension-related brain activation patterns showed near-complete normalization ten years after successful shoulder stabilisation, although subjective apprehension remained higher than in healthy controls.

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Conflicts of Interest

Alexandre Lädermann is a paid consultant for Arthrex, Stryker, Medacta, and Enovis. He received royalties from Stryker and Medacta. He is the (co-)founder of FORE, Med4Cast, and BeeMed. He owns stock options in Medacta and Follow Health. He is on the board of the French Arthroscopic Society.

Data availability

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

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