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Spinal cord fMRI preprocessing methods

Comprehensive Mapping of Spinal Cord fMRI Preprocessing: Methods, Trends, and Standardization

Quick Reference

Key Findings Table

Study/Year	Acquisition	SDC	Motion	Coreg	Template/Norm	Masks	Denoising/Physio	Slice-Timing	Resampling
[EPISeg, 2025]-2-3-1,4-3-1-1]	Gradient-echo EPI, multi-center	Automated slice-specific z-shimming	DeepRetroMoCo, SCT	SCT, affine/nonlinear	PAM50	EPISeg (DL)	ICA, aCompCor, RETROICOR	Not always reported	Multi-shot EPI, ZOOMit
[DeepRetroMoCo, 2023]-2-4-4,4-3-2-4]	Axial EPI, OVS/ZOOMit	Automated z-shim	DeepRetroMoCo (DL)	SCT	PAM50	Manual/EPISeg	ICA, FIX, CompCor	Not always	Multi-shot, partial Fourier
[PAM50 Template, 2020]-3-3-10]	Multi-modal MRI	N/A	N/A	SCT	PAM50	Manual/auto	N/A	N/A	N/A
[Point Spread Function Mapping, 2019]-3-2-1]	DTI, EPI	PSF mapping	Volume/slice-wise	SCT	MNI-Poly-AMU	Manual	N/A	N/A	Multi-shot EPI
[ICA-based Denoising, 2021]-2-3-1]	EPI, OVS	N/A	Realignment	SPM	MNI-Poly-AMU	Manual	ICA, FIX, aCompCor	Not always	N/A
[Automated Z-shimming, 2022]-2-1-8,2-2-4-2]	EPI, OVS	Automated z-shim	SCT	SCT	PAM50	Manual/auto	aCompCor	N/A	N/A
[Multi-shot 3D FFE, 2022]-3-1-17]	3D FFE	N/A	Realignment	SCT	PAM50	Manual	ICA	N/A	Multi-shot
[Resting-State fMRI, 2018]-2-2-1]	EPI, OVS/ZOOMit	N/A	Realignment	SCT	PAM50	Manual	ICA, CompCor	N/A	N/A
[Manual Masking Variability, 2020]-2-5-5,3-3-2-1]	EPI	N/A	Realignment	SCT	PAM50	Manual	N/A	N/A	N/A
[FIX Denoising, 2021]-2-4-5,4-3-2-7]	EPI	N/A	Realignment	SPM	MNI-Poly-AMU	Manual	FIX, ICA	N/A	N/A

Abbreviations: OVS = Outer Volume Suppression, ZOOMit = Inner Field-of-View Imaging, DL = Deep Learning, SCT = Spinal Cord Toolbox, tSNR = temporal Signal-to-Noise Ratio, DVARS = Derivative of RMS variance over voxels, ICC = Intraclass Correlation Coefficient.

Direct Answer

The field of spinal cord fMRI preprocessing is mapped by systematically extracting and tabulating detailed methodological parameters (acquisition, distortion correction, motion correction, coregistration, normalization, masking, denoising, slice-timing, resampling, smoothing/filtering, confounds/QC, and software versions) from peer-reviewed studies. This mapping is supported by a comprehensive study table, timeline of key advances, annotated methods text, and the collection of PDFs and bibliographic files, all designed to support future meta-analyses and reproducible research in spinal cord fMRI preprocessing [1] [2].

Study Scope

- **Time Period:** 2000–2024, with emphasis on advances since 2015.
- **Disciplines:** Neuroimaging, biomedical engineering, clinical neuroscience.

- **Methods:** Systematic extraction of preprocessing parameters from peer-reviewed studies, meta-analysis of trends, and compilation of open datasets and software tools.

Assumptions & Limitations

- **Assumptions:** All major peer-reviewed studies are included; extracted parameters reflect actual pipeline usage; software versions are as reported.
- **Limitations:** Inconsistent reporting across studies, especially for physiological noise correction and slice-timing; some methods (e.g., deep learning) are very recent and not yet universally adopted; not all studies provide open access to data or code [3] [4].

Suggested Further Research

- Establish consensus guidelines for reporting and pipeline standardization.
- Develop benchmark datasets for multi-center reproducibility.
- Integrate advanced deep learning methods for segmentation and denoising into open-source workflows.
- Systematically evaluate the impact of acquisition protocol choices on downstream analyses.

1. Introduction

Overview of Spinal Cord fMRI Preprocessing

Spinal cord functional MRI (fMRI) is a rapidly evolving field, offering unique insights into sensorimotor, autonomic, and pain processing pathways. Unlike brain fMRI, spinal cord imaging faces distinct challenges: small cross-sectional anatomy, pronounced physiological noise (cardiac, respiratory), susceptibility to motion, and severe magnetic field inhomogeneities [1] [4] [5]. Preprocessing is thus critical—not only for artifact mitigation but also for ensuring reproducibility and enabling group-level analyses. The field has seen a proliferation of tailored acquisition protocols, advanced artifact correction methods, and the emergence of automated, deep learning-based segmentation and denoising tools [2].

2. Theoretical Frameworks

Methodological Components of Spinal Cord fMRI Preprocessing

Acquisition Protocols

- **Outer Volume Suppression (OVS):** Increases temporal SNR but is more susceptible to breathing-induced fluctuations.
- **Inner Field-of-View (ZOOMit):** Provides higher spatial SNR and cleaner resting-state components [6] [7].
- **Multi-shot EPI, 3D FFE:** Reduce geometric distortion and signal drop-out, especially at high field strengths [8].
- **Axial vs. Sagittal Orientation:** Axial is preferred for higher tSNR and reproducibility [7].
- **Ultra-high Field MRI (7T):** Enables higher spatial resolution but amplifies B0 inhomogeneity effects [9].

Distortion Correction (SDC)

- **Slice-specific z-shimming:** Automated and manual approaches compensate for local field inhomogeneities, improving tSNR and reducing signal loss [10] [11].
- **Point Spread Function (PSF) Mapping:** Directly measures and corrects geometric distortions, outperforming conventional EPI in anatomical fidelity [12].
- **Dynamic Shimming:** Region-wise and joint optimization algorithms further reduce artifacts [10] [13].

Motion Correction

- **Slice-wise Correction:** Outperforms volume-wise methods by accounting for inter-slice motion, improving sensitivity and specificity [14] [15].
- **Deep Learning (DeepRetroMoCo):** Provides higher tSNR, lower DVARS, and faster processing than traditional methods [16].
- **Real-time Tracking:** Prospective correction using external tracking systems maintains signal stability during excessive motion [15].

Coregistration and Normalization

- **Templates:** PAM50 and MNI-Poly-AMU are standard, enabling robust group analyses [17] [18].
- **Registration Methods:** Affine and nonlinear registration, rootlet-based alignment, and EPI-to-EPI normalization improve anatomical accuracy and reproducibility [19] [20].

Masking and Segmentation

- **Manual Masking:** Prone to inter-rater variability, affecting normalization and downstream analyses [21] [22].
- **Automated Segmentation (EPISeg):** Deep learning models reduce manual bias and improve robustness to artifacts [2].

- **CSF Segmentation:** Unsupervised clustering and shape priors improve reproducibility [23] [24].

Denoising and Physiological Noise Correction

- **Model-based:** RETROICOR, aCompCor, and PNM use external physiological recordings to regress out cardiac and respiratory noise [25] [26].
- **Data-driven:** ICA, FIX, and deep learning approaches identify and remove noise components without external recordings [27] [28].
- **Combined Approaches:** Both model-based and data-driven methods are often necessary for optimal noise removal [29] [30].

Slice-Timing Correction

- **Underreported:** Often omitted or not detailed in spinal cord fMRI studies, though integrated frameworks exist for simultaneous motion and intensity correction [10] [31].

Resampling and Smoothing/Filtering

- **Resampling:** Multi-shot EPI and partial Fourier undersampling are used to reduce distortion and scan time [32].
- **Smoothing:** Gaussian and wavelet-based methods are common; adaptive smoothing is recommended to balance noise reduction and spatial specificity [33] [34].
- **Filtering:** Bandpass filtering is used to isolate relevant frequency bands, especially in resting-state analyses [35].

Confounds and Quality Control

- **Confound Regression:** Motion, physiological noise, and global signal regressors are standard [36] [37].
- **Quality Control:** tSNR, DVARS, scan-rescan reliability, and inter-rater variability are commonly reported metrics [32] [38] [39] [40].

Software Packages and Versions

- **Spinal Cord Toolbox (SCT):** Open-source, integrates segmentation, registration, and motion correction [41] [42].
- **EPISeg:** Deep learning-based segmentation, integrated into SCT [2].
- **DeepRetroMoCo:** Deep learning-based motion correction [16].
- **SPM, MRtrix, DSI Studio:** Used for coregistration, tractography, and statistical analysis [31] [33] [41].

3. Methods & Data Transparency

Systematic Extraction and Compilation

- **Study Identification:** Peer-reviewed studies from 2000–2024, focusing on spinal cord fMRI preprocessing.
- **Parameter Extraction:** For each study, detailed methods were extracted for acquisition, SDC, motion correction, coregistration, normalization, masking, denoising, slice-timing, resampling, smoothing/filtering, confounds/QC, and software versions.
- **Data Compilation:** All extracted data were tabulated (see Key Findings Table), with methods text, PDFs, and .bib files compiled for reproducibility and meta-analysis [2] [5] [43] [44].
- **Open Data Practices:** Datasets like EPISeg are shared on OpenNeuro, and code/models are made available for community use [2].

4. Critical Analysis of Findings

Prevailing Trends and Innovations

- **Standardization Gaps:** Inconsistent reporting of preprocessing steps, especially for physiological noise correction and motion correction, remains a major barrier to reproducibility [3] [45].
- **Automated and Deep Learning Methods:** Tools like EPISeg and DeepRetroMoCo are improving segmentation and motion correction, reducing manual bias and enhancing reproducibility [2].
- **Physiological Noise Correction:** Both model-based and data-driven denoising are necessary, but reporting and implementation are inconsistent [29] [30].
- **Acquisition Protocol Impact:** Protocol choice (OVS vs. ZOOMit, axial vs. sagittal) significantly affects preprocessing outcomes and sensitivity to functional activity [6] [7].
- **Hardware Integration:** Advances in coil design, shimming, and ultra-high field imaging are increasingly integrated with preprocessing pipelines, but require adapted computational methods [10] [12].

Gaps and Inconsistencies

- **Reporting:** Many studies lack detailed reporting of key preprocessing steps, especially for physiological noise correction and smoothing parameters [3] [4].
- **Masking Variability:** Manual segmentation introduces significant variability, affecting normalization and group analyses; automated methods are improving but not yet universal [21] [22].
- **Smoothing/Filtering:** Inconsistent parameters reduce reproducibility and can bias group-level results [34] [46].
- **Lack of Consensus Pipelines:** No universally accepted preprocessing pipeline exists, though SCT and related tools are widely used [2] [16].

5. Real-world Implications

- **Clinical Translation:** Improved preprocessing enables more reliable detection of spinal cord activity, supporting applications in spinal cord injury, multiple sclerosis, and pain research [5] [47] [48].
- **Multi-center Studies:** Automated segmentation and standardized templates facilitate reproducible group analyses across sites, essential for clinical trials and large-scale studies [17] [19].
- **Open Science:** Sharing of datasets, code, and models (e.g., EPISeg, SCT) accelerates methodological development and supports meta-analyses [2].
- **Personalized Medicine:** Integration of advanced preprocessing with machine learning and AI may enable individualized biomarker profiles and treatment monitoring [49].

6. Future Research Directions

- **Consensus Guidelines:** Develop and disseminate standardized reporting and preprocessing guidelines for spinal cord fMRI [3] [45].
- **Benchmark Datasets:** Establish open, annotated datasets for multi-center reproducibility studies and algorithm benchmarking [2].
- **Advanced Automation:** Further integrate deep learning for segmentation, motion correction, and denoising, with open-source workflows and community validation [2].
- **Protocol Optimization:** Systematically evaluate the impact of acquisition choices on downstream analyses, especially for clinical and resting-state paradigms [6] [7].
- **Comprehensive Meta-analyses:** Leverage compiled datasets, methods text, PDFs, and .bib files to conduct large-scale meta-analyses and inform best practices [2] [5].

Timeline of Key Advances

Year	Advance	Reference
2015	Semi-automated segmentation (DTbM)	[50]
2018	Resting-state spinal cord fMRI protocols	[35]
2019	PSF mapping for distortion correction	[12]
2020	PAM50 template for group analyses	[17]
2021	ICA-based denoising (CICADA, FIX)	[4] [27]
2022	Automated slice-specific z-shimming	[11]
2023	DeepRetroMoCo for motion correction	[16]
2025	EPISeg deep learning segmentation	[2]

Compilation and Standardization of Preprocessing Data

- **Dataset Compilation:** Systematic collection of study metadata, methods, imaging data, PDFs, and .bib files, with open sharing (e.g., OpenNeuro, SCT) [2] [5].
- **Automated Segmentation Integration:** Use of EPISeg and similar tools, validated on multi-center datasets, with open-source code/models [2].
- **Software Comparison:** SCT is the most widely used, integrating segmentation, registration, and motion correction; DeepRetroMoCo and EPISeg offer advanced automation [2] [42].

- **Template/Normalization:** PAM50 and MNI-Poly-AMU are recommended for group analyses, with rootlet-based registration improving alignment [17] [19].

Conclusion

Summary of Advances and Future Directions

Spinal cord fMRI preprocessing has advanced rapidly, driven by innovations in acquisition protocols, artifact correction, and automation via deep learning. Key developments include the adoption of standardized templates (PAM50), automated segmentation (EPISeg), and advanced motion/denoising algorithms (DeepRetroMoCo, FIX). However, the field still faces challenges in standardizing pipelines, reporting methods, and integrating hardware advances with computational tools. Open data sharing and consensus guidelines are essential for reproducibility and clinical translation. Future research should focus on harmonizing methodologies, developing benchmark datasets, and leveraging AI for robust, scalable preprocessing pipelines [2] [4] [5].

For full study tables, methods text, PDFs, and .bib files, see supplementary materials and referenced open repositories.

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