

Cerebral metabolic alterations and network disruption in pulmonary fibrosis assessed with [18F] FDG PET/CT

Yongguang chang

changyongguang2024@163.com

The First Affiliated Hospital of Zhengzhou University <https://orcid.org/0009-0008-4697-4130>

Xiaoxian Wang

The First Affiliated Hospital of Zhengzhou University

Xiaoman Cui

The First Affiliated Hospital of Zhengzhou University

Shasha Xu

The First Affiliated Hospital of Zhengzhou University

Keliu Wu

The First Affiliated Hospital of Henan Polytechnic University

Baoping Liu

The First Affiliated Hospital of Zhengzhou University

Yujie Bai

The First Affiliated Hospital of Zhengzhou University

Ruihua Wang

The First Affiliated Hospital of Zhengzhou University <https://orcid.org/0009-0008-5194-9829>

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Abstract

Background

Emerging evidence highlights the roles of lung-brain axis in the systemic effects of chronic pulmonary disease, but cerebral metabolic and network manifestations in pulmonary fibrosis (PF) remain poorly characterized. The relationship between cerebral metabolism and clinical outcomes in PF was therefore investigated.

Results

Compared with healthy controls, patients with PF exhibited hypometabolism in frontal, temporal, insular, cingulate, and caudate regions (all $P < 0.05$). Significant disruption was identified within the parasympathetic-associated subnetwork ($P < 0.001$), whereas no significant alteration was detected in the sympathetic-associated subnetwork ($P = 0.1582$). Cerebral metabolism was modestly associated with pulmonary function and systemic inflammatory markers ($|r| = 0.213\text{--}0.373$, $P < 0.05$). After adjustment for age, sex, forced vital capacity (FVC), and diffusing capacity of the lung for carbon monoxide (DLCO), hypometabolism in selected autonomic and association regions remained associated with poorer EFS (HR = 0.426–0.632, $P \leq 0.048$).

Conclusions

PF was associated with widespread cerebral hypometabolism and metabolic network disruption, particularly within the parasympathetic-associated network. Cerebral metabolic alterations may provide prognostic information beyond conventional pulmonary function measures.

Background

Fibrosis is a common endpoint of chronic tissue injury and is increasingly recognized as a systemic rather than exclusively local process. Cognitive impairment and alterations in brain structure and function have been documented in liver fibrosis, myocardial fibrosis, and systemic sclerosis^[1–5]. These observations raise the possibility that pulmonary fibrosis (PF) may also involve the brain, yet its cerebral manifestations remain poorly understood.

Bidirectional lung-brain communication is mediated through immune, neural, metabolic, endocrine, and vascular pathways^[6, 7]. In chronic pulmonary disease, these pathways may be disrupted by inflammation, hypoxaemia, oxidative stress, blood-brain barrier dysfunction, and altered visceral afferent signaling^[7, 8]. Grey-matter atrophy, white-matter injury, perfusion abnormalities, and disrupted functional connectivity have been reported mainly in chronic obstructive pulmonary disease (COPD) and, less extensively, in asthma^[9–11]. By contrast, evidence of cerebral involvement in PF remains limited and

heterogeneous. Clinical studies have indicated cognitive vulnerability, most consistently involving memory and information processing, although the affected domains and their associations with physiological impairment have varied across cohorts^[12–17]. Direct neuroimaging evidence is even scarcer. A population-based imaging-genetics study associated idiopathic pulmonary fibrosis susceptibility variants with anterior cingulate cortical thinning and white-matter microstructural differences, while finding no significant associations with functional imaging-derived phenotypes^[18]. In particular, cerebral glucose metabolism, metabolic network organization, and their prognostic relevance in PF have not been systematically characterized.

Accordingly, brain [¹⁸F]FDG PET/CT was used to characterize cerebral metabolism and metabolic connectivity in PF at the whole-brain and autonomic-network levels. Associations with pulmonary function, systemic inflammatory markers, and event-free survival (EFS) were examined to assess the clinical and prognostic relevance of these alterations.

Materials and Methods

Study population

A total of 86 patients with PF and 103 matched healthy controls (HC) from the First Affiliated Hospital of Zhengzhou University between April 2020 and June 2025 were retrospectively included. Adults aged ≥ 18 years were eligible if PF was demonstrated on high-resolution computed tomography (HRCT), the underlying fibrotic interstitial lung disease was established by multidisciplinary evaluation, and technically adequate brain [¹⁸F]FDG PET/CT data were available^[19]. Exclusion criteria comprised a history of dementia, stroke, epilepsy, traumatic brain injury, major psychiatric illness, structural intracranial lesions, active malignancy, or alcohol or substance abuse. Patients with incomplete clinical data, inadequate PET/CT image quality, or blood glucose exceeding the prespecified threshold before tracer administration were also excluded.

Clinical data collection

Baseline clinical characteristics were systematically recorded for all participants. Pulmonary function parameters included the percentage of predicted forced vital capacity (FVC), forced expiratory volume in one second (FEV₁), total lung capacity (TLC), and diffusing capacity of the lung for carbon monoxide (DLCO). Inflammatory biomarkers included serum Krebs von den Lungen-6 (KL-6), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and procalcitonin (PCT).

Image acquisition and processing

All participants underwent baseline [¹⁸F]FDG PET/CT using a Biograph TruePoint 64 PET/CT system (52-ring, Siemens Healthineers, Germany). Participants fasted for at least 6 h, and blood glucose was

measured before injection to confirm a level below 11.1 mmol/L. [^{18}F]FDG was administered intravenously at 3.70–4.44 MBq/kg, and imaging began 45–60 min after injection. Low-dose CT was performed for attenuation correction and anatomical localisation at 120 kVp, with automatic tube current modulation between 100 and 200 mA. The reconstructed slice thickness was 3 mm.

Brain PET images were processed using SPM12 (Wellcome Department of Cognitive Neurology, London, UK) implemented in MATLAB (MathWorks). Images were spatially normalised to Montreal Neurological Institute (MNI) space and smoothed with an 8 mm full-width-at-half-maximum Gaussian kernel. Regional uptake was extracted from 90 cortical and subcortical regions of interest (ROIs) defined by the Automated Anatomical Labeling (AAL) atlas. The standardised uptake value ratio (SUVR) was calculated by dividing each ROI's mean SUV by the mean cerebellar SUV. Sympathetic- and parasympathetic-associated subnetworks were defined using prior neuroimaging evidence^[20]. Metabolic network topology was visualised using BrainNet Viewer^[21].

Follow-up and Study Endpoints

The primary outcome was EFS, defined as the interval from baseline PET/CT to the first occurrence of acute exacerbation of fibrotic interstitial lung disease (AE-fILD) or respiratory-related death. AE-fILD was defined by acute worsening of respiratory symptoms, typically within 1 month, accompanied by new bilateral ground-glass opacities and/or consolidation superimposed on pre-existing fibrotic abnormalities on HRCT. Deterioration attributable to cardiac failure or fluid overload was excluded^[22]. Patients experiencing either component of the composite outcome were classified as having an event. Follow-up information was obtained from electronic medical records and structured telephone interviews. Patients without an event were censored at the date of their last confirmed follow-up.

Statistical Analysis

All analyses were performed using R software (version 4.5.2, R Core Team, 2025). Normality was assessed using the Shapiro-Wilk test. Regional SUVR were compared between the PF and HC groups using independent-samples Student's *t*-tests or Mann–Whitney *U*-tests, as appropriate. These exploratory regional comparisons were reported using uncorrected two-sided *P* values.

Metabolic connectivity was evaluated at the whole-brain and predefined autonomic-network levels. Group-specific connectivity matrices were constructed from pairwise Pearson correlations of regional SUVR, and between-group differences were assessed using Fisher's *r*-to-*z* transformation. For network-based statistics (NBS), edges meeting an uncorrected threshold of $P < 0.05$ were used to form candidate components. Component-level significance was assessed using 5,000 permutations with family-wise error rate (FWER) control based on the maximum component statistic^[23].

Potential clinical correlates of the observed cerebral metabolic alterations were explored by relating regional SUVR to pulmonary function indices and systemic inflammatory biomarkers using Spearman

correlations. For prognostic analyses, regional SUVR were standardized as Z-scores and assessed using Cox proportional hazards regression. Regions associated with EFS in univariable analyses were entered separately into multivariable models adjusted for age, sex, FVC, and DLCO. Hazard ratios (HR) were reported per one-standard-deviation (SD) increase in SUVR with 95% confidence intervals (CI). A two-sided $P < 0.05$ was considered statistically significant.

Results

Participant Characteristics

A total of 103 HC participants and 86 patients with PF were included. Age and sex distribution were comparable between the PF and HC groups ($P = 0.052, 0.055$). According to whether the composite endpoint occurred during follow-up, patients with PF were classified into event-free ($n = 31$) and event ($n = 55$) groups (Table 1).

Table 1
Baseline characteristics of the study participants

Characteristics	HC (n = 103)	PF (n = 86)	P value	Event-free group (n = 31)	Event group (n = 55)	P value
Male Sex	54 (52.4%)	58 (67.4%)	0.052	17 (54.8%)	41 (74.5%)	0.102
Age (years)	64.0 (60.0, 68.0)	68.0 (61.2, 71.0)	0.055	64.0 (54.5, 70.5)	69.0 (64.0, 73.0)	0.014
FVC (% pred)	-	80.0 ± 20.0	-	100.0 ± 20.0	70.0 ± 20.0	< 0.001
FEV ₁ (% pred)	-	80.0 ± 20.0	-	100.0 ± 20.0	80.0 ± 20.0	< 0.001
TLC (% pred)	-	70.0 ± 20.0	-	90.0 ± 10.0	60.0 ± 10.0	< 0.001
DLCO (% pred)	-	40.0 (30.0, 60.0)	-	60.0 (50.0, 80.0)	40.0 (30.0, 50.0)	< 0.001
KL-6 (U/mL)	-	1546.0 (811.0, 2274.0)	-	966.0 (440.0, 1967.0)	1932.0 (1066.0, 2829.0)	0.004
CRP (mg/L)	-	5.0 (2.4, 19.1)	-	3.9 (1.7, 6.5)	9.7 (3.2, 27.5)	0.065
ESR (mm/h)	-	27.0 (10.0, 52.0)	-	22.0 (9.0, 45.0)	27.5 (10.2, 53.5)	0.608
PCT (ng/mL)	-	0.1 (0.0, 0.1)	-	0.1 (0.0, 0.1)	0.1 (0.0, 0.1)	0.584
Values are presented as mean ± standard deviation (SD), median (25th, 75th), or n (%).						
Comparisons between the PF and HC groups were performed to assess demographic balance. Clinical characteristics were compared between the event and event-free groups within the PF cohort. Continuous variables were analysed using Student's <i>t</i> -test or the Mann-Whitney <i>U</i> test, as appropriate; categorical variables were analysed using the chi-square test. The event group included patients with AE-fILD or respiratory-related death during follow-up.						

Within the PF cohort, the event group was older than the event-free group ($P = 0.014$), whereas sex distribution did not differ significantly between the groups ($P = 0.102$). The event group had lower predicted FVC, FEV₁, TLC, and DLCO values (all $P < 0.001$) and higher KL-6 levels ($P = 0.004$). No significant between-group differences were observed in ESR, CRP, or PCT.

Cerebral Hypometabolism and Metabolic Decoupling

As shown in Fig. 1, cerebral hypometabolism was detected in the PF group compared with the HC group (all $P < 0.05$). Hypometabolism predominantly involved the frontal and temporal cortices, insula,

cingulate cortex, and caudate nucleus. Representative cases are shown in Fig. 2. Detailed regional comparisons are provided in Additional file 1: Table S1.

As shown in Fig. 3, widespread attenuation of interregional metabolic correlations was observed in the PF group (all $P < 0.05$). The most pronounced decoupling involved the temporal cortex, where connectivity with distributed brain regions was markedly reduced. Group-specific matrices, between-group differences, and complete edge-wise statistics are provided in Additional file 1: Tables S2–S5.

Autonomic Network Disruption

As shown in Fig. 4, no significant topological difference was detected in the sympathetic-associated subnetwork ($P = 0.1582$). By contrast, significant connectivity disruption was identified within the parasympathetic-associated subnetwork in PF group ($P < 0.001$). Connectivity matrices, between-group differences, and complete edge-wise statistics for the sympathetic- and parasympathetic-associated subnetworks are provided in Additional file 1: Tables S6–S13.

Clinical Correlates of Cerebral Metabolism

As shown in Fig. 5, cerebral metabolism was associated with pulmonary function and systemic inflammatory markers, with absolute correlation coefficients ranging from 0.213 to 0.373 ($P < 0.05$). Complete correlation coefficient and P value matrices are provided in Additional file 1: Tables S14 and S15.

Prognostic Value of Cerebral Metabolism

As shown in Table 2, metabolism in several autonomic-related regions was associated with EFS in univariate analysis and after adjustment for age and sex. After additional adjustment for FVC and DLCO, some associations were attenuated, whereas hypometabolism in frontal, parietal, insular, and angular regions remained independently associated with poorer EFS (HR = 0.426–0.632, $P \leq 0.048$). Fully adjusted Cox models are provided in Additional file 1: Tables S16 and S17.

Table 2
Cox regression analyses of cerebral glucose metabolism and event-free survival

SUVR		Univariate HR (95% CI)	Univariate <i>P</i> value	Adjusted HR (95% CI)	Adjusted <i>P</i> value
Frontal_Mid_left	Per unit change	0.008 (0.000- 0.141)	0.001	0.007 (0.000- 0.134)	0.001
	Per SD change	0.637 (0.488– 0.832)	0.001	0.625 (0.472– 0.827)	0.001
Frontal_Mid_right	Per unit change	0.002 (0.000- 0.063)	0.001	0.002 (0.000- 0.069)	0.001
	Per SD change	0.561 (0.410– 0.769)	0.001	0.563 (0.409– 0.775)	0.001
Frontal_Mid_Orb_left	Per unit change	0.016 (0.001– 0.232)	0.002	0.010 (0.001– 0.161)	0.001
	Per SD change	0.687 (0.539– 0.876)	0.002	0.655 (0.506– 0.847)	0.001
Frontal_Mid_Orb_right	Per unit change	0.005 (0.000- 0.160)	0.003	0.005 (0.000- 0.162)	0.003
	Per SD change	0.629 (0.464– 0.851)	0.003	0.628 (0.463– 0.852)	0.003
Cingulum_Ant_left	Per unit change	0.002 (0.000- 0.081)	0.001	0.004 (0.000- 0.165)	0.004
	Per SD change	0.626 (0.477– 0.823)	0.001	0.650 (0.486– 0.870)	0.004
Cingulum_Ant_right	Per unit change	0.002 (0.000- 0.052)	0.001	0.006 (0.000- 0.178)	0.003
	Per SD change	0.578 (0.433– 0.770)	0.001	0.634 (0.467– 0.859)	0.003
Parietal_Inf_left	Per unit change	0.003 (0.000- 0.046)	0.001	0.004 (0.000- 0.074)	0.001
Adjusted HR indicates the hazard ratio after adjusting for age and sex.					

SUVR		Univariate HR (95% CI)	Univariate <i>P</i> value	Adjusted HR (95% CI)	Adjusted <i>P</i> value
	Per SD change	0.525 (0.385– 0.715)	0.001	0.550 (0.402– 0.752)	0.001
Parietal_Inf_right	Per unit change	0.001 (0.000- 0.025)	0.001	0.002 (0.000- 0.047)	0.001
	Per SD change	0.459 (0.322– 0.655)	0.001	0.491 (0.342– 0.704)	0.001
Angular_left	Per unit change	0.001 (0.000- 0.015)	0.001	0.001 (0.000- 0.017)	0.001
	Per SD change	0.495 (0.368– 0.667)	0.001	0.499 (0.368– 0.676)	0.001
Angular_right	Per unit change	0.001 (0.000- 0.020)	0.001	0.001 (0.000- 0.046)	0.001
	Per SD change	0.475 (0.337– 0.670)	0.001	0.512 (0.359– 0.729)	0.001
Insula_left	Per unit change	0.008 (0.000- 0.280)	0.008	0.016 (0.000- 0.730)	0.034
	Per SD change	0.697 (0.535– 0.909)	0.008	0.732 (0.549– 0.977)	0.034
Insula_right	Per unit change	0.002 (0.000- 0.221)	0.010	0.011 (0.000- 1.461)	0.07
	Per SD change	0.666 (0.490– 0.906)	0.010	0.742 (0.538– 1.025)	0.07
Adjusted HR indicates the hazard ratio after adjusting for age and sex.					

Discussion

Main Findings

This study characterized cerebral metabolism and metabolic network organization in PF and evaluated their clinical relevance. PF was associated with cerebral hypometabolism and metabolic network

disruption, particularly within the parasympathetic-associated network. Associations between cerebral metabolic measures and EFS persisted after adjustment for conventional clinical covariates, suggesting potential prognostic information beyond pulmonary function.

Cerebral metabolic dysfunction

Previous neuroimaging studies of fibrosing interstitial lung diseases have primarily relied on structural magnetic resonance imaging (MRI) or resting-state functional MRI ^[16, 17]. In the present study, [¹⁸F]FDG PET/CT was combined with whole-brain metabolic connectivity analysis to extend these observations to cerebral glucose metabolism and interregional metabolic organization. Widespread hypometabolism and attenuation of metabolic connectivity were identified, indicating distributed rather than isolated cerebral metabolic dysfunction in PF.

Hypometabolism was concentrated in frontal, temporal, insular, cingulate, and caudate regions, broadly corresponding to neural systems implicated in the bidirectional lung-brain axis ^[6]. Several mechanisms may contribute to this pattern ^[24]. Impaired alveolar gas exchange and systemic hypoxaemia may reduce cerebral oxygen availability and constrain oxidative metabolism in vulnerable regions ^[25–27]. Associations between lower cerebral metabolism and poorer FVC and DLCO further support a relationship between pulmonary disease severity and central metabolic dysfunction.

Systemic inflammation may provide an additional pathway linking PF to cerebral metabolic dysfunction. Persistent fibrotic lung injury can increase circulating pro-inflammatory mediators, which may affect blood-brain barrier function, cerebral microvasculature and neuroimmune signaling ^[7, 28]. Altered synaptic activity, cellular energy utilization, and neurovascular coupling may therefore contribute to the observed abnormalities ^[29]. Consistently, higher CRP and ESR levels were associated with lower metabolism in several affected brain regions.

Widespread attenuation of interregional metabolic connectivity was also identified in PF. Particularly marked temporal decoupling suggested impaired integration of systems supporting memory, affective processing, semantic cognition, and interoception. The known vulnerability of temporal regions to hypoxaemia, microvascular dysfunction, and inflammatory stress may contribute to this pattern ^[30–32].

Parasympathetic network disruption

Differential involvement of central autonomic networks was identified in PF. Extensive connectivity loss was observed in the parasympathetic-associated network, whereas no significant group-level alteration was detected in the sympathetic-associated network. Parasympathetic network disruption may therefore represent a prominent cerebral metabolic feature of PF.

The pulmonary parasympathetic inflammatory reflex provides a plausible biological framework for this observation. Inflammatory and mechanical signals are detected by vagal sensory endings and conveyed to brainstem integrative centres. Efferent vagal signaling can subsequently suppress macrophage cytokine production through acetylcholine-dependent activation of alpha7 nicotinic acetylcholine

receptors^[33–35]. Homeostatic regulation of pulmonary and systemic inflammation is thereby supported by this afferent-central-efferent circuit.

This circuit may be disturbed by parenchymal remodelling, altered pulmonary mechanics, hypoxaemia, and persistent inflammatory signaling^[36]. The observed parasympathetic decoupling is consistent with impaired lung-to-brain feedback, which could weaken cholinergic restraint of inflammation. However, peripheral deafferentation and central metabolic dysfunction cannot be distinguished by the present imaging data.

Prognostic metabolic signature

A distinct pattern was identified in the survival analyses. Metabolism in selected autonomic and association regions remained independently associated with EFS after adjustment for age, sex, FVC, and DLCO, whereas other regional associations were attenuated. These findings suggest that cerebral metabolism may provide prognostic information beyond conventional measures of pulmonary impairment.

The insula, together with frontal and parietal association regions, contributes to interoception, salience processing, and autonomic regulation^[37]. Respiratory sensations, affective responses, and contextual information are integrated within these systems to support adaptive physiological responses. Sustained dyspnoea, impaired pulmonary compliance, and recurrent inflammatory signaling may impose persistent demands on these networks. Reduced metabolism may therefore indicate diminished integrative and autonomic capacity^[38, 39]. However, neuronal exhaustion cannot be distinguished from reduced synaptic activity, altered afferent input, or other metabolic effects by resting FDG uptake.

This framework may explain why cerebral metabolic markers remained prognostic value after adjustment for FVC and DLCO. Pulmonary function reflects mechanical restriction and gas-transfer impairment, whereas cerebral metabolism may capture complementary dimensions of interoceptive integration, autonomic regulation, and allostatic capacity. Reduced metabolic reserve could impair adaptive responses to infectious, inflammatory, or environmental stressors and increase vulnerability to acute exacerbation.

Translational relevance

Cerebral metabolic markers may complement FVC and DLCO in AE-fILD risk stratification by capturing regulatory information not reflected by pulmonary function alone. Clinical utility will require external validation and confirmation of incremental predictive performance. Parasympathetic network disruption also provides a rationale for further investigation of vagal neuromodulation. However, resting hypometabolism does not establish vagal failure or neuronal exhaustion. Longitudinal PET combined with autonomic, inflammatory, and physiological measurements should therefore precede interventional studies of vagus nerve stimulation or repetitive transcranial magnetic stimulation.

Limitations

Selection bias and limited generalizability may have resulted from the retrospective, single-centre design. The absence of contemporaneous blood gases, inflammatory cytokines, and direct autonomic measurements prevented separation of hypoxaemic, inflammatory, and neural mechanisms. Prospective multicentre studies with longitudinal imaging, multimodal physiological profiling, and external prognostic validation are required.

Conclusions

PF was associated with widespread cerebral hypometabolism and disrupted metabolic connectivity, particularly within the parasympathetic-associated network. Cerebral hypometabolism remained associated with poorer EFS after adjustment for age, sex, FVC, and DLCO. Cerebral metabolic imaging may therefore provide prognostic information beyond conventional pulmonary-function measures, although causality and clinical utility require prospective external validation.

Abbreviations

PF	
pulmonary fibrosis	
COPD	
chronic obstructive pulmonary disease	
EFS	
event-free survival	
HC	
healthy control	
HRCT	
high-resolution computed tomography	
FVC	
forced vital capacity	
FEV ₁	
forced expiratory volume in one second	
TLC	
total lung capacity	
DLCO	
diffusing capacity of the lung for carbon monoxide	
KL-6	
Krebs von den Lungen-6	
CRP	
C-reactive protein	
ESR	
erythrocyte sedimentation rate	

PCT
procalcitonin
MNI
Montreal Neurological Institute
ROI
region of interest
AAL
Automated Anatomical Labeling
SUVR
standardized uptake value ratio
AE-fILD
acute exacerbation of fibrotic interstitial lung disease
NBS
network-based statistic
FWER
family-wise error rate
HR
hazard ratio
SD
standard deviation
CI
confidence interval
MRI
magnetic resonance imaging.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the Ethics Committee of the First Affiliated Hospital of Zhengzhou University (Approval No. 2025-KY-1046) and written informed consent was waived because of its retrospective design. The study was conducted in accordance with the Declaration of Helsinki. This study was registered with ClinicalTrials.gov (NCT07203495).

Consent for publication

The authors affirm that human research participants provided informed consent for publication of the images in Fig. 2A, 2B, 2C and 2D.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

XXW and XMC contributed to study data collection. RHW and BPL conceived of the current work, with YJB and YGC contributing to study design. KLW implemented the statistical analysis. YJB and SSX contributed to the interpretation of data. YGC and XXW drafted the initial version of the manuscript, and all authors read and approved the final manuscript.

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Not applicable.

Availability of data and materials

The datasets analysed during the current study are not publicly available because they contain clinical and imaging data from human participants, but de-identified data are available from the corresponding author upon reasonable request and in accordance with applicable ethical and data-protection requirements.

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Figures

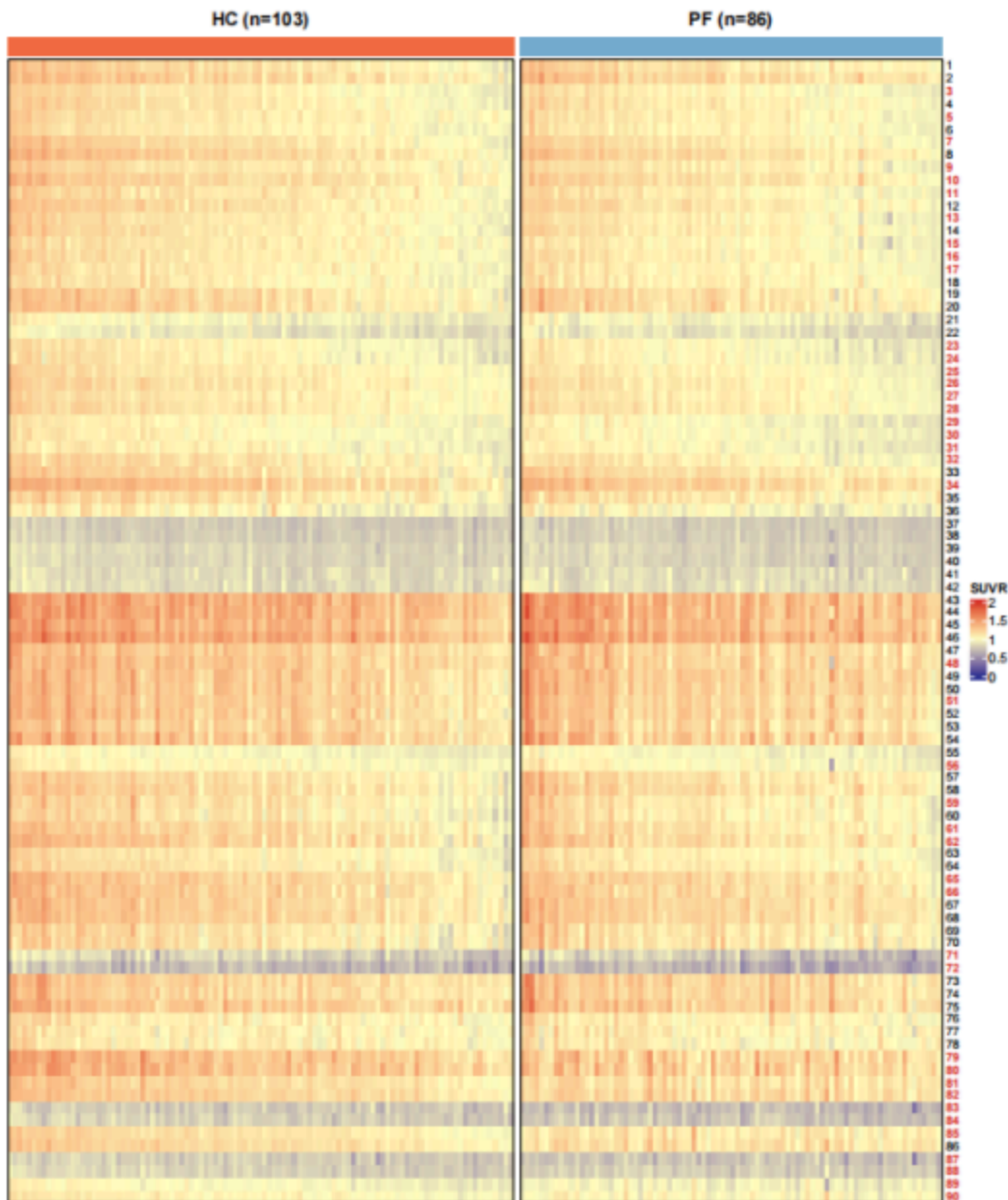


Figure 1

Cerebral glucose metabolism in healthy controls and patients with pulmonary fibrosis

Each column represents one participant, and each row represents one brain region. Region numbers correspond to the Automated Anatomical Labeling (AAL) atlas. Colors represent standardized uptake value ratio (SUVR) values, from blue (lower SUVR) to red (higher SUVR). Regional SUVR values were compared using Student's *t*-test or the Mann-Whitney *U* test, as appropriate. Red region labels indicate lower metabolism in the PF group than in the HC group ($P < 0.05$).

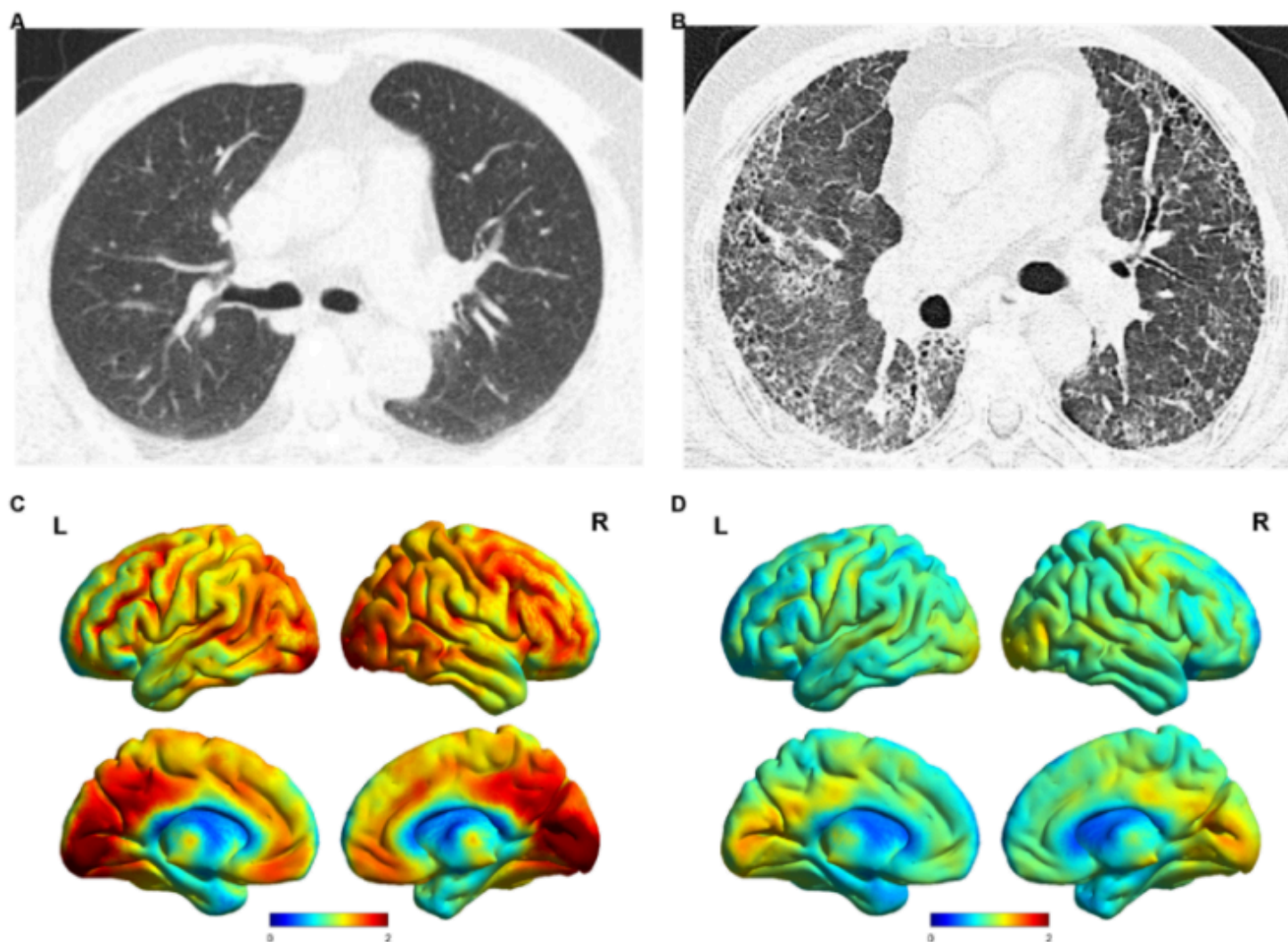


Figure 2

Representative pulmonary CT images and cerebral metabolic patterns

(A) Pulmonary CT image from a 64-year-old male healthy control. (B) Pulmonary CT image from a 64-year-old male patient with pulmonary fibrosis. (C, D) Corresponding cerebral metabolic patterns for the healthy control and patient, respectively. The patient experienced an acute exacerbation during the 6-month follow-up.

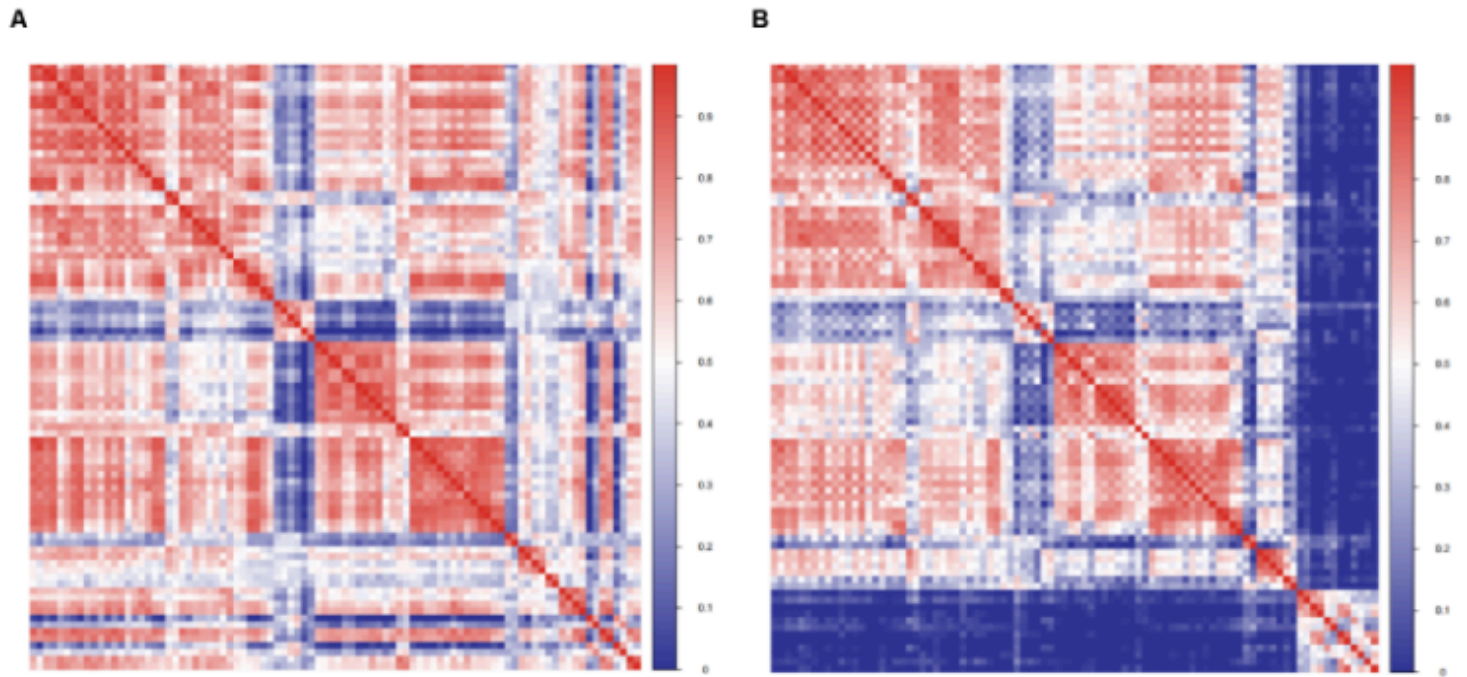


Figure 3

Whole-brain metabolic correlation matrices in healthy controls and patients with pulmonary fibrosis

(A) Metabolic correlation matrix for the HC group. (B) Metabolic correlation matrix for the PF group. Matrices show pairwise interregional correlations in standardized uptake value ratios across 90 predefined brain regions. Colors indicate correlation strength from 0 (blue) to 1 (red).

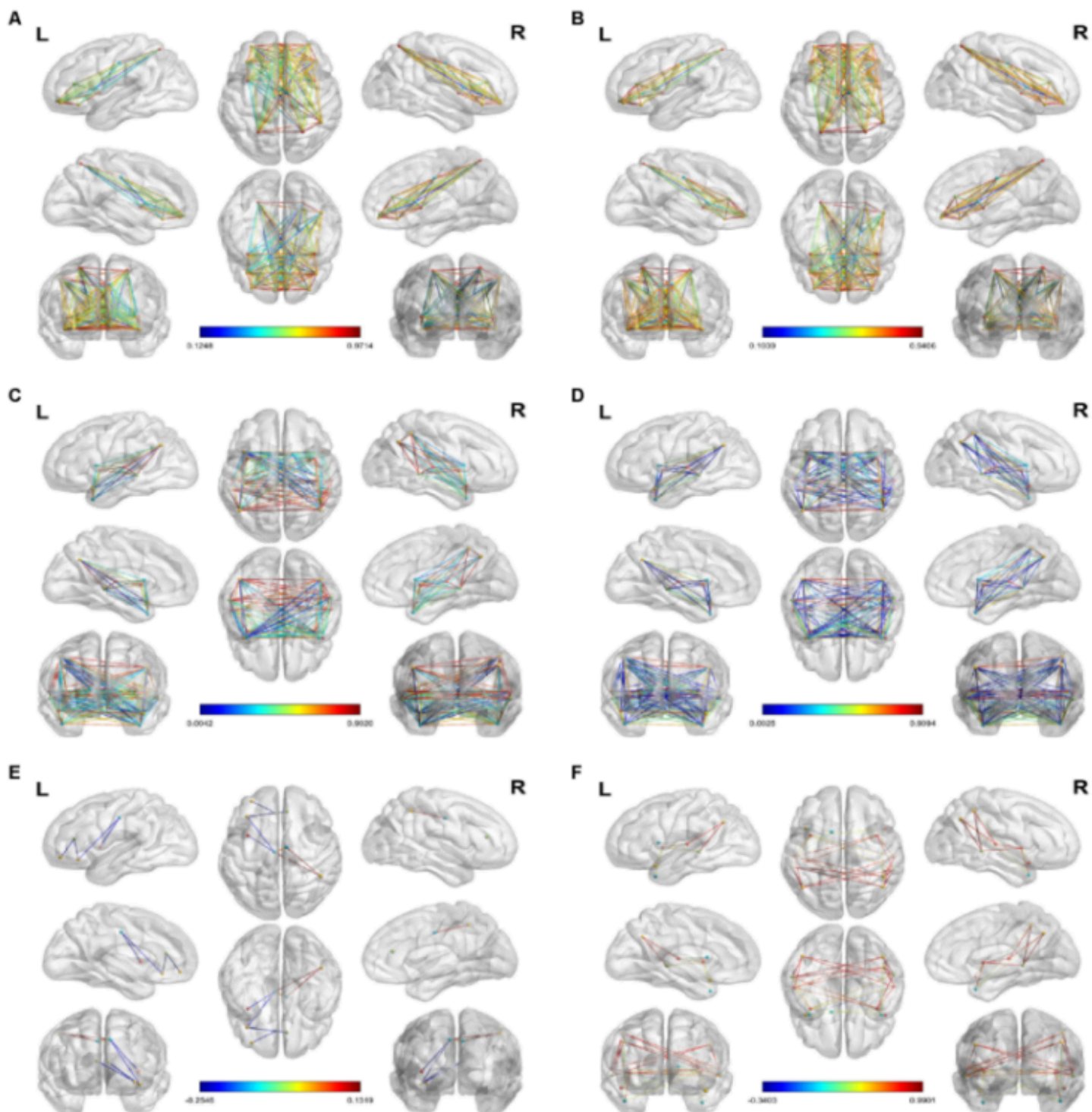


Figure 4

Autonomic metabolic subnetworks and network-based comparisons between groups

(**A, B**) Sympathetic-associated neural subnetworks in the HC and PF groups, respectively. (**C, D**) Parasympathetic-associated neural subnetworks in the HC and PF groups, respectively. (**E, F**) Between-group differential networks for the sympathetic- and parasympathetic-associated systems, respectively.

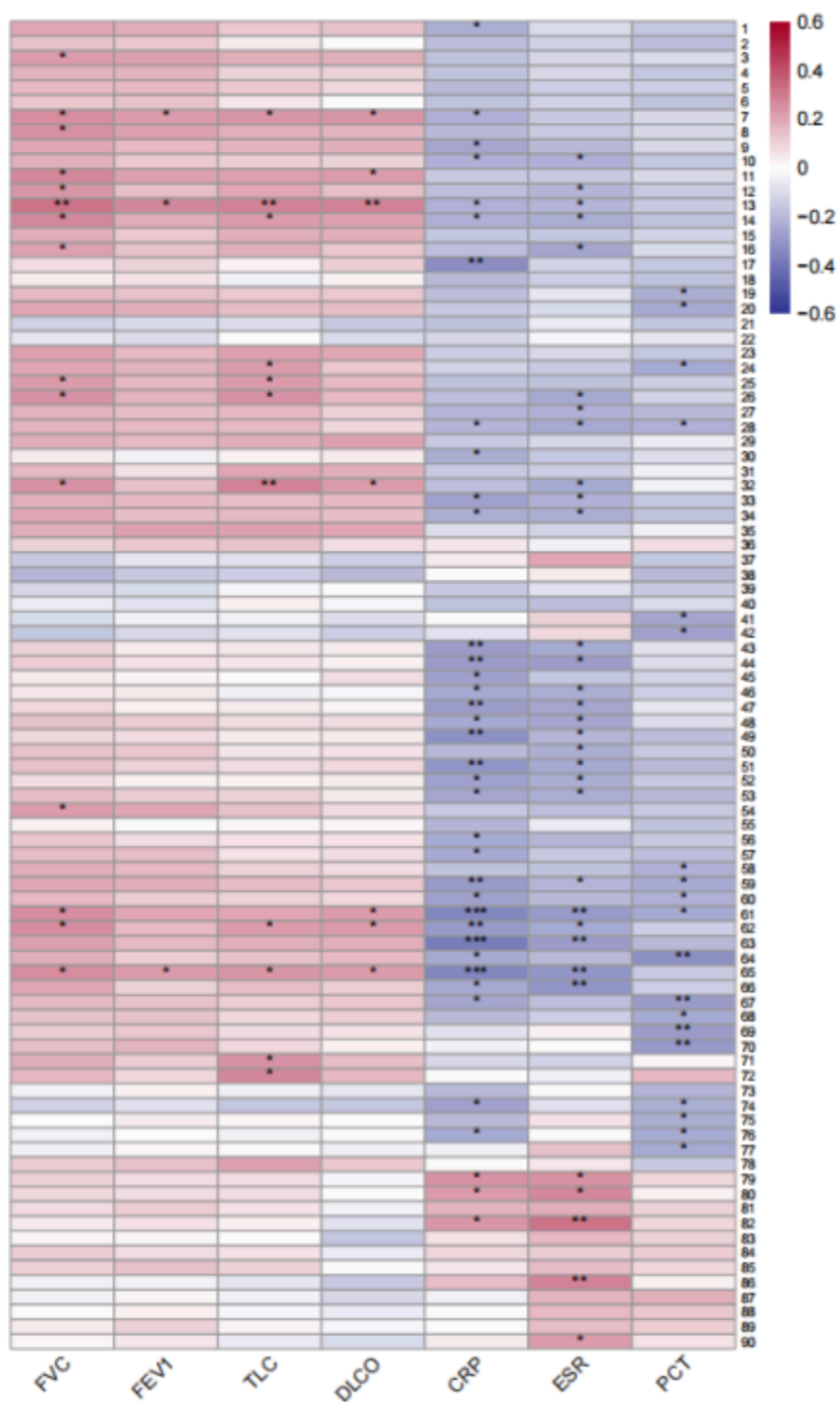


Figure 5

Associations of cerebral glucose metabolism with pulmonary function and inflammatory markers

Colors indicate the strength and direction of correlations, from blue (negative) to red (positive). Asterisks indicate statistical significance: * $P < 0.05$, ** $P < 0.01$, and *** $P < 0.001$.

Supplementary Files

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