

The Neuro-Fluid Paradigm in Microgravity: A Bibliometric Mapping of Spaceflight-Associated Neuro-Ocular Syndrome (SANS) and Intracranial Hypertension

Arylic Singh

asingh62@health.ucdavis.edu

University of California, Davis

Katrina Shute

Ministry of Health Fiji

Muhammed Sulman

University of California, Davis

Cameron Hawk

California Northstate University

Cristian Mendieta

Universidad San Francisco Xavier

Article

Keywords: SANS, Glymphatic system, Spaceflight-associated neuro-ocular syndrome, Intracranial hypertension, Optic disc edema, Gravity

Posted Date: September 14th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10923731/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Additional Declarations: No competing interests reported.

Abstract

Background

Spaceflight-associated neuro-ocular syndrome (SANS) remains a critical physiological barrier to long-duration space exploration. While historically characterized by isolated ocular pathology, emerging evidence suggests a complex etiology rooted in central nervous system fluid dynamics. This study provides a quantitative bibliometric synthesis mapping the conceptual transition toward intracranial and glymphatic mechanics.

Methods

A comprehensive search of the Web of Science Core Collection was executed in April 2026. Bibliometric metadata from 194 strictly curated peer-reviewed documents were extracted, specifically capturing document types, prolific authors, active journals, and funding agencies. Programmatic network analysis then evaluated annual production, conceptual clusters, institutional collaboration, and citation impact to map the thematic evolution of the field.

Results

Analysis reveals a 2011 inflection point initiating an exponential publication surge that peaked in 2025. Keyword mapping connects microgravity to idiopathic intracranial hypertension via optic disc edema and intracranial pressure, alongside a recently emerging glymphatic node. Institutional matrices reveal a highly centralized research infrastructure heavily anchored by The National Aeronautics and Space Administration (NASA) and Texas Medical Center ecosystem. Lee et al. and npj Microgravity emerged as the most prolific author and journal, respectively. However, citation analysis confirms the highest impact foundational literature is consistently published in mainstream terrestrial clinical journals. Curatorial extraction shows the 194 English documents feature a high concentration of theoretical reviews necessitated by the constrained astronaut population, bridging ophthalmology and neuroscience. Finally, the dataset maintains a cumulative impact of 4,621 citations averaging 23.8 per document.

Conclusion

The literature has definitively transitioned from descriptive ocular observations toward complex mechanistic models of glymphatic clearance and systemic cerebrospinal fluid dynamics. This conceptual evolution establishes microgravity as an invaluable analog for terrestrial intracranial hypertension and underscores the critical necessity for automated precision surveillance during future interplanetary exploration.

1. Introduction

As humanity transitions from low Earth orbit missions to long duration exploration of the Moon and Mars, physiological preservation of the central nervous system has emerged as a primary mission constraint. Among the most significant risks identified by global space agencies is spaceflight-associated neuro-ocular syndrome (SANS), a constellation of clinical findings including optic disc edema, posterior globe flattening, choroidal folds, and hyperopic refractive shifts [1]. Historically, this pathology was termed Visual Impairment Intracranial Pressure (VIIP). This legacy nomenclature reflected early hypotheses that isolated intracranial hypertension was the primary driver of the visual changes. However, as the medical community increasingly recognized the pathology as a broader manifestation of systemic neuro-fluid stasis rather than simply elevated pressure, the terminology officially transitioned to SANS [2, 3].

The pathophysiology of SANS is largely attributed to the persistent cephalad fluid shift that occurs in the absence of a hydrostatic gradient. In microgravity, significant fluid volume migrates from the lower extremities toward the cranium, resulting in chronic venous congestion and elevated intracranial pressure [4]. This environment provides a unique operational model of intracranial hypertension that mirrors terrestrial idiopathic intracranial hypertension (IIH), yet lacks the confounding metabolic variables typically associated with the latter [3]. Consequently, the study of SANS offers a profound opportunity to refine our understanding of cerebrospinal fluid production, venous outflow, and the recently characterized glymphatic system [5].

Despite the critical nature of these neurological risks, the literature has historically been fragmented across aerospace engineering, clinical ophthalmology, and basic physiology. There is a notable lack of high-level synthesis regarding how the field has matured conceptually. Specifically, the literature lacks a quantitative mapping of the shift from descriptive ocular morphology toward complex neuro-fluid mechanics. As deep space missions demand autonomous health monitoring, identifying the thematic pillars and key contributors of this research is essential for developing effective mitigation strategies.

The objective of this study is to perform a comprehensive bibliometric analysis of the microgravity neuro-fluid and SANS literature spanning the past five decades. By utilizing programmatic network analysis and topological mapping of the Web of Science Core Collection, this research quantifies the temporal acceleration of scientific production and identifies the dominant research hubs bridging aerospace medicine with clinical neurosurgery. This study visualizes the thematic evolution toward mechanistic, glymphatic, and precision medicine models. Through this quantitative lens, we provide a roadmap for the next generation of neurosurgical interventions required to sustain human life beyond terrestrial gravitational influence.

2. Methods

2.1 Search strategy and data acquisition

The Web of Science Core Collection was exclusively selected as the primary database because it provides the highly standardized cited reference metadata and rigid export architecture required for precise programmatic network analysis, avoiding the indexing inconsistencies prevalent in other repositories. A comprehensive literature search was executed in April 2026. To capture the full historical and modern scope of the pathology, the search string utilized a combination of legacy acronyms and contemporary terminology. The exact primary query executed was: ("Spaceflight-Associated Neuro-ocular Syndrome" OR "SANS" OR "Visual Impairment Intracranial Pressure" OR "VIIP" OR ("microgravity" AND ("intracranial pressure" OR "optic disc edema" OR "glymphatic")))). The search spanned from database inception to April 2026. No language restrictions were applied during the initial query to ensure comprehensive coverage of international space agency outputs, though English served as the primary indexing language for downstream keyword co-occurrence analysis.

2.2 Data curation and exclusion criteria

The initial search yielded a raw dataset of 222 metadata records. These records were exported in plain text format containing full bibliometric indicators and cited references. Two authors (K.S. and M.S.) independently performed a manual title and abstract screen to filter out "bycatch" literature that shared keywords but lacked mechanistic relevance to the central nervous system. Any discrepancies regarding inclusion were resolved through consensus discussion with a third author (A.S.). Exclusion criteria were strictly applied to remove 28 off topic documents. These excluded papers primarily consisted of strictly terrestrial exercise physiology lacking microgravity context, basic in vitro cell biology, unrelated terrestrial ophthalmological pathologies such as primary open angle glaucoma, and generalized administrative reviews of space programs. Importantly, studies utilizing high fidelity microgravity analogs on Earth, including head down tilt bed rest, dry immersion, and lower body negative pressure countermeasure testing, were explicitly retained due to their direct relevance to systemic fluid shifts. Following this filtration, a finalized, high yield dataset of 194 peer reviewed documents was established for downstream computational analysis. A complete, itemized bibliography of the utilized dataset, including digital object identifiers (DOIs), is provided in the Supplementary document.

2.3 Data processing and variable extraction

Custom programmatic pipelines were developed using Python to deterministically parse the structured raw metadata exported from the Web of Science. The extracted data points included document type, publication year, contributing authors, source journals, total citations, Web of Science categories, and funding agencies. Author Keywords and Web of Science generated Keywords Plus were both extracted to capture the maximum conceptual footprint of each document. Documents lacking indexed keyword metadata were excluded from the co-occurrence analysis. The pandas library was utilized to construct dataframes, resolve minor indexing inconsistencies, and aggregate descriptive statistics regarding annual scientific production and citation density, thereby ensuring absolute computational reproducibility and eliminating the risk of manual transcription errors.

2.4. Programmatic network analysis and visualization

To map the thematic evolution and collaborative infrastructure of the field, computational network analysis was performed. Rather than relying on proprietary black box graphical user interfaces common in standard bibliometric software, this study utilized deterministic, open source Python libraries (NetworkX and pandas) to perform the topological mapping. This custom programmatic approach ensures absolute computational reproducibility and provides complete transparency regarding the matrix calculations utilized to generate the network and institutional matrices. For the conceptual mapping of the pathology, a keyword co-occurrence matrix was constructed. To eliminate transient or isolated research topics and highlight the core structural pillars of the literature, a rigorous mathematical threshold was applied, retaining only conceptual relationships that co-occurred a minimum of six times across the dataset. The resulting topological map was visualized using the matplotlib library. Institutional collaboration matrices were similarly generated using programmatic heatmaps to identify the primary global hubs driving the transition toward automated precision space medicine. The full pipeline source code is provided in the supplementary documents for reproducibility.

3. Results

3.1 Literature retrieval and characteristics

The primary database query yielded an initial dataset of 222 documents spanning from database inception to April 2026. Following the manual screening protocol to eliminate terrestrial bycatch and non mechanistic physiological studies, a finalized cohort of 194 highly relevant peer reviewed documents was retained for downstream topological analysis (Fig. 1). The curatorial demographics of the finalized dataset demonstrate a strong foundation of primary clinical and experimental research. The cohort consists predominantly of original research articles ($n = 114$, 58.8%), followed by comprehensive literature reviews ($n = 52$, 26.8%), and formalized proceedings papers ($n = 8$, 4.1%). Despite the lack of language restrictions during the initial query, the indexed literature is entirely consolidated within the English language ($n = 192$), reflecting the standardized communication protocols of global aerospace agencies. While the literature remains anchored in Ophthalmology (55 documents), it branches heavily into Multidisciplinary Sciences (38 documents), Physiology (32 documents), and increasingly into dedicated Neurosciences (17 documents), confirming the clinical shift from isolated ocular observations toward complex systemic neurology.

3.2 Annual publication trends and dataset growth

Analysis of the publication timeline reveals a distinct biphasic trajectory in the microgravity neurofluid literature (Fig. 2). Prior to 2011, scientific production was characterized by a low volume historical baseline. A quantitative inflection point was observed after 2011, coinciding directly with the publication of the highly cited clinical report by Mader et al. Following this event, the annual growth rate of publications accelerated rapidly, initiating a sustained exponential increase in scientific output. This trajectory culminated in a historic maximum of annual publications in the year 2025. The temporal

distribution confirms that the vast majority of the 194 finalized documents were published during the post 2011 era, reflecting a rapid and quantitative expansion of the research domain.

*This chronological distribution quantifies the publication volume of the curated 194 document dataset from database inception through April 2026. The temporal trajectory demonstrates a low volume historical baseline prior to a critical inflection point after 2011. This structural break corresponds with the initial clinical formalization of the pathology, which served as a catalyst for subsequent research. Following this event, the field demonstrates a sustained exponential surge in scientific output, culminating in a historic maximum. This rapid acceleration visually reflects the active transition of the discipline from passive observation toward high priority operational intervention and neurosurgical modeling. **Note:** *2026 data represents a partial year (January–April).*

3.3 Citation impact and prolific contributors

Citation analysis of the 194 document dataset yielded a cumulative total of 4,621 citations. The literature maintains an average of 23.8 citations per document and utilizes an average of 50.5 references per manuscript. The distribution of academic production is heavily concentrated among a specific cohort of neuro-ophthalmologists and aerospace physiologists (Table 1). Lee et al. emerged as the most prolific contributor with 31 publications, followed by Gibson et al. (n = 24) and Mader et al. (n = 23). Source analysis indicates that Npj Microgravity is the primary venue for this literature (n = 22), bridging the gap to high impact clinical journals including the Journal of Applied Physiology (n = 14) and JAMA Ophthalmology (n = 13). Analysis of the top ten most highly cited documents (Table 2) confirms the foundational status of the 2011 clinical report by Mader et al., which has accumulated 551 total citations.

Table 1

Top ten most prolific authors and active journals in spaceflight associated neuro-ocular syndrome literature This table quantifies the primary academic contributors and publication venues within the curated 194 document dataset. The distribution highlights a high concentration of research output among a specialized cohort of neuro ophthalmologists and aerospace physiologists. Furthermore, it demonstrates that specialized aerospace venues such as npj Microgravity publish the highest volume of related literature, bridging the aerospace domain with mainstream clinical journals including the Journal of Applied Physiology and JAMA Ophthalmology.

Rank	Most Prolific Authors	Publications [N (%)]	Most Active Journals	Publications [N (%)]
1	Lee et al.	31 (15.9%)	npj Microgravity	22 (11.3%)
2	Gibson et al.	24 (12.3%)	Journal Of Applied Physiology	14 (7.2%)
3	Mader et al.	23 (11.8%)	Jama Ophthalmology	13 (6.7%)
4	Macias et al.	21 (10.8%)	Aerospace Medicine And Human Performance	12 (6.1%)
5	Ong et al.	21 (10.8%)	Life Sciences In Space Research	10 (5.1%)
6	Laurie et al.	15 (7.7%)	Aviation Space And Environmental Medicine	9 (4.6%)
7	Wostyn et al.	15 (7.7%)	Investigative Ophthalmology & Visual Science	7 (3.6%)
8	Stenger et al.	14 (7.2%)	Eye	7 (3.6%)
9	Marshall-Goebel et al.	13 (6.7%)	Physiological Reports	4 (2.1%)
10	Hargens et al.	13 (6.7%)	Current Opinion In Ophthalmology	3 (1.5%)

Table 2

Top ten most highly cited documents in spaceflight-associated neuro-ocular syndrome literature This table presents the foundational literature driving the conceptual evolution of the field, ranked by total citation count within the curated 194 document dataset. The distribution mathematically confirms the seminal status of the 2011 clinical report by Mader and colleagues, which initiated the exponential surge in contemporary scientific production. Furthermore, the prominent inclusion of mainstream terrestrial clinical journals specifically Ophthalmology, Physiological Reviews, and JAMA Ophthalmology, demonstrates that the highest impact literature has successfully transcended specialized aerospace venues to influence the broader neurosurgical and ophthalmological communities

Rank	First Author	Year	Title	Journal	Total Citations [N]	Citations Per Year
1	Mader et al.	2011	Optic Disc Edema, Globe Flattening, Choroidal Folds, And Hyperopic Shifts Observed In Astronauts After Long-Duration Space Flight.	Ophthalmology	551	36.7
2	Lee et al.	2020	Spaceflight Associated Neuro-Ocular Syndrome (Sans) And The Neuro-Ophthalmologic Effects Of Microgravity: A Review And An Update.	npj Microgravity	243	40.5
3	Zhang et al.	2018	Spaceflight-Induced Intracranial Hypertension And Visual Impairment: Pathophysiology And Countermeasures.	Physiological Reviews	181	22.6
4	Lee et al.	2018	Space Flight-Associated Neuro-Ocular Syndrome (Sans).	Eye	123	15.4
5	Lee et al.	2017	Space Flight-Associated Neuro-Ocular Syndrome.	Jama Ophthalmology	96	10.7
6	Macias et al.	2020	Association Of Long-Duration Spaceflight With Anterior And Posterior Ocular Structure Changes In Astronauts And Their Recovery.	Jama Ophthalmology	94	15.7
7	Laurie et al.	2020	Optic Disc Edema And Choroidal Engorgement In Astronauts During Spaceflight And Individuals Exposed To Bed Rest.	Jama Ophthalmology	92	15.3

Rank	First Author	Year	Title	Journal	Total Citations [N]	Citations Per Year
8	Kawai et al.	1993	Cerebral Blood-Flow Velocity In Humans Exposed To 24-H Of Head-Down Tilt.	Journal Of Applied Physiology	80	2.4
9	Petersen et al.	2019	Lower Body Negative Pressure To Safely Reduce Intracranial Pressure.	Journal Of Physiology-London	79	11.3
10	Feola et al.	2016	Finite Element Modeling Of Factors Influencing Optic Nerve Head Deformation Due To Intracranial Pressure.	Investigative Ophthalmology & Visual Science	77	7.7

3.4 Conceptual evolution and network mapping

Topological mapping of author keywords and Web of Science Keywords Plus generated a co-occurrence network reflecting the conceptual architecture of the field (Fig. 3). Applying a strict visualization threshold of six co-occurrences eliminated transient topics and isolated the core pathophysiological pillars. The resulting network structure mathematically bridges operational aerospace triggers with terrestrial neuropathologies. Specifically, the node for microgravity shares robust edge weights with intracranial pressure, cephalad fluid shift, and optic disc edema. Furthermore, the network confirms a direct structural link to idiopathic intracranial hypertension. Notably, the glymphatic system emerged as a distinct node in the modern literature, establishing direct network connections to cerebrospinal fluid dynamics and neuro-fluid stasis.

A strict visualization threshold of six co-occurrences was applied to isolate core pathophysiological pillars. Node size represents the frequency of keyword occurrence. The lines linking the nodes represent direct conceptual co-occurrences within the literature, with the layout algorithm clustering highly associated terms in close physical proximity. The network explicitly maps the structural bridge between aerospace operational triggers (microgravity) and terrestrial clinical pathologies (idiopathic intracranial hypertension). Notably, central hubs such as intracranial pressure and optic disc edema serve as primary connectors, while the glymphatic system emerges as a distinct node, reflecting the modern paradigm shift toward systemic neuro fluid stasis

3.5 Global infrastructure and institutional collaboration

Evaluation of the economic and institutional infrastructure supporting this research reveals a highly centralized funding ecosystem. The National Aeronautics and Space Administration (NASA) serves as the primary financial catalyst, directly funding 26 explicit publications, supplemented by the NASA Human Research Program (n = 7) and the National Space Biomedical Research Institute (n = 5).

Heatmap visualization of institutional collaboration (Fig. 4) demonstrates the dense international networks required to execute these studies. The matrices highlight strong structural ties between federal aerospace operational centers, such as the Johnson Space Center, and terrestrial academic medical institutions.

This programmatic heatmap visualizes the coauthorship frequency and collaborative network density among the most prolific institutions publishing on spaceflight-associated neuro-ocular syndrome. Color intensity correlates directly with the volume of joint publications. The matrix highlights a highly centralized domestic infrastructure anchored by NASA and the broader Texas Medical Center ecosystem, notably including Baylor College of Medicine, KBRwyle, and the University of Texas Medical Branch. Additionally, the map identifies a distinct European collaborative cluster centered around the University of Antwerp and associated Belgian clinical institutions, reflecting the international, multi institutional effort required to map microgravity induced fluid shifts. Abbreviations for truncated labels: BCM, Baylor College of Medicine; HMMH, Houston Methodist Hospital; MDACC, University of Texas MD Anderson Cancer Center; UIHC, University of Iowa Hospitals & Clinics.

4. Discussion

4.1 The neuro-fluid paradigm shift

The primary finding of this bibliometric analysis is the definitive conceptual evolution of SANS from a localized ophthalmological anomaly into a complex neurosurgical and hydrodynamic pathology. Historically, visual impairment in astronauts was treated as an isolated consequence of microgravity [1, 6, 7]. However, the topological mapping in this study visualizes a stark paradigm shift. The robust structural linkages connecting optic disc edema to intracranial pressure and cephalad fluid shift indicate that ocular remodeling is now widely recognized by the scientific community not as the primary disease, but as the visible biomarker of systemic intracranial fluid stasis [2, 8].

Most notably, the emergence of the glymphatic system as a distinct node in recent literature highlights a critical advancement in mechanistic modeling. Microgravity induces chronic venous congestion in the jugular outflow tract [9, 10]. This venous impedance cascades backward, disrupting the delicate pressure gradients required for cerebrospinal fluid clearance and glymphatic drainage [11, 12, 13]. The persistent mathematical connection between microgravity and terrestrial idiopathic intracranial hypertension (IIH) mapped in our network suggests that the aerospace and neurosurgical communities are actively merging these pathologies [3, 14, 15]. SANS effectively represents an accelerated, metabolically pure analog of IIH, providing a unique environment to study neuro-fluid dynamics without the confounding variables of terrestrial obesity or endocrine dysfunction [16, 17].

Furthermore, the literature highlights a critical demographic paradox between terrestrial and microgravity intracranial hypertension. Terrestrial idiopathic intracranial hypertension predominantly affects overweight females of childbearing age, driven heavily by endocrine and metabolic factors [15, 18].

Conversely, the historical incidence of SANS has been disproportionately documented in male astronauts [19]. It is critical to acknowledge that this disparity is likely influenced by an artifact of historical space agency demographics, as the astronaut corps has traditionally been overwhelmingly male. However, the current literature suggests this divergence is not merely a statistical illusion. Emerging evidence points to a true physiological divergence, indicating that while the mechanical cephalad fluid shift acts as the primary trigger in space, underlying hormonal, anatomical, or genetic variables modulate individual susceptibility. As international space agencies diversify their astronaut corps for the Artemis lunar missions, resolving this sex specific pathophysiological divergence remains a critical gap in the current literature.

4.2 Bibliometric markers of a resource constrained frontier

Beyond thematic mapping, the curatorial metadata extracted in this study reveals several highly unusual characteristics that reflect the unique logistical constraints of space medicine. First, the dataset exhibits an exceptionally high ratio of literature reviews to original research articles. In mature terrestrial medical fields, original research vastly outpaces review literature. The dense concentration of reviews in the SANS literature reflects a field grappling with an inherently limited N size of astronaut subjects [2, 5, 20]. Researchers are utilizing theoretical synthesis and mathematical modeling to bridge the gaps in sparse operational data.

Second, this multidisciplinary synthesis is mathematically proven by the abnormally high reference density across the dataset, averaging over 50 references per document. This metric demonstrates that aerospace researchers must aggressively pull data from diverse terrestrial disciplines including exercise physiology, ophthalmology, and basic neuroscience to contextualize their findings [21, 22, 23]. Furthermore, the institutional collaboration matrices explicitly confirm that research dominance in this field is heavily dictated by physical geographic proximity to federal aerospace infrastructure. The dense concentration of output from the Texas Medical Center ecosystem, including Baylor College of Medicine and the University of Texas Medical Branch, directly reflects their integration with the neighboring NASA Johnson Space Center and associated federal funding mechanisms.

Finally, our analysis identifies a significant divergence between publication volume and citation impact. While specialized aerospace venues produce the highest volume of SANS literature, the most highly cited foundational documents are consistently published in mainstream terrestrial clinical journals [1, 4, 24]. This paradox proves that SANS has successfully crossed the disciplinary boundary and it is no longer viewed merely as operational aerospace trivia, but as a high priority pathology with direct translational value for terrestrial neurosurgery and ophthalmology.

4.3 Countermeasures and the imperative for autonomous surveillance

The exponential surge in scientific production peaking in 2025 aligns directly with the escalating timelines for the Artemis lunar missions and planned Martian exploration. Current mitigation strategies

rely heavily on mechanical countermeasures, such as lower body negative pressure, to temporarily reverse the cephalad fluid shift and relieve intracranial hypertension [25, 26, 27]. However, the transition from low Earth orbit to deep space introduces communication latency and strict mass limitations, rendering current Earth dependent diagnostic protocols obsolete [28, 29].

The bibliometric trajectory mapped in this study identifies a distinct gap in the current translational literature. While the publication landscape is heavily saturated with mechanistic fluid models, our network mapping reveals a lack of literature addressing how to operationalize these findings. To safely execute interplanetary missions, future research must pivot toward translating this massive volume of mechanistic fluid data into automated precision health surveillance systems. As deep space medical infrastructure evolves, we anticipate a future surge in literature focusing on autonomous, artificial intelligence-driven integration of portable conventional magnetic resonance imaging and ocular ultrasound to monitor subtle changes in intracranial compliance in real time.

While mechanical fluid models dominate the highly cited literature, predicting individual risk requires a transition toward precision medicine. The bibliometric data indicates that the aerospace community is beginning to investigate molecular and genetic biomarkers to explain why only a subset of astronauts develop SANS despite uniform exposure to microgravity. Specifically, polymorphisms in one carbon metabolism and B vitamin status have been proposed as significant modulators of endothelial compliance and neurovascular vulnerability [30, 31]. Integrating these genomic and metabolomic profiles with the automated neuroimaging surveillance systems proposed earlier will be essential for creating individualized risk stratification models for deep space crew members.

Crucially, the development of these autonomous, artificial intelligence-driven diagnostic tools will yield massive translational benefits for terrestrial medicine. The engineering constraints of deep space necessitate medical devices that are portable, radiation hardened, and capable of operating without specialist interpretation [32]. Transitioning this spaceflight technology to Earth will directly enhance neurocritical care in resource limited environments, rural hospitals, and military deployments, democratizing access to complex intracranial pressure monitoring and neuro-ophthalmological diagnostics.

4.4 Limitations

This study has several inherent limitations. By restricting data acquisition exclusively to the Web of Science Core Collection to ensure high fidelity citation mapping, this analysis inherently excludes internal government technical reports and unindexed symposium proceedings commonly utilized by aerospace agencies. Furthermore, while the search strategy was not restricted by language, the English indexing bias of major scientific databases may underrepresent historical data from non Western space programs.

Finally, while standard bibliometric network analyses frequently utilize datasets comprising thousands of documents, our finalized cohort of 194 papers is relatively small. However, this volume accurately

reflects the inherently niche domain of spaceflight medicine and our deliberate methodological choice to prioritize pathophysiological rigor over dataset volume. By manually screening out 28 off-topic documents, such as strictly terrestrial exercise physiology or unrelated ocular pathologies like primary open-angle glaucoma, we generated a high-fidelity dataset. This strict curation ensures that the resulting topological networks represent a pure, highly concentrated mapping of the microgravity neuro-fluid paradigm, free from the dilutive effects of extraneous terrestrial clinical noise.

5. Conclusion

Over the past five decades, the scientific conceptualization of spaceflight neuro-ocular pathologies has undergone a radical transformation. This bibliometric mapping demonstrates that the literature increasingly emphasizes a conceptual transition away from descriptive ocular assessments toward complex, mechanistic models of cerebrospinal fluid dynamics and glymphatic clearance. The microgravity environment serves as an invaluable accelerator for understanding terrestrial neurosurgical pathologies like idiopathic intracranial hypertension. While current research extensively documents the pathophysiology of SANS, our analysis indicates that the literature has not yet adequately addressed operational countermeasures. Resolving the SANS pathology through the deployment of automated, precision diagnostic surveillance remains a critical research frontier for the future of human interplanetary exploration.

Declarations

Funding: The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

Competing interests: The authors have no relevant financial or non-financial interests to disclose.

Ethics approval: Not applicable. This study is a quantitative bibliometric analysis of previously published, publicly available literature and did not involve human participants or animal subjects.

Consent to participate: Not applicable.

Consent for publication: Not applicable.

Availability of data and material: The finalized, curated dataset of 194 documents is provided in Supplementary Document attached.

Code availability: The custom Python scripts utilized for NetworkX programmatic analysis and topological mapping are attached in the supplementary documents.

Authors' contributions: A.S. and K.S. conceived the study design. A.S. and M.S. performed the data extraction and programmatic Python analysis. K.S., C.H. and C.M. performed the manual curation of the dataset. The first draft of the manuscript was written by A.S., and all authors commented on previous

versions of the manuscript. A.S provided critical manuscript revisions and supervised the study. All authors read and approved the final manuscript.

References

1. Mader TH, Gibson CR, Pass AF, Kramer LA, Lee AG, Fogarty J, Tarver WJ, Dervay JP, Hamilton DR, Sargsyan A, Phillips JL, Tran D, Lipsky W, Choi J, Stern C, Kuyumjian R, Polk JD. Optic disc edema, globe flattening, choroidal folds, and hyperopic shifts observed in astronauts after long-duration space flight. *Ophthalmology*. 2011;118(10):2058–69. doi: 10.1016/j.ophtha.2011.06.021. Epub 2011 Aug 17. PMID: 21849212.
2. Lee AG, Mader TH, Gibson CR, Tarver W, Rabiei P, Riascos RF, Galdamez LA, Brunstetter T. Spaceflight associated neuro-ocular syndrome (SANS) and the neuro-ophthalmologic effects of microgravity: a review and an update. *NPJ Microgravity*. 2020;6:7. doi: 10.1038/s41526-020-0097-9. Erratum in: *NPJ Microgravity*. 2020;6:23. doi: 10.1038/s41526-020-00114-8. PMID: 32047839; PMCID: PMC7005826.
3. Zhang LF, Hargens AR. Spaceflight-Induced Intracranial Hypertension and Visual Impairment: Pathophysiology and Countermeasures. *Physiol Rev*. 2018;98(1):59–87. doi: 10.1152/physrev.00017.2016. PMID: 29167331.
4. Laurie SS, Lee SMC, Macias BR, Patel N, Stern C, Young M, Stenger MB. Optic Disc Edema and Choroidal Engorgement in Astronauts During Spaceflight and Individuals Exposed to Bed Rest. *JAMA Ophthalmol*. 2020;138(2):165–172. doi: 10.1001/jamaophthalmol.2019.5261. PMID: 31876939; PMCID: PMC6990717.
5. Lee AG, Mader TH, Gibson CR, Brunstetter TJ, Tarver WJ. Space flight-associated neuro-ocular syndrome (SANS). *Eye (Lond)*. 2018;32(7):1164–1167. doi: 10.1038/s41433-018-0070-y. Epub 2018 Mar 12. PMID: 29527011; PMCID: PMC6043524.
6. Alperin N, Bagci AM. Spaceflight-Induced Visual Impairment and Globe Deformations in Astronauts Are Linked to Orbital Cerebrospinal Fluid Volume Increase. *Acta Neurochir Suppl*. 2018;126:215–219. doi: 10.1007/978-3-319-65798-1_44. PMID: 29492564.
7. Ong J, Tavakkoli A, Strangman G, Zaman N, Kamran SA, Zhang Q, Ivkovic V, Lee AG. Neuro-ophthalmic imaging and visual assessment technology for spaceflight associated neuro-ocular syndrome (SANS). *Surv Ophthalmol*. 2022 Sep-Oct;67(5):1443–1466. doi: 10.1016/j.survophthal.2022.04.004. Epub 2022 Apr 21. PMID: 35461882.
8. McGregor HR, Hupfeld KE, Pasternak O, Beltran NE, De Dios YE, Bloomberg JJ, Wood SJ, Mulavara AP, Riascos RF, Reuter-Lorenz PA, Seidler RD. Impacts of spaceflight experience on human brain structure. *Sci Rep*. 2023;13(1):7878. doi: 10.1038/s41598-023-33331-8. PMID: 37291238; PMCID: PMC10250370.
9. Lawley JS, Petersen LG, Howden EJ, Sarma S, Cornwell WK, Zhang R, Whitworth LA, Williams MA, Levine BD. Effect of gravity and microgravity on intracranial pressure. *J Physiol*. 2017;595(6):2115–2127. doi: 10.1113/JP273557. Epub 2017 Feb 14. PMID: 28092926; PMCID: PMC5350445.

10. Marshall-Goebel K, Lee SMC, Lytle JR, Martin DS, Miller CA, Young M, Laurie SS, Macias BR. Jugular venous flow dynamics during acute weightlessness. *J Appl Physiol* (1985). 2024;136(5):1105–1112. doi: 10.1152/japplphysiol.00384.2023. Epub 2024 Mar 14. PMID: 38482574; PMCID: PMC11365546.
11. Wostyn P, Gibson CR, Mader TH. The odyssey of the ocular and cerebrospinal fluids during a mission to Mars: the "ocular glymphatic system" under pressure. *Eye (Lond)*. 2022;36(4):686–691. doi: 10.1038/s41433-021-01721-9. Epub 2021 Aug 9. PMID: 34373611; PMCID: PMC8956714.
12. Wostyn P, Mader TH, Gibson CR, Nedergaard M. New insights in brain-to-eye transport: can excess cerebrospinal fluid in astronauts escape into the eye? *Eye (Lond)*. 2025;39(2):210–212. doi: 10.1038/s41433-024-03430-5. Epub 2024 Nov 4. PMID: 39496741; PMCID: PMC11751437.
13. Ong J, Mader TH, Gibson CR, Mason SS, Lee AG. Spaceflight associated neuro-ocular syndrome (SANS): an update on potential microgravity-based pathophysiology and mitigation development. *Eye (Lond)*. 2023;37(12):2409–2415. doi: 10.1038/s41433-023-02522-y. Epub 2023 Apr 18. PMID: 37072472; PMCID: PMC10397180.
14. Kramer LA, Sargsyan AE, Hasan KM, Polk JD, Hamilton DR. Orbital and intracranial effects of microgravity: findings at 3-T MR imaging. *Radiology*. 2012;263(3):819–27. doi: 10.1148/radiol.12111986. Epub 2012 Mar 13. PMID: 22416248.
15. Rodrigues GA, Russomano T, Santos Oliveira E. Understanding the relationship between intracranial pressure and spaceflight associated neuro-ocular syndrome (SANS): a systematic review. *NPJ Microgravity*. 2025;11(1):22. doi: 10.1038/s41526-025-00464-1. PMID: 40456790; PMCID: PMC12130532.
16. Hargens AR, Richardson S. Cardiovascular adaptations, fluid shifts, and countermeasures related to space flight. *Respir Physiol Neurobiol*. 2009;169 Suppl 1:S30-3. doi: 10.1016/j.resp.2009.07.005. Epub 2009 Jul 15. PMID: 19615471.
17. Eklund A, Jóhannesson G, Johansson E, Holmlund P, Qvarlander S, Ambarki K, Wåhlin A, Koskinen LO, Malm J. The pressure difference between eye and brain changes with posture. *Ann Neurol*. 2016;80(2):269–76. doi: 10.1002/ana.24713. Epub 2016 Jul 15. PMID: 27352140.
18. Mollan SP, Davies B, Silver NC, Shaw S, Mallucci CL, Wakerley BR, Krishnan A, Chavda SV, Ramalingam S, Edwards J, Hemmings K, Williamson M, Burdon MA, Hassan-Smith G, Digre K, Liu GT, Jensen RH, Sinclair AJ. Idiopathic intracranial hypertension: consensus guidelines on management. *J Neurol Neurosurg Psychiatry*. 2018;89(10):1088–1100. doi: 10.1136/jnnp-2017-317440. Epub 2018 Jun 14. PMID: 29903905; PMCID: PMC6166610.
19. Platts SH, Bairey Merz CN, Barr Y, Fu Q, Gulati M, Hughson R, Levine BD, Mehran R, Stachenfeld N, Wenger NK. Effects of sex and gender on adaptation to space: cardiovascular alterations. *J Womens Health (Larchmt)*. 2014;23(11):950–5. doi: 10.1089/jwh.2014.4912. PMID: 25401939; PMCID: PMC4236093.
20. Ong J, Waisberg E, Masalkhi M, Suh A, Kamran SA, Paladugu P, Sarker P, Zaman N, Tavakkoli A, Lee AG. "Spaceflight-to-Eye Clinic": Terrestrial advances in ophthalmic healthcare delivery from space-

- based innovations. *Life Sci Space Res (Amst)*. 2024;41:100–109. doi: 10.1016/j.lssr.2024.02.003. Epub 2024 Feb 13. PMID: 38670636.
21. Macias BR, Patel NB, Gibson CR, Samuels BC, Laurie SS, Otto C, Ferguson CR, Lee SMC, Ploutz-Snyder R, Kramer LA, Mader TH, Brunstetter T, Stenger MB. Association of Long-Duration Spaceflight With Anterior and Posterior Ocular Structure Changes in Astronauts and Their Recovery. *JAMA Ophthalmol*. 2020;138(5):553–559. doi: 10.1001/jamaophthalmol.2020.0673. PMID: 32239198; PMCID: PMC7118682.
 22. Hargens AR, Whalen RT, Watenpaugh DE, Schwandt DF, Krock LP. Lower body negative pressure to provide load bearing in space. *Aviat Space Environ Med*. 1991;62(10):934–7. PMID: 1764003.
 23. Zahid AM, Martin B, Collins S, Oshinski JN, Ethier CR. Quantification of arterial, venous, and cerebrospinal fluid flow dynamics by magnetic resonance imaging under simulated micro-gravity conditions: a prospective cohort study. *Fluids Barriers CNS*. 2021;18(1):8. doi: 10.1186/s12987-021-00238-3. PMID: 33579319; PMCID: PMC7879666.
 24. Petersen LG, Lawley JS, Lilja-Cyron A, Petersen JCG, Howden EJ, Sarma S, Cornwell WK 3rd, Zhang R, Whitworth LA, Williams MA, Juhler M, Levine BD. Lower body negative pressure to safely reduce intracranial pressure. *J Physiol*. 2019;597(1):237–248. doi: 10.1113/JP276557. Epub 2018 Nov 20. PMID: 30286250; PMCID: PMC6312426.
 25. Marshall-Goebel K, Laurie SS, Alferova IV, Arbeille P, Auñón-Chancellor SM, Ebert DJ, Lee SMC, Macias BR, Martin DS, Pattarini JM, Ploutz-Snyder R, Ribeiro LC, Tarver WJ, Dulchavsky SA, Hargens AR, Stenger MB. Assessment of Jugular Venous Blood Flow Stasis and Thrombosis During Spaceflight. *JAMA Netw Open*. 2019;2(11):e1915011. doi: 10.1001/jamanetworkopen.2019.15011. Erratum in: *JAMA Netw Open*. 2020;3(1):e1920195. doi: 10.1001/jamanetworkopen.2019.20195. PMID: 31722025; PMCID: PMC6902784.
 26. Yang JW, Song QY, Zhang MX, Ai JL, Wang F, Kan GH, Wu B, Zhu SQ. Spaceflight-associated neuro-ocular syndrome: a review of potential pathogenesis and intervention. *Int J Ophthalmol*. 2022;15(2):336–341. doi: 10.18240/ijo.2022.02.21. PMID: 35186696; PMCID: PMC8818462.
 27. Norsk P, Asmar A, Damgaard M, Christensen NJ. Fluid shifts, vasodilatation and ambulatory blood pressure reduction during long duration spaceflight. *J Physiol*. 2015;593(3):573–84. doi: 10.1113/jphysiol.2014.284869. PMID: 25774397; PMCID: PMC4324706.
 28. Cheung HC, De Louche C, Komorowski M. Artificial Intelligence Applications in Space Medicine. *Aerosp Med Hum Perform*. 2023;94(8):610–622. doi: 10.3357/AMHP.6178.2023. PMID: 37501303.
 29. Meer EA, Church LE, Johnson BA, Rohde J, Sinclair AJ, Mollan SP, Petersen L, Polk JD, Sawyer AJ. Non invasive monitoring for spaceflight associated neuro ocular syndrome: responding to a need for In flight methodologies. *NPJ Microgravity*. 2025;11(1):61. doi: 10.1038/s41526-025-00502-y. PMID: 40890229; PMCID: PMC12402340.
 30. Zwart SR, Gibson CR, Mader TH, Ericson K, Ploutz-Snyder R, Heer M, Smith SM. Vision changes after spaceflight are related to alterations in folate- and vitamin B-12-dependent one-carbon metabolism. *J Nutr*. 2012;142(3):427 – 31. doi: 10.3945/jn.111.154245. Epub 2012 Feb 1. PMID: 22298570.

31. Carter KJ, Ferguson CR, O'Grady CS, Poczatek MJ, Chen X, Young M, Huang AS, Laurie SS, Macias BR. Prediction of Optic Disc Edema Progression During Spaceflight. JAMA Ophthalmol. 2026;144(1):34–40. doi: 10.1001/jamaophthalmol.2025.4635. PMID: 41264263; PMCID: PMC12635925.

32. Ong J, Tavakkoli A, Zaman N, Kamran SA, Waisberg E, Gautam N, Lee AG. Terrestrial health applications of visual assessment technology and machine learning in spaceflight associated neuro-ocular syndrome. NPJ Microgravity. 2022;8(1):37. doi: 10.1038/s41526-022-00222-7. PMID: 36008494; PMCID: PMC9411571.

Figures

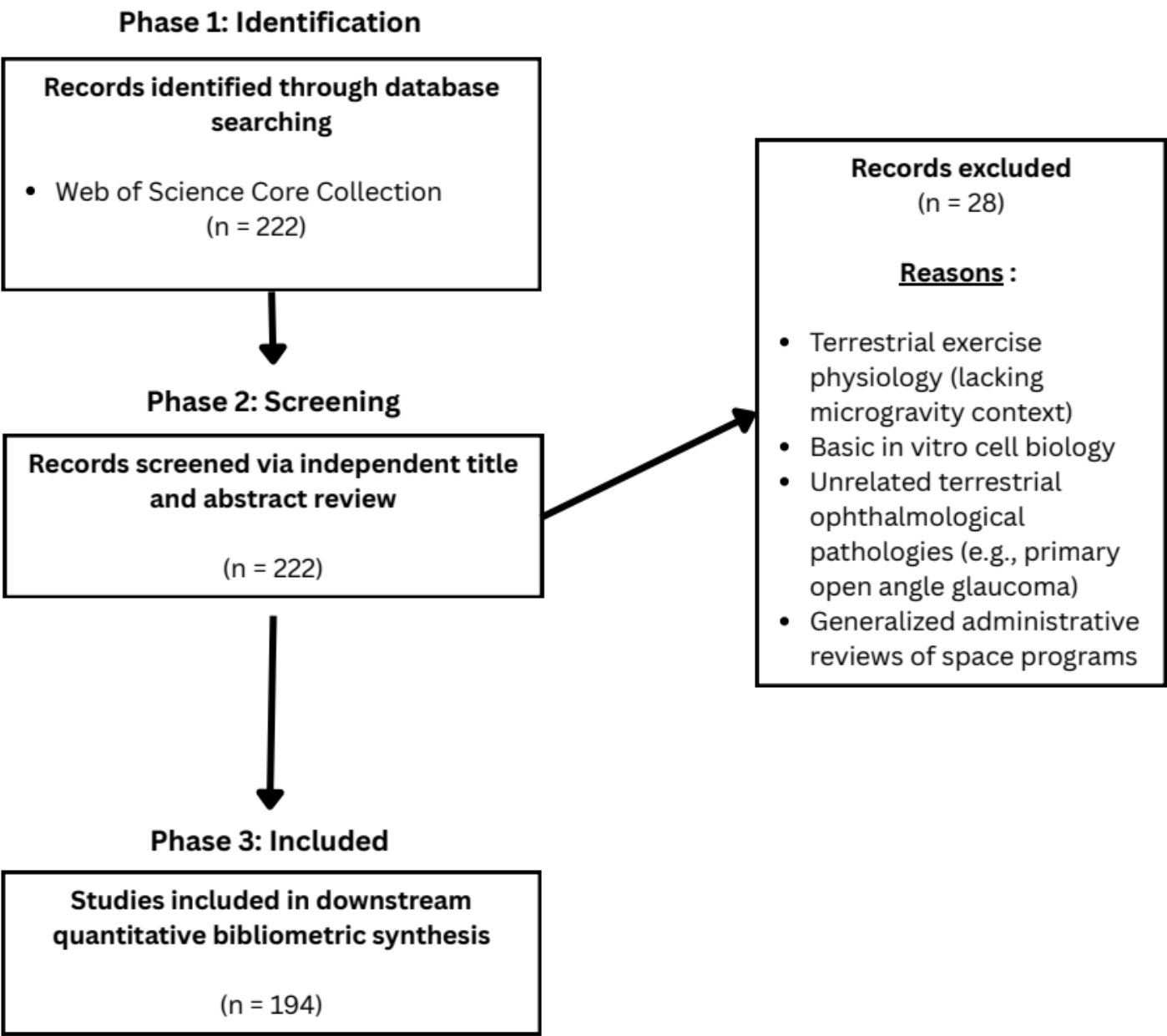


Figure 1

Flow Diagram detailing the literature curation process. An initial query of the Web of Science Core Collection yielded 222 records. Following independent manual screening and the application of strict exclusion criteria to remove off-topic bycatch, a finalized cohort of 194 documents was retained for quantitative network analysis.

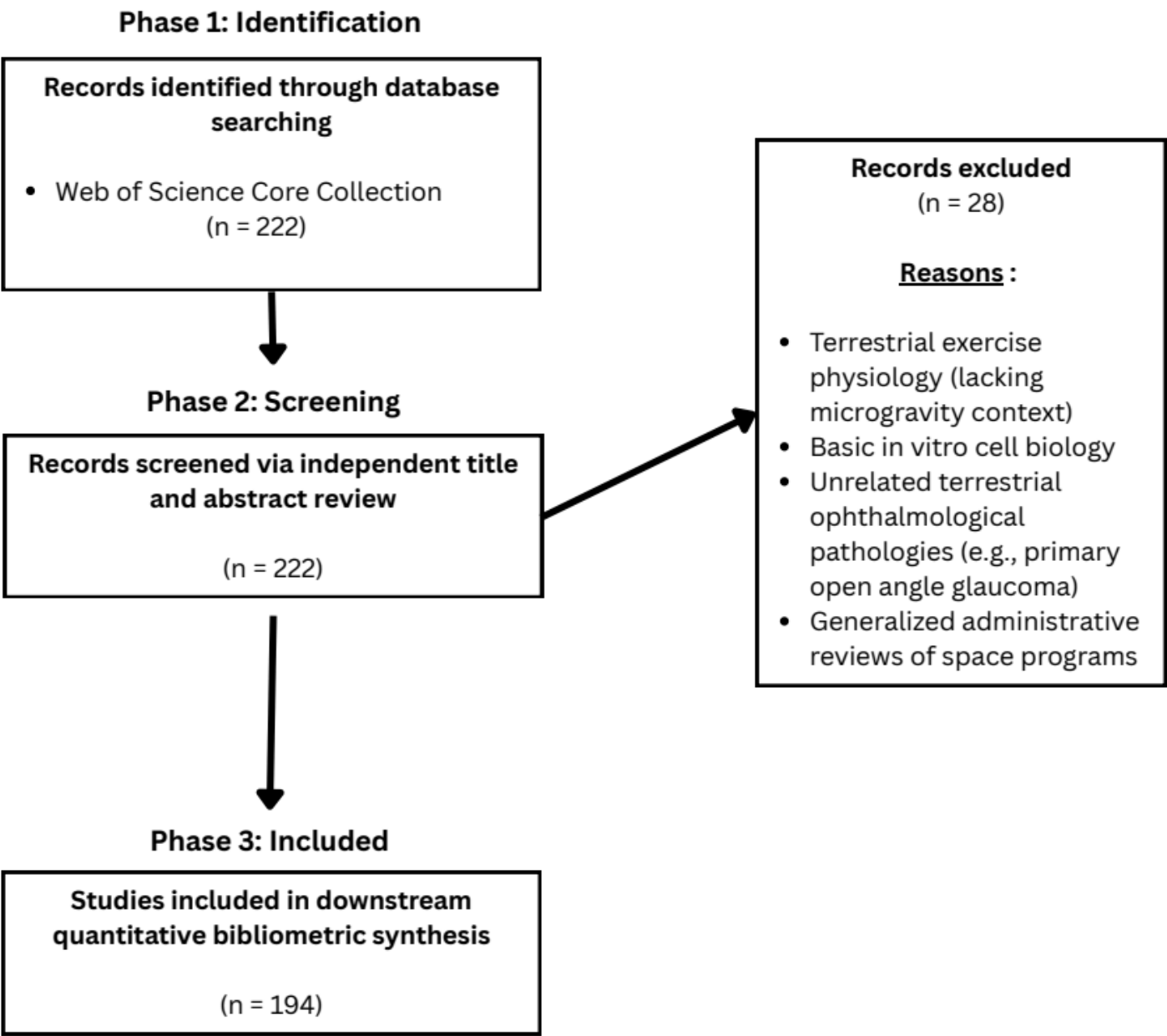


Figure 1

Flow Diagram detailing the literature curation process. An initial query of the Web of Science Core Collection yielded 222 records. Following independent manual screening and the application of strict

exclusion criteria to remove off-topic bycatch, a finalized cohort of 194 documents was retained for quantitative network analysis.

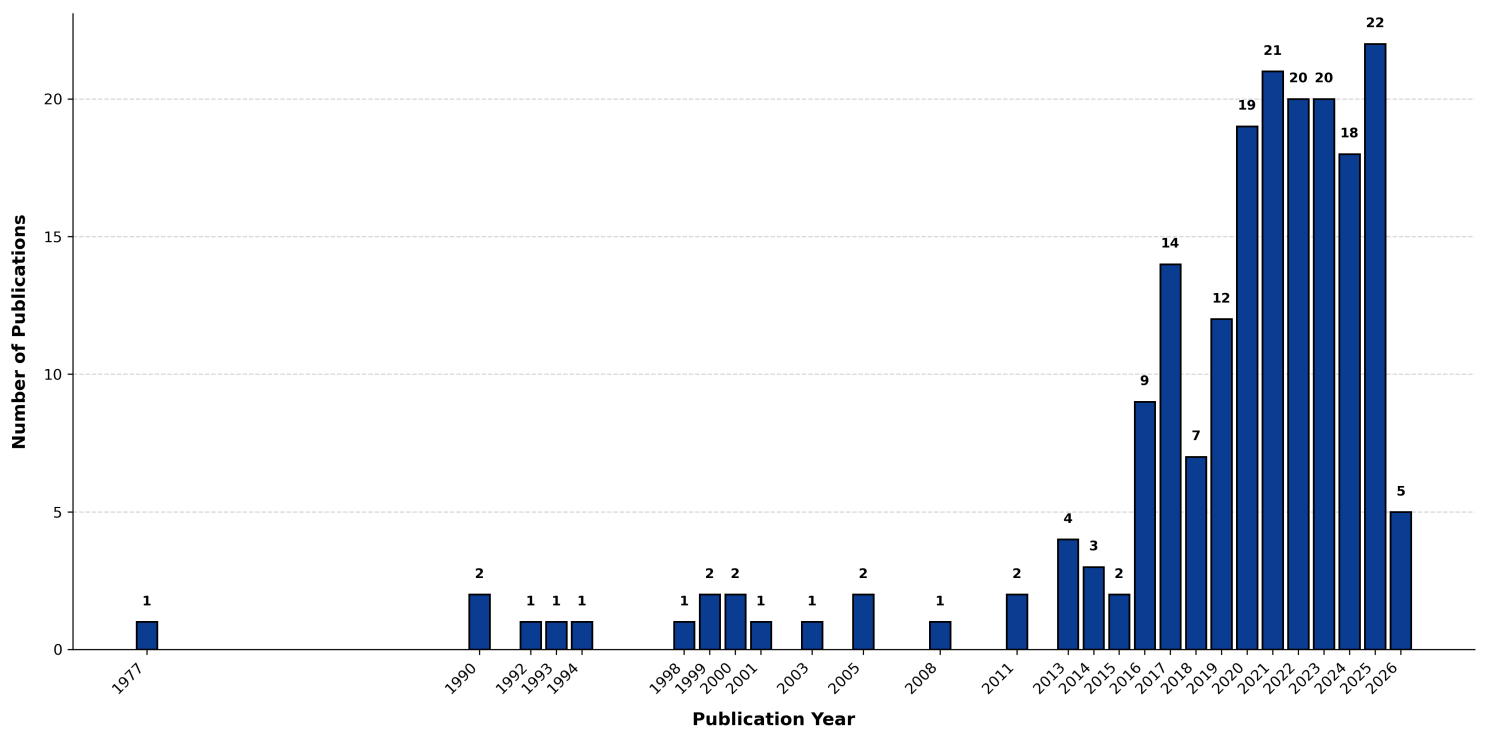


Figure 2

Annual scientific production of spaceflight-associated neuro-ocular syndrome literature

This chronological distribution quantifies the publication volume of the curated 194 document dataset from database inception through April 2026. The temporal trajectory demonstrates a low volume historical baseline prior to a critical inflection point after 2011. This structural break corresponds with the initial clinical formalization of the pathology, which served as a catalyst for subsequent research. Following this event, the field demonstrates a sustained exponential surge in scientific output, culminating in a historic maximum. This rapid acceleration visually reflects the active transition of the discipline from passive observation toward high priority operational intervention and neurosurgical modeling. **Note:** *2026 data represents a partial year (January–April).

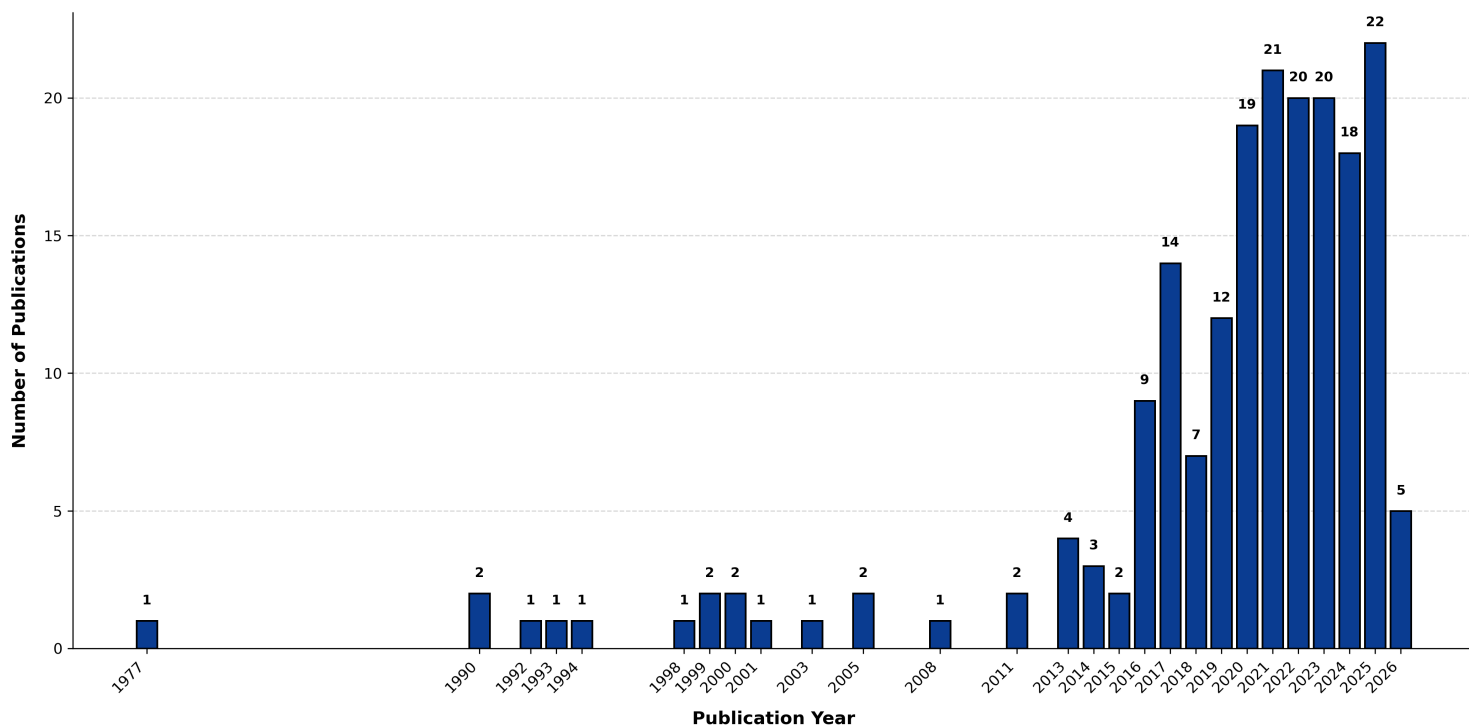


Figure 2

Annual scientific production of spaceflight-associated neuro-ocular syndrome literature

*This chronological distribution quantifies the publication volume of the curated 194 document dataset from database inception through April 2026. The temporal trajectory demonstrates a low volume historical baseline prior to a critical inflection point after 2011. This structural break corresponds with the initial clinical formalization of the pathology, which served as a catalyst for subsequent research. Following this event, the field demonstrates a sustained exponential surge in scientific output, culminating in a historic maximum. This rapid acceleration visually reflects the active transition of the discipline from passive observation toward high priority operational intervention and neurosurgical modeling. **Note:** *2026 data represents a partial year (January–April).*

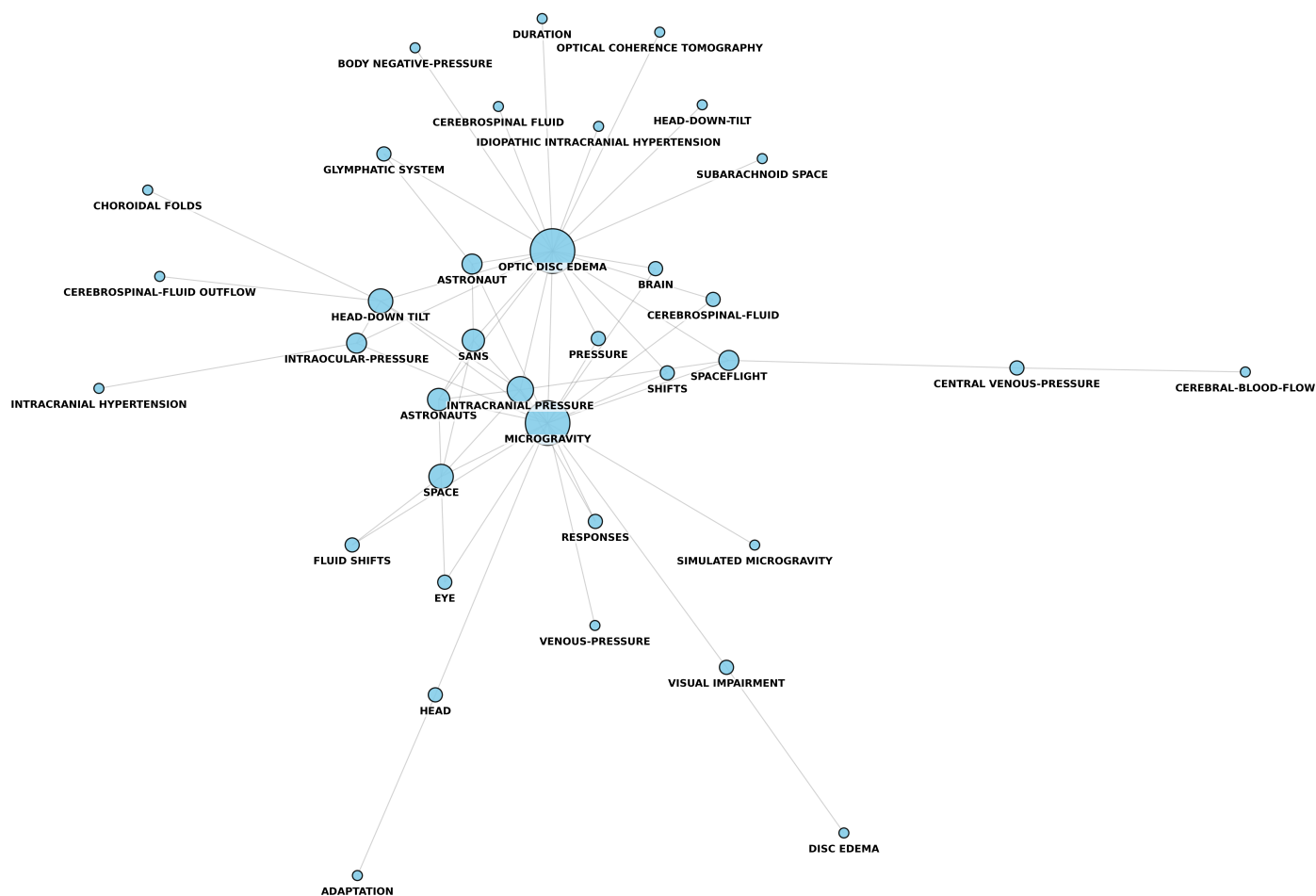


Figure 3

Topological network mapping of keyword co-occurrence in spaceflight-associated neuro-ocular syndrome literature

A strict visualization threshold of six co-occurrences was applied to isolate core pathophysiological pillars. Node size represents the frequency of keyword occurrence. The lines linking the nodes represent direct conceptual co-occurrences within the literature, with the layout algorithm clustering highly associated terms in close physical proximity. The network explicitly maps the structural bridge between aerospace operational triggers (microgravity) and terrestrial clinical pathologies (idiopathic intracranial hypertension). Notably, central hubs such as intracranial pressure and optic disc edema serve as primary connectors, while the glymphatic system emerges as a distinct node, reflecting the modern paradigm shift toward systemic neuro fluid stasis

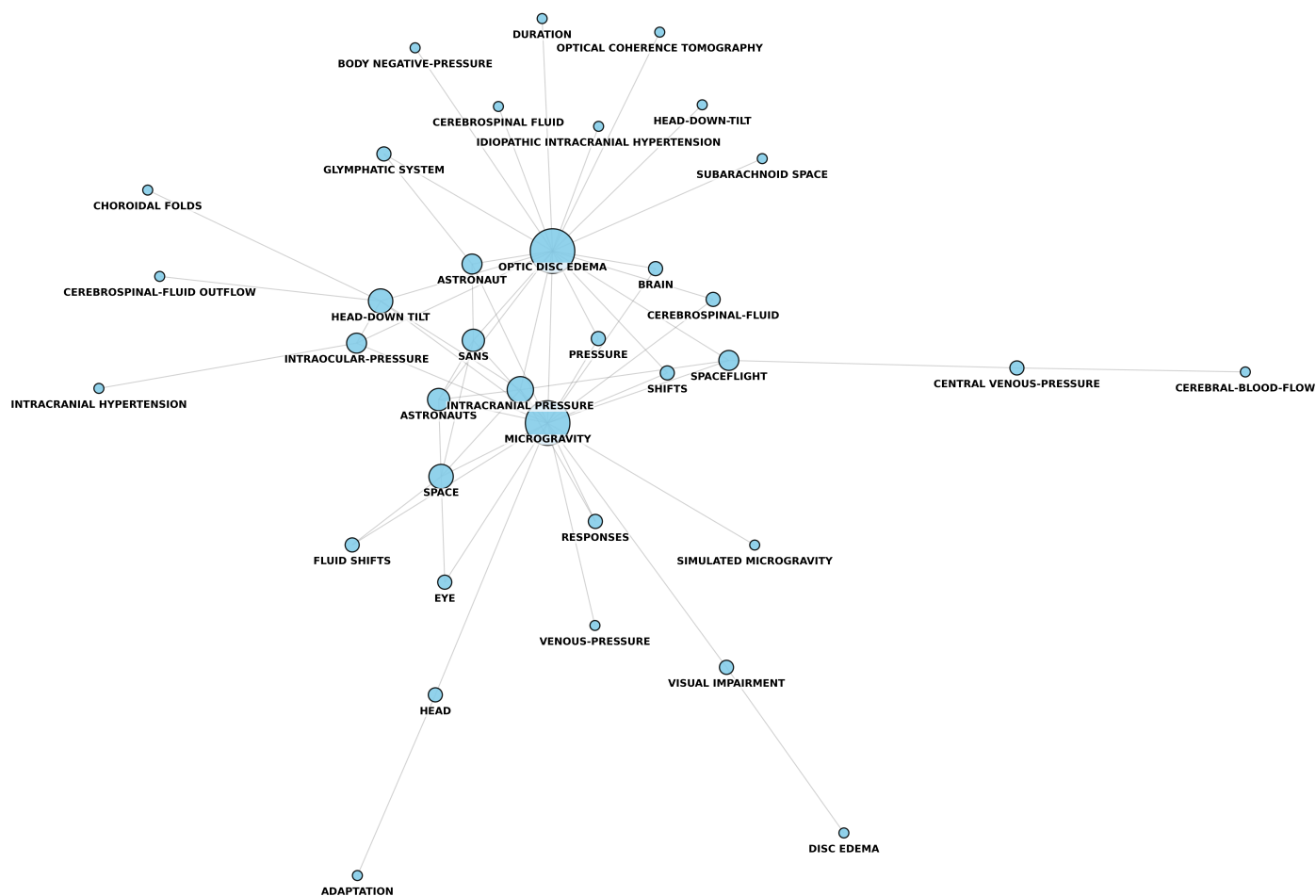


Figure 3

Topological network mapping of keyword co-occurrence in spaceflight-associated neuro-ocular syndrome literature

A strict visualization threshold of six co-occurrences was applied to isolate core pathophysiological pillars. Node size represents the frequency of keyword occurrence. The lines linking the nodes represent direct conceptual co-occurrences within the literature, with the layout algorithm clustering highly associated terms in close physical proximity. The network explicitly maps the structural bridge between aerospace operational triggers (microgravity) and terrestrial clinical pathologies (idiopathic intracranial hypertension). Notably, central hubs such as intracranial pressure and optic disc edema serve as primary connectors, while the glymphatic system emerges as a distinct node, reflecting the modern paradigm shift toward systemic neuro fluid stasis

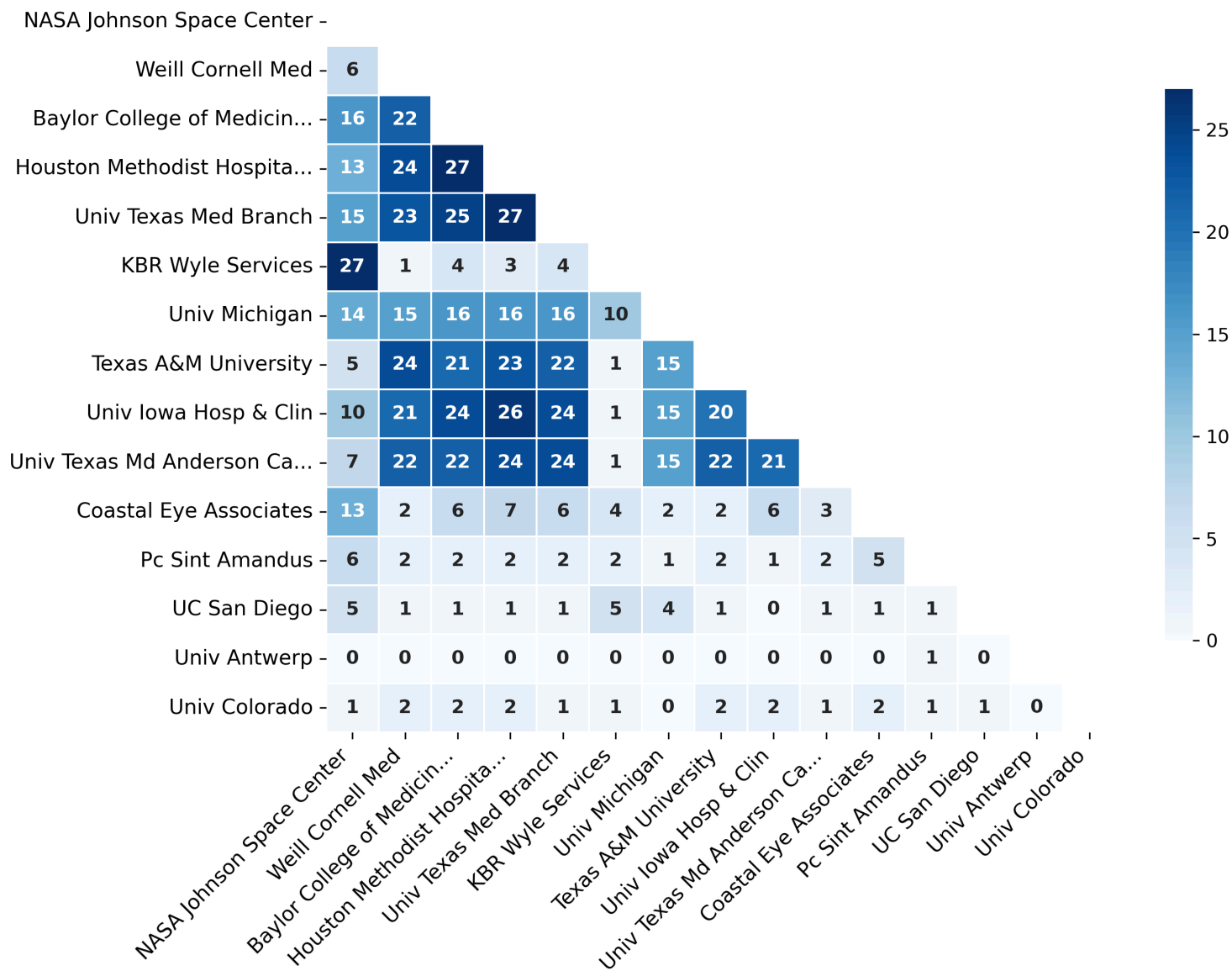


Figure 4

Institutional collaboration matrix of the top 15 global research hubs

This programmatic heatmap visualizes the coauthorship frequency and collaborative network density among the most prolific institutions publishing on spaceflight-associated neuro-ocular syndrome. Color intensity correlates directly with the volume of joint publications. The matrix highlights a highly centralized domestic infrastructure anchored by NASA and the broader Texas Medical Center ecosystem, notably including Baylor College of Medicine, KBRwyle, and the University of Texas Medical Branch. Additionally, the map identifies a distinct European collaborative cluster centered around the University of Antwerp and associated Belgian clinical institutions, reflecting the international, multi institutional effort required to map microgravity induced fluid shifts. Abbreviations for truncated labels: BCM, Baylor College of Medicine; HMH, Houston Methodist Hospital; MDACC, University of Texas MD Anderson Cancer Center; UIHC, University of Iowa Hospitals & Clinics.

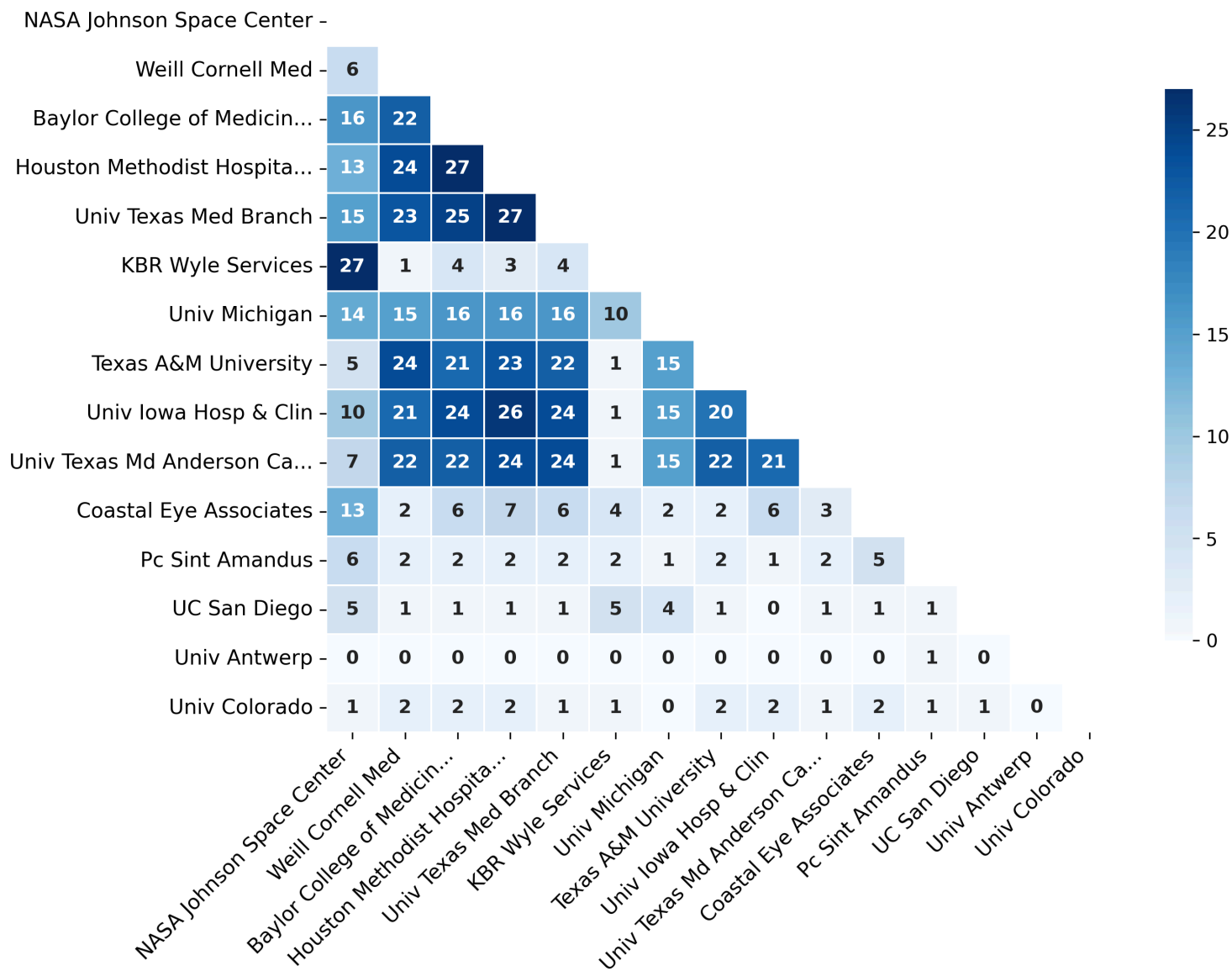


Figure 4

Institutional collaboration matrix of the top 15 global research hubs

This programmatic heatmap visualizes the coauthorship frequency and collaborative network density among the most prolific institutions publishing on spaceflight-associated neuro-ocular syndrome. Color intensity correlates directly with the volume of joint publications. The matrix highlights a highly centralized domestic infrastructure anchored by NASA and the broader Texas Medical Center ecosystem, notably including Baylor College of Medicine, KBRwyle, and the University of Texas Medical Branch. Additionally, the map identifies a distinct European collaborative cluster centered around the University of Antwerp and associated Belgian clinical institutions, reflecting the international, multi institutional effort required to map microgravity induced fluid shifts. Abbreviations for truncated labels: BCM, Baylor College of Medicine; HMH, Houston Methodist Hospital; MDACC, University of Texas MD Anderson Cancer Center; UIHC, University of Iowa Hospitals & Clinics.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [includedpaperstable.csv](#)
- [includedpaperstable.csv](#)
- [spacepaper.ipynb](#)
- [spacepaper.ipynb](#)