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APPLICATIONS OF FUNCTIONAL NEAR-INFRARED SPECTROSCOPY (FNIRS) FOR TINNITUS ASSESSMENT: A SCOPING REVIEW

APLICAÇÕES DA ESPECTROSCOPIA FUNCIONAL EM INFRAVERMELHO PRÓXIMO (FNIRS) PARA AVALIAÇÃO DO ZUMBIDO: UMA REVISÃO DE ESCOPO

APLICACIONES DE LA ESPECTROSCOPÍA FUNCIONAL DEL INFRARROJO CERCANO (FNIRS) PARA LA EVALUACIÓN DE TINNIS: UNA REVISIÓN DEL ALCANCE

Mariana Lopes Martins[1], Amanda Camara Miranda[1], Daniel Gomes da Silva Machado[2], Thaís Mendonça Maia Wanderley Cruz de Freitas[1], Marine Raquel Diniz da Rosa[1]

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ABSTRACT
PURPOSE: identify the applications of fNIRS in tinnitus assessment and ascertain variations in oxyhemoglobin and deoxyhemoglobin levels among empirical studies involving individuals with tinnitus. METHODS: The present scoping review involved a systematic search of peer-reviewed journals, focusing on empirical studies featuring human participants with tinnitus assessed via fNIRS. The terms were combined Near-Infrared Spectroscopy and Tinnitus. Searches across databases such as PubMed, Medline, Web of Science, Scopus, Cochrane Library, LILACS, Virtual Health Library (Bireme), and EMBASE, covering articles published up until July 21st, 2023. Two independent researchers conducted the initial selection, with discrepancies resolved by a third. RESULTS: Ten studies were included. Four compared oxy-hemoglobin changes in participants with tinnitus and controls. One adapted a probe in the external auditory canal to use in the fNIRS equipment, while another assessed their functional efficacy. The fNIRS evaluated improved auditory cortex function through transcranial direct current stimulation in chronic tinnitus. Longitudinal studies employed fNIRS to assess the effectiveness of Transcranial Magnetic Stimulation, notched sound therapy, and acupuncture for tinnitus treatment. Five experimental designs encompassed block-design, three developed resting-state experiments, and two studies utilizing both. These explored changes in brain activity using pure tones stimuli and masking noise. CONCLUSION: fNIRS has proven advantageous. Variability exists in stimulus types, experiment duration, methods of data processing and statistical analysis, and descriptions of the results.

KEYWORDS: Tinnitus. Near-Infrared Spectroscopy. Brain Mapping. Functional Neuroimaging. Review Literature. Audiology.

RESUMO
OBJETIVO: identificar as aplicações da fNIRS na avaliação do zumbido e verificar as variações nos níveis de oxihemoglobina e desoxihemoglobina entre estudos empíricos envolvendo indivíduos com zumbido. MÉTODOS: A presente revisão de escopo envolveu uma pesquisa sistemática de periódicos revisados por pares, foco em estudos empíricos, participantes humanos com zumbido avaliados por meio da fNIRS. Foram combinados os termos *Near-Infrared Spectroscopy* e *Tinnitus*. Foram pesquisados bancos de dados, *PubMed, Medline, Web of Science, Scopus, Cochrane Library, LILACS,* Biblioteca Virtual em Saúde e *EMBASE*, abrangendo artigos publicados até 21 de julho de 2023. Dois pesquisadores independentes realizaram a seleção inicial, com discrepâncias resolvidas por um terceiro. RESULTADOS: Dez estudos foram incluídos. Quatro compararam as mudanças da oxi-hemoglobina em participantes com zumbido e controles. Um adaptou uma sonda no canal auditivo externo para uso no equipamento de fNIRS, enquanto outro avaliou sua eficácia funcional. A fNIRS avaliou a melhora da função do córtex auditivo por meio da estimulação transcraniana por corrente contínua no zumbido crônico. Estudos longitudinais empregaram a fNIRS para avaliar a eficácia da estimulação magnética transcraniana, da terapia *notched* e da acupuntura no tratamento do zumbido. Cinco desenhos experimentais abrangeram projetos de avaliação em bloco, três desenvolveram experimentos de estado de repouso e dois estudos utilizaram ambos. Estes exploraram as mudanças na atividade cerebral usando estímulos de tons puros e ruído de mascaramento. CONCLUSÃO: A

[1] Universidade Federal da Paraíba.
[2] Universidade Federal do Rio Grande do Norte.

fNIRS demonstrou ser vantajosa. Existe variabilidade nos tipos de estímulo, duração do experimento, métodos de processamento de dados e análise estatística, e descrições dos resultados.

PALAVRAS-CHAVE: Zumbido. Espectroscopia em Infravermelho Próximo. Mapeamento Cerebral. Neuroimagem Funcional. Revisão de Literatura. Audiologia.

RESUMEN
OBJETIVO: identificar las aplicaciones de fNIRS en la evaluación del tinnitus y verificar variaciones en los niveles de oxihemoglobina y desoxihemoglobina entre estudios empíricos que involucran individuos con tinnitus. MÉTODOS: La presente revisión de alcance implicó una búsqueda sistemática de revistas revisadas por pares, centrándose en estudios empíricos, participantes humanos con tinnitus evaluados mediante fNIRS. Se combinaron los términos espectroscopia de infrarrojo cercano y tinnitus. Se buscaron en bases de datos, PubMed, Medline, Web of Science, Scopus, Cochrane Library, LILACS, Biblioteca Virtual em Saúde y EMBASE, cubriendo artículos publicados hasta el 21 de julio de 2023. Dos investigadores independientes realizaron la selección inicial, con discrepancias resueltas por un tercero. RESULTADOS: Se incluyeron diez estudios. Cuatro compararon los cambios de oxihemoglobina en participantes con tinnitus y controles. Uno adaptó una sonda en el canal auditivo externo para su uso en equipos fNIRS, mientras que otro evaluó su eficacia funcional. fNIRS evaluó la mejora de la función de la corteza auditiva mediante estimulación transcraneal de corriente directa en el tinnitus crónico. Los estudios longitudinales han utilizado fNIRS para evaluar la eficacia de la estimulación magnética transcraneal, la terapia con muescas y la acupuntura en el tratamiento del tinnitus. Cinco diseños experimentales abarcaron diseños de evaluación en bloques, tres desarrollaron experimentos en estado de reposo y dos estudios utilizaron ambos. Estos exploraron cambios en la actividad cerebral utilizando estímulos de tonos puros y ruidos enmascarantes. CONCLUSIÓN: fNIRS ha demostrado ser ventajoso. Existe variabilidad en los tipos de estímulos, la duración del experimento, los métodos de procesamiento de datos y análisis estadístico y las descripciones de los resultados.

PALABRAS CLAVE: Tinnitus. Espectroscopia de infrarrojo cercano. Mapeo cerebral. Neuroimagen funcional. Revisión de la literatura. Audiología

INTRODUCTION

fNIRS has the advantage of localizing the source of response in comparison with other techniques, such as electroencephalography (EEG) and magnetoencephalography (MEG), but the technique has a worse temporal resolution in comparison with these techniques(2). In comparison with functional magnetic resonance imaging (fMRI), both techniques assess cortical oxygenation changes(3) and have similar vascular sensitivity(1, 4). However, fMRI techniques use only deoxyhemoglobin, and NIRS is based on the intrinsic optical absorption of blood (allowing the detection of changes in oxyhemoglobin and deoxyhemoglobin)(4). A limitation of NIRS is that cap recordings are limited to three centimeters of signal penetration depth due to the skull thickness(5) and the difficulty in locating the cortical activity source because it relies on localized absorption change relative to the source/detector position and light wavelength which is affected by optical properties of the tissue(2).

Despite these limitations, fNIRS is a beneficial device for auditory research because it is quiet, non-invasive, and safe to measure and repeat the procedure (2, 6). Therefore, it is an advantageous method to assess tinnitus, since tinnitus subjects generally have an increased activation observed in primary auditory cortex and surround auditory belt areas, including the parietal, frontal, cingulate areas, somatosensory, and limbic system(7-10).

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Tinnitus is a condition characterized as the presence of sound in the absence of an external sound source. It can be evaluated subjectively by hearing exams and questionnaires, with no relation between audiological exams and tinnitus distress[(11)]. Objective methods have been sought to understand the symptomatology of the condition, such as imaging exams[(12)]. For instance, the use of Near-infrared spectroscopy (NIRS) to analyze and evaluate the brain flow variations that occur in the human brain due to tinnitus, study the pathophysiology of the symptom, and the response to treatments performed[(13)].

To the best of our knowledge, no scoping or systematic reviews assessing the use of NIRS in tinnitus evaluation are available. Only one literature review used fNIRS to measure cochlear implant performance and tinnitus perception [(2)]. This review included three papers on tinnitus [(14-16)] and concluded that, while unable to define the exact plasticity underlying tinnitus perception, the proof-of-concept study provided a foundation for subsequent research.

Thus, the present scoping review was used to answer the broad question of "How is near-infrared spectroscopy used to assess tinnitus?", while still ensuring the quality and methodological rigor of a high-standard review. In turn, the scoping review enables the identification of the key features of the evaluation technique to direct future studies.

The purpose of the review is to identify how fNIRS is used to assess tinnitus. Additionally, it aims to verify differences in oxyhemoglobin and deoxyhemoglobin levels in empirical studies that evaluated people with and without tinnitus, or people with tinnitus at different moments.

METHODS

This review is reported according to the PRISMA extension for scoping reviews (PRISMA-ScR) [(14, 15)].

Eligibility criteria

A search for original full-text published articles was performed without language or publication date restrictions. The selection criteria followed the strategy: (a) involved participants with tinnitus; (b) used NIRS as an assessment method; (c) Compared with participants without tinnitus or participants with tinnitus pre- and post-treatment; (d) The outcome is oxy and/or deoxy hemoglobin; (e) empirical studies with humans; and (f) published in a peer-reviewed journal.

Information sources

The online PubMed, Medline, Web of Science, Scopus, Cochrane Library, LILACS, Virtual Health Library (VHL; https://bvsalud.org/en/) (Bireme), and EMBASE databases were explored for articles published up until July 21st, 2023.

Search strategy

The keywords and Boolean terms were established to identify literature related to the NIRS assessment for tinnitus participants. The terms were included in the Medical Subject Headings (MeSH) and Health Sciences Descriptors (https://decs.bvsalud.org/I/homepagei.htm):

- “Spectroscopy, Near-Infrared”,
- “Spectrophotometry, Infrared”,
- “Tinnitus”.

The following additional terms were also included:

- “Near-Infrared Spectroscopy”,
- “Near-Infrared Spectroscopies”,
- “NIR Spectroscopy”,
- “NIR Spectroscopies”,
- “Near-Infrared Spectrometry”,
- “Functional near-infrared spectroscopy”,
- fNIRS,
- NIRS,
- “Functional near-infrared spectroscopic”,
- “Optical imaging system”,
- “Optical topography”.

Thus, the following term combinations were used: (“Spectroscopy, Near-Infrared”[Mesh]) OR (“Spectrophotometry, Infrared”[Mesh]) OR “Near-Infrared Spectroscopy” OR “Near-Infrared Spectroscopies” OR “NIR Spectroscopy” OR “NIR Spectroscopies” OR “Near-Infrared Spectrometry” OR “functional near-infrared spectroscopy” OR fNIRS OR NIRS OR “functional near-infrared spectroscopic” OR “optical imaging system” OR “optical topography” AND “Tinnitus”[Mesh] OR “Tinnitus” (for more details about the combination in each database, please access the Supplementary Material – Table 1).

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Table 1. Combination of descriptors and terms in each database

Database	Restrictions	Combination of terms	Number of articles
PubMed	No restrictions	(((((((((((("Spectroscopy, Near-Infrared"[Mesh] OR "Spectrophotometry, Infrared"[Mesh]) OR "Near-Infrared Spectroscopy"[All Fields]) OR "Near-Infrared Spectroscopies"[All Fields]) OR "NIR Spectroscopy"[All Fields]) OR "NIR Spectroscopies"[All Fields]) OR "Near-Infrared Spectrometry"[All Fields]) OR "functional near-infrared spectroscopy"[All Fields]) OR fNIRS[All Fields]) OR ("spectroscopy, near-infrared"[MeSH Terms] OR ("spectroscopy"[All Fields] AND "near-infrared"[All Fields]) OR "near-infrared spectroscopy"[All Fields] OR "nirs"[All Fields])) OR "functional near-infrared spectroscopic"[All Fields]) OR "optical imaging system"[All Fields]) OR "optical topography"[All Fields]) AND ("tinnitus"[MeSH Terms] OR "tinnitus"[All Fields])	301
MEDLINE	Reduction of the terms due to incompatibility in the combination	(AllFields:"Near-Infrared Spectroscopy") OR (AllFields:"Functional near-infrared spectroscopy") OR (AllFields:NIRS) OR (AllFields:fNIRS) AND (AllFields:Tinnitus)	24
Web of Science	Reduction of the terms due to incompatibility in the combination	("Spectroscopy, Near-Infrared"[Mesh]) (All Fields) OR ("Spectrophotometry, Infrared"[Mesh]) (All Fields) OR "functional near-infrared spectroscopy" (All Fields) AND Tinnitus (All Fields)	12
Scopus	No restrictions	(ALL (("Spectroscopy, Near-Infrared" [mesh])) OR ALL (("Spectrophotometry, Infrared"[mesh])) OR ALL ("Near-Infrared Spectroscopy") OR ALL ("Near-Infrared Spectroscopies") OR ALL ("NIR Spectroscopy") OR ALL ("NIR Spectroscopies") OR ALL ("Near-Infrared Spectrometry") OR ALL ("functional near-infrared spectroscopy") OR ALL (fnirs) OR ALL (nirs) OR ALL ("functional near-infrared spectroscopic") OR ALL ("optical imaging system") OR ALL ("optical topography") AND ALL ("Tinnitus"))	370
Cochrane Library	Terms identified in the title, abstract, or keywords	"Spectroscopy, Near-Infrared" in Title Abstract Keyword OR "Spectrophotometry, Infrared" in Title Abstract Keyword OR "functional near-infrared spectroscopy" in Title Abstract Keyword OR "NIRS" in Title Abstract Keyword AND "Tinnitus" in Title Abstract Keyword	763
Virtual Health Library (Bireme)	Reduction of the terms due to incompatibility in the combination. Terms identified in the title, abstract, or subject	((Spectroscopy, Near-Infrared)) OR ((functional near-infrared spectroscopy)) AND (Tinnitus)	12
EMBASE	No restrictions	('spectroscopy, near-infrared'/exp OR 'spectroscopy, near-infrared' OR 'spectrophotometry, infrared' OR 'near-infrared spectroscopy' OR 'near-infrared spectroscopies' OR 'nir spectroscopy' OR 'nir spectroscopies' OR 'near-infrared spectrometry' OR 'functional near-infrared spectroscopy' OR fnirs OR nirs OR 'functional near-infrared spectroscopic' OR 'optical imaging system' OR 'optical topography') AND 'tinnitus'	16
LILACS	Reduction of the terms due to incompatibility in the combination.	("Spectroscopy, Near-Infrared"[Mesh]) OR ("Spectrophotometry, Infrared" [Mesh]) OR "functional near-infrared spectroscopy" AND "Tinnitus"	38

Selection of evidence sources

The list of results after the electronic search was combined. A separate selection was performed by two independent researchers (MLM and MRDR), and any disagreements were resolved and analyzed by a third researcher (DGSM). Each researcher screened the titles and abstracts of the results found in the search. All pre-selected records proceeded to full-text screening, in which the eligibility criteria were applied again.

The inter-reviewer agreement for the article selection was assessed using Kappa statistic (K) and the results showed "perfect" agreement between the reviewers ($k = 0.925$; $p < 0.0001$)[16].

Data charting process

Data extraction was independently performed by the researcher MLM. Then, the researchers MRDR and DGSM discussed the results and updated the information.

Data items

The following data were extracted:

- (1) Authors and year of publication.
- (2) Study design definition.
- (3) Study aim, purpose, or questions.
- (4) Sample Size.
- (5) Population characteristics (age, gender, tinnitus laterality, tinnitus duration in months, tinnitus distress, and loudness).
- (6) Eligibility criteria.
- (7) Hearing assessments and questionnaires.
- (8) fNIRS parameters: wave, channels, optode placement, brain location – region of interest (ROI), source-detector separation, sample rate, stimulus: duration and type, number of blocks and trials, run time, randomization, sound equipment type.
- (9) Summary of main results: Hemodynamic data during block design, hemodynamic data during resting state, hemisphere differences, behavioral data.
- (10) Conclusion.

Synthesis of results

The data were summarized in tables and compiled into images to enable a comparison of the studies already conducted on the subject.

RESULTS

Selection of evidence sources

A total of 1,536 unique records were screened, and 12 full texts were assessed for eligibility criteria. Finally, 10 studies were included in the synthesis (Figure 1). The most common reasons for exclusion in the screening phase were: (a) studies without tinnitus participants; (b) articles using another assessment method for tinnitus' and (c) use of fNIRS for assessment of another disease (Figure 2).

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Figure 1

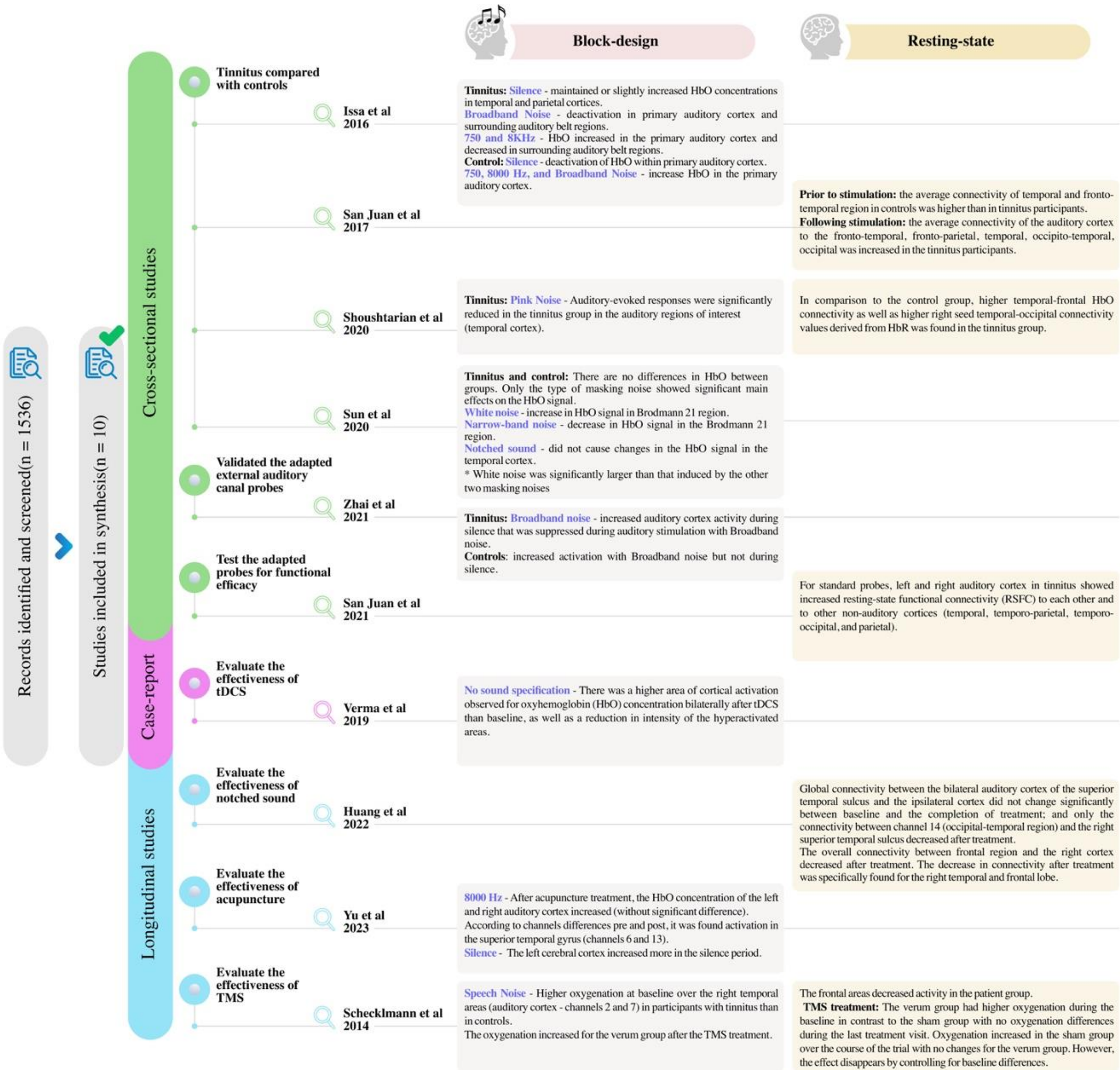

Figure 1. Visual summary of the scoping review, showing all included articles and their respective results.

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Figure 2

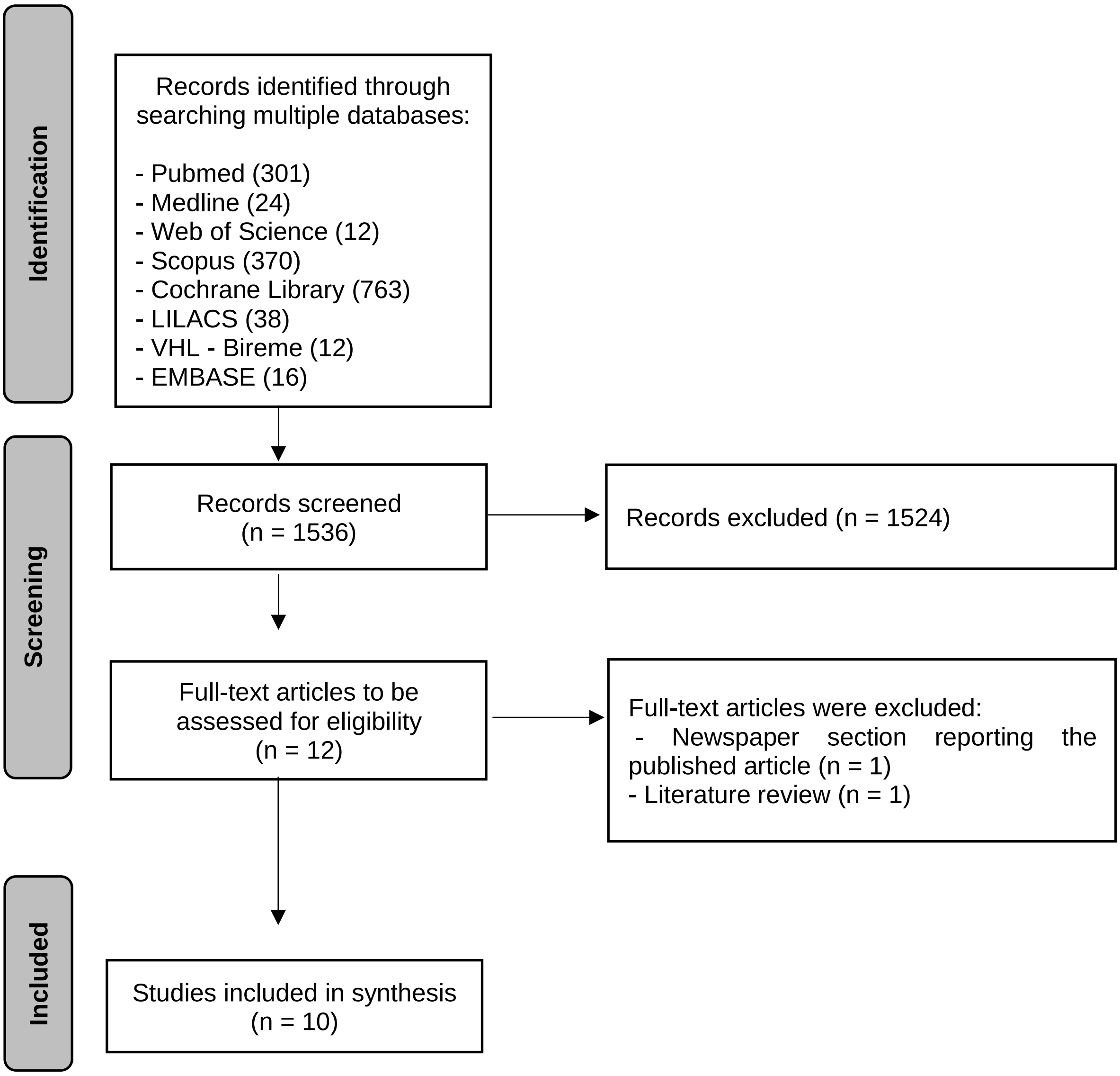

Figure 2. Study flow diagram adapted from PRISMA 2018, 2020 guidelines[15, 17].

Characteristics of evidence sources

Thus, 10 studies[18-27] included were published between 2014 and 2023, which demonstrates this novel way to assess tinnitus. It is important to note that one of the research groups published four of the included articles[19, 24, 25, 28], and another group published two articles[23, 26].

The review included six cross-sectional studies[19, 20, 22-25], one case report[21], and three longitudinal studies[18, 26, 27]. All studies totaled 149 participants with tinnitus and 88 controls in the qualitative synthesis.

Results of individual evidence sources

Summaries of the sampling and design information of the included articles are shown in the Supplementary Material - Table 2. The NIRS parameters and characteristics of the experiments are presented in Table 3, and the main results and conclusions are shown in Table 4. The articles are organized in alphabetical order.

Table 2. Sampling and design information of the ten included articles

AUTHOR AND YEAR	STUDY DESIGN	AIM / KEY PURPOSE / QUESTIONS	SAMPLE SIZE	POPULATION CHARACTERISTICS	HEARING AND IMAGING ASSESSMENTS	QUESTIONNAIRES
Huang et al., 2022	Longitudinal study	Explore whether notched sound could regulate tinnitus by affecting the emotional center.	29 = Tinnitus	**Tinnitus group:** 18 males and 11 females, age 19–52 years, with an average age of 31.45±9.68 years. The course of disease ranged from 3 to 36 months, with an average course of 10.90± 9.34 months.	The outpatient doctors assessed each patient for tinnitus. Collection of some essential information was also conducted at this time, such as a routine medical history, examination of the ear, including a physical examination of the external auditory canal and tympanic membrane. In addition, audiology tests were conducted, including conventional pure-tone audiometry (PTA) (125 Hz–8 kHz), emittance measurement, otoacoustic emission. CT/MRI imaging examinations were also performed according to the specific condition.	It was performed at baseline and after sound therapy. Tinnitus Handicap Inventory (THI), Beck Anxiety Inventory (BAI), and the Center for Epidemiologic Studies-Depression (CES-D) Scale.
Issa et al., 2016	Cross-sectional	Measure changes in oxy-hemoglobin concentration from regions of interest (ROI; auditory cortex) and adjacent non-auditory	10 = tinnitus and normal/ near-normal hearing; 7 = controls (non-tinnitus and normal/near -normal hearing)	**Tinnitus group:** average age: 48.7±16 years, average SRT: 19dB, WDS: 100%). **Control group:** average age: 25.7 ± 7.8 years, average SRT: 15dB, WDS: 99%.	Both groups performed pure tone averages (PTA) across all frequencies, including high-frequency regions such as 8000Hz. Moreover, the speech reception	Tinnitus Handicap Inventory - THI

	cortices (non-ROI) during auditory stimulation and silence in participants with subjective tinnitus appreciated equally in both ears and in non-tinnitus controls using functional near-infrared spectroscopy (fNIRS).		thresholds (SRTs) and word discrimination scores (WDS) were also found to be within the normal range between both groups.	

San Juan et al., 2017 *(Same methods and sample as in Issa et al., 2016, but analyzing the resting state)*	Cross-sectional	Investigate changes in the baseline resting state functional connectivity between human auditory and non-auditory brain regions in normal-hearing, bilateral subjective tinnitus and controls before and after auditory stimulation.	10 = tinnitus and normal hearing; 8 = controls (non-tinnitus and normal hearing) *(Same participants as in Issa et al., 2016, plus an additional control)*	**Tinnitus group:** average age: 48.7±16 years; 6 men. **Control group:** average age: 25.4±7.3 years, 5 men.	*(Same as in Issa et al., 2016)*	*(Same as in Issa et al., 2016)*
San Juan et al., 2021 *(Same methods and sample as in Zhai et al., 2020 - but analyzing only the resting state)*	Cross-sectional	Validate and extend our previously published changes in RSFC (in human tinnitus) as a measurable objective platform to validate the adapted probes for functional efficacy and application going forward (San Juan et al., 2017).	*(Same as in Zhai et al., 2020)*	*(Same as in Zhai et al., 2020)*	*(Same as in Zhai et al., 2020)*	*(Same as in Zhai et al., 2020)*
Schecklmann et al., 2014	Longitudinal study *(Participants with tinnitus received treatment with transcranial magnetic stimulation, in a neuronavigated trial. However, the fNIRS of the tinnitus group was compared with the control group in a cross-sectional study.)*	In this proof-of-principle study we probed the capability of functional near-infrared spectroscopy (fNIRS) for the measurement of brain oxygenation in auditory cortex in dependence from chronic tinnitus and from intervention with transcranial magnetic stimulation.	23 = tinnitus (12 = active TMS; 11 = placebo) and 12 = healthy controls	1. **Active group** - Age [years]: 48.2 ± 10.7, Sex [female/male]: 5/7, Mean hearing loss [dB HL]: 20.5 ± 11.0, Tinnitus duration [months]: 68.9 ± 61.4, Tinnitus laterality [unilateral/not unilateral]: 2/10. **Sham group** - Age [years]: 46.5 ± 11.5, Sex [female/male]: 4/7, Mean hearing loss [dB HL]: 21.4 ± 6.7, Tinnitus duration [months]: 96.8 ± 120.4, Tinnitus laterality [unilateral/not unilateral]: 2/8. **Healthy group** - Age [years]: 43.6 ± 15.0, Sex [female/male]: 3/9, Mean hearing loss [dB	Otologic assessment included micro-otoscopy, pure-tone audiometry, tympanometry, and stapedius reflex measurement to verify normal middle ear function. Mean hearing loss in dB HL was defined as the average pure-tone hearing threshold of both ears at 0.125, 0.250, 0.500, 1, 2, 3, 4, 6, and 8 kHz.	-

				HL]: —, Tinnitus duration [months]: —, Tinnitus laterality [unilateral/not unilateral]: —.		
Shoushtarian et al., 2020	Cross-sectional	1) Assess the sensitivity of fNIRS to differentiate individuals with tinnitus from controls, and 2) identify fNIRS features associated with subjective ratings of tinnitus severity and whether these could differentiate between perceived loudness of tinnitus and annoyance.	25 = Tinnitus (23 bilaterally) and 21 = healthy adults *(18 controls included – two excluded due to long hair and poor signal quality, and one due to technical issues with the cap.)*	**Tinnitus group:** gender (male: female) 16:9; Age, mean (SD), range: 48.4 (12.9), 25–68; Handedness: R: 21, L: 2, both: 2; Tinnitus duration, mean (SD), range: 11.5 (8.8), 0.5–25; Tinnitus laterality: R: 2, bilateral: 23. **Control group:** 18 healthy adults with no history of tinnitus, neurological or hearing disorders were also tested.; gender (male: female): 11:7; Age, mean (SD), range: 45.5 (16.7), 25–76; Handedness: R: 18.	Pure tone audiometry was performed on all participants at frequencies of 0.25, 0.5, 1, 2, 4, and 8 kHz	Tinnitus Handicap Inventory (THI) and visual analogue scale to access tinnitus loudness and annoyance.
Sun et al., 2020	Cross-sectional	This study aimed to use fNIRS to clarify whether different masking noises and variational amplitude of oxygenated hemoglobin (HbO) in the corresponding cortical regions, with contrasting spectra (e.g., narrow-band noise, notched sound, and white noise) induce distinguishable activation patterns and if the amplitude in the corresponding region of interest (ROI) correlates with clinical indicators (i.e. residual inhibition) in patients with	13 = Tinnitus and 20 = controls	**Tinnitus group:** age (year) 36.77±9.56; tinnitus side: 9 bilateral, 3 right, 1 left; tinnitus duration (months): mean - 16.30. **Control group:** age (year) 30.85±5.68	Pure tone hearing threshold test for both groups at a frequency range of 250–8,000 Hz. Tinnitus matching, Residual inhibition.	-

		tinnitus. We also assessed near-infrared spectroscopy brain function imaging (NIRS) as an objective assessment tool in acoustic therapy.				
Verma et al., 2019	Case Report	The current case report depicts the use of functional near-infrared spectroscopy (fNIRS) based on the assessment of improvement in auditory cortex functioning in chronic tinnitus by transcranial direct current stimulation (tDCS).	1 = tinnitus	Mr. R, a 28-year-old, right-handed, with no family history of psychiatric or neurological illness, progressively diminution of hearing (right more than left) in the last 5 years. He did not have any history of diabetes, hypertension, hypothyroidism, seizure, any neurological illness, or any form of surgical intervention. Over the last 2 years, he also started to have ringing in his ear, which gradually increased over 2-3 months. Ringing was continuous and more prominent in his right than in his left ear. Ringing would interfere with his work and interaction with people. It would increase in a noisy environment and when he would speak in a louder tone. However, it did not interfere with his sleep.	Tuning fork tests revealed conduction of sound to the left ear with no other abnormality. Pure tone audiometry revealed profound sensory neural hearing loss (>100 dB) in the right ear and mild conductive hearing loss in the left ear. MRI brain scan specifically focusing on the inner ear along with the temporal bone revealed no abnormality.	Tinnitus Handicap Inventory (THI) score was 60 (severe) at baseline.
Yu et al., 2023	Longitudinal study	The purpose of this study was to investigate the effect of acupuncture treatment on cortical activation in patients with tinnitus and to explore the	18 = Tinnitus	**Tinnitus group:** 18 participants (8 females and 10 males, age 27-67 years, average age 49.38 years, average duration 20.44 months) with bilateral subjective tinnitus.	Before the treatment, all participants were tested using an audiogram, within the measured frequency range (including 8000 Hz), the	Before and after the treatment, it was applied Tinnitus disorder inventory (THI), tinnitus evaluation questionnaire (TEQ),

		ability to use fNIRS as a potential indicator to assess the efficacy of acupuncture treatment for tinnitus.			average pure-tone threshold was lower than 30 dB HL.	Hamilton anxiety scale (HAMA), and Hamilton depression scale (HAMD).
Zhai et al., 2020	Cross-sectional	The primary purpose was not to identify underlying mechanisms of tinnitus, but rather to use our previously published changes in human HA as a measurable objective platform to validate the adapted EAC probes for functional efficacy and application going forward. Our second goal was to validate and extend our previous observation of basal hyper-activation of AC and its suppression with broad band noise (BBN) in tinnitus.	20 = tinnitus; 20 = controls (non-tinnitus)	**Tinnitus group:** bilateral Tinnitus (10 females; 10 males; average age 38.2 years). **Control group:** non-tinnitus controls (10 females; 10 males; average age 48 years).	Speech reception thresholds (SRTs) and word discrimination scores (WDS) were within the normal range for all.	-

Note: Not Reported = It could be reported but was not; - = It does not need to be done.

Table 3. NIRS parameters and characteristics of the experiments of the ten included articles

AUTHOR AND YEAR	METHODS										
	Wave	Channels	Optode placement	Brain Location - Region of Interest (ROI)	Source-detector separation	Sample rate	Stimulus: Duration and Type	Number of blocks and trials	Run time	Randomization	Sound Equipment type
Huang et al., 2022	*(Same as in Sun et al., 2020)*	*(Same as in Sun et al., 2020)*	*(Same as in Sun et al., 2020)*	ROI: bilateral superior temporal sulcus - STC	*(Same as in Sun et al., 2020)*	*(Same as in Sun et al., 2020)*	-	-	*(Same as in Sun et al., 2020)*	-	-

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				(channels 7, 11, 12) and Broadmann Area 46 (dorsolateral prefrontal lobe) (channels 18 and 14)							
Issa et al., 2016	Continuous wave with two wavelengths (690 and 830 nm)	(30 optodes - 15 per hemisphere). 8 detectors and 7 sources = 22 channels per hemisphere.	Emitters and detectors were arranged into 5 × 3 arrays over the frontal, temporal, and parietal cortices of the right and left hemispheres. T3 and T4 are the reference points.	**ROI:** primary auditory cortex (temporal lobe including superior temporal plane). **non-ROI:** surrounding auditory belt regions (temporal and parietal cortices).	3 cm	20Hz	18 seconds each: pure tones (750 or 8000 Hz), broadband noise (BBN), and silence.	9 rounds of 18-second blocks of sound (750, 8000, or BBN) separated by intervening 18-second blocks of silence. Each experimental run per participant consisted of 54 blocks: 27 silent and 27 stimulation blocks equally distributed amongst the three experimental stimuli (750Hz, 8000Hz, or BBN).	20 minutes	The order of auditory stimuli presentation was randomized across the experiment.	Standard fixed volume through two loudspeakers placed at a distance approximately 2 feet from the subject in a sound field orientation that was held constant for all participants at 70dBSPL
San Juan et al 2017 *(Same methods and sample as in Issa et al.,*	*(Same as in Issa et al., 2016)*	*(Same as in Issa et al., 2016)*	*(Same as in Issa et al., 2016 adding occipital in the*	*(Same as in Issa et al., 2016)*	*(Same as in Issa et al., 2016)*	*(Same as in Issa et al., 2016 adding “except for one participant*	*(Same as in Issa et al., 2016) (750 Hz was descri*	60-second baseline /period of silence before + *(Same as in Issa et*	*(Same as in Issa et al., 2016)*	*(Same as in Issa et al., 2016)*	*(Same as in Issa et al., 2016)*

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2016, but analyzing the resting state).			*description)*			*whose recording was performed at 50Hz and subsequently down-sampled" in the description).*	*bed in the figure, but in the text it was 700Hz).*	al., 2016) + 60-second baseline /period of silence after			
San Juan et al 2021 *(Same methods and sample as in Zhai et al., 2020 - but only the resting state period was analyzed)*	*(Same as in Issa et al., 2016, San Juan et al., 2017, and Zhai et al., 2020)*	Traditional cap: 30 optodes (15 per hemisphere). 12 detectors and 6 sources = 23 channels per hemisphere. *(They used the same methods as Zhai et al., 2020, but the channels were reported differently)*	*(Same as in Zhai et al., 2020)*	*(Same as in Zhai et al., 2020)*	2.8 cm *(They used the same methods as Zhai et al., 2020, but the distance between source and detector were reported differently)*	50Hz *(They used the same methods as Zhai et al., 2020, but the sample rate was reported differently)*	*(Same as in Zhai et al., 2020)*	*(The methods are described in the article by Zhai et al., 2020, however the figure included is the same as the article by San Juan et al., 2017 - with the BBN, 750Hz, and 8KHz stimuli)*	*(The methods are described in the article by Zhai et al., 2020, however the figure included is the same as the article by San Juan et al., 2017)*	Not reported	*(Same as in Issa et al., 2016, San Juan et al., 2017, and Zhai et al., 2020)*
Schecklmann et al., 2014	Continuous wave with two wavelengths (695 ± 20 nm and 830 ± 20 nm)	7 detectors and 8 sources = 22 channels covered an area of 6 x 12 cm on the scalp	The channel over the middle inferior optode was placed over T3/T4 with vertical orientation in direction to C3/C4.	*(No Description. However, by the placement of the electrodes the region of interest is the primary auditory*	3 cm	10 Hz	20 seconds: Speech Noise and silence.	**Block design:** 12 blocks of 20 seconds of Speech Noise followed by 20 seconds of resting period. **Event-related design:** Stimuli were	Not reported	Not reported	Insert earphones (E-A-RTONE 3A) binaurally at 70 dBSPL.

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				cortex) .				presented 40 times with a variable inter-stimulus interval of 12-14 s for 1.75 s.			
Shoushtarian et al., 2020	Continuous wave with two wavelengths (760 and 850 nm)	16 detectors and 16 sources = 36 long channels and 4 short channels	Over or around the Auditory cortex.	Frontal, temporal and occipital cortical regions.	Long channels: 3 cm; Short channels: 1.1 cm	7.8125 Hz per channel	15 seconds: pink noise and visual stimuli + 20 or 25 seconds: silence	**Recording 1:** 6-minute resting-state recording + ***Break*** *(3-5 min)* + **Recording 2:** Auditory or visual stimulus blocks (six 15-second auditory and six 15-second visual stimuli) +***Break*** *(3-5 min)* **+ Recording 3:** Auditory or visual stimulus blocks (four 15-second auditory and four 15-second visual stimuli). / In total, 10 trials of each stimulus type were collected (six in recording 2 and four in recording 3).	Approximately 20 minutes	Stimuli were randomized across blocks with no more than two blocks of the same type in a row and 20 or 25 second non-stimulus intervals between stimuli.	Insert earphones (E-A-RTONE 3A) binaurally at 65 dBSPL.
Sun et al., 2020	two wavelengths (695	16 sources and 14	Sources and detectors were	Two ROIs: channels 7,	3 cm	10Hz	20 seconds: Maski	15 blocks of 5 trials -	620 seconds =	The blocks were distribute	Auditory stimuli were present

	and 830 nm)	detectors	arranged into 3 × 5 arrays over the left and right temporal cortex, frontal and parietal lobe.	11, 12, 29, 33, and 34, and the BA21 region was drawn according to the activation pattern of different acoustic stimuli in this study (including channels 1, 2, 3, 23, 24, and 25).			ng Noise (Narrow-band, notched sound, and white noise) and silence.	each of three masking sounds followed by 20 seconds of silence	*10.33 minutes*	d randomly to avoid uneven influence upon the results of different masking sounds	ed through a sound speaker placed 75 cm in the front of the subject. The sound intensity was coordinated at 70 dB SPL.
Verma et al., 2019	Continuous wave with two wavelengths (760 and 850 nm)	8 detectors and 8 sources = 10 Channels per hemisphere	Auditory cortex	Bilateral temporal cortical areas	3 cm	15.625 Hz	3 seconds: sound and silence. *(What type of sound was used?)*	6 blocks with 12 trials in each block. Each trial consisted of a sound presented for 3 s, followed by 3 s of silence. *(What type of sound was used?)*	Not reported	Not reported	Philips headphone at Not reported *(Intensity - dB)*
Yu et al., 2023	Two wavelengths (730 and 850 nm)	8 detectors and 8 sources = 10 Channels per hemisphere (total channels: 20)	T3 and T4 are the reference points of the International 10-20 System. Covering an area of 4 x 10	Not reported	3 cm	10 Hz	18 seconds: 8,000 Hz and silence	12 blocks: 6 blocks of auditory stimulation and 6 blocks of silence. The auditory stimulation paradigm	Approximately 8.6 minutes.	Not reported	Headset (Edifier, W800BT) at 50 dBSPL

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			cm^2 on each side of the measuring cap. Temporal, occipital frontal and parietal lobe.					consists of 6 rounds of sequentially selected 18-second blocks of 8000 Hz, and 18-second blocks of silence from the interval between every two blocks of sound.			
Zhai et al., 2020	*(Same as in Issa et al., 2016 and San Juan et al., 2017)*	Traditional cap: 36 optodes (18 per hemisphere), 12 detectors and 6 sources = 23 channels per hemisphere.	Sources and detectors were arranged into 5 × 3 arrays over the frontal, temporal, and parietal cortices of both hemispheres.	*(Same as in Issa et al., 2016 and San Juan et al., 2017)*	*(Same as in Issa et al., 2016 and San Juan et al., 2017)*	*(Same as in Issa et al., 2016 and San Juan et al., 2017)*	18 seconds each: Silence and BBN.	5 minutes baseline /period of silence before + 9 rounds of 18-second blocks of sound (BBN) separated by intervening 18-second blocks of silence (inter-stimulus rest - ISR) + 5 minutes baseline /period of silence after	17 minutes of the entire block-paradigm design protocol *(17 min for the experiment plus 5 min before and after the stimulation)*	The stimulus (BBN or silence was randomly presented *(How was it randomized? The first stimulus that would be presented? Since there are only 2 stimuli and it is not possible to randomize since they are interleaved).*	*(Same as in Issa et al., 2016 and San Juan et al., 2017)*

Note: Not Reported = It could be reported but was not; - = It does not need to be done.

Table 4. Main results and conclusions of the ten included articles

AUTHOR AND YEAR	SUMMARY OF MAIN RESULTS				CONCLUSION
	HEMODYNAMIC DATA DURING BLOCK DESIGN	HEMODYNAMIC DATA DURING RESTING STATE	HEMISPHERE DIFFERENCES	BEHAVIORAL RESULTS	
Huang et al., 2022	-	The results showed that: (1) global connectivity between	-	The analyses of the questionnaires for tinnitus,	Notched sound treatment for 1 month can

		the bilateral auditory cortex of the superior temporal sulcus and the ipsilateral cortex did not change significantly between baseline and the completion of treatment; and (2) only the connectivity between channel 14 (Brodmann areas 19 and 39 = occipital-temporal region) and the right superior temporal sulcus decreased after treatment. The overall connectivity between the right Brodmann 46 region (frontal region) and the right cortex decreased after treatment. The decrease in connectivity after treatment were specifically found for the right temporal lobe (channels 10 and 14), the frontal lobe (channels 16, 20, 21, and 22), while there was no significant change on the left side.		anxiety, or depression (THI general, THI emotional, THI functional, THI catastrophe, BAI, or CES-D) found that there were no significant differences before and after sound treatment.	restructure the cerebral cortex of tinnitus patients. Notched sound can decrease connectivity between the auditory cortex and specific brain regions. Notched sound treatment not only regulates the auditory center through lateral inhibition, but it also improves tinnitus by reorganizing the emotional control center. The results of the study indicate that cerebral cortex reorganization occurs in tinnitus patients after submitted to treatment with notched sound for one month, and that notched sound decreases the connectivity between the auditory cortex and specific brain regions. Notched sound also alleviated tinnitus by reorganizing the emotion-related cortical center.
Issa et al., 2016	**During silence:** tinnitus participants maintained or slightly increased HbO concentrations in ROI and non-RO. Controls had deactivation of HbO within ROI, with a larger HbO decrease than tinnitus. **During auditory stimulation** (750Hz, 8000Hz, and BBN): 1. control participants showed increases during 750Hz, 8000Hz, and BBN when compared with silence in the primary auditory cortex, but not in the surrounding auditory belt regions.; 2. Following stimulation with BBN, tinnitus participants showed a deactivation in ROI	-	There were no differences between right and left hemispheres within specific experimental conditions pooled across the length of the experiment.	There was no correlation between age, hearing threshold, and audiogram findings with hemodynamic activity during the various experimental paradigms (ISR, BBN, 750Hz, and 8000Hz) in both ROI and non-ROI. The only significant effect was a negative correlation between THI score and hemodynamic activity in non-ROI during 750Hz tone stimulation.	Both auditory and select non-auditory cortices have elevated hemodynamic activity in participants with tinnitus in the absence of an external auditory stimulus, a finding that may reflect basic science neural correlates of tinnitus that ultimately contribute to phantom sound perception.

	and non-ROI. For 750 and 8KHz, the HbO increased in the tinnitus group in the ROI and decreased in non-ROI. The comparison between ROI and non-ROI during acoustic stimulation (750Hz, 8000Hz, and BBN) revealed a significant difference in response only to 750Hz in controls and tinnitus participants, revealing the expected result of increased auditory cortex activity following acoustic stimulations as compared to non-ROI.				
San Juan et al., 2017 *(Same methods and sample as in Issa et al., 2016, but analyzing the resting state)*	-	Prior to stimulation, the average connectivity of temporal and fronto-temporal region in controls was higher than in tinnitus participants. Following stimulation, the average connectivity of the auditory cortex to the fronto-temporal, fronto-parietal, temporal, occipito-temporal, occipital was increased in the tinnitus participants. Interestingly, all channels that changed significantly in tinnitus exhibited an increase in connectivity, while all channels that changed in controls exhibited a decrease in connectivity.	There was no asymmetry between the left and right hemisphere involving ROI and "n-1" non-ROI channels for all experimental conditions.	There was no correlation between hemodynamic responses and age, hearing threshold and audiogram findings during the stimulation paradigm conditions (750Hz, 8000Hz, BBN, silence) in either ROI or "n-1" non-ROI.	Our data demonstrate significant changes in RSFC involving both auditory and non-auditory cortical regions in human tinnitus and controls. Altered RSFC observed throughout the brain following sound stimulation in tinnitus suggests that multiple central auditory and non-auditory regions may contribute to phantom perception.
San Juan et al., 2021 *(Same methods and sample as in Zhai et al., 2020 - but only the resting state period was analyzed)*	-	For standard probes, left and right auditory cortex in tinnitus showed increased resting-state functional connectivity (RSFC) to each other and to other non-auditory cortices (temporal, temporo-parietal, temporo-occipital, and parietal). These were all significant in both the pre- and	-	-	While many areas for the adapted probes did not reach significance, these data using a highly innovative and newly created probe adapting fNIRS technology to the EAC substantiates our previously published data in human tinnitus and concurrently

		post-stimulation conditions (5-min silence periods before and after the block silence-BBN stimulation paradigm) and none of the changes from pre- to post-stimulation were significantly different. **fNIRS probes adapted to the external auditory canal:** Two channels demonstrated connectivity values similar to channels of the scalp/cap configuration, but none of the adapted probe channels, neither individually nor combined, showed a statistically significant connection to any of the regions.			validates this technology as a useful and expanded brain imaging modality.
Schecklmann et al., 2014	1. Higher oxygenation at baseline over the right temporal areas (auditory cortex - channels 2 and 7) in participants with tinnitus than in controls (healthy controls). 2. TMS treatment: the oxygenation increased for the verum group	1. Statistical values were higher for the event-related design in contrast to the block-design experiment. 2. We only found significant activity for the event-related design (left hemisphere: channel 11, 16; right hemisphere: channel 2, 6, 7, 11, 16, 20). 3. Differences between patients and controls in channel 12 for the event-related design were found for the baseline measurements. 4. The significant channel of the event related design was related to frontal areas showing decreased activity in the patient group. 5. There were no clear differences in the left hemisphere between patient groups and the control group. 6. TMS treatment: The verum group had higher oxygenation during the baseline in contrast to the sham group with no oxygenation differences during the last treatment visit. Oxygenation increased in the	-	-	1.The fNIRS has sensitivity for detecting rTMS changes in brain activity; 2. The increased auditory cortical activity as measured by fNIRS may be related to tinnitus perception. To sum up the pre-post effects, the activity of the right hemisphere was not sensitive to specific treatment effects. For the left hemisphere, increased oxygenation during baseline decreased over the course of the treatment and lowered oxygenation during the baseline increased over the course of the treatment with reversed patterns between the verum and sham group and between the block and event-related design.

		sham group over the course of the trial with no changes for the verum group. However, the effect disappears by controlling for baseline differences.			
Shoushtarian et al., 2020	Auditory-evoked responses were significantly reduced in the tinnitus group in the auditory regions of interest.	In comparison to the control group, higher right temporal-frontal HbO connectivity, as well as higher right seed temporal-occipital HbR connectivity was found in the tinnitus group.	There was no significant difference between left and right auditory responses.	HbO-derived connectivity between right seeds and frontal channels increased with duration of tinnitus. HbR- derived connectivity between right seed and occipital channels increased significantly with subjective ratings of loudness. Auditory-evoked responses in the tinnitus group were significantly reduced but did not change significantly with tinnitus severity. There is an increasing trend between temporal-frontal connectivity and duration of tinnitus.	Our findings show the feasibility of using fNIRS and machine learning to develop an objective measure of tinnitus.
Sun et al., 2020	The HbO signal in selected ROIs induced by white noise was significantly larger than that induced by the other two masking noises, while the results between narrow-band noise and the notched sound did not show significant differences. The group analysis results from 33 individuals (tinnitus and controls) showed that the narrow-band noise caused a marginally significant decrease in HbO signal in the Brodmann area 21 region (BA21), while	-	-	The depth of residual inhibition induced by the narrow-band noise and white noise significantly correlated with ΔHbO in the region of interest (ROI). However, neither the depth nor the duration of the residual inhibition induced by notched sound correlated with the ΔHbO. The duration of RI by the white noise showed a marginally significant correlation with	Thus, NIRS showed three cortical activation patterns induced by three different masking noises, and correlations between residual inhibition effects and change of HbO amplitude were found. NIRS could therefore be applied in objective assessment of acoustic therapy.

	white noise caused a significant increase in HbO signal in BA21. Notched sound did not cause significant changes in the HbO signal in the temporal cortex. In addition, none of the three masking noises caused significant changes in the HbR signal in the temporal cortex.			the amplitude of ΔHbO in the ROI.	
Verma et al. 2019	There was a higher cortical activation area observed for oxyhemoglobin (HbO) concentration bilaterally after tDCS than baseline, as well as a reduction in intensity of the hyperactivated areas. 1. Assessment of cortical functioning revealed a reduction in intensity of hyperactivated cortical areas, as well as spreading of the cortical HbO concentration during the presentation of sound stimuli to a larger cortical area in comparison with baseline before receiving tDCS. 2. Sound-evoked hemodynamic activation was asymmetrically distributed over the bilateral auditory cortex region prior to tDCS, higher contralateral rather than ipsilateral to the tinnitus side at baseline. 3. The contralaterally localized hyperactivity was reduced with regard to intensity, and there was a greater spread of HbO concentration observed over the bilateral auditory cortex region after receiving tDCS.	-	-	-	fNIRS is a valuable tool to assess auditory cortex activation. There is improvement in tinnitus symptoms after tDCS. In addition, there is improvement in functional cortical activity as assessed by fNIRS in chronic tinnitus after tDCS.
Yu et al., 2023	Acupuncture increased the concentration of oxygenated hemoglobin in the left temporal lobe of tinnitus patients and	-	-	The changes in the scores of THI and TEQ were significantly correlated with the changes in the concentration of	In this study, acupuncture reduced the severity of tinnitus in patients with tinnitus and reduced symptoms

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	affected the activation of the auditory cortex during silence. According to channels differences pre and post, it was found activation in the superior temporal gyrus (channels 6 and 13).			HbO2 in the auditory cortex.	of anxiety and depression. According to the fNIRS detection results of tinnitus patients, acupuncture increased the concentration of oxygenated hemoglobin in the temporal lobe of tinnitus patients, and affected the activation of the auditory cortex, which may reflect the potential plasticity of acupuncture on the auditory central nervous system.
Zhai et al., 2020	Standard fNIRS measurements in participants with tinnitus revealed increased auditory cortex activity during silence that was suppressed during auditory stimulation with BBN. Conversely, controls displayed increased activation with BBN but not during silence. A strong correlation was observed between the cap and adapted probe-generated waveforms. Importantly, adapted ear canal fNIRs probes showed similar hemodynamic responses seen with cap probes in both tinnitus and controls.	-	-	-	In this proof of concept study, we successfully fabricated, adapted, and utilized a novel fNIRS technology that replicates established findings from traditional cap fNIRS probes. This exciting new innovation, validated by replicating previous and current cap findings in auditory cortex, may have applications in future studies to not only investigate brain changes in tinnitus, but also in other pathologic states that may involve the temporal lobe and surrounding brain regions.

Note: Not Reported = It could be reported but was not; - = It does not need to be done.

Synthesis of results

- Type of studies:

Among the cross-sectional studies, four aimed to compare changes in oxy-hemoglobin of participants with tinnitus and controls[19, 20, 22, 23], one study adapted external auditory canal probes for NIRS equipment[24], and one study tested the adapted probes for functional efficacy[25]. The case report used fNIRS to evaluate the improvement in auditory cortex functioning in chronic tinnitus by tDCS[21]. The longitudinal studies used fNIRS to evaluate the benefit of Transcranial Magnetic Stimulation (TMS)[18], the effectiveness of notch sound to regulate tinnitus[26], and the use of acupuncture for tinnitus treatment[27].

- Sample characteristics and evaluation forms:

The number of participants was relatively similar in the cross-sectional and longitudinal studies[18-20, 22-27], and ranged from 10-29 people with tinnitus and 7-21 controls.

The main evaluation form in the studies was NIRS, but some studies used complementary instruments, such as hearing procedures: pure tone averages (PTA) performed at frequencies 0.25-8kHz[19-23, 26, 27], speech reception thresholds (SRTs) and word discrimination scores (WDS)[19, 20, 24, 25], emittance measurement and otoacoustic emission[26], tinnitus matching and residual inhibition[23]. In addition, the questionnaires were used: Tinnitus Handicap Inventory – THI[19-22, 26, 27], visual analog scale[22], Beck Anxiety Inventory (BAI)[26], Center for Epidemiologic Studies-Depression (CES-D) Scale[26], tinnitus evaluation questionnaire (TEQ)[27], Hamilton anxiety scale (HAMA)[27], and Hamilton depression scale (HAMD)[27]. Complementary exams, such as physical and systemic examination, blood investigations, and imaging studies – TC or MRI brain scans were also performed[21, 26].

- Characteristics of the experiments:

Five studies performed a block-design experiment[19, 21, 23, 24, 27], three developed resting-state[20, 24, 26], and two did both[18, 22]. The evaluation time of the resting state ranged from one minute before and after the block design[20], five minutes before and after the block design[25], and six minutes before the block design[22], while in two studies it was not clear for how long it was evaluated[18, 26].

There is no consensus in block-design studies on the duration of the auditory stimulus and baseline nor on the minimum number of blocks and trials needed to identify change in hemodynamic activity[18, 19, 21-24, 27]. Pure tones (750Hz and 8000Hz) and masking noise (Broadband Noise, Speech Noise, Narrow-band, Pink Noise, Notched Sound, and White Noise) were explored. The stimulus and silence duration varied between 3, 15, 18, and 20 seconds, with each stimulus type repeated 9, 10, 12, 20, 72, and 75 times. The experiment duration varied from 8 to 20 minutes.

Regarding supplementary assessments, three studies compared the interhemispheric difference[19, 20, 22], and six correlated the NIRS findings with behavioral data[19, 20, 22, 23, 26, 27].

- Main results of block design:

The case study used block design to verify the effect of neuromodulation. It was observed higher cortical activation area for oxyhemoglobin concentration bilaterally after tDCS than baseline, as well as a reduction in intensity of the hyperactivated areas. However, the study did not present statistical analysis and the type of sound used during the evaluation was not described(21).

During silence:

Controls decreased HbO levels within primary auditory cortex. However, tinnitus participants maintained or increased HbO concentrations in temporal and parietal cortices(19, 24), and another study only observed an increase in HbO in the right temporal areas(18). This indicates that central tinnitus origins may also exhibit physiological changes over other brain regions(19). The tinnitus participants presented greater primary auditory cortex metabolic activity during periods of silence(19, 27).

During auditory stimulation with pure tones (750Hz, and 8000Hz):

Control participants showed HbO increases during 750 and 8000Hz when compared with silence in the primary auditory cortex, but not in the surrounding auditory belt regions. An HbO increase in the primary auditory cortex and a decrease in non-ROI (temporal and parietal cortices) were found in the tinnitus group(19). A significant difference in response was only found for 750Hz in controls and tinnitus participants, revealing increased auditory cortex activity following acoustic stimulations as compared to non-ROI (temporal and parietal cortices)(19).

Another study(27) used 8000Hz to analyze the benefit of acupuncture in tinnitus participants, showed that acupuncture increased HbO concentration in the temporal lobe, but that difference was not significant. Although there was no significant difference in oxygenation levels when stimulated with pure tone, the concentration of HbO in the silence period was higher than that in the sound period, which may also be related to the inhibition of auditory cortical activity by sound stimulation(27).

During auditory stimulation with masking noises (Broadband Noise, Speech Noise, Pink Noise, Narrow-band, Notched Sound, and White Noise):

Control participants showed increases during BBN when compared with silence in the primary auditory cortex, but not in the surrounding auditory belt regions. The opposite was found for tinnitus participants, with decreased in temporal and parietal cortices(19, 24).

The sound-evoked activity in right temporal areas during speech noise was increased in tinnitus participants in contrast to healthy controls(18), while another study used Pink Noise and observed reduced auditory responses (negative variation in right auditory cortex) in patients with tinnitus, explained by reduced neural activity(22).

The HbO signal in selected ROIs induced by White Noise was significantly larger than that induced by the other two masking noises (Narrow-band and Notched Sound), while the results between Narrow-band Noise and the Notched Sound did not show significant differences(23). The tinnitus and

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controls showed that the narrow-band noise caused a marginally significant decrease in HbO signal in the Brodmann area 21, while White Noise caused a significant increase. Although, predictably, the White Noise induced an activation response in the Brodmann area 21, the decreased induced by Narrow-Band Noise was unexpected[(23)].

- Main results of Resting-state:

Before stimulation, the average connectivity of temporal and frontotemporal regions in controls was higher than in tinnitus participants. Following stimulation, the average connectivity of the primary auditory cortex to the temporal, frontotemporal, frontoparietal, occipitotemporal, and occipital regions was lower in controls than in tinnitus participants[(20)].

There were differences between tinnitus and controls in the average change in connectivity in frontotemporal, temporoparietal, temporal, occipital, temporooccipital, and parietal regions[(20, 22, 25)]. The changes observed for all the brain regions in tinnitus involved increases in connectivity, whereas multiple regions in controls experienced a decrease in connectivity[(20)]. These results are congruent with the hypothesis that tinnitus perception may also be generated by non-auditory brain regions that are connected to auditory cortex neurons[(25)].

The tinnitus participants showed more focused activation during the event-related design as mirrored by decreased activation in frontal areas. There were no clear differences between patient and control group in the left hemisphere[(18)].

Another study[(26)] analyzed the benefit of Notched Sound and showed that global connectivity between the bilateral auditory cortex of the superior temporal sulcus and the ipsilateral cortex did not change significantly between baseline and the completion of treatment. It was found a decrease in the overall connectivity in the right temporal and frontal cortex after treatment, while there was no significant change on the left side.

- Interhemispheric difference assessment:

Among the 10 included studies, three studies compared the interhemispheric difference[(19, 20, 22)]. The studies did not found differences between right and left temporal and parietal cortices[(19, 20)], nor between frontal, temporal and occipital cortical regions[((22)].

- Relation of HbO/HbR levels with behavioral results:

The association of HbO/HbR levels with tinnitus characteristics is controversial. Two studies conducted with the same participants, evaluating block design and resting state, did not find a correlation between age, hearing threshold, and audiogram findings with hemodynamic activity during the various experimental paradigms (ISR, BBN, 750Hz, and 8000Hz) in temporal and parietal cortices[(19, 20)].

However, it was observed association between tinnitus severity[(27)] and residual inhibition with HbO in the auditory cortex[(23)]. It was also seen that HbO-derived connectivity between right seeds and frontal channels increased with duration of tinnitus; while HbR- derived connectivity between right seed and occipital channels increased significantly with subjective ratings of loudness[22].

Finally, a study used THI, BAI and CES-D to assess the effectiveness of notched sound to treat tinnitus and found no differences[26].

DISCUSSION

The findings demonstrate that fNIRS has been used in a variety of ways to assess tinnitus. Its applications encompass the observation of brain responses to pure tones of varying frequencies, diverse noise types, and silence. Moreover, this technique has been adapted for auditory research purposes and holds promise in evaluating diverse tinnitus treatment modalities.

The silence in the resting state analysis revealed distinct impacts on connectivity between tinnitus and control participants. Tinnitus participants exhibited elevated connectivity in various regions, including auditory and non-auditory areas such as frontotemporal, frontoparietal, temporal, occipitotemporal and occipital regions[20, 22].

Alterations in functional interactions among neural circuits of the brain provide insight into certain tinnitus characteristics[29]. Distress modifies the functional connectivity between the auditory cortex and the cingulate[30], as also tinnitus-related distress appears associated with the executive control network, suggesting a likely consequence of hyperactive attention condition[29].

The observed increase in brain connectivity among tinnitus participants may indicate a central auditory and non-auditory plasticity, leading to distorted sound processing and potentially contributing to phantom perception[20]. Although research demonstrates heightened connectivity between brain regions in tinnitus individuals, there is substantial variability in neural functional connectivity between subjects[31, 32]. Further investigation is necessary to uncover shared patterns among subjects. In this context, fNIRS emerges as a valuable tool for objectively mapping tinnitus-related neural correlations within the complex subjective disease[20].

Although functional near-infrared spectroscopy (fNIRS) offers important advantages, such as portability, low cost, and tolerance to movement artifacts [1], it also presents notable technical limitations when compared to well-established neuroimaging methods like functional magnetic resonance imaging (fMRI) and electroencephalography (EEG). Unlike fMRI, which provides high spatial resolution and whole-brain coverage, fNIRS is limited to superficial cortical areas and has reduced spatial resolution due to its reliance on optical signal penetration, typically restricted to 2–3 cm beneath the scalp [33]. Furthermore, while EEG captures neuronal electrical activity with millisecond precision, allowing detailed temporal resolution of brain dynamics, fNIRS measures slow hemodynamic responses associated with neural activity, resulting in lower temporal resolution [34]. These highlights suggest the importance of methodological triangulation and that fNIRS may be best used in conjunction with other techniques to provide a more comprehensive understanding of the neural correlates of tinnitus.

In the other way of analyzing with fNIRS through sound presentation analysis, tinnitus participants exhibited increased HbO concentration in the primary auditory cortex during 750Hz and

8KHz presentations. In contrast, the surrounding auditory belt cortex (parietal and temporal cortices) experienced decreased HbO concentration. During the Broadband Noise presentation, tinnitus participants demonstrated HbO decrease in the temporal and parietal cortices(19).

During pink noise presentation, the auditory-evoked responses were reduced in the tinnitus participants, possibly indicating decreased neural activity(22). In distinct noise types, such as white noise, narrow-band noise, and notched sound, it was observed that the white noise exhibited an increase in HbO levels compared to the masking noises. Surprisingly, Narrow-band deactivated and Notched Sound activated the Brodmann region 21(23).

The findings reinforce the idea that auditory cortical regions and the surrounding auditory belt cortex exhibit spontaneous activation in tinnitus participants even without external stimulation. Additionally, the presentation of Broadband Noise decreased hemodynamic responses, indicative of cortical suppression resembling forward masking and residual inhibition (RI) mechanisms(19). RI involves a temporary suppression of the tinnitus perception following a sound stimulation, it can be obtained in most tinnitus participants(35), with complete RI observed in over a third of individuals(36). The variability in RI within the tinnitus population might be a result of diverse oscillatory patterns associated with acoustic tinnitus suppression(37).

The NIRS was also adapted and validated for auditory studies to reduce signal penetration limitations. An innovative approach involved adapting probes for use within the external auditory canal (EAC(24) and subsequently validating their functional efficacy(25). The results indicated a correlation in oxygenation levels between standard cap probes and the adapted EAC probes(24). However, the EAC probes exhibited smaller response amplitudes compared to the standard probes, and it was explained that the optical paths of the two probes may not completely overlap. Notably, these pioneering studies introduced the concept of deeper within the skull through the EAC probe fabrication.

The application of fNIRS extends to the assessment of tinnitus treatment effectiveness. In a case report, enhanced bilateral cortical activation, reflected by increased oxyhemoglobin concentration, was observed post-neuromodulation. This was accompanied by an expanded cortical response area during sound stimulus presentation(21). Despite the improvement in tinnitus symptoms and an improvement in functional cortical activity after neuromodulation, the case report lacked the type of sound presented and statistical analysis. Therefore, more methodologically rigorous studies are required for comprehensive treatment evaluation.

Longitudinal fNIRS studies investigating tinnitus treatment include Notched Sound(26), acupuncture(27), and neuromodulation – specifically TMS(18). The Notched Sound study examined resting-state oxygen levels, revealing no global connectivity changes between bilateral auditory cortices, yet identifying reduced connectivity in the right temporal and frontal cortex(26).

Acupuncture treatment led to increased oxygenated hemoglobin concentration in the left temporal lobe, influencing auditory cortex activity during silence. Notably, changes in THI and TES questionnaire scores correlated significantly with auditory cortex HbO concentration changes(27). In the TMS study, verum group oxygenation increased in block design, though no significant differences emerged in resting state analyses between groups[18]. Hence, fNIRS proves advantageous for assessing auditory cortical activity across diverse tinnitus treatments and holds promise for auditory-related imaging studies.

Limitations arise from experimental variability, hindering comprehensive inter-paper comparisons in this scoping review. Notably, the wide range of tinnitus symptoms encompass loudness, pitch, cause, duration, laterality, association with psychiatric symptoms, and concurrent hearing loss.

CONCLUSION

The fNIRS technique shows promise for identifying hemodynamic differences in individuals with tinnitus, offering a non-invasive and accessible approach to explore neural correlates of this condition. Although variability across studies remains, due to factors such as stimulus type, experimental duration, and analytical methods, fNIRS may contribute valuable insights into the underlying mechanisms of tinnitus. Future research should aim to standardize experimental protocols, compare fNIRS findings with established methods such as fMRI and EEG, and investigate its potential for longitudinal monitoring and clinical intervention. It is also interesting explore the potential of fNIRS in assessing neuropsychiatric comorbidities associated with tinnitus, such as anxiety and depression, as well as its application in more rigorous longitudinal studies.

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