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# Subcortical aphasia: a systematic review

## Afasia subcortical: uma revisão sistemática da literatura

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## Abstract

**Introduction:** Language is defined as the ability to communicate from several cognitive processes, while aphasia is an acquired disorder characterized by receptive and expressive problems in oral and written language. Subcortical structures may play an important role in speech production and processing, and recent studies have suggested that damage to these structures induces aphasia. Therefore, this study aimed to relate subcortical structures to language function and disorders. **Methods:** This systematic review of the literature was developed from March 2022 to May 2023 using questions from the PICO strategy and following the PRISMA guidelines. Blind and independent searches were conducted on PubMed, Cochrane Library, CAPES periodic, LILACS, Medline, and SciELO databases, considering studies published between 2018 and 2023. A manual search was performed to ensure the inclusion of ongoing or unpublished studies. **Results:** Of the 9,888 studies retrieved, 11 met the eligibility criteria and were included in the qualitative synthesis. **Conclusions:** A broad thalamocortical interaction was suggested for language functions and tasks, with special involvement of the left anterior thalamus.

**Keywords:** Aphasia; Basal ganglia; Thalamus; Language disorders; Systematic review.

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## Resumo

**Introdução:** A linguagem é definida como a capacidade de comunicação a partir de diversos processos cognitivos, enquanto a afasia é um distúrbio adquirido caracterizado por problemas receptivos e expressivos na linguagem oral e escrita. As estruturas subcorticais podem desempenhar um papel importante na produção e processamento da fala, e estudos recentes sugeriram que danos a essas estruturas induzem afasia. Portanto, este estudo teve como objetivo relacionar estruturas subcorticais com funções e distúrbios de linguagem. **Métodos:** Esta revisão sistemática da literatura foi desenvolvida de março de 2022 a maio de 2023 utilizando questões da estratégia PICO e seguindo as diretrizes PRISMA. Foram realizadas buscas cegas e independentes nas bases de dados PubMed, Cochrane Library, periódico CAPES, LILACS, Medline e SciELO, considerando estudos publicados entre 2018 e 2023. Foi realizada busca manual para garantir a inclusão de estudos em andamento ou não publicados. **Resultados:** Dos 9.888 estudos recuperados, 11 atenderam aos critérios de elegibilidade e foram incluídos na síntese qualitativa. **Conclusões:** Foi sugerida uma ampla interação tálamo-cortical para funções e tarefas de linguagem, com envolvimento especial do tálamo anterior esquerdo.

**Palavras-chave:** Afasia, Núcleos da base, Tálamo, Transtornos da linguagem, Revisão sistemática.

## INTRODUCTION

Language is defined as the ability to communicate from several cognitive processes, including visual perception, semantic processing, selection and recovery of phonological or orthographic representations, and motor output planning and execution. Also, naming is a key language process for effective communication that involves attaching a word or label to an object or concept, which is essential for speech. Difficulty with naming is reported in most types of aphasia[1].

Aphasia is a disorder characterized by receptive and expressive problems with oral and written language[2]. It typically arises from damage to the left frontotemporal cerebral cortex, which was associated with lesions in the basal ganglia, thalamus, lentiform nucleus, and caudate nucleus[3]. These structures play an important role in speech production and processing and contribute to naming and language correlation and modulation[1,3,4,6-13].

Studies have shown that thalamic hemorrhages often impair cognition, regardless of the damage location. However, different cognitive subdomains are affected depending on the location of the lesion within the thalamus. In this context, lesions in the lateral region of the thalamus may be associated with language, the posterior region to memory, and the anteromedial region to other cognitive subdomains[4]. . Common causes of language disorders include subcortical stroke and intracerebral hemorrhages, and individuals with thalamic aphasia present decreased comprehension[2]. In this sense, this systematic review aimed to relate subcortical structures to language

function and disorders, such as verbal fluency, listening comprehension, repetition, reading, and writing.

## METHODS

A systematic review was conducted between March 2022 and May 2023 using questions according to the PICO strategy (Population, Intervention, Control group, and Outcome). Chart 1 describes definitions and eligibility criteria.

**Chart 1.** Eligibility criteria for studies using the PICO strategy.

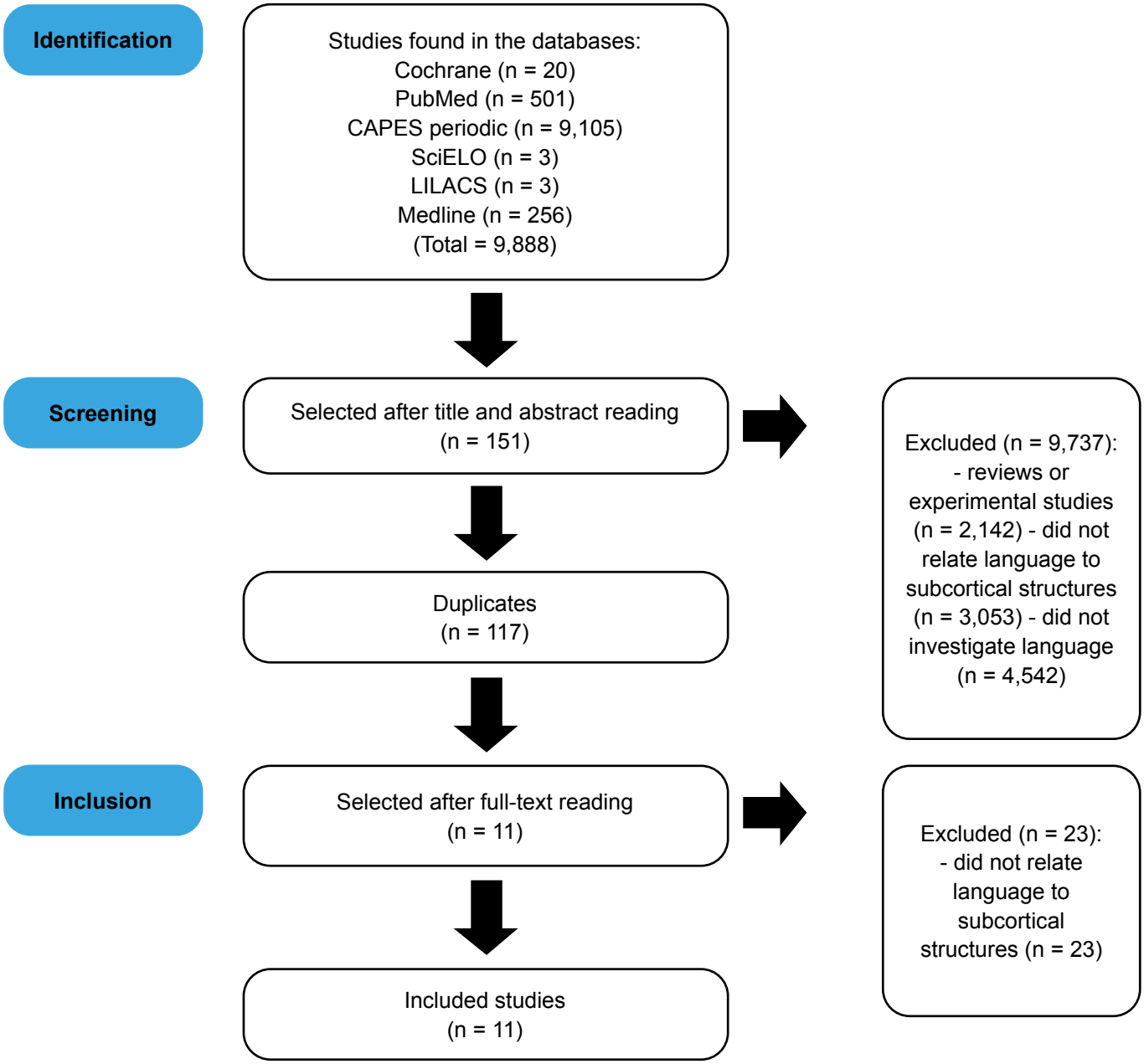
| **Guiding question: "what is the relationship between aphasia and cerebral subcortical structures?"** | | |
|---|---|---|
| Selection criteria | Inclusion criteria | Exclusion criteria |
| Population | Healthy or unhealthy humans, without age, sex, or color restriction | Experimental studies and animal models |
| Intervention | Not used as study criteria | Not used as study criteria |
| Control group | Not used as study criteria | Not used as study criteria |
| Outcomes | Study relating subcortical structures to language | Study not relating subcortical structures to language |
| Study type | Population-based studies. Descriptive or analytical studies in which the design investigated and related subcortical structures to language | Reviews, editorials, conference reports and scientific annals, events, theses, study cases, and studies that did not relate subcortical structures to language |

Source: the authors.

An independent and blind search of studies was conducted using PubMed, Cochrane Library, Coordination for the Improvement of Higher Education Personnel (CAPES) periodic, Latin American and Caribbean Health Sciences Literature (LILACS), Medical Literature Analysis and Retrieval System Online (Medline), and Scientific Electronic Library Online (SciELO) databases. Studies published in the last five years (2018 to 2023) were selected. A manual search was performed on websites and reference lists, and abstracts were reviewed to ensure the inclusion of relevant studies.

The first screening was performed on titles and abstracts without language restrictions. Literature reviews, experimental or irrelevant studies, and studies not correlating or investigating language and subcortical structures were excluded. Next, a full-text reading was performed to select the relevant studies for descriptive analysis (Figure 1).

**Figure 1.** Flowchart of the study selection.




Source: the authors.

The study selection was guided by the question: “what is the relationship between aphasia and cerebral subcortical structures?”. Four groups of descriptors from the Medical Subject Headings (MeSH) were used for the search strategy in Portuguese, English, and Spanish, and each group had two descriptors combined with the Boolean operator “AND”: “globus pallidus” AND “Language”; “corpus striatum” AND “Language”; “Caudate nucleus” AND “Language”; and “thalamus” AND “Language” (Chart 2).

**Chart 2.** Search strategy.

| Search strategy of databases with respective descriptors | | n |
|---|---|---|
| Medline | "globus pallidus" (MESH) AND "Language" (MESH), "corpus striatum" (MESH) AND "Language" (MESH), "Caudate nucleus" (MESH) AND "Language" (MESH), "thalamus" (MESH) AND "Language"(MESH). | 256 |
| Cochrane Library | "globus pallidus" (MESH) AND "Language" (MESH), "corpus striatum" (MESH) AND "Language" (MESH), "Caudate nucleus" (MESH) AND "Language" (MESH), "thalamus" (MESH) AND "Language"(MESH). | 20 |
| LILACS | "globus pallidus" (MESH) AND "Language" (MESH), "corpus striatum" (MESH) AND "Language" (MESH), "Caudate nucleus" (MESH) AND "Language" (MESH), "thalamus" (MESH) AND "Language"(MESH). | 3 |
| SciELO | "globus pallidus" (MESH) AND "Language" (MESH), "corpus striatum" (MESH) AND "Language" (MESH), "Caudate nucleus" (MESH) AND "Language" (MESH), "thalamus" (MESH) AND "Language"(MESH). | 3 |
| CAPES periodic | "globus pallidus" (MESH) AND "Language" (MESH), "corpus striatum" (MESH) AND "Language" (MESH), "Caudate nucleus" (MESH) AND "Language" (MESH), "thalamus" (MESH) AND "Language"(MESH). | 9,105 |
| PubMed | "globus pallidus" (MESH) AND "Language" (MESH), "corpus striatum" (MESH) AND "Language" (MESH), "Caudate nucleus" (MESH) AND "Language" (MESH), "thalamus" (MESH) AND "Language"(MESH). | 501 |

Source: the authors

Independent and blind researchers assessed each group of descriptors, and another researcher resolved any disagreements. The researchers followed a search protocol developed previously for this study, and all studies were included in a posterior consensus according to eligibility criteria and assessed critically for their methodology. The PRISMA[5] protocol was used to guide this systematic review.

## RESULTS

A total of 9,888 studies were retrieved from the searches. After analyzing titles and abstracts, 2,142 reviews or experimental studies, 3,053 studies without relationship between language and subcortical structures, and 4,542 studies not investigating language were excluded. Of the 151 remaining studies, 117 were duplicates. A total of 34 studies were selected for full-text reading; 23 were excluded for not addressing the relationship between language and subcortical structures. Therefore, 11 studies were included in the qualitative synthesis.

The included studies were from nine different countries (Canada, Germany, United States, Italy, Russia, Austria, China, Palestine, and Turkey). Nine studies were developed in universities[3,6-13] and two in medical or hospital centers[1,4]. All studies addressed the relationship between subcortical structures and language (Chart 3).

**Chart 3.** Analysis of the included studies.

| Author/ year | Study location | Number of individuals and characteristics | Studied structures | Assessed language function |
|---|---|---|---|---|
| Braun *et al*., 2019 | Austria | 23 healthy individuals | Hippocampus, globus pallidus, and caudate nucleus | Orthographic input in the long-term memory |
| Manes *et al*., 2018 | USA and Europe | 89 (77 individuals with Parkinson's disease and 12 healthy individuals) | Putamen, caudate nucleus, and external and internal globus pallidus | Speech |
| Cheema *et al*, 2018 | Canada | 33 (19 individuals with reading skills and 14 with difficulty in reading) | Caudate nucleus, putamen, and thalamus | Reading |
| Zhang *et al*., 2021 | China | 51 (25 individuals with subacute stroke and 26 healthy individuals) | Thalamus | Naming |
| Rangus *et al*., 2021 | Germany | 52 individuals with acute ischemic lesions isolated in the thalamus | Thalamus | Complex comprehension of speech and verbal fluency |
| Wang *et al*., 2021 | USA | 30 individuals with essential tremor (before and after DBS surgery) | Thalamus | Verbal abstraction |
| Lahiri *et al*., 2020 | India | 515 individuals after stroke (175 with an acute subcortical condition) | Putamen, striatocapsular region, thalamus, and white periventricular substance | Speech, comprehension, lexico-semantics functions, and work, reading, and naming memories |
| Campanella *et al*., 2020 | Italy | One individual with hemorrhagic stroke in the thalamus | Thalamus | Repetition, writing, and comprehension |
| Fritsch *et al*., 2019 | Germany | 1,064 individuals after stroke (52 with isolated thalamic lesion) | Thalamus | Integration of cortical information, lexical selection, and speech |
| Samara *et al*.,2020 | USA | One individual with glioblastoma multiforme | Thalamus | Speech and comprehension |
| Temel *et al*., 2021 | Turkey | 28 individuals with thalamic hemorrhage | Thalamus | Speech, comprehension, repetition, naming, reading, and writing |

Source: the autors.

A total of 1,887 individuals were analyzed; the sample size ranged from 23 to 1,064, and two case studies assessed only one individual. Several language functions were studied. Eight studies[3,4,6-9,11,12] investigated aspects related to speech or comprehension and their relationship with subcortical structures, and other functions, such as orthographic input in long-term memory,

reading, writing, naming, repetition, and work memory were also approached[1,4,7,10,12,13].

Among imaging tests, brain magnetic resonance imaging, especially functional magnetic resonance imaging (fMRI), was the main test analyzing brain structures[1,3,6-13]. Only one study[4] did not use magnetic resonance imaging but used clinical parameters and non-contrast head computerized tomography to assess these structures. Although these tests were also present in some studies, they were complementary to the fMRI.

The thalamus was the most studied subcortical structure related to subcortical aphasia: of the 11 selected studies, 9 assessed the thalamic function and its association with language functions[1,3,4,6-10,12]. Other structures were also studied, such as the putamen, caudate nucleus, globus pallidus, hippocampus, striatocapsular region, and white periventricular substance[10-13]. The involvement of a thalamic subregion, influence of the perfusion level, and functional connection with the temporal cortex was observed in the naming performance. Thus, the thalamus was considered a component of the lexico-semantic system[1].

Individuals with thalamic aphasia presented language dysfunctions, including complex comprehension of speech and verbal fluency, highlighting the involvement of the thalamus in domains of high-level language[6] It may occur due to the thalamus projection to all neocortex areas, including frontal and temporal regions associated with language, establishing reciprocal connections between the subregions of the Broca's area and subcortical structures[7]. Also, left anterior thalamus nuclei might play an important role in integrating left cortical information in the thalamocortical language networks[3]. Considering the lateralization and regionalization of the thalamic language function[8], these factors may explain thalamic aphasia, which is associated with lesions affecting exclusively the thalamus, usually on the left side[9].

The putamen was associated with the performance of reading words and non-words, reinforcing its fundamental role in executing highly familiar motor plans; however, this action is only possible when interacting with the thalamus[10]. Also, highly severe subcortical aphasia is related to the left region of the putamen compared with the thalamus, striatocapsular region, and white periventricular substance[12].

The caudate nucleus participated in tasks requiring information from sounds, such as phonemes and syllables, since individuals with dyslexia became slower when the activity in this nucleus increased[10]. Also, the caudate nucleus is involved in work memory and selection and inhibition of lexical candidates during silent reading, with involvement of the globus pallidus[13].

Activation of the hippocampus was associated with strong and weak memories of the perirhinal cortex and memories and familiarity of stimuli. This finding corroborated the hypothesis of the declarative and procedural model, which suggests that the hippocampus is part of a declarative memory system and involved in the storage of lexico-semantical information[13].

The association between language and the capsular striatum and periventricular white matter regions was not deeply studied. However, subcortical strokes in both structures were associated with aphasia[12].

## DISCUSSION

An adult fluent in any language has a daily active vocabulary ranging from 17,000 to 45,000 words. The efficacy, speed, and ease of the human brain in recognizing words are complex and intriguing. Also, the adequate processing of words requires activation, recovery, and reconstruction of orthographic information stored by memory[13].

Aphasia is an acquired disorder characterized by receptive and expressive problems with oral and written language[2]. It usually occurs due to lesions on the left frontotemporal cerebral cortex, which is part of a complex language network to comprehend the production and processing of speech[3]. However, research involving this adequate comprehension indicated that subcortical structures, such as the thalamus, should be recognized as part of the complex language networks and investigated as potential aphasia foci[3].

In the mid-19th century, aphasia was recognized as a possible derivation from subcortical pathologic processes, and the traditional classification of aphasia by Wernicke included subcortical aphasia among the subtypes. However, some authors rejected this idea at the beginning of the 20th century since subcortical disorders involving base nuclei and other structures would result in dysarthria instead. The idea of subcortical aphasia was abandoned when Dejerine et al. investigated the language zones, corresponding to the perisylvian region of the left hemisphere. Recently, lesions in subcortical structures were constantly associated with aphasia due to the development of precise imaging tests (e.g., computerized tomography), restarting the discussion on the topic[12].

Although literature have described the striatocapsular region and thalamus as the two structures most affected by subcortical aphasia, recent studies indicated other subcortical structures related to dysarthria (mostly initiated by mutism), hypophonic, slow, and melodic speech, and aphasia[12]. A study in individuals with subcortical disorders identified several language components associated with these structures, including sentence length, grammatical form, ease of initiating speaking, articulation, voice volume, and comprehension[12]. Manes et al.[11] investigated the involvement of subcortical structures in language disorders of individuals with Parkinson's disease and suggested that these disorders were associated with changes in connections of cortical structures with the putamen and left internal globus pallidus.

The fMRI is one of the main methods used to analyze anatomical structures related to language function and has been used in many studies[1,6,10,11]. The structures related to language may be approached by assessing cerebral hemodynamic activity during language comprehension and

statistical analysis. Also, three regions subjacent to language comprehension are consistently found in fMRI of adults: the left inferior frontal, left middle temporal, and left superior temporal gyrus[14].

Zhang et al.[11] developed a study on the importance of thalamocortical connections for the naming skill in the context of cerebral perfusion. The naming process consists of the assignment of a lexical label to an object or concept, which is essential for efficient communication. It also comprehends distinct cognitive executions, including visual perception, semantic processing, lexical selection, recovery of phonologic or orthographic representations, and planning and execution of speech motor output. The difficulty in naming is commonly observed in aphasia, and its complexity may justify the liability to a series of pathologies, including vascular events and chronic neurodegenerative processes[1].

The naming process usually occurs in specific networks of the left perisylvian cortex, including the Broca area, posterior temporal gyrus, motor cortex, middle frontal gyrus, bilateral fusiform regions, and anterior temporal lobes. Recent studies reported that different types of errors in naming depend on the specific location of the cerebral damage. Also, subcortical structures (particularly the thalamus) and cortical-subcortical connections were recognized as having a relevant impact on this process[1].

Basal ganglia and its complex network are related to motor skills and naming. For example, language lateralization (characterized by anomie and impaired repetition or listening comprehension) was identified in up to 64% of left thalamic lesions. This might result from the thalamic influence on the temporal and frontal cortex through connectivity with the thalamic middle pulvinar nuclei[1].

## CONCLUSION

The results supported the notion of language lateralization in the thalamus and suggested a predominant involvement of the left anterior nuclei. However, the mechanism of how a left anterior thalamic lesion leads to aphasic symptoms needs further investigation. In general, a wide thalamocortical interaction in language functions and involvement of the thalamus in the information integration needed for language tasks were suggested. Thus, this study evidenced a possible specific left anterior thalamus involvement in the language function.

## CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

## AUTHOR CONTRIBUTIONS

**ABA**: conceptualization, data curation and analysis, methodology and project administration, research, and writing, review, and edition of the manuscript; **IFGG**: methodology administration, data analysis, and writing, review, and edition of the manuscript; **GSSGM**: data analysis and research; **WHSB**: data analysis and research; **KFSV**: data analysis and research; **DECB**: data analysis and research; and **LCAA**: conceptualization, supervision, project administration, data and experiment validation, and review and edition of the manuscript. All authors approved the final version to be published.

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