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Childhood apraxia of speech in cases with comorbidities

Apraxia de fala Infantil em quadros com comorbidades

Apraxia de fala Infantil com comorbidades

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Abstract

Introduction: Childhood apraxia of speech (CAS) can result from neurological impairments associated with complex neurobehavioral disorders or have an unknown nosological entity. **Objective**: To relate the comorbidities combined with CAS and its clinical manifestations. **Data sources:** This systematic review was conducted according to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The search for scientific articles was carried out in the Medline database (via Pubmed), LILACS, Scopus and SciELO. The search terms used in English were: Comorbidity, Apraxias, Childhood apraxia of speech, Dyspraxia, Speech, and the terms in between. All studies whose subjects had some diagnosed syndrome and / or disorder and apraxia of speech were included. Initially, titles and abstracts of the articles were analyzed. Three independent reviewers evaluated the full articles and made their selections according to the eligibility criteria. At all stages, disagreements were sorted out by consensus. The main data collected was in relation with the occurrence of comorbidities in subjects with CAS. **Summary of the findings:** The most common comorbidities connected with CAS were Autism Spectrum Disorder, Rolandic Epilepsy and Down Syndrome. Genetic causes come as a predictor of the association between CAS and these comorbidities. **Conclusions:** Since CAS is a disorder of heterogeneous manifestation, it can come along with several comorbidities, which generates a late diagnosis, for CAS and the secondary disorder, hindering the process of assessment and early intervention, compromising the development of important speech skills.

Keywords: Comorbidity; Apraxias; Speech Disorders; Child Speech Apraxia.

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Authors' contributions:
AMO, LGG: Study design; Methodology; Outline of the article; Critical review; Guidance.
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Resumo

Introdução: A apraxia de fala na infância (AFI) pode resultar de comprometimentos neurológicos, estar associada a distúrbios neuro-comportamentais complexos ou ter entidade nosológica desconhecida**. Objetivo:** Relacionar as comorbidades associadas à Apraxia de Fala Infantil (AFI) e suas manifestações clínicas. **Método:** A presente revisão sistemática foi conduzida conforme recomendações do Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). A busca por artigos científicos foi realizada na base de dados Medline (via Pubmed), LILACS, Scopus e SciELO. Os termos de busca utilizados foram: Comorbidity, Apraxias, Childhood apraxia of speech, Dyspraxia, Speech, e seus entretermos, em inglês. Foram incluídos todos estudos cujos sujeitos apresentavam alguma síndrome e/ou transtorno diagnosticado e apraxia de fala. Inicialmente, títulos e resumos dos artigos foram analisados. Três revisores independentes avaliaram os artigos completos e realizaram suas seleções de acordo com os critérios de elegibilidade. Em todas as etapas, as discordâncias foram resolvidas por consenso. O dado principal coletado foi quanto à ocorrência de comorbidades em sujeitos com AFI. **Resultados:** As comorbidades mais presentes associadas à Apraxia de Fala Infantil foram Transtorno do Espectro Autista, Epilepsia Rolândica e Síndrome de Down. As causas genéticas vêm como preditor da associação entre Apraxia de Fala Infantil e estas comorbidades. **Conclusão:** Como a AFI é um distúrbio de manifestação heterogênea, pode se apresentar em conjunto com diversas comorbidades, o que gera um diagnóstico tardio, para AFI e o distúrbio secundário. Ainda, dificultando o processo de avaliação e intervenção precoce, comprometendo o desenvolvimento de habilidades importantes de fala.

Palavras-chave: Comorbidade; Apraxias; Distúrbios da Fala. Apraxia de Fala na Infância.

Resumen

Introducción: La apraxia del habla infantil (AFI) puede ser el resultado de deficiencias neurológicas, estar asociada con trastornos neuroconductuales complejos o tener una entidad nosológica desconocida. **Objetivo**: relacionar las comorbilidades asociadas a la apraxia del habla infantil y sus manifestaciones clínicas. **Fuentes de datos**: Esta revisión sistemática se llevó a cabo de acuerdo con las recomendaciones de los elementos de informe preferidos para revisiones sistemáticas y metaanálisis (PRISMA). La búsqueda de artículos científicos se realizó en la base de datos Medline (vía Pubmed), LILACS, Scopus y SciELO. Los términos de búsqueda utilizados fueron: Comorbilidad, Apraxias, Apraxia del habla infantil, Dispraxia, Habla y sus entretenimientos, en inglés. Se incluyeron todos los estudios cuyos sujetos tenían algún síndrome y / o trastorno diagnosticado y apraxia del habla. Inicialmente se analizaron títulos y resúmenes de los artículos. Tres revisores independientes evaluaron los artículos completos y realizaron sus selecciones de acuerdo con los criterios de elegibilidad. En todas las etapas, los desacuerdos se resolvieron por consenso. Los principales datos recopilados fueron sobre la aparición de comorbilidades en sujetos con PIA. **Resumen de los hallazgos:** Las comorbilidades más comunes asociadas con la apraxia del habla infantil fueron el trastorno del espectro autista, la epilepsia rolándica y el síndrome de Down. Las causas genéticas vienen como un predictor de la asociación entre la apraxia del habla en los niños y estas comorbilidades. **Conclusiones:** Como la PIA es un trastorno de manifestación heterogénea, puede presentarse junto con varias comorbilidades, lo que genera un diagnóstico tardío, para la PIA y el trastorno secundario. Aún así, dificulta el proceso de evaluación e intervención temprana, comprometiendo el desarrollo de importantes habilidades del habla.

Palabras clave: Comorbilidad; Apraxias; Trastornos del Habla; Apraxia del habla infantil.

Introduction

In child development, when there is a disability in the execution of speech planning and motor programming with nonappearance of neuromuscular damage, Childhood Apraxia of Speech (CAS) makes its presence known. In accordance with the American Speech-Language-Hearing Association - ASHA[1] - CAS is a neurological disorder that affects the accuracy and consistency of movements used in speech production in the absence of neuromuscular deficits, such as abnormal reflexes and paralysis. The literature shows numerous clinical signs of speech sound disorder mentioned above; nonetheless, three of them are consensus among the authors: inconsistent errors of consonants and vowels, inadequate coarticulation in the transition between phonemes and disturbance of prosody, especially regarding lexical and phrasal stress[2, 3].

CAS may result from neurological impairments, be accompanied with c'" omplex neurobehavioral disorders, or have an unknown nosological entity. Over the years, studies have identified that CAS sometimes co-occurred with other diagnoses, including Autism Spectrum Disorder, Down Syndrome, Benign Rolandic Epilepsy (BRE) and Attention Deficit Hyperactivity Disorder[4,10]. Notwithstanding, in the current literature, there is a dearth of studies investigating the association between the Speech Sound Disorder aforementioned and other disorders.

It is noteworthy that the presence of comorbidities can generate a late diagnosis, both for CAS and secondary disorder, which can hinder the evaluation and intervention process, bringing unfavorable prognosis for such cases. Due to the scarcity of studies that discuss the relationship between CAS and comorbidities, both nationally and internationally, it is of paramount importance that studies on this subject be accomplished in order to serve as a theoretical basis for the practice of professionals involved in multidisciplinary teams.

In light of the foregoing, the present study aims to review in the literature the co-occurrence of CAS in developmental disorders, verifying the main comorbidities associated with CAS, exploring its clinical manifestations.

Methods Data collection and synthesis

The following electronic databases (up to May 2020) were used: MEDLINE (accessed via PubMed), LILACS, Scopus and SciELO. The search terms used were "Comorbidity", "Apraxias", "Childhood apraxia of speech", "Dyspraxia", "Speech", in English, in a combined way. There was no restriction as to the type of comorbidity studied.

Study Selection

This systematic review was developed in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (Prisma)[15] checklist. Two independent evaluators, according to pre-established criteria for the present review, carried out the study selection. In case of discrepancies, a third evaluator reached the consensus. In the first step, after searching the databases, duplicate articles were removed. In the second stage, the articles were selected in relation to their titles and abstracts and, finally, in the third stage, the articles selected during the second stage were read thoroughly, and the eligibility criteria were applied to the composition of the final sample of this review. In addition, manual secondary searches were made in the references of the studies included in the final review process to complement the sample of this review.

Inclusion and exclusion process

Two reviewers performed the inclusion process of the studies independently, while a third reviewer made the consensus if discrepancies were observed. It was included all the studies in which the subjects had comorbidities (syndromes and others) associated with CAS, and which were empirical or experimental. Exclusion criteria were: studies that included individuals who were not within the age group of zero to twelve years old; presentation of an unreliable definition of what was considered CAS or diagnosis of the regarded comorbidity, and presentation of a methodological design different from the one proposed in the inclusion criteria.

Data extraction

Two independent reviewers performed data extraction concerning methodological and sample characteristics, interventions, and study outcomes, using standardized forms created specifically for this purpose, also considering the eligibility criteria. At all stages of the study, disagreements were sorted out by consensus. The main data collected was in connection with the occurrence of comorbidities in subjects with CAS.

Results

According to the findings for this analysis, it is noticed that there are still few studies that relate CAS to any comorbidity. 261 articles were found in this systematic review. According to the eligibility criteria, 237 articles were rejected, leaving 15 articles that were submitted to full reading. After this stage, it was observed that only 09 articles were in accordance with the inclusion criteria, composing the sample of the present study. In Figure 1, the diagram presents the selection steps of the studies of this review.

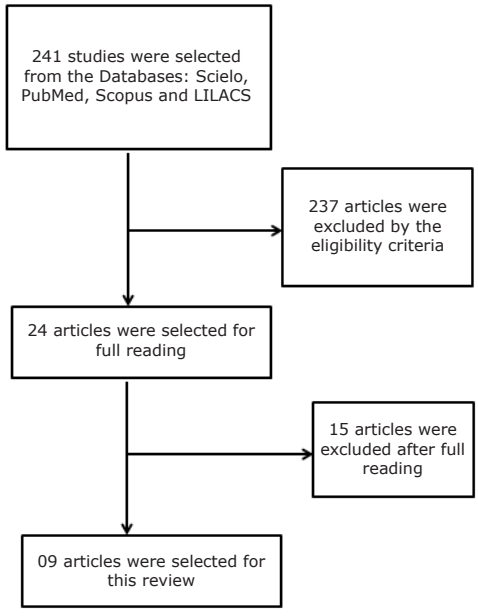

Figure 1. Study selection diagram

Characteristics of the selected studies

The nine studies included in this review scrutinized several comorbidities. Three were the most commonly addressed disorders as comorbid to CAS. The first was Epilepsy, observed in the studies by Pal et al (2010)[11] and Scheffer et al (2000)[12], with Rolandic Epilepsy being the subtype addressed. The second most observed theme among the studies included in this review was Autism Spectrum Disorder (ASD), discussed in the papers of Schumacher et al (2009)[5] and Newmeyer et al (2009)[13]. The study by Schumacher et al (2009)[5], while examining the relationship between CAS and ASD, mentions ADHD as a possible comorbidity. The genetic questions studied by Dechow et al (2019)[6], Pal et al (2011)[11] and Scheffer (2001)[6, 11, 12] comprised the third category of disorders mingled with genetic comorbidities.

The fourth category of studies refers to the deficits in cognitive functions (CF) studied by Nijland et al (2015)[14] establishing a relationship between CAS and its comorbidities. The authors exposed the importance of these functions for the performance of connected speech and orofacial movements.

The studies by Printz et al (2018)[16] and Iuzzini-Seigel et al (2017)[25] relate CAS to oromotor dyspraxias (OD) and language disorder (LD), composing, thus, the fifth category. Down Syndrome (DS), with the study of Kumin (2006)[17], is the fifth category.

Table 1 shows the study design with the characteristics of each study included in this review, considering the authors, journals in which they were published, year of publication and the impact factor (IF) of the journal.

The nine studies included in this review range from methodologies related to case studies to clinical trials. There are also studies involving family groups, focusing on genetic mapping. Table 2 shows the objectives of each study, as well as information about the participants and the outcomes of the studies. In Table 3, the comorbidities related to CAS and the characteristics of each of them can be observed, according to the selected studies.

Table 1. Characteristics of selected studies

Authors and year of publication	Original Title	Journals and Impact Factor (IF)	Outline
NIJLAND, L et al, 2015.[14]	Cognitive functions in childhood apraxia of speech.	Journal of Speech, Language, and Hearing Research 1.900 (2019)	Case-Control Observational Qualitative and quantitative
PAL, DK et al, 2010.[11]	Pleiotropic effects of the 11p13 locus on developmental verbal dyspraxia and eeg centrotemporal sharp waves.	Genes, Brain and Behavior 4.760 (2019)	Case-Control Observational Quantitative
IUZZINI-SEIGEL, J et al, 2017.[25]	Inconsistency in Children With Childhood Apraxia of Speech, Language Impairment, and Speech Delay: Depends on the Stimuli.	Journal of Speech, Language, and Hearing Research 1.900 (2019)	Qualitative and Quantitative Experimental Clinical Trial.
SCHUMACHER, J et al, 2017.[5]	Apraxia, Autism, Attention-Deficit Hyperactivity Disorder: Do We Have a New Spectrum?	Journal of Developmental and Behavioral Pediatrics 1.950 (2019)	Case study Descriptive Qualitative.
NEWMEYER, AJ et al, 2009.[13]	Results of the Sensory Profile in Children with Suspected Childhood Apraxia of Speech	Physical & Occupational Therapy In Pediatrics 1.540 (2019)	Clinical Trial Qualitative e quantitative
DUCHOW, H et al, 2019.[6]	The Co-Occurrence of Possible Developmental Coordination Disorder and Suspected Childhood Apraxia of Speech	Canadian Journal of Speech-Language Pathology and Audiology 0.280 (2019)	Clinical Trial Quantitative
PRINTZ, T et al, 2018.[16]	Verbal and oral dyspraxia in children and juveniles	Downs Syndr Res Pract. 1.440 (2010)	Qualitative and descriptive study
KUMIN, L, 2006.[16]	Speech intelligibility and childhood verbal apraxia in children with Down syndrome	Developmental Medicine & Child Neurology 3.870 (2019)	Exploratory clinical trial Qualitative
SCHEFFER, IE, 2001.[12]	Autosomal dominant rolandic epilepsy with speech dyspraxia	Annals of Neurology: Official Journal of the American Neurological Association e da Child Neurology Society 2.782 (2018)	Clinical trial Qualitative and quantitative Descriptive

Table 2. Objectives, participants and outcome of selected studies

Authors and Year	Objectives	Participants	Outcome found
NIJLAND, L et al, 2015.[14]	Determine the limit of nonverbal deficits presented by children with CAS who may offer clinical evidence of comorbidity.	34 children (17 with CAS without comorbidity and 17 with normal speech development).	Children with CAS have deficits in sequential speech memory, motor and sensory complexes, as well as delay in cognitive functions. Apraxia may present as comorbidity nonverbal dyspraxia.
PAL, DK et al, 2010.[11]	To relate BRE and SSD, from genetic mapping and acoustic analysis with a view to affirming that there is a neural network favorable to SSD.	38 families with SSD (16 children between 3 and 12 years old, with BRE and orofacial complaints). In addition to the children, 15 parents also participated in the study	The study revealed that families with BRE had, among the comorbidities, SSD, showing abnormalities in the acoustic analysis, and VD is the basis for SSD in these individuals, having in the same locus (CTS), concluding that BRE is a neurodevelopmental disorder

Authors and Year	Objectives	Participants	Outcome found
IUZZINI-SEIGEL, J et al, 2017.[25]	Determine whether speech inconsistency is an essential feature of CAS or it is caused by a comorbid LD that affects a large subset of children with CAS. Determine whether speech inconsistency is a sensitive and specific diagnostic marker that can differentiate CAS from speech delay.	48 children within the age group of 4;7 to 17;8 (years; months), being: 10 with CAS; 10 with CAS + language impairment; 10 with Speech Delay; 09 with language impairment; 09 with typical development.	Children with language disorder + CAS and CAS + a comorbidity presented equivalent performance in all evaluations of speech sound inconsistency, which is the main differentiation between children with CAS and speech delay.
SCHUMACHER, J et al., 2017.[5]	Discuss with experts a case of a child with CAS and suspected ASD and ADHD in order to identify characteristics of the syndrome and verify if it is a new spectrum.	A bilingual child (Portuguese and English) 6 years and 10 months of age, with the possibility of presenting ASD and ADHD.	Differentiated and limited language movement was observed for speech motor planning or programming, inconsistent phoneme errors and altered prosody, expressive language restrictions. Social anxiety, hypersensitivity and distraction justified comorbid diagnoses of ASD and ADHD. It showed language processing delay.
NEWMEYER, AJ et al., 2009.[13]	Review and compare the results of the Sensory Profile of children with CAS in an attempt to explore the relationship between sensory processing and sound production deficits	Thirty-eight children from 3 to 10 years of age with suspected CAS were evaluated from July 2003 to July 2005.	Children with suspected CAS may present differences in sensory processing, in addition to speech impairment. When present, these differences in sensory processing can be treated with specific therapeutic approaches through OT or an appointment with an OT.
DUCHOW, H et al., 2019.[6]	Explore the prevalence of a potential for DCD in children with suspected VD	35 children with CAS.	Children with suspected CAS are at higher risk of DCD than typical children.
PRINTZ, T et al, 2018.[16]	Differentiate VD from OD and verify the reasons for the increase in referrals of such conditions to professionals such as speech-language therapists and otorhinolaryngologists. Explore clinical and epidemiological aspects of apraxia subtypes.	Children and young people with subtypes of apraxia. Information on the cases was provided by the National Council for Public Health and Welfare to carry out the study.	The study confirmed the increase in notifications for both types of apraxia, being categorized by a neurological disorder and suggests early treatment for a better quality of life of these individuals.
KUMIN, L, 2006.[16]	Examine the answers given by parents of children with DS, through a questionnaire, in order to know how CAS has been identified and treated in children with this syndrome.	Parents of children with DS answered 1,620 questionnaires and 15% of the parents who answered the survey were informed that the child had CAS.	Symptoms of CAS can be found in children with Down syndrome, since there is a significant correlation between CAS and parents' intelligibility classifications, as well as between speech intelligibility and the age at which the child began to speak (after 5 years old). The diagnosis of difficulty with oral motor skills is more frequent than the diagnosis of CAS.
SCHEFFER, IE, 2001.[12]	To study a family with ADRESD from tests such as EEG aiming to understand, in genetic and symptomatic terms, ADRESD and BRE, alone.	Three generations with BRE + CAS had seven living members affected with CAS, of which 6 had BRE, and 2 deceased family members affected had seizures and speech problems.	Epilepsy is age dependent when along with chronic speech disorder. Chronic speech and language difficulties in BRE + CAS occur due to epistatic interactions of a second gene closely linked to the BRE locus.

CAPTION: ASD = Autism Spectrum Disorder; ADHD = Attention Deficit Hyperactivity Disorder; SSD = Speech Sound Disorders; ADRESD = Autosomal Dominant Rolandic Epilepsy with Speech Dyspraxia; (B)RE = (Benign) Rolandic Epilepsy; DCD = Developmental Coordination Disorder; EEG = Electroencephalogram; OT = Occupational Therapy; VD = Verbal Dyspraxia; OD = Oral Dyspraxia; LD = Language Disorder.

Table 3. Characteristics of comorbidities and CAS in selected studies

Authors and year of publication	Comorbidity researched	Main characteristics of the comorbidity	Characteristic of CAS
NIJLAND, L et al, 2015.[14]	Cognitive Functions (CF)	Set of cognitive skills necessary to perform various activities that require planning and monitoring of intentional behaviors related to an objective or environmental demands.	CAS is diagnosed based on specific speech characteristics, in the absence of hearing problems, intelligence and language comprehension.
PAL, DK. et al., 2010.[11]	Rolandic Epilepsy (RE)	Rolandic epilepsy is a common epilepsy of development that contains a complex genetic inheritance and it is difficult to map. In this subtype of epilepsy, the individual does not always present seizures.	Speech sound disorder (including CAS), defined as inappropriate errors in speech production that reduce intelligibility. CAS has comorbidity with BRE. This condition usually persists and provokes intelligible speech in adults.
IUZZINI-SEIGEL, J et al, 2017.[25]	Language Disorder (LD)	Children with LD acquire simultaneously the structure of the organized language and the coordination domain of articulators. Still, they have decreased oromotor coordination; impaired syntax, discourse and semantics in the absence of cognitive deficits; decreased articulatory stability and oromotor coordination; often show to have fine and gross motor capacity; have difficulties in integrating sensory information, low learning capacity of procedures or processing of information.	Difficulty in programming the motor commands that activate the speech muscles, generating: inconsistent errors in speech sounds (variable production of phonemes, in words or sentences, in multiple opportunities); decreased vowel contrasts, prosodic disorders and difficulty in transitioning and coarticulating sounds and syllables.
SCHUMACHER, J et al., 2017.[5]	ASD ADHD	Case study - diagnosis of ASD, ADHD and CAS: limited interest in interaction with other children, poor eye contact and hypersensitivity, needs constant support and redirection during school, difficulties to get dressed and follow the daily classroom routines, significant impairment in their performance. In addition, the boy presents productions of isolated words and unintelligible phrases. He tries to start a conversation, but looks away and gets frustrated when asked to repeat again.	Children with ASD or ADHD and suspected CAS may present more general difficulties with general motor programming, inconsistent sound production, groping for articulatory point search, inability to mimic sounds, increased difficulty with longer emission length and poor sound sequencing.
NEWMEYER, AJ et al., 2009.[13]	ASD	Sensory deficits in children with ASD and CAS: sensory search, oral sensory sensitivity, inattention/distraction and impaired fine and perceptual motor coordination; emotionally reactive, low resistance/tone.	AFI is a childhood neurological speech sound disorder (pediatric), in which the accuracy and consistency of movements underlying speech are impaired in the absence of neuromuscular deficits (e.g., abnormal reflexes, abnormal tone).
DUCHOW, H. et al., 2019.[6]	Developmental Coordination Disorder (DCD)	DCD is a neurodevelopmental disorder in which "the acquisition and execution of coordinated motor skills is substantially below expected, given the individual's chronological age and the opportunity to learn and use skills" (American Association of Pediatrics, 2013, p. 76 apud DUCHOW et al, 2019).	CAS is a communication disorder characterized by planning and programming deficits of motor speech movements.

Authors and year of publication	Comorbidity researched	Main characteristics of the comorbidity	Characteristic of CAS
PRINTZ, T et al, 2018.[16]	Oral Dyspraxia (OD) Verbal Dyspraxia (VD)	DO - achieves orofacial movements not related to speech, such as sucking, chewing and swallowing function. It may or may not be associated with CAS. DV - achieves movements related to speech production.	VD and OD are subtypes of dyspraxia: a neurological motor disorder with no neuromuscular deficits. Dyspraxia can affect motor skills in defined muscle groups. In the case of CAS, the involvement is specifically on speech. The commitment in central dyspraxia is in the planning and/or programming of space-time parameters of movement sequences, which results in errors in the production of speech sounds and prosody, or in oral motor movements and gestures.
KUMIN, L., 2006.[16]	Down Syndrome (DS)	The author does not define DS. The study selects parents of children with DS to answer a questionnaire about their children's speech intelligibility.	Difficulty in voluntarily programming, combining, organizing and sequencing the movements necessary for speech. Children with DS present decreased intelligibility with increased enunciation time, inconsistency of speech errors, difficulty in sequencing oral movements and sounds, and a receptive language pattern superior to the expressive one. Difficulties in oral motor skills, such as weak facial muscles. Children with SD + CAS usually do not start speaking before the age of 5.
SCHEFFER, IE, 2001.[12]	Epilepsy Cognitive Functions	Individuals in the study had epileptic seizures from early childhood. In most cases, seizures occurred at night during sleep and presented the same characteristics of rolandic crises, starting with an aura of perioral or hand paraesthesia. Motor manifestations varied, including unilateral or bilateral tonic and or clonic activity of the face and upper limbs. In some cases, there was loss of consciousness, ataxia and problems in salivation.	Apraxia is a difficulty with the organization and coordination of high-speed movements, impairing the ability to produce fluent and intelligible speech.

CAPTION: CAS = Childhood Apraxia of Speech; ASD = Autism Spectrum Disorder; ADHD = Attention Deficit Hyperactivity Disorder; SSD = Speech Sound Disorders; ADRESD = Autosomal Dominant Rolandic Epilepsy with Speech Dyspraxia; (B)RE = (Benign) Rolandic Epilepsy; DCD = Developmental Coordination Disorder; EEG = Electroencephalogram; OT = Occupational Therapy; VD = Verbal Dyspraxia; OD = Oral Dyspraxia; LD = Language Disorder.

Discussion

The study systematically reviewed in the literature the co-occurrence of CAS in developmental disorders, identifying the clinical conditions associated with CAS, exploring its clinical manifestations.

Epilepsy, one of the comorbidities with the highest frequency of onset in the studies included in the present review, consists of a heterogeneous disorder of neurological issues that leads the individual to develop convulsive seizures, especially during sleep or immediately upon awakening. This neurological disorder can affect children and adults and presents itself in several ways, and may injure the brain in several regions or in a specific area, but the impact can be generalized even with these focal crises[9, 11, 12]. The epileptic individual may present from changes in consciousness to seizures. Due to that, these individuals might have, as a result,

cognitive and neurological disorders as well as social disabilities[17].

The epilepsy subtype most correlated with CAS, according to the results of the present review, is Benign Rolandic Epilepsy (BRE), addressed in the studies by Scheffer (2000)[12] and Pal et al (2010)[11]. This neurological disorder is classified as idiopathic, dependent on the patient's age and benign evolution. There are studies that relate attention and language deficits to BRE. Yet, individuals with or without seizures may present other disorders and/or their comorbidities[18, 19].

ASD is a disorder of unknown etiology and high prevalence. It is a behavioral syndrome that brings motor, social and psychoneurological deficits to the individual, hindering language acquisition and other cognitive skills[19, 21]. Neurological comorbidities, including motor abnormalities, epilepsy and epileptiform EEG abnormalities and sleep disorders are relatively common in ASD[5,13] .

The study by Schumacher et al[5], selected for this study, which analyzed the case of a six-year-old bilingual boy with CAS and suspected ASD and/or ADHD, sought to identify characteristics of the syndrome so as to verify whether it was a new spectrum. The authors of the aforementioned study observed that the participant's connected speech and oral motor signals showed differentiated and limited movements of the tongue for the planning and/or motor programming of speech, besides presenting inconsistent errors in the production of phonemes and altered prosody, proving to be CAS. Social anxiety, hypersensitivity and distraction, present in the child's behavior, justified the comorbid diagnoses of ASD and ADHD.

ASD and CAS, as comorbid, generate late diagnoses. Consequently, a child with CAS will possibly have a late diagnosis for ASD and vice versa. Ergo, it is recommended that children with ASD undergo evaluation for CAS, because both disorders may be associated and, for an effective intervention, it is necessary a therapeutic plan that addresses both conditions, because the earlier the intervention, the better the prognosis[22].

Among the selected articles, a study explores deficits in cognitive functions (CG) as a comorbid condition to CAS[14]. The authors found that, in these individuals, there are comorbidities related to sequential speech memory, motor and sensory complexes, as well as delay in cognitive functions. For this reason, the authors refuted CAS as a unitary disorder; as there is evidence that, in these children, executive functions contain deficits.

BRE and CAS are highly comorbid. Electrical discharges in the brain resulting from epilepsy usually focus on perisylvian areas, that is, in a place where language and oral praxia skills are found[18, 19]. It was found that epilepsy might affect not only one individual, but also a complete family group. The study by Scheffer (2000)[12] observed that three generations of the same family were affected by a type of disorder that consisted of the simultaneous occurrence of CAS and BRE, because the study participant presented more intense epileptic seizures, while the members of his family presented greater damage in speech. Sleep-related tests, electromyography, electroencephalograms and language evaluations of the members of this family found that motor speech deficits were related to epileptic seizures.

Deficits in CF were explored by two studies[14, 15]. Nijland et al (2015)[14] questioned the possibility of children with CAS presenting deficit in nonverbal processes and/or in a disorder that resulted in delays in cognitive functions. With a sample of 34 children (17 diagnosed with CAS without other associated comorbidities and the others with typical language development) the study compared the two groups and concluded that CAS is not a unitary disorder, since children with CAS presented, as comorbidity, deficit in nonverbal sequencing at different levels for each individual. Teverovsky, Bickel and Feldman (2018)[15] emphasize that children with CAS may present impairments in CF, presenting difficulties in maintaining attention, learning deficits (reading, writing and calculating) and in memory. The authors pointed out that both disorders tend to coexist and, as comorbid, the damage goes beyond those of articulatory deficits.

Genetic studies of translocation of the FOXP2 gene have been cited to justify speech alterations. The study by Pal et al (2010)11, for instance, when establishing a relationship between BRE and Speech Sound Disorders (SSD), made genetic mapping and acoustic analysis of the speech of members of 38 families with the aim of investigating the possibility of a neural network favorable to SSDs. The authors detected the occurrence of pleiotropic effects of locus 11p13 in CAS and acute centrotemporal waves of the EEG, revealing that families with BRE also had SSD.

It is imperative to point out that several areas in the brain, among those related to language, are affected by synchronous, excessive and abnormal electrical discharges of nerve cells that cause epileptic seizures. Therefore, epilepsy is a network disorder in which even focal crises have a generalized impact on many parts of the brain, interfering with cognitive functions, language, behavior, fine and gross motor programming, among other consequences, of the affected individual[19, 9].

Newmeyer et al (2009)[13], when exploring the relationship between sensory processing and sound production deficits in children with CAS, showed differences between these individuals, justifying the need for a follow-up carried out by a multidisciplinary team. Another recent study[6] concluded that children with suspected verbal dyspraxia (DV) might have the potential for developmental coordination disorder (DCD). The results reinforced the importance of the role of the speech-language therapist throughout evaluation, diagnosis and intervention, as well as multidisciplinary practice to obtain better prognoses.

The paper of Printz et al (2018)[16] explored the relationship between CAS and Oromotor Dispraxia, due to the increased notification of cases of both disorders generating, thus, a greater demand for speech-language therapists and otorhinolaryngologists in Denmark, the region where the study occurred. The authors, at first, conceptualized and differentiated Verbal Dyspraxia (VD) from Oral Dyspraxia (OD) and concluded that, after anamnesis with the individuals in the sample, clinical observations and analysis of tests, focusing on motor function, for both disorders, early intervention should be recommended.

They also observed that children born prematurely, with and without corticobulbar involvement, were more likely to return OD[24]. According to Printz et al (2018)[16], OD causes difficulties in oral motor areas beyond speech production, manifesting itself as the lack of coordination of movements that are performed voluntarily or on request (as opposed to spontaneous movements). Subsequently, in isolation, OD can generate implications for oral motor control, food deficit and, consequently, impair speech development[24].

The treatment of children with CAS and OD, when concomitant, needs to be multidisciplinary, early, frequent and repetitive. It is also worth mentioning that, for these cases, methods based on planning and motor programming are chosen according to the child's age, the severity of O/VD and possible comorbidity, besides the need to complement the intervention with alternative and supplementary forms of communication. The correct diagnosis of these disorders is decisive, since prognosis and treatment differ from prognosis and treatment of other types of speech and oromotor difficulties[16].

The main characteristic of CAS, as already mentioned, is the inconsistency in articulatory movements that results in unintelligible speech. The child knows what he/she means, but he/she does not know how to program the movements and produce the phonemes in an effort to articulate them clearly and accurately.

Iuzzini-Seigel et al (2017)[25] reported in their studies on this topic that there is no validated list of pathognomonic characteristics of CAS. Still, the present symptoms, variable among individuals affected by the disorder - such as lack of consistency in the production of phonemes, difficulty in co-articulation, decreased vowel and voice contrasts - are also present in other language disorders, hindering and, on that account, requiring a differential diagnosis.

Children with language disorder (LD) have speech characteristics that are similar to CAS, revealing deficient oromotor performance. Having said that, the impairment for these cases is also revealed in other levels, such as syntactic and semantic. The authors[25] concluded that children with CAS (associated with LD or CAS associated with LD and a comorbidity) present equivalent performances in all evaluations of speech sound inconsistency, demonstrating that this is the main characteristic that differentiates children with CAS from those with speech delay. The study by Crestani et al (2013)[26] corroborates the view presented above, stating that LD may contain several subtypes, among them those involving motor deficits. In addition, CAS and LD contain common traits, such as the high prevalence of cases in the family group and the difficulties presented in the acquisition of written language.

It is known that the treatment of CAS should begin early, during the period in which the child is learning how to produce the sounds. CAS in children with Down Syndrome (DS) is a very recent diagnosis. The study by Kumin (2006)[17], with a view to learning more about a specific factor af-

fecting speech intelligibility in patients with SD, examined the responses of an interview conducted with parents of children with this condition. As a conclusion, the researcher[17] observed that the most common characteristics presented by these subjects included decreased intelligibility with increased enunciation time, inconsistency of speech errors, difficulty in sequencing oral movements and sounds and a receptive language pattern superior to the expressive one, characteristics which are also present in CAS. According to the author[17], these children have been diagnosed with difficulties in oral motor skills, making it necessary to evaluate and intervene as early as possible. The results of this study indicated that 15.1% of children with SD were diagnosed with CAS, suggesting that these children are being underdiagnosed.

The speech of children with SD, according to Kumin (2006)[17], presents characteristics of CAS, such as: inconsistency in the production of phonemes; increased pronunciation difficulty as words, phrases and sentences become more or less familiar; difficulties with consonant and vowel sounds, with omissions of sounds and syllables; limited repertoire of sounds; difficulty in imitation, prosody and the rhythm of speech; articulatory groping, in addition to difficulties with fast speech speed and vowel extensions, at least, a few times.

According to some studies, it was found that children with SD who were diagnosed with CAS began to speak later, around five years of age[27, 28, 29]. Therefore, children with this syndrome need early intervention to improve prognosis[17], since they present not only oromotor difficulties (specific to DS), but also deficits in programming skills and sequencing of speech movements (characteristic of CAS).

The presence of comorbidities may generate a late diagnosis, both for CAS and for secondary disorder, which may hinder early evaluation and intervention, bringing an unsatisfactory prognosis for such cases. It is thereupon essential to identify CAS and possible comorbid disorders, so that adequate interdisciplinary follow-up can occur. Such follow-up should meet the needs of the child and family, as well as contemplate an individualized and personalized therapeutic plan to develop the individual's cognitive, linguistic, behavioral and psychological skills to the fullest.

As limitations of the present study, we observe the scarcity of national and international studies on CAS and comorbidities that compare diverse and different groups, generating a small number to make up this sample, which may impair, in a certain way, the interpretation of the results obtained. To this end, the importance of studies related to this theme is highlighted and it is suggested that research be carried out to advance this field of knowledge.

Conclusion

It was found that, in order of higher frequency of occurrence in the studies, the main comorbidities linked with CAS were BRE and ASD. The comorbidity with the highest prevalence, according to this review, was epilepsy, more specifically rolandic epilepsy, because it affects the neural pathways responsible for language, impairing the child's development.

Another disorder that was present was ASD. In this case, the characteristics that stand out are the low social interest, deficits in prosody and errors in speech production that become more evident when the individual has CAS. Furthermore, studies in the area of genetics play a fundamental role, since changes and mutations in certain genes responsible for language can bring the possibility of a comorbid manifestation to CAS, especially if there are already cases in the family, such as the FOXP2 gene.

In this current review, there was a scarcity of studies discussing the relationship between CAS and comorbidities, both in national and international scenario. Thus, it is recommended that the topic be more deeply studied, and more studies involving CAS and its comorbidities should be carried out, with diverse populations and different age groups.

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