From the DEPARTMENT OF CLINICAL SCIENCE,
INTERVENTION AND TECHNOLOGY, CLINTEC
Division of Speech and Language Pathology
Karolinska Institutet, Stockholm, Sweden

EXPLORING CHILDHOOD APRAXIA OF SPEECH: SPEECH AND LANGUAGE PROFILES IN 5-YEAR-OLDS WITH SUSPECTED APRAXIA OF SPEECH OR CLEFT PALATE

Ann Malmenholt

Karolinska Institutet

Stockholm 2020

Cover illustration by Ann Malmenholt

Published by Karolinska Institutet.
Printed by Universitetsservice US-AB, Stockholm, Sweden

ISBN 978-91-7831-761-5

Exploring childhood apraxia of speech: Speech and language profiles in 5-year-olds with suspected apraxia of speech or cleft palate

THESIS FOR DOCTORAL DEGREE (Ph.D.)

which, by due permission from Karolinska Institutet, will be publicly defended in lecture hall **Månen**, Alfred Nobels Allé 8, Karolinska Institutet, Campus Flemingsberg

Friday, May 29th, 2020 at 9 a.m.

By

Ann Malmenholt
M.Sc., Speech and Language Pathologist

Principal Supervisor:
Associate Professor Per Östberg
Karolinska Institutet
Department of Clinical Science,
Intervention and Technology
Division of Speech and Language Pathology

Co-supervisors:
Professor Anette Lohmander
Karolinska Institutet
Department of Clinical Science,
Intervention and Technology
Division of Speech and Language Pathology

Associate Professor Anita McAllister
Karolinska Institutet
Department of Clinical Science,
Intervention and Technology
Division of Speech and Language Pathology

Opponent:
Dr Sara Wood, PhD
Queen Margaret University Edinburgh,
United Kingdom
Division of Speech and Hearing Sciences

Examination Board:
Associate Professor Margareta Dahl
Uppsala University
Department of Women's and Children's Health
Neuropediatrics/Pediatric Oncology

Associate Professor Christina Samuelsson
Linköping University
Department of Biomedical and Clinical Sciences
Division of Sensory Organs and Communication

Associate Professor Avni Abdiu
Linköping University
Department of Biomedical and Clinical Sciences

TABLE OF CONTENTS

ABSTRACT

Introduction and aims: Childhood apraxia of speech (CAS) is a speech sound disorder (SSD) lacking a quantifiable measure discriminating all cases of CAS from other SSDs. This project aimed at exploring CAS using different perspectives when examining speech and language difficulties commonly seen in 5-year-old children with suspected CAS or children with repaired cleft palate (CP±L). Children with CP±L were added to broaden and differentiate the knowledge base on CAS and to search for factors explaining unfavorable speech outcome in this group.

Material and methods: In **study I**, a questionnaire was constructed and used**,** anonymously surveying Swedish SLPs (n=178) knowledge and praxis about CAS features and assessment. Findings were compared to earlier survey findings from English contexts. **Study II** examined articulation proficiency and orofacial function of children with CP±L (n=52) based on SLP examination and parental interview. For measurement of intelligibility, both parent reports and SLP ratings were compared. **Study III** included children with CP±L and disordered speech (n=19) and children with suspected CAS (n=15). Phonetic transcription and CAS diagnostics were based on audio-recordings of single word naming. The diagnosis was built on judgement of presence or absence of speech features using a checklist constructed for English speakers. The cross-linguistic applicability of the operationalized features and checklist was tested. In **study IV** language competence of children with CAS and CP±L was directly assessed, and parental ratings of everyday life communication were added, and results compared.

Results: Swedish SLP's views on typical speech characteristic of CAS, surveyed in **study I**, corresponded in large with reports of SLP's from English-speaking contexts. The top seven characteristics were inconsistent speech production, sequencing difficulties, oro-motor deficits, vowel errors, voicing errors, consonant cluster deletion and prosodic disturbance. In **study II**, 37% of children with CP±L were found to have orofacial dysfunction; however, this was not an explanatory factor for speech outcome for these children. A distinct CAS profile, found in **study III**, included the five features: phonemic speech inconsistency for consonants and vowels plus vowel error, voicing error, difficulty achieving initial articulatory configurations or transitionary movement gestures and stress errors. In **study IV**, expressive language disorder was found in 67% of children with CAS. Receptive language ability was significantly better than expressive language in all children with CAS. No such difference was observed in the group of children without CAS (non-CAS SSD). Parent ratings of communication skills reflected an increased burden on communication in everyday life when difficulties within both speech and language domains were present.

Conclusions: Despite relevant theoretical and/or clinical knowledge about CAS, Swedish SLPs reported a need for further education. Swedish-speaking 5-year-olds with CAS shared a distinct speech profile including five features, with prosodic impairment almost exclusively seen in children with CAS. Findings supported cross-linguistic applicability of CAS speech feature operationalization between English and Swedish speakers. In children with CP±L and SSD, a heightened cooccurrence of CAS, compared to clinical prevalence, should be anticipated. Expressive language ability in children with CAS was worse than receptive language ability. Poor articulation proficiency in children with CP±L did not correlate with orofacial dysfunction. Parental ratings of communication abilities in everyday life added ecological validity and confirmed validity of the clinical assessment procedures.

SAMMANFATTNING

Introduktion och syfte: Taldyspraxi (TD) är en talstörning som är svår att diagnostisera eftersom det saknas ett kvantifierbart mått som särskiljer alla barn med TD från barn med andra typer av talstörningar. Syftet med detta projekt var att utforska tal- och språkförmågan hos 5-åringar med TD och hos barn med gomspalt. Barnen med gomspalt inkluderades för att bredda och nyansera kunskapen om TD men också för att söka efter faktorer som kan förklara kvarstående talstörning hos en andel 5-åringar behandlade för gomspalt.

Material och metoder: I s**tudie I** utvecklades en enkät med frågor kring kunskap och praxis gällande särdrag och undersökning av TD som besvarades anonymt av svenska barnlogopeder (n=178). Svaren jämfördes med tidigare enkätstudiesvar av logopeder i engelskspråkiga kontexter. I **studie II** undersöktes tal och orofacial funktion hos 52 barn med gomspalt, direkt av logoped och indirekt genom frågor till barnets föräldrar, talförståelighet skattades av både logoped och föräldrar och skattningarna jämfördes. I **studie III** deltog 19 barn med gomspalt och talstörning samt 15 barn med förmodad TD. Talet spelades in vid bildbenämning samt transkriberades. TD-diagnosen byggde på logopedbedömning av olika särdrag i talet, utifrån en checklista utformad för engelskspråkiga barn. Checklistan och validiteten i beskrivningen av särdragen undersöktes avseende användning på svenska. I **studie IV** undersökte logoped den språkliga förmågan hos barn med TD eller gomspalt och kommunikationsförmågan i det dagliga livet skattades av föräldrarna, varefter resultaten jämfördes.

Resultat: Svenska logopeders kunskap om typiska särdrag i talet hos barn med TD, som undersöktes i **studie I**, överensstämde i stort med engelskspråkiga logopeders. De sju mest frekvent rapporterade dragen var inkonsekvent tal, svårigheter med sekvensering av talljud, oralmotoriska svårigheter, vokalfel, svårigheter med distinktionen tonande-tonlös, förenklingar av konsonantkluster samt avvikande prosodi. I **studie II** uppvisade 37 % av barnen med gomspalt en orofacial dysfunktion, som dock inte förklarade barnens talstörning. I **studie III** framkom en särskild TD-profil med fem särdrag: inkonsekvent uttal av konsonanter och vokaler samt vokalfel, svårigheter med distinktionen tonande-tonlös, svårigheter att hitta artikulatorisk rörelse för ordstart och koartikulation mellan språkljud samt avvikande prosodi. Expressiv språkstörning konstaterades hos 67 % av barnen med TD i **studie IV.** Språkprofilen, med en signifikant bättre receptiv än expressiv förmåga, sågs enbart hos barn med TD. Föräldraskattningen av kommunikationsförmågan i det dagliga livet pekade på större svårigheter för barn med både tal- och språkstörning.

Slutsatser: Trots relevant teoretisk/klinisk kunskap om TD uppgav de flesta svenska barnlogopeder ett utbildningsbehov. En specifik talprofil hos svensktalande femåringar med TD framkom. Talprofilen bestod av fem talkarakteristika och inkluderade prosodiska svårigheter noterades i princip uteslutande hos barn med TD. Resultaten stödjer användningen av beskrivna och operationaliserade talkaraktäristika för engelsktalande barn också för svensktalande barn. Hos barn med gomspalt och talstörning borde en högre andel barn förväntas ha TD, jämfört med kliniska prevalensuppgifter. Expressiv språkförmåga hos barn med TD var generellt sämre än receptiv förmåga. Avvikande artikulationsförmåga hos barn med gomspalt förklarades inte av orofacial dysfunktion. Föräldraskattningar av vardaglig kommunikationsförmåga visade att det fanns större svårigheter hos barn med både tal- och språkstörning. Dessa föräldraskattningar tillförde information om kommunikationsförmågan i det dagliga livet och stärkte den ekologiska validiteten hos de kliniska bedömningsmetoderna för TD.

LIST OF SCIENTIFIC PAPERS

I. **Malmenholt, A.**, Lohmander, A. & McAllister, A.
Childhood apraxia of speech: A survey of praxis and typical speech characteristics. *Logopedics Phoniatrics Vocology* 2017, 42(2): 84-92.

II. **Malmenholt, A.**, McAllister, A. & Lohmander, A.
Orofacial function, articulation proficiency, and intelligibility in 5-year-old children born with cleft lip and palate. *The Cleft Palate-Craniofacial Journal* 2019, 56(3): 321-330.

III. **Malmenholt, A.**, McAllister A., Lohmander, A. & Östberg, P.
Speech feature profiles in 5-year-olds with speech sound disorder related to suspected childhood apraxia of speech or cleft palate. *Manuscript submitted*, 2020.

IV. **Malmenholt, A.**, Östberg, P., McAllister, A. & Strömbergsson, S.
Language profiles in 5-year-olds with speech sound disorder related to suspected childhood apraxia of speech or cleft palate. *Manuscript under review*.

LIST OF ABBREVIATIONS

22q11.2DS	22q11.2 deletions syndrome, earlier called CATCH22, DiGeorge syndrome, velo-cardio-facial syndrome
AOS	Acquired apraxia of speech
ASHA	American Speech-Language-Hearing Association
BCLP	Bilateral cleft lip and palate
CAS	Childhood apraxia of speech
CELF-4	Clinical Evaluation of Language Fundamentals
CP±L	Cleft palate with/without cleft lip
CPH	Cleft of the hard and soft palate
CPO	Isolated cleft palate (including CPH+CPS)
CPS	Cleft of the soft palate only
DLD	Developmental language disorder
ICS	Intelligibility in context scale
ISPc	Inconsistency severity percentage of consonants
ISPv	Inconsistency severity percentage of vowels
MRI	Magnetic resonance imaging
non-CAS SSD	SSD but not CAS
NOT-S	Nordic Orofacial Test - Screening
PCC	Percentage of consonants correct
sCAS	Suspected childhood apraxia of speech
SLP	Speech language pathologist
SMCP	Submucous cleft palate
SSD	Speech sound disorder
SVANTE	Swedish articulation and nasality test
UCLP	Unilateral cleft lip and palate

1 INTRODUCTION

Speech is the common way for humans to express thoughts, opinions and emotions. In unity with language skills the spoken output makes it possible to communicate in a reciprocal way with others. In typical development speech and language skills mature and develop without effort. Children with delayed or deviant speech and/or language development face limitations when communicating.

1.1 GENERAL MOTIVATION

This thesis project was based on my professional curiosity and frustration as a clinical speech language pathologist (SLP) concerning the lack of treatment progress in children with childhood apraxia of speech (CAS) and in children with speech disorders related to cleft palate with/without cleft lip (CP±L). Anecdotal reports and my clinical experience of these children indicated some overlap of speech difficulties between the two groups. In addition, meeting children with their parents in the clinic made it clear that communication in everyday life is not only influenced by the severity of the speech disorder, but also by comorbid language or neurodevelopmental disorders and the child's and significant other's environment.

Delays in speech and language acquisition are the most common problems in preschool children. Their prevalence in 5-year-olds has been estimated to ~12% for speech and language delay, ~7% for language delay only and ~8% for speech delay only (Law, Boyle, Harris, Harkness, & Nye, 2000). More recently the prevalence of language disorder in 4-5-year-olds has been reported to be ~10% (Norbury et al., 2016). At ages 4-5 years, 12% of parents judged that their child's "speech (is) not clear to others" and 6% that "speech (is) not clear to the family" (McLeod & Harrison, 2009). This thesis project is mainly concerned with the latter group of children, whose ability to communicate with others is markedly restricted at age 5.

Including only a restricted age group in this project had several reasons. At 5 years of age, most children cooperate reliably during standardized assessments and normative data on speech and language competence are available. Swedish-speaking 5-year-olds typically master the Swedish phoneme inventory, with phonemes /s/ and /r/ being the last to be established (Blumenthal & Lundeborg Hammarström, 2014). It has been suggested that 5-year-old children with speech disorder are not yet aware of their speech problem but aware of the inability of their communication partners to "hear" and understand what they say (McCormack, McLeod,

McAllister & Harrison, 2010). Language competence at 5 years of age typically includes the ability to tell or re-tell a coherent story, to understand what is read or listened to, and to follow or remember spoken instructions (Bishop et al., 2016). In addition, school entry is approaching and maximizing communication skills, including speech ability, is an important goal for the child, family and the professionals involved (Kuehn & Moller, 2000). Language problems at 5 years of age are likely to persist (Stothard, Snowling, Bishop, Chipchase & Kaplan, 1998; Institute of Medicine, 2016) and there is little evidence that the gap between children with and without language disorder closes over time (Lundeborg, McAllister, Samuelsson, Ericsson, & Hultcrantz, 2009; Rice & Hoffman, 2015; Institute of Medicine, 2016). Despite the close relationship between speech motor and language production (Vuolo & Goffman, 2018), children with atypical development may present with isolated speech, language, or mixed difficulties.

1.2 CHILDHOOD APRAXIA OF SPEECH

Already 129 years ago, three clinical cases of children with 'defects in articulation', fitting the description of the speech sound disorder we today call CAS, were published in the Journal of Mental Science (Hadden, 1891). In 'The development and disorders of speech in childhood' by Muriel Morley (1957), the clinical history and signs of twelve cases with 'developmental articulatory apraxia' were described and followed longitudinally. These clinical cases are strikingly alike present patients diagnosed with CAS. Morley addressed important points to assist in diagnostics, still relevant in today's clinical settings, such as information about family history, motor, speech, social and personal development of the child. Phonetic analysis of speech sounds from several speech tasks (realizations of phonemes in different word positions, repetition of phrases and spontaneous speech) were proposed as well as screening of language competence. Difficulties with differential diagnosis of less severe cases of CAS, dysarthria and dyslalia, or a combination of these, were highlighted. However, Morley did not present a list of diagnostic speech features but rather acknowledged the heterogeneity of the diagnosis. In large, Morley's understanding of the disorder and awareness of similarities with the acquired form of apraxia of speech after brain damage in both children and adults was sharp-eyed.

1.2.1 Terminology

The term ‘childhood apraxia of speech’ was endorsed by the American Speech-Language–Hearing Association (ASHA, 2007). Previous terms for the disorder include: ‘developmental articulatory apraxia’ (Morley, Court & Miller, 1954), ‘developmental apraxia of speech’ (Rosenbek & Wertz, 1972), ‘developmental verbal dyspraxia’ (Crary, Landess, & Towne, 1984) to speech delay–apraxia of speech (SD-AOS) (Shriberg et al., 2003) to name a few (for the early history of terminology, see Hall, Jordan & Robin, 1993). The term apraxia had traditionally been used to describe the inability to produce purposeful movements in the absence of paralysis, sensory impairment, comprehension problems or intellectual disorders (Liepmann, 1900). Using the term apraxia for a developmental speech problem caused confusion, indicating the loss of a skill not yet acquired. Both research approaches and terminology in apraxia in childhood have been based on knowledge about the adult form of the disorder, acquired apraxia of speech (AOS). The description of AOS as a distinct speech impairment occurring independently or in combination with language disturbance (aphasia) and/or neuromuscular involvement (dysarthria) (e.g. Darley, 1982), resembles our understanding of the childhood form, as does the definition: AOS is a “neurologic speech disorder that reflects an impaired capacity to plan or program sensorimotor commands necessary for directing movements that result in phonetically and prosodically normal speech” (Duffy, 2020, p. 4). However, AOS results from a known, acquired brain damage typically following stroke (Duffy, 2020), degenerative processes (progressive AOS) (e.g. Josephs et al., 2012), tumor or traumatic injury (Duffy, 2020). Isolated AOS is rare, complicating the identification of the specific location of the damage to the brain. In addition, different lesion locations have been reported to result in similar clinical presentations. More recent studies suggest that AOS is associated with lesions in brain areas involved in speech motor control (for an overview of brain damage associated with AOS, see Moser, Basilakos, Fillmore & Fridriksson, 2016). Neurological evidence for brain dysfunction in children, in analogy to the adult form, was studied on during the 1970s, using electroencephalography (EEG) (e.g. Rosenbek & Wertz, 1972; Yoss & Darley, 1974; Williams, Ingham & Rosenthal, 1981). Findings were inconclusive and reports mainly indicated none, mild or nonspecific abnormalities. Routine clinical MRI scans are not sensitive enough to identify neural anomalies in children with idiopathic CAS (Morgan & Webster, 2018). However, advances in genetic research and the use of voxel-based morphometry have shown morphological abnormalities in the supramarginal gyrus and planum temporale for children with a subtype of speech sound disorder characterized by persistent speech sound errors (Preston et al., 2014). The discovery

that a mutation of FOXP2 was associated with CAS, started a new era of etiologic research (Lai, Fisher, Hurst, Vargha-Khadem, & Monaco, 2001). FOXP2 is widely expressed in the fetal and adult brain, where it regulates the expression of other genes (Spiteri et al., 2007). It is now evident that CAS is associated to several genetic conditions and different gene pathways.

The debate on criteria and diagnosis of CAS started with a critical review by Guyette and Diedrich (1981), who challenged the evidence for CAS as a specific diagnostic entity. The authors surveyed more than 100 publications and found contradictions, confusions and questionable designs in both clinical and experimental studies. Difficulties with study selection or inclusion and varying ages, intellectual levels, language abilities and severity of problems hampered cross-study comparisons and the knowledge base of CAS. Apparently, many clinicians based their diagnoses on the duration of difficulties and results of speech-language training (e.g. Rosenbek, 1978; Yoss & Darley, 1974). In a literature review of management strategies for 'developmental apraxia of speech' Pannbacker (1988) stated that therapy techniques used for children were based on clinical experience and the literature about therapy for acquired apraxia.

1.2.2 Classification

In this context, the seminal work of Lawrence D. Shriberg and colleagues must be acknowledged. They developed the speech disorders classification system (SDCS) which has been updated over several decades, and finalized in 2017 (e.g. Shriberg, 1993; Shriberg, 2010a; Shriberg, 2010b; Shriberg et al., 2010; Shriberg et al., 2017a). It is a major contribution to the development of the field of speech sound disorders in general and to CAS in particular. The SDCS is a framework consisting of four levels. The levels are linking 'etiological processes' (level I) (distal causes including explanatory pathways of a specific speech disorder) to 'speech processes' (level II) (proximal causes including fundamental processes underlying speech production, e.g. representation, transcoding and execution of speech, mediated by feedforward and feedback processes) to 'clinical typology' (level III) (behavioral phenotype) which are the actual speech behaviors that can be classified using 'diagnostic markers' (level IV) (criterial signs of the phenotypes). The goal is to identify a single, conclusive, behavioral, diagnostic marker (level III and IV) for each of the eight speech disorders in the typology. This means finding a marker that maximizes sensitivity and specificity for every speech disorder leading to correct prediction of true positives and true negatives. Another goal has been to use this

diagnostic marker (level IV) to identify and validate biomarkers (level I) of that same disorder, connecting the marker to proximal causes fitting into the underlying speech production processes (level II). By linking all four levels, circular reasoning can be avoided. CAS characteristics will thus not be found in participants included in studies just because they are suspected of having CAS. Such circularity cannot be overcome without a line of arguments convincingly connecting all levels. The 'Pause Marker' (PM) was presented as a behavioral diagnostic marker for CAS (level IV) both for research and clinical use (Shriberg et al., 2017a, 2017b, 2017c, 2017d). The PM is an acoustically aided perceptual sign quantifying the speech precision of phrasing, that is, inappropriate pauses of different types (Shriberg et al., 2017c). It is built on data reduction and analyses computed in the PEPPER (Programs to Examine Phonetic and Phonological Evaluation Records, Shriberg et al., 2010) platform, freely available (http://www.waisman.wisc.edu) for analysis of American English speech material. The PM is quantified using 24 utterances, or at least 40 between-words opportunities, from a continuous speech sample. However, this requirement excludes participants who do not produce longer utterances and/or those with extremely low intelligibility, making the PM inapplicable to speakers with very low verbal output, such as young children and those with severe CAS.

The American Speech-Language–Hearing Association's Technical Report on CAS was presented in 2007 and is still referred to as the guideline for CAS. The content was produced by the Ad Hoc Committee on Apraxia of Speech in Children. The Committee had reviewed and summarized the research background, addressed terminology and provided a definition of the disorder. The three diagnostic criteria of the disorder were described as: (a) inconsistent errors on consonants and vowels in repeated productions of syllables or words (b) lengthened and disrupted co-articulatory transitions between sounds and syllables, and (c) inappropriate prosody, especially in the realization of lexical or phrasal stress (ASHA, 2007).

Despite much promising work on CAS for more than 60 years, a number of questions about the etiology, pathology and validity of reported symptoms still remain. The current understanding of the underlying difficulty in CAS is that of an impairment of transcoding linguistic content into speech movements. The core disability is in *sensorimotor planning*, which identifies the acoustic goals and the spatial configurations of the vocal tract to achieve them and in *programming*, which provides the muscle-specific requirements so that structures move with the correct range of motion, strength, speed and direction (Strand, 2020). CAS is defined as a neurological childhood speech sound disorder in which the precision and consistency of movements underlying speech are impaired in the absence of neuromuscular deficits. CAS is said to occur as a result of known neurological impairment, in association with

complex neurobehavioral disorders of known or unknown origin, or as an idiopathic neurogenic speech sound disorder (ASHA, 2007). The clinical prevalence of CAS in English-speaking children has recently been estimated to 2.4% for the idiopathic form and 4.3% when associated with complex neurodevelopmental disorder (Shriberg, Strand, Jakielski, & Mabie, 2019). An additional clinical prevalence has been reported for concurrent CAS and dysarthria (4.9%) in children with complex neurodevelopmental disorder (Shriberg et al., 2019). Following the raised awareness of CAS, high rates of possibly false positive cases have been reported (Shriberg & McSweeny, 2002; Shriberg, Potter, & Strand, 2011). On the other hand, CAS may also be underdiagnosed in populations with genetic or complex neurodevelopmental disorders (Cleland, Wood, Hardcastle, Wishart & Timmins, 2010).

1.2.3 Speech characteristics

Several checklists of diagnostic speech features for CAS have been surveyed (e.g. Forrest, 2003; Joffe & Pring, 2008; Meredith & Potter, 2011) and published for research purposes (Shriberg et al., 2011), but so far no quantifiable measures have been presented and operationalized that accurately discriminates all cases of CAS from other communication disorders. In addition, overlapping speech symptoms within individuals and between groups of individuals with SSD are commonly reported (e.g. Ballard, Granier, & Robin, 2000; McNeil, Robin & Schmidt, 2009). Furthermore, no single neurological or behavioral diagnostic marker has been found yielding for all cases of CAS (e.g. ASHA, 2007; Shriberg, Lohmeier, Strand & Jakielski, 2012). Two studies have attempted to identify quantifiable speech characteristics for a diagnosis of CAS (Murray, McCabe, Heard, & Ballard, 2015; Shriberg et al., 2017a). Both investigated prosodic features of speech such as lexical stress and syllable segregation (Murray et al., 2015) or between-words pauses (PM) (Shriberg et al., 2017a). Four measures in combination were found to significantly predict a CAS diagnosis in a regression model (R^2 = .91): syllable segregation, percentage of stress matches, percentage phonemes correct on polysyllables and the accuracy on a diadochokinesis (DDK) task (Murray et al., 2015). However, in this model children with CAS plus DLD and participants with submucous cleft palate were omitted, making the findings less generalizable to unselected groups of children with SSD. Arguing that clinical SLPs need to diagnose and treat children with CAS despite the current lack of evidence-based procedures, Iuzzini-Seigel and Murray (2017) proposed a 12-feature checklist for clinical use, based on a previous checklist published for research (Shriberg et al., 2011). Most importantly, the Iuzzini-Seigel and Murray checklist (2017) included operationalized definitions of all features listed. As a cut-off for a positive diagnosis of CAS

five optional features as a minimum in addition to the mandatory feature *speech sound inconsistency* were required, that is, six features from the list observed at least once. The 12 CAS features commonly associated with CAS with operational definitions (Iuzzini-Seigel & Murray, 2017) are summarized in table 1 (based on table 1 in Malmenholt et al., submitted 2020) and structured with respect to the three primary ASHA criteria (ASHA, 2007).

Table 1. Operational definitions for the 12-feature checklist of CAS proposed by Iuzzini-Seigel and Murray (2017) structured with respect to primary criteria for CAS (ASHA, 2007)

ASHA's three primary criteria (2007)	Speech features commonly associated with CAS	Operational definition according to Iuzzini-Seigel & Murray (2017)
a) inconsistent errors on consonants and vowels in repeated productions of syllables or words	Vowel error	both vowel substitutions and distortions are considered incorrect
	Consonant distortion	the speech sound is recognizable as a specific consonant but not produced accurately
	Speech sound inconsistency	variable production of phonemes (i.e., phonemic inconsistency) words or phrases (i.e., token-to-token inconsistency across multiple opportunities)
	Nasal resonance	hypo- or hypernasal resonance
b) lengthened and disrupted coarticulatory transitions between sounds and syllables	Intrusive schwa	addition of a schwa between consonants
	Voicing error	a sound produced between voicing categories or as its voicing cognate
	Groping	prevocalic, silent articulatory searching prior onset of phonation and speech production
	Difficulty achieving initial articulatory configurations or transitionary movement gestures	lengthened or disrupted, hence uncoordinated, movements or coarticulatory gestures at word start or between sounds within words
	Increased difficulty with multisyllabic words	the number of errors increases disproportionately if number of syllables increase
c) inappropriate prosody, especially in the realisation of lexical or phrasal stress	Stress errors	appropriate stress is not correctly produced at the word or sentence level
	Syllable segregation	inappropriate pauses between sounds, syllables or words leading to segregation and lack of smooth transitions within words
	Slow rate	atypically slow speech rate

1.2.4 Childhood apraxia of speech comorbidity

The literature on language abilities in children with CAS is rather sparse. Possibly, the search for reliable diagnostic markers and defining the speech disorder per se has had priority. The reported cooccurrence of CAS with language disorder varies from 46 to 82% (Thoonen, Maassen, Gabreels, Schreuder, & de Swart, 1997; Lewis, Freebairn, Hansen, Iyengar, & Taylor, 2004; Iuzzini, 2012; Vuolo & Goffman, 2018; Zuk, Iuzzini-Seigel, Cabbage, Green, & Hogan, 2018; Murray, Thomas, & McKechnie, 2019). Research in the 1970s described a gap between receptive and expressive language ability in patients with CAS, with better receptive than expressive abilities (e.g. Rosenbek & Wertz, 1972). This gap has also been reported in a more recent study (Murray et al., 2019). In that study, morphological disorder was found in 48% of 4-5-year old children with CAS. The question raised was whether the cooccurrence of difficulties with motor speech and morphology was to be seen as speech motor difficulties affecting language or cooccurrence of both speech and language disorder (Murray et al., 2019). Also, interactions between language and gross and fine motor skills in children with language disorder have been reported (e.g. DiDonato Brumbach & Goffman, 2014; Hill, 2001; Zelaznik & Goffman, 2010). After reviewing the literature on cooccurrence of motor and language impairment in children, Hill (2001) concluded that shared cognitive processes could be a plausible explanation. Two processing streams, the ventral and dorsal stream, have been proposed for higher-order cognitive processes, including language production and comprehension (for a detailed review, see Cloutman, 2013). The dual stream model of speech processing (e.g. Hickock & Poeppel, 2004, 2007, Poeppel, Emmorey, Hickock & Pylkkänen, 2012) attributes the role of supporting speech comprehension to the ventral stream (e.g. semantic and phonological processing, long-term storage of semantic information, sound recognition); it represents a sound-to-meaning interface. The dorsal stream is attributed the role of sensory-motor integration (e.g. auditory-motor transcoding, syntactic analysis, phonological memory); an auditory-to-motor translation. Although functionally specialized and anatomically separate, the streams need to interact closely for successful production and comprehension of language (Hickock, 2012) and synergies between these white matter tracts for language functioning are proposed (Rolheiser et al., 2011). It is evident that the language network is much more extended than previously suggested and that the lateralization to the left hemisphere is not as exclusive as proposed in earlier research (Hagoort, 2017). Taking advantage of the technical development of functional MRI and voxel-based morphometry, brain anomalies can be studied in greater detail than before. Nevertheless, in children with DLD, structural brain changes have not been found in the classical language tracts, that is, the

ventral or dorsal stream. However, findings across studies have been inconsistent, possibly explained by the heterogeneity of DLD (e.g. Liégeois et al., 2014; Morgan et al., 2018).

The discovery of the KE family in the 1990s changed the understanding of CAS. Because of a mutated FOXP2 gene, affected members had CAS, orofacial dyspraxia and language disorder including difficulties producing morphosyntax and the comprehension of complex grammatical structures; some also had dysarthria (Watkins, Dronkers, Vargha-Khadem, 2002; Morgan & Liégeois, 2010). Developments in neurogenetics followed, and structural and functional brain images in affected and unaffected family members were compared. Reduced gray matter volumes were found in for example Broca's area, and abnormally large volumes of gray matter in Wernicke's area. In analogy to the anatomical finding, there were functional differences in affected members, such as, low activations in speech-related cortical regions but overactivations of regions not typically speech-related (Vargha-Khadem et al., 1998; Vargha-Khadem, Gadian, Copp, & Mishkin, 2005). However, FOXP2 mutations were found to be rare in children with non-syndromic CAS (Laffin et al., 2012). Since the discovery of the KE family, several copy number variations in diverse locations on different chromosomes have been reported in sporadic cases of CAS (Laffin et al., 2012). Another multigenerational family with autosomal dominant inheritance of CAS, but with no causal gene identified, has been described (Peter, Button, Stoel-Gammon, Chapman, & Raskind, 2013) as has a family with CAS not explained by a FOXP2 variant (Liégeois et al., 2019). This latter family is especially intriguing, because family members are primarily affected by CAS without cooccurring language or literacy impairment. Neuroanatomical findings indicate an atypical developmental of the dorsal language network responsible for auditory-motor translation as an explanation for CAS in this family.

To summarize, advances in neuroimaging methods have uncovered both functional and sub-macroscopic brain anomalies in individuals with CAS. These have mainly been presented as gray and/or white matter reductions or elevations in brain regions typically activated during speech or language processes (Liégeois, Mayes, & Morgan, 2014) or atypically activated, probably indicating compensatory strategies (Vargha-Khadem et al., 2005). A new functional connectivity approach has been recently presented to explain CAS (Liégeois et al., 2019). For individuals with DLD, examined in adolescence and young adulthood, altered brain structures in both the dorsal and ventral pathways have been reported (Lee, Dick & Tomblin, 2020). Further studies investigating the underlying neurobiological networks for typical and atypical development of speech and language abilities are to be expected in the future.

1.3 CLEFT PALATE ± LIP

Worldwide about a quarter of a million babies with cleft lip and/or palate (CLP) are born every year (Mars, Sell, & Habel, 2008). The corresponding figure for Sweden is 150-200 (Hagberg, Larson, & Milerad, 1998). Clefts are the result of an interruption in embryologic growth and arise during the 4th and 10th week of the developing embryo (Peterson-Falzone, Hardin-Jones & Karnell, 2010). Children born with CP±L form a heterogeneous group: the extent and etiology of the cleft differ with a high frequency of associated anomalies or syndromes. Clefts are described based on the structures involved which are the lip, alveolus, hard palate and soft palate. Cleft types affecting the palate (CP±L) are usually divided into bilateral cleft lip and palate (BCLP), unilateral cleft lip and palate (UCLP), cleft affecting the hard and soft palate (CPH), cleft of the soft palate only/isolated cleft (CPO) and submucous cleft (SMCP).

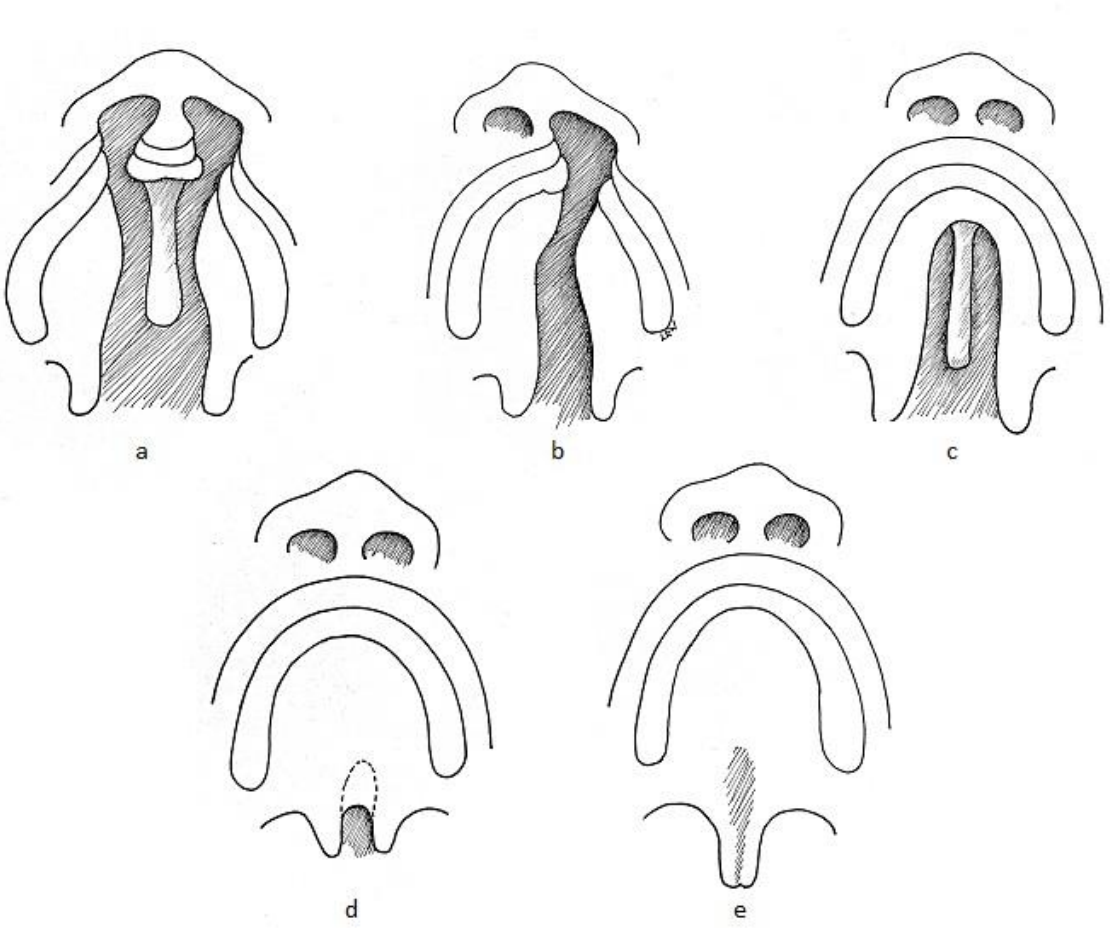

Figure 1. (a) bilateral cleft lip and palate, (b) unilateral cleft lip and palate, (c) cleft affecting the hard and soft palate, (d) cleft of the soft palate only/isolated cleft and (e) submucous cleft. *Illustrations by Liisi Raud Westberg*

A cleft palate affects eating, speech development, ear function/hearing, dentition and facial appearance. For optimal development of these structures, the cleft is surgical closed. While it is the cleft in the palate that may cause difficulties with eating, speech, and ear function/hearing, and should therefore be closed early, early surgery in the hard palate may cause problems with maxillofacial growth. One- or two-stage protocols for cleft palate repair are nowadays usually performed between 6 and 24 months of age. However, different techniques, staging and timing are in practice and there is still no standard protocol to attain optimal results for all affected areas (Leow & Lo, 2008; Reddy, Gosla Reddy, Vaidhyanathan, Berge, & Kuijpers-Jagtman, 2017).

Prerequisites for speech production in children with CP±L are altered owing to both structural and functional limitations. Following surgical interventions, structure and function are repeatedly altered during the first years of speech development in children with CP±L. Although lip and tongue strength and endurance have been found to be normal in children with UCLP (Van Lierde et al., 2014) and tongue structure and function per se is considered unaffected in children born with CP±L (Peterson-Falzone et al., 2010), adaptive behaviors are reported. These behaviors are linked to velopharyngeal inadequacy resulting in articulatory or compensatory strategies. Compared to non-cleft peers, speakers with a repaired cleft lip evidence considerable functional differences in motor activity (Atkinson & Howard, 2011) and atypical patterns of tongue to palate contact have been observed, including retracted articulation and overuse of the tongue dorsum (e.g. Morley, 1970; Gibbon, 2004; Howard, 2004). In addition, atypical complete tongue-palate constriction during production of high vowels have been reported (e.g. Gibbon, Smeaton-Ewins, & Crampin, 2005) and increased variability of lip movements during speech production (Rutjens, Spauwen, & van Lieshout, 2001). Difficulties with tongue grooving, needed for production of vowels (Stone, Shawker, Talbot & Rich, 1988), have been reported in some children with CP±L. Tongue grooving is also required for production of sibilant sounds, known to be frequently affected in children with CP±L (e.g. Harding & Grunwell, 1996; Morley, 1970).

1.3.1 Speech characteristics

Speech difficulties in children born with CP±L were traditionally categorized as ‘articulation disorders’, primarily related to the anatomical relationships and alterations within the oral cavity and vocal tract before and after surgical repair. In the 1990s, however, cleft speech

characteristics were reconsidered in the context of phonological development (e.g. Harding & Grunwell, 1996). Speech characteristics in cleft palate speech can be divided into two types: active and passive (Harding & Grunwell, 1996, 1998; Hutters & Brønsted, 1987).

Passive speech characteristics occur as a direct consequence of limited structures or muscle functions, that is, children speak in a way that would have sounded typical, if there had not been a structural abnormality or dysfunction. Commonly reported passive speech characteristics include hypernasality, audible nasal airflow errors, and weak and/or nasalized consonants. Consequently, passive speech characteristics require surgery and are not treatable with speech therapy. In contrast, active speech characteristics appear to be a child's spontaneous attempt to compensate for the structural abnormality and are used to create phonological contrast. Intended consonants are produced using compensatory articulatory gestures, resulting in for example backing or glottal stops and may also include speech sounds not found in the language in question.

Active cleft speech characteristics can be the result of early mislearning and are associated with velopharyngeal insufficiency and/or a fistula and may persist despite successful surgical intervention (Harding & Grunwell, 1998; Hutters & Brønsted, 1987). Active cleft speech characteristics can be considered in a phonological context and treated with speech therapy. Every child's acquisition of the speech sound system includes learning of the language-specific phonological structure and organization (Gierut & Morrisette, 2005). Articulatory placement and movements to produce correct sounds, that is, articulation and motor learning, are required (Fey, 1992). In children born with CP±L, not all develop normal speech despite surgical intervention. Actually, speech in 5-year-olds with CP±L varies from typical articulation proficiency and intelligibility to severe difficulties (Chapman, 2017; Klintö, Salameh, & Lohmander, 2016). It has been reported that about 20% to 50% of children with UCLP display speech difficulties at 5 years (e.g. Lohmander & Persson, 2008; Nyberg, Peterson, & Lohmander, 2014; Sell et al., 2015) and at least 50% when including children with several cleft types and syndromes (Britton et al., 2014).

Differences in speech outcome related to different surgical protocols have been sparsely investigated (Lohmander, 2011). However, in the Scandcleft trials the outcome after four different surgical protocols for primary repair of the cleft palate in 450 children born with UCLP was compared (Semb et al., 2017). Whereas the results confirmed the high prevalence of speech disorders, none of the protocols were found favorable except for one speech error type, namely the retracted oral consonant error or backing. This error type was most commonly found in children who had the cleft in the hard palate repaired later, even if the soft palate cleft

was closed early (Willadsen et al., 2017). No differences in perceived velopharyngeal function or hypernasality were significantly related to the different protocols (Lohmander et al., 2017).

1.3.2 Cleft palate ± lip and comorbidity

Reports on the prevalence of additional malformations in the cleft population vary depending on cleft type and definition of associated anomalies and syndromes. Several studies report an overall prevalence of about 30% (Chetpakdeechit, Mohlin, Persson, & Hagberg, 2010; Impellizzeri, Giannantoni,Polimeni, Barbato, & Galluccio, 2019; Milerad, Larson, Hagberg, & Ideberg, 1997). A consistent finding is that patients with CPO (including submucous clefts), although having the rarest form of oral clefting, have the highest likelihood of associated anomalies. Also, children with BCLP have a higher prevalence of associated anomalies than children with UCLP (e.g. Peterson-Falzone et al., 2010).

Language abilities in children with CP±L has not received much attention (Hardin-Jones & Chapman, 2011). This could be owing to the overt nature of cleft speech characteristics, potentially masking language difficulties. Language competence in 5-year-olds with nonsyndromic cleft lip and/or palate has been suggested to be delayed rather than disordered. A catch-up due to maturation is reported, resulting in non-significant differences compared to language competence in non-cleft peers (Boyce, Kilpatrick, Reilly, Da Costa, & Morgan, 2018; Collett, Leroux, & Speltz, 2010). In a recent meta-analysis, the conclusions were similar, after examining the literature (n=31) on speech and language development in children with non-syndromic cleft lip ± palate from 1950 to 2018, including ages 0 through 8:11 (Lancaster et al., 2020). Both expressive and receptive language competence were examined, resulting in an average effect size of -0.57 SD unit lower for expressive language competence and -0.59 SD unit lower for receptive language skills for children with non-syndromic CP±L compared to competence of peers without clefts. The overall conclusion about language development and competence in children with non-syndromic CP±L was that of early onset language delay but with a decreasing negative impact over time (Lancaster et al., 2020). However, two studies not included in the analysis targeting language competence in preschool and early school-aged children with non-syndromic CP±L reported DLD in 14% to 20% (Klintö et al., 2019; Morgan et al., 2017), indicating that there are both children with and without cooccurring DLD in the heterogeneous group of children born with non-syndromic CP±L.

A significantly increased risk for comorbidities (e.g. psychiatric disorder, intellectual disability, language disorder, autism spectrum disorder, psychotic disorder, attention deficit/hyperactivity disorder) was found in a large Swedish register cohort study on children with orofacial clefts (Tillman et al., 2018). In total ~19% with CLP and ~23% with CPO received at least one psychiatric diagnosis, compared to 11% of children without cleft. The highest hazard ratio of the different comorbidities was found for language disorder (aHR = 4.89) and intellectual disability (aHR = 4.19). A sibling analyses suggested that the heightened risk for comorbidities could not be explained by familial influence.

Dyspraxia, or speech features typically associated with CAS, have been reported with a high frequency in syndromic cleft populations with 22q11.2 deletion syndrome (22q11.2DS) (D'Antonio, Scherer, Miller, Kalbfleisch, & Bartley, 2001; Kummer, Lee, Stutz, Maroney, & Brandt, 2007) suggesting a phenotypic overlap between CAS and CP±L. Thus, the highest clinical prevalence of CAS (11.8%) among complex neurodevelopmental disorders was recently reported for 22q11.2DS (Shriberg et al., 2019). Not all children with 22q11.2DS are born with a cleft, but 49% to 82% were reported to have a palatal abnormality (e.g. D'Antonio et al., 2001; Márquez-Ávila et al., 2015; Persson, Lohmander, Jönsson, Óskarsdóttir, & Söderpalm, 2003; Solot et al., 2019), so that a substantial proportion of children with 22q11.2DS present with a cleft and CAS. Furthermore, there have been reports of submucous clefts being found when patients are assessed for suspected CAS (Murray et al., 2015) and CAS was identified in a patient with unilateral cleft lip and palate and hard to treat SSD including glottal stops (Lohmander & Persson, 2008). These cases with a potentially dual diagnosis raise interest in the overlapping speech characteristics and cooccurrence of CAS in children born with CP±L.

2 AIMS

2.1 GENERAL AIM

The overall aim of the project was to explore and investigate speech and language difficulties in children with childhood apraxia of speech and in children with repaired cleft palate at age 5 years to broaden the knowledge base on CAS and search for factors explaining unfavorable speech outcome in children with cleft palate. Both children with suspected CAS, diagnosed CAS, and CP±L were of interest for assessment and comparison of speech and language abilities.

2.2 SPECIFIC AIMS

The specific aims were to:

- survey the knowledge among Swedish SLPs' about speech characteristics and other deficits commonly associated with suspected CAS (Study I)
- examine if orofacial function in children born with CP±L differs from that in children without clefts and could be an explanatory factor for speech outcome (Study II)
- evaluate a checklist for diagnosis of CAS, constructed for English-speaking children (Study III)
- describe the prevalence of CAS speech features in children with severe speech sound disorders of different origins, looking for similarities and differences in speech feature profiles (Study III)
- describe the prevalence and profile of cooccurring language disorder in children with severe SSDs of different origins (Study IV)
- investigate the correspondence between SLP assessments of speech and language in children with severe SSDs and parental ratings of intelligibility and functional communication in their children's everyday lives (Studies II and IV)

3 METHOD

3.1 PARTICIPANTS

For the survey study (study I), 289 Swedish SLPs working with pre- and primary school-aged children (ages 3 to 9) throughout Sweden were contacted per email and invited to anonymously answer the web-based questionnaire. In total 178 questionnaires were returned, which equals a survey response rate of 62%. Questions targeting the background of the SLPs revealed graduation from different universities between the years 1972 and 2011. The largest proportion of answers came from SLPs' with less than five years (41%) or more than ten years (37%) of clinical experience. Most respondents worked in hospitals or public speech and language clinics (44%). Other workplaces were child habilitation services (24%), university hospitals (12%), special pre- and primary schools for children with speech and language disorders (8%), and private clinics (8%).

In total 67 five-year-old children (4:10-5:11) were included in studies II-IV, as illustrated in figure 1. All children had at least one native Swedish-speaking parent. They came from two different patient groups: children born with cleft palate (CP±L) and children with suspected CAS (sCAS). Fifty-two children, born with a cleft affecting the palate also including additional malformations, came from the original cohort of 88 children born between July 2009 and June 2011. These children were treated by the Stockholm Craniofacial Team and were included in study II. Children with no speech production and internationally adopted children were excluded. Study III included a subgroup of participants with CP±L from study II, children with disordered speech, who scored at least two standard deviation units below the mean on a standardized articulation test (n=19). Study IV included children with CP±L from study III who volunteered for additional language testing (n=8). For study III and IV children with suspected or diagnosed CAS (n=16) born between April 2010 and March 2012 were referred for a second opinion by community-based SLPs. One child was excluded owing to difficulties with participation.

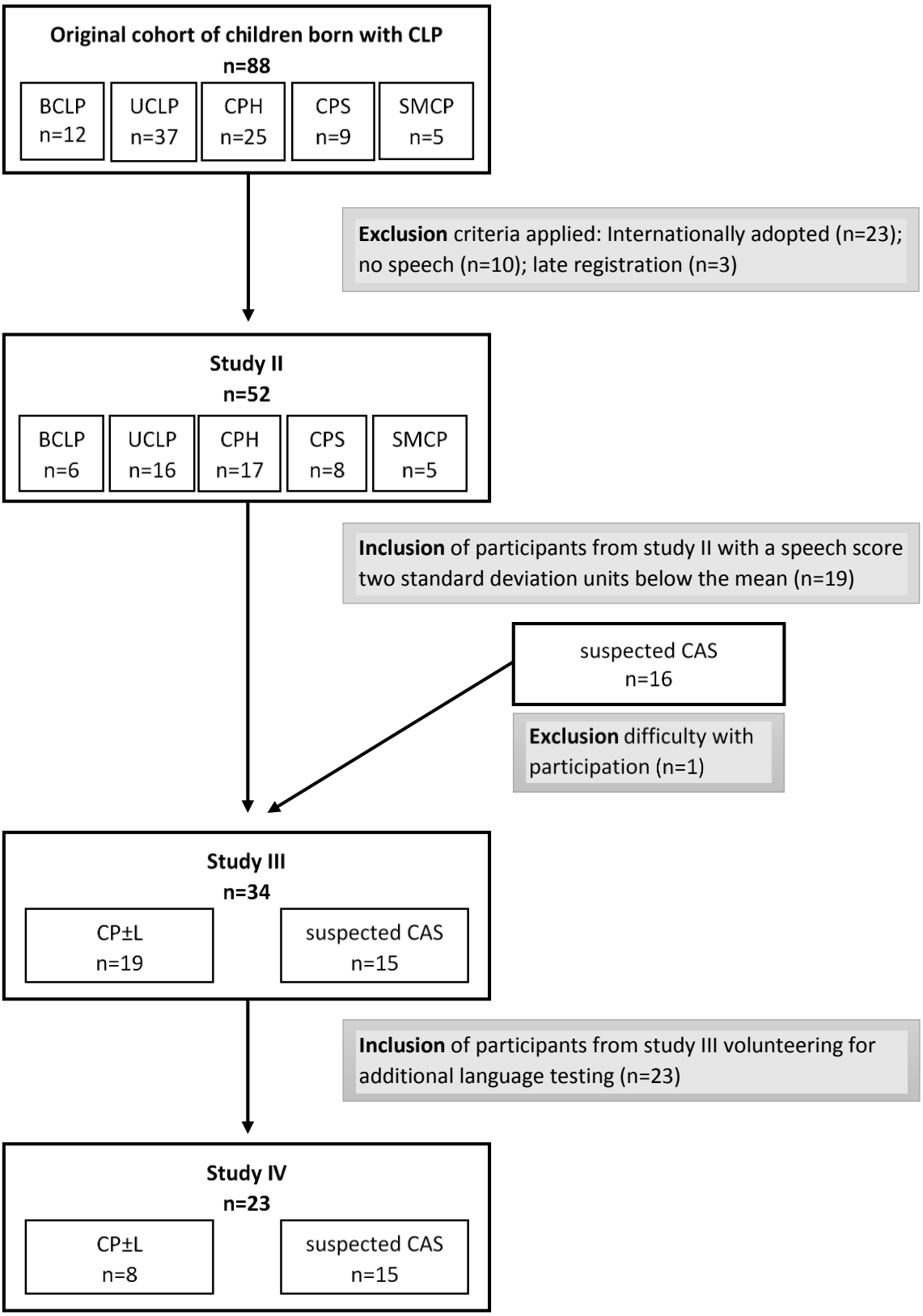

Figure 2. Flowchart over participants in study II, III and IV. BCLP, bilateral cleft lip and palate; UCLP, unilateral cleft lip and palate; CPH, cleft of the hard and soft palate; CPS, cleft of the soft palate only; SMCP, submucous cleft; CP±L, cleft palate with or without cleft lip; CAS, childhood apraxia of speech.

3.2 MATERIAL

3.2.1 Speech samples

All speech samples came from the Swedish Articulation and Nasality Test (SVANTE) (Lohmander et al., 2005).

Single word naming: For single word naming the 74 pictures from the test were used. The test primarily targets the production of consonants vulnerable to a cleft condition but is also recommended for the analysis of speech disorders related to, for example, motor speech disorders (Lohmander, Lundeborg, & Persson, 2017).

Sentence repetition: Thirteen short sentences, with different types of consonants (high-pressure, low-pressure, nasal or mixed), were produced through imitation by the children.

Connected speech: To elicit connected speech the children freely described the events from a picture of a day on the beach.

3.2.2 Observations of orofacial function

All information about orofacial function came from the Nordic Orofacial Test - Screening (NOT-S) (Bakke, Bergendal, McAllister, Sjögreen, & Åsten, 2007).

Orofacial function: Twelve domains are included; six domains through SLP examination and six through interviewing parents about orofacial function of the child. The domains included sensory function, breathing, habits (e.g. sucking fingers, grinding teeth during daytime), masticatory muscles and jaw function, chewing and swallowing, drooling, dryness of the mouth, the face at rest, facial expression, oral motor function, and speech.

3.2.3 Language samples

All language samples came from the Clinical Evaluation of Language Fundamentals (CELF-4) (Semel, Wiig, & Secord, 2003; Swedish version 2013).

Receptive Language: All subtests targeting receptive language skills were administered: ‘Concepts and Following Directions’, ‘Word Classes’ and ‘Sentence Structure’.

Expressive Language: All subtests targeting expressive language skills were administered: ‘Word Structure’, ‘Recalling Sentences’ and ‘Formulated Sentences’.

3.2.4 Questionnaires

3.2.4.1 SLP questionnaires

The author was responsible for the construction of the survey questionnaire, data collection and phonetic transcription.

Data collection for study I was based on a survey questionnaire. The questionnaire was constructed and pilot tested with four clinically and academically experienced SLPs. The 22 questions targeted the background of the SLPs, their clinical and theoretical knowledge and experience of CAS, estimation of own competence and prevalence of children with CAS in the SLPs' clinical settings.

3.2.4.2 Parental questionnaires

The Intelligibility in Context Scale (ICS) (McLeod et al., 2012a; Swedish translation, 2012b) and Children's Communication Checklist (CCC-2) (Bishop, 2003: Swedish translation 2011) were used.

Parental ratings: Parents filled in two questionnaires, one rating the degree to which their child's speech was understood by different communication partners and one rating functional communication in everyday life.

3.2.5 Audio and video recordings

For participants with sCAS, speech and language samples were documented with audio and simultaneous video recordings (Digital Video Camrecorder, Canon FS100 and Zoom Handy Recorder H4n). For participants with CP±L, speech was audio recorded using a Zoom Handy Recorder H4n and RØDE Microphone NT4-P48. Language samples were simultaneously video recorded (JVC Pro HD Camera, GY-HM100E). For analysis of speech measures audio recordings were used. CAS feature analysis of groping was based on video recordings.

3.3 ANALYSIS

Table 2 summarizes the different instruments used in studies II, III, and IV. As can be seen, measures of speech were included in all three studies, whereas measures of orofacial function, language and communication were used in study II and study IV respectively.

Table 2. Overview of measures analyzed, based on tests assessing speech, orofacial function, language and communication and used in studies II, III and IV

Measures	Study II	Study III	Study IV
Speech			
Swedish Articulation and Nasality Test (SVANTE) (Lohmander et al., 2005)			
Features commonly associated with CAS and their operational definitions (Iuzzini-Seigel & Murray, 2017)			
Percentage of Consonants Correct (PCC)	x		
Percent Words Correct (PWC)			x
Inconsistency Severity Percentage of consonants and vowels (ISPc and ISPv)		x	
Number and type of CAS features		x	
Intelligibility in connected speech rated by SLP	x		
Orofacial function			
Orofacial screening (NOT-S) (Bakke et al., 2007)			
Orofacial function examination	x		
Orofacial function interview	x		
Language			
Clinical Evaluation of Language Fundamentals (CELF-4) (Semel et al., 2003; Swedish version, 2013)			
Core Language Score			x
Expressive Language Index			x
Receptive Language Index			x
Communication			
Children's Communication Checklist (CCC-2) (Bishop, 2003; Swedish translation, 2011)			
Intelligibility in Context scale (ICS) (McLeod et al., 2012a; Swedish translation, 2012b)			
General Communication Composite			x
Social Interaction Deviance Composite			x
Intelligibility in Context rated by parents	x		

3.3.1 Measures of speech

3.3.1.1 Articulation

For study II, narrow phonetic transcription of targeted consonants was performed according to IPA and ExtIPA conventions (IPA, 2005, 2008). For study III, semi-narrow phonetic transcription of the whole words, consonants and vowels was performed (SVANTE; Lohmander et al., 2005). The percentage of consonants correct score (PCC score) (Shriberg, Aram, & Kwiatkowski, 1997; Shriberg & Kwiatkowski 1982) was based on the same single word material but included different numbers of consonants for calculations in study II and III. In study II, including children with CP±L only, PCC scores were based on narrow phonetic transcription of 59 targeted consonants, with nasality variables subtracted, following the

routine speech registration at 5 years reported into the National Quality Registry for Cleft Lip and Palate (https://lkg-registret.se/?page_id=96). For inclusion in study III and subsequently study IV, the PCC score was based on semi-narrow transcription of the whole words (161 consonants) for all participants. The reported percentage of words correct (PWC) in study IV was based on semi-narrow transcription of 161 consonants and 69 vowels. The calculation of the inconsistency severity percentages for consonants and vowels (ISPc and ISPv respectively) used in study III, was based on semi-narrow phonetic transcriptions of 112 consonants and 69 vowels.

3.3.1.2 Childhood apraxia of speech

For diagnosis of CAS, two SLPs jointly judged the presence or absence of the operationalized 12 CAS features (Iuzzini-Seigel & Murray, 2017). Ten features were judged perceptually using the audio/video recordings of single words, whereas two features were calculated based on semi-narrow phonetic transcriptions of the same single words.

3.3.1.3 Intelligibility

The assessing SLP rated to which degree connected speech was intelligible using a 3-point ordinal scale (0 = good/normal, 1 = mildly reduced and 2 = moderately to severely reduced) (SVANTE; Lohmander et al., 2005).

3.3.2 Measures of orofacial function

Scoring of the 12 domains was made on a binary scale (yes/no), that is 0 or 1 point per domain. The maximum total test score of 12 would indicate difficulties within all tested domains (NOT-S; McAllister & Lundeborg Hammarström, 2014).

3.3.3 Measures of language

Three subtests respectively are included in the expressive and receptive language indexes and were scored live during assessment. The subtests included in the receptive index were scored on a binary scale (correct/incorrect). The three subtests included in the expressive index all use ordinal scales, although differing between binary, 3-point and 4-point ordinal scales. The scoring of the three expressive subtests was controlled a second time, directly after assessment, using the video recording. Consequently, the core language score was composed of a combination of one receptive subtest score and the three expressive subtests scores (CELF-4; Semel et al., 2003, Swedish version, 2013).

3.3.4 Measures of communication

Functional intelligibility was quantified using parental ratings of the degree to which their child's speech was understood in everyday life by themselves, immediate family members, extended family members, friends, acquaintances, teachers and strangers on a 5-point scale (0 = never, 1 = rarely, 2 = sometimes, 3 = usually, 4 = always) (ICS; McLeod., et al., 2012a, 2012b).

Functional communication was quantified sorting the 70 parental questions into 10 subscales representing different communication areas and calculating the frequency of subscale behaviors rated by parents on a 4-point scale (0 = less than once a week or never, 1 = at least once a week but not every day, 2 = once or twice a day, 3 = every day or always). Two index scores, named the general communication composite and the social interaction deviance composite, were calculated including several, thus different, of the subscales (CCC-2; Bishop, 2003, Swedish translation, 2011).

3.4 RELIABILITY

Reliability of transcriptions was calculated as point-by-point percentage agreement between two transcribers. In order to be considered an agreement, the compared consonants had to be identically transcribed for place, manner, and voicing. Vowels had to be identically transcribed to be considered an agreement. In study II, the mean intra-transcriber agreement on 30% of randomly chosen transcriptions of target consonants was calculated and resulted in 96% for the main transcriber and 95% for the second transcriber. The mean inter-transcriber agreement between the two transcribers based on 41% of target consonants was 92%. In study III the intra-transcriber agreement for the main transcriber was based on 29% of the material including both consonants and vowels, this is, randomly chosen re-transcriptions of ten children, including five children from group sCAS and five from group CP±L. The mean intra-transcriber agreement was 86% for consonants and 96% for vowels. Inter-transcriber agreement between the two transcribers, the main transcriber and second transcriber from study II, was based on re-transcription of the same 29% of the material, resulting in a mean inter-transcriber agreement of 88% for consonants and 90% for vowels.

Reliability assessment of expressive language scoring in study IV was based on rescoring 30% of randomly chosen recordings from both participant groups by a second SLP. The intraclass

correlation coefficient (ICC) was calculated for single measures with absolute agreement using a two-way mixed model. ICC was .97 with a 95% confidence interval from .92 to .99.

3.5 STATISTICAL ANALYSES

Nonparametric statistics were chosen because of skewed data and small sample sizes. All analyses were performed using SPSS (versions 23, 26) and for all statistical analyses, $p < .05$ (two tailed) was considered significant.

Results from study I and III were presented using descriptive statistics. In study II, correlations between variables within the study group were tested with Kendall τ_B. The Mann-Whitney U test was used to compare the study groups' outcome measures with reference data. Differences between subgroups in study II and IV were tested using the Mann-Whitney U test or Kruskal-Wallis test, depending on the number of subgroups. In study IV, within-subgroup differences between subtests were analyzed using the Wilcoxon signed-rank test.

3.6 ETHICAL APPROVALS

Ethical approval was obtained from the Regional Ethical Review Board in Stockholm, Sweden for studies II-IV. The ethical approval for study II, with Dnr: 2014/609-31/2, was the main approval. For studies III and IV, the same main approval and two supplements, Dnr: 2015/251-32 and 2015/1305-32, used in both studies, were obtained. No application for ethical approval was filed for study I. The anonymous participation when completing the questionnaire was one reason for this choice, as was the content of questions asked, targeting professional know-how and not patient-specific information. Participation in study I was consented to by responding to the web-based questionnaire.

4 RESULTS

4.1 STUDY I

The SLPs selected seven main speech characteristics, from a list of 17, as typical for children with CAS. These were: inconsistent speech production (85%), sequencing difficulties (71%), oro-motor deficits (63%), vowel errors (62%), voicing errors (61%), consonant cluster deletion (54%) and prosodic disturbance (53%). Underlying motor-programming difficulties were perceived by 82%. Twenty-nine percent considered CAS as being a separate disorder, 10% as a disorder cooccurring with another disorder, and 51% agreed with the alternative that there are both clear cases of CAS as well as cases cooccurring with other disorders. The proposition that children with CAS typically display phonological deficits was agreed on by 44%, and cooccurring language disorder was perceived by 10% of the SLPs. The mode of the estimated clinical occurrence of CAS in Swedish speaking pre- and primary school-aged children was 5%.

4.2 STUDY II

Orofacial dysfunction was found in 37% of children born with CP±L, which is significantly more frequent compared to reference data for 5-year-olds (McAllister & Lundeborg Hammarström, 2014) on children without CP±L. Age-appropriate articulation proficiency was found in 39%, whereas 49% presented below 2 SD scores. Just above 50% had good intelligibility and were always understood by different communication partners according to both SLP and parent rating. No significant correlations were found between orofacial dysfunction and PCC or between orofacial function and intelligibility. Compared to reference data, sensory function and drooling were the domains where children born with CP±L were significantly more affected than the reference group. However, the degree of impairment did not differ between cleft types. Orofacial function was not different between children with CP±L plus additional malformations compared to children with CP±L only. Children with CP±L plus language disorder on the other hand had significantly more often difficulties within the domain of oral motor function, compared to children without additional difficulties.

4.3 STUDY III

A distinct CAS profile was shared by 12 of the 34 participants. The profile included *phonemic speech inconsistency for consonants and vowels* plus *vowel error*, *voicing error*, *difficulty achieving initial articulatory configurations or transitionary movement gestures* and *stress errors*. This CAS profile met the three consensus-based ASHA criteria. Sixty-seven percent (n=10) of children with sCAS were diagnosed with CAS, whereas 33% (n=5) had non-CAS SSD. For group CP±L the corresponding figures were 11% (n=2) with CAS and 89% (n=17) with non-CAS SSD. For participants with non-CAS SSD no specific speech profile was found, and prosodic impairment was rare.

4.4 STUDY IV

Expressive language disorder was found in 67% of children diagnosed with CAS. Tasks targeting morphological ability and verbatim repetition of sentences were particularly affected. In all children with CAS, receptive language was significantly stronger than expressive language, whereas no such difference was observed in the group of children with non-CAS speech sound disorder (non-CAS SSD). Developmental language disorder, including significant difficulties within both receptive and expressive domains, was found in 18% of children with non-CAS SSD, while expressive language disorder was found in 9%. Parent ratings of communication skills reflected an increased burden on communication in everyday life when difficulties within both speech and language domains were present.

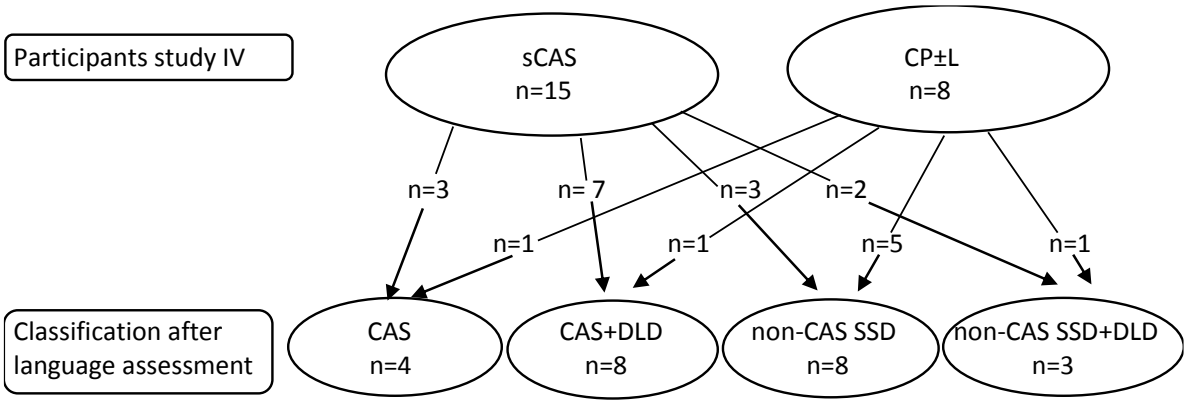

Figure 3. Participants in study IV and classification after assessment of language (study IV). sCAS, suspected childhood apraxia of speech; CP±L, cleft palate with/without cleft lip; CAS, childhood apraxia of speech, DLD, developmental language disorder; non-CAS SSD, speech sound disorder but not CAS.

5 DISCUSSION

In this doctoral project, childhood apraxia of speech was explored from different perspectives: the knowledge and praxis of CAS among SLPs was investigated and the speech and language abilities of children with suspected CAS were examined. Results were also compared to children with speech difficulties related to cleft palate, that is, a different but comparably severe speech sound disorder, in order to explore the speech profile of CAS. Furthermore, explanatory factors for unfavorable speech outcome in children born with CP±L, such as orofacial dysfunction and language disorder, were examined.

5.1 A SPEECH PROFILE ASSOCIATED WITH CHILDHOOD APRAXIA OF SPEECH

When comparing the views of SLPs on typical speech characteristics of CAS in English and Swedish speakers, they corresponded in large. The most prevalent characteristic of CAS in all surveys, study I included, was *inconsistent production* or *inconsistency of errors* (Forrest, 2003; Joffe & Pring, 2008; Meredith & Potter, 2011). There were no contradicting results found for CAS speech characteristics between the studies on Swedish and English language contexts, indicating that research could be valid cross-linguistically for the two languages. Swedish SLPs' top seven speech characteristics of CAS were *inconsistent speech production* (85%), *sequencing difficulties* (71%), *oro-motor deficits* (63%), *vowel errors* (62%), *voicing errors* (61%), *consonant cluster deletions* (54%) and *prosodic disturbance* (53%). Some of these characteristics cannot not be translated directly into a feature from the 12-feature list used in study III (Iuzzini-Seigel & Murray, 2017). However, these top speech characteristics reflect the three ASHA diagnostic criteria (ASHA, 2007).

The cross-linguistic validity of CAS speech characteristics suggested in study I led to the design of study III, aiming at evaluating a checklist for CAS constructed for English-speaking children. When the work on this thesis project began, there were no evidence-based assessment protocols or standardized tests available in Swedish, for differential diagnosis of CAS. However, in 2016 the Swedish version and extension of the Dynamic Evaluation of Motor Speech Skills (DEMSS; Strand & McCauley, 2019) was published (DYMTA; Rex, McAllister & Hansson, 2016). In study III, a CAS speech feature list was investigated that was operationalized by Iuzzini-Seigel and Murray (2017). This list has also been used in other recent studies (e.g. Centanni, Green, Iuzzini-Seigel, Bartlett, & Hogan, 2015; Iuzzini-Seigel,

Hogan, Guarino, & Green, 2015a; Iuzzini-Seigel, 2019; Zuk et al., 2018). By replicating the diagnostic procedure for CAS used in research on English-speaking children, we evaluated the procedures applicability for diagnosis in another Germanic language. In addition, we investigated the diagnostic relevance of the checklist by including two groups with disordered speech of different origin and with some hypothesized overlap of speech characteristics.

The most prevalent characteristic of CAS, according to SLPs in study I and in line with earlier surveys, was inconsistency of production errors (Forrest, 2003; Joffe & Pring, 2008; Meredith & Potter, 2011). This was also the only mandatory CAS feature on the checklist used (Iuzzini-Seigel, Hogan, & Green, 2017; Iuzzini-Seigel & Murray, 2017). For judgment of *inconsistent errors*, the phonemic speech inconsistency was calculated based on phonetic transcription. The calculation of the inconsistency severity percentage (ISP) (Iuzzini-Seigel et al. 2017) was developed and advocated for its ability to differentiate suspected CAS from phonological disorder in preschool children (Iuzzini, 2012; Iuzzini & Forrest, 2010). Speech inconsistency was also used as a diagnostic marker and could differentiate between CAS and speech delay (Iuzzini-Seigel et al., 2017). In studies on school-aged children, an ISP of 18% or higher on production of sounds-in-words was proposed to distinguish children with CAS. The calculation of the ISP was also promoted because of its clinical applicability, reusing transcriptions of a custom word list or an articulation test already included in standardized test batteries (Iuzzini-Seigel & Murray, 2017). Iuzzini-Seigel and colleagues (2017) concluded that speech inconsistency can contribute to the differential diagnosis of school-aged children with CAS; however, they emphasized the impact of stimuli selection on results. Further, they declared that stimuli too simple for participants would not tax phonemic inconsistency. On the other hand, stimuli too challenging for children with speech disorder would not be efficacious in differentiating CAS from other speech disorders. In this project, inconsistency of phoneme production in simple, single words was used owing to the severe speech disorder of the participating 5-year-old children. This task was also perceived as relatively free from both language load and higher-order planning; thus, results were hypothesized to primarily reflect inconsistency of speech production due to CAS. Owing to the simple speech material used, ISP results were lower than reported in studies using materials including challenging multisyllabic words and non-words. When using this simpler speech material, the ISP for participants ranged from 0 to 34% with just five participants (15%) scoring 0%, indicating no ceiling effect. To determine a cut-off, in accordance to the 18% reported for older children using more complex materials (Iuzzini-Seigel, 2012) the distribution of scores was examined. However, it did not indicate a cut-off differentiating CAS from non-CAS SSD. Because inconsistent consonant *and* vowel production is a prerequisite for a CAS diagnosis (ASHA, 2007), it is unclear why the

ISP reported so far has been calculated based on consonants only. Consequently, the inconsistency severity percentage for vowels (ISPv) was constructed in analogy to the calculation of the ISP for consonants (Iuzzini-Seigel et al., 2017). The ISPv calculated from the simple, single word material ranged from 0 to 7% with 20 of all participants (59%) scoring 0%. Interestingly, all participants with the CAS feature profile (n=12) scored above 0%. Additionally, one of the three participants with CP±L fulfilling the ASHA primary criteria, as discussed in a following section, scored 3%. None of the participants classified as non-CAS SSD presented with inconsistent vowel errors, making the ISPv a promising measure for further validation.

The emerged CAS speech profile consisted of a distinct set of five features: the mandatory *speech inconsistency* plus four features (*vowel errors, voicing errors, difficulty achieving initial articulatory configurations or transitionary movement gestures and speech errors*), when using Iuzzini-Seigel and Murray's (2017) checklist and operationalized definitions. In other words, of the possible 10 features from the list that could be evaluated within this project, five (50%) were shared by all cases with CAS. However, for a CAS diagnosis according to Iuzzini-Seigel and Murray (2017) an additional optional feature was needed. It should be noted that the number of CAS features needed for a CAS diagnosis is arbitrary and differs between research groups (e.g. studies of Iuzzini-Seigel and colleagues contra Shriberg and colleagues), as does the frequency of occurrences of a specific feature needed to be considered for the feature to be present. This means that the number of different features and the frequency of that feature's presence are two different measures, the first indicating variation in feature criteria (e.g. ASHA's three primary criteria), the latter the frequency of a feature observed. To my knowledge, there has been no attempt made to quantify feature frequency related to severity of the speech disorder. In this project, one observation of a CAS feature, agreed upon by both raters, was enough for that feature to be judged as present (a procedure further discussed under methodological considerations, see 5.5.3). The used procedure could, therefore, explain the relatively high occurrence of several CAS features seen in all included participants having disordered speech in common.

Exploring the possible cooccurrence of CAS in children with CP±L and severely disordered speech led to intriguing findings. Despite the reduced number of CAS features assessed, from 12 to 10 (for the discussion of this methodological limitation, see 5.5.3), at the same time keeping the cut-off for a positive diagnosis of CAS stable, two out of 19 children (11%) with CP±L fulfilled diagnostic criteria for CAS. Another three children fulfilled the three consensus-based ASHA criteria. They were thus short of one feature, not reaching the minimal number of

CAS features needed for a diagnosis according to Iuzzini-Seigel and Murray (2017). None of the presumably five children with CP±L who met the ASHA criteria for CAS had a diagnosis of 22q11.2DS, a syndrome known to include a high percentage of children with cooccurring CAS (e.g. Shriberg et al., 2019). However, of the two children with CP±L+CAS one had additional malformations as had two of the additional three who met ASHA criteria. These five children with CP±L represented different cleft types and malformations.

The three CAS features representing inappropriate prosody and stress were not found in any children with non-CAS SSD, except for the three cases with CP±L fulfilling the ASHA criteria presented in the section above. This finding, upraising stress errors as a diagnostic marker for CAS, is well in line with current research and understanding (e.g. Morgan & Webster, 2018; Shriberg et al., 2017c).

The proportion of Swedish children with sCAS, classified as non-CAS SSD (33%) in study III, was in agreement with earlier research. Murray and colleagues (2015), also used community-based SLPs for referral and inclusion of Australian children with sCAS, diagnosing 32% with non-CAS. Both studies add to the body of evidence indicating that CAS is suspected and overdiagnosed in the general SSD population (e.g. Forrest, 2003; Shriberg et al., 2011) and in different language contexts.

5.2 A LANGUAGE PROFILE ASSOCIATED WITH CHILDHOOD APRAXIA OF SPEECH

The reported gap between receptive and expressive language competence in children with CAS (e.g. Rosenbek & Wertz, 1972; Murray et al., 2019) was confirmed in study IV. The proportion of children having an expressive language disorder (67%) was similar to the reported proportions of Dutch and English-speaking children (46-82%) (Thoonen et al., 1997; Lewis et al., 2004; Iuzzini, 2012; Vuolo and Goffman, 2018; Zuk et al., 2018; Murray et al., 2019). Receptive language competence in children with CAS could be considered a relative strength.

The most severely impaired language ability was expressive morphology and morphosyntax, shared by all children with CAS+DLD in this project. However, here the influence of stimuli tasks on the results needs to be considered. As outlined by Murray and colleagues (2019) when assessing morphology, many articulatory challenging sounds are targeted, and speech

production is anticipated to include inconsistency due to CAS. In addition, children with CAS have difficulties with increased word length and complexity as well as producing weak syllables (Murray et al., 2015; Shriberg et al., 2011). For assessment of morphology in this project the 'Word Structure' subtest (CELF-4; Semel et al., 2003, Swedish version, 2013) was used. The task requires mainly one-word answers using a sentence completion format, targeting production of grammatical morphemes in a simple phonological context. To ensure reliability, this subtest was rescored immediately after testing and later by a second SLP to determine agreement. Production did not need to be correctly pronounced but signaled. Interestingly, results on the two subtests used for assessment of morphosyntax, 'Recalling Sentences' and 'Formulated Sentences', requiring formulating or recalling a full sentence, were somewhat less impaired compared to the morphology task and to reference data. This finding is in line with conclusions made by Murray and colleagues (2019), that the 'Word Structure' subtest included more linguistic-based morphological errors than did results from the subtest using sentence level sampling contexts in children with CAS.

The finding of an association with a morphological language deficit in CAS, as found in this project and previously reported (Murray et al., 2019; McNeill & Gillon, 2013) could be explained using the dual stream model of speech processing (e.g. Hickock & Poeppel, 2004, 2007; Poeppel, Emmorey, Hickock & Pylkkänen, 2012). The suggested dorsal stream's importance for both auditory-motor transcoding and syntactic analysis could explain the cooccurrence of such difficulties. Structural correlates of the dorsal stream are the posterior temporal, temporo-parietal and inferior frontal regions and their corresponding white matter connections through the superior longitudinal and arcuate fasciculi. Fiori and colleagues (2016) found that one of the subnetworks disrupted in CAS involved the left inferior frontal gyrus, classically related to speech motor connectivity correlated with oral diadochokinesis, oromotor skills, expressive grammar and lexical difficulties.

5.3 FUNCTIONAL COMMUNICATION ASSOCIATED WITH SEVERELY DISORDERED SPEECH

Intelligibility is a term describing how successful a speaker manages to convey a message to the listener. Functional intelligibility, as measured by the intelligibility in context scale (ICS) (McLeod et al., 2012a, 2012b) is a complex concept taking different aspects of communication, different listeners and everyday life into account (Lagerberg, Hellström, Lundberg, & Hartelius, 2019). The ICS screening tool was used for children with CP±L to obtain a measure of intelligibility when communicating with different communication partners in everyday life, adding ecological validity. For the same reason these parental ratings were compared to SLP ratings of overall intelligibility in connected speech. Intelligibility, rated by parents and SLPs, were largely in agreement for both children with good intelligibility which were always understood by different communication partners as for children with moderate to severe reduced intelligibility which were never/rarely/sometimes understood during conversation. About 50% of 5-year-old children with CP±L were always understood according to parental rating and scores of these children were almost identical compared to ICS-scores reported for children with no speech difficulties (McLeod et al., 2012a). The results indicate that parental rating of functional intelligibility using the ICS for children with CP±L could reliably differentiate between children with and without associated communication disorder. The ICS was also used when assessing children with sCAS in this project; however, results for this group have not yet been presented.

Another parental rating instrument, The Children's Communication Checklist (CCC-2; Bishop, 2003; Swedish translation, 2011), targets functional communication in everyday life. It was completed by parents of children with sCAS and children with CP±L, intended to add ecological validity to the standardized language assessment by the SLP (Semel et al., 2003, Swedish version, 2013). The questionnaire targeted the domains speech, language, communication and pragmatic/social interaction skills. Speech was rated to cause the greatest difficulties with communication in everyday live, which is in line with a previous study on children with SMCP aged 5 to 12:8 (Boyce et al., 2019). In addition, interesting results were found in the parental rating of Syntax, which was below -2 SD scores for all participants with CAS+DLD (n=7). Parent responses demonstrated an awareness of their child's deviant production, and in fact, an ability to differentiate between speech and language difficulties when answering questions about sentence structure and grammar. Consequently, marked difficulties with morphology are in line with results from formal assessment and should be seen as part of the language profile associated with CAS.

5.4 EXPLANATORY FACTORS FOR SPEECH OUTCOMES IN CHILDREN WITH CLEFT PALATE ± LIP

In the project factors explaining the large variation in speech outcome in the heterogeneous group of children born with CP±L were explored. Orofacial function (study II), speech features typically associated with CAS (study III) and language competence (study IV) were examined.

Age-appropriate articulation proficiency was found in just 39% of children with CP±L, an even lower proportion compared to the previously reported 48% in a study of 5-year-olds including several cleft types and syndromes (Britton et al., 2014). Varying results between study II and the National audit standard study from Great Britain and Ireland (Britton et al., 2014) could be owing to different study sizes and/or different conceptions of the label "speech within normal range." In study II, reference data from children without clefts and a cut-off at - 1 SD were applied to meet criteria for normal articulation proficiency. Moreover, articulation proficiency correlated significantly with intelligibility in study II.

Prior to study II, orofacial function had not been examined and reported systematically for children with CP±L. Orofacial dysfunction was found to be more frequent in 5-year-old children born with CP±L (37%) compared to children born without cleft (11%) (McAllister & Lundeborg Hammarström, 2014). However, the findings were mainly within non-speech areas, such as breathing, drooling, chewing and swallowing. Consequently, when correlating orofacial function and articulation proficiency (PCC) the results indicated that orofacial dysfunction was not an explanatory factor for speech outcome in children born with CP±L.

Focusing on speech features commonly associated with CAS, when exploring the speech of children with CP±L, resulted in interesting findings. They indicated that 11% (n=2) of children with CP±L fulfilled criteria for CAS based on Iuzzini-Seigel and Murray criteria (2017). As many as 26% (n=5) would have met the three primary ASHA criteria (ASHA, 2007). The dual diagnosis of CP±L and CAS could in fact explain the unfavorable speech outcome in a subgroup of children with CP±L including both children with and without additional malformations.

Cooccurrence of language disorder in children born with CP±L was examined. In study II, children with CP±L plus DLD were the subgroup with the lowest articulation proficiency (16%). Information about cooccurring DLD for all children with CP±L was based on data from the National Quality Registry for Cleft Lip and Palate (https://lkg-registret.se/?page_id=96). Unfortunately, only a small proportion of children with CP±L and severe speech disorder

volunteered for inclusion in study IV and the assessment of language abilities. Results indicated cooccurring DLD in two of the eight (25%) participants with CP±L. This suggests, that cooccurring DLD could be a factor explaining unfavorable speech outcome in children with CP±L.

5.5 METHODOLOGICAL CONSIDERATIONS

5.5.1 Participants

The representativeness of the sample of children with CAS and CP±L included in this project presents a methodological dilemma. Owing to participant heterogeneity and relatively small sample sizes, especially after subgrouping, group results could have been influenced by atypical performance in a few participants. No genetic or neuropsychiatric tests were conducted of the participants. The ability to participate in formal testing was a prerequisite, although several children within both included patient groups had attention difficulties, although undiagnosed at the time. Three children needed an extra visit for test completion and a fourth child two additional visits. On the other hand, the inclusion of a relatively unselected group of children with cooccurring additional malformations or undiagnosed neuropsychiatric disorders increase the samples clinical representativeness. Inclusion of a narrow age range minimized age-driven changes as confounders. On the other hand, results might not be generalizable to other age groups.

5.5.2 Phonetic transcription

Although narrow phonetic transcription has been advocated for highly unintelligible speech (e.g. Ball, Müller, Klopfenstein, & Rutter, 2009), semi-narrow transcription of single words was performed. This was motivated because transcription in finer detail than needed is not time efficient. Moreover, there needs to be a balance between level of detail in transcription and reliable and replicable intra- and inter-transcriber agreement used in research to facilitate methods to be transferable into clinical settings (Heselwood & Howard, 2008).

5.5.3 Diagnostic procedure

When directly replicating a method, one should follow the original parameters as close as possible (for a discussion of study replication, see Zwaan, Etz, Lucas, & Donnellan, 2018). In this project the diagnostic procedure proposed by Iuzzini-Seigel and Murray (2017) was replicated, using definitions, operationalized features and diagnostic cut-offs as required for CAS diagnosis. Despite failure to rate two out of the 12 features from the checklist in this project, the cut-off was retained, thereby changing the proportion of speech features needed for a CAS diagnosis. Iuzzini-Seigel and Murray (2017) specified six (one mandatory plus five optional features) of the twelve that equal 50% of the total number of features. For children with CP±L in this thesis this resulted in six of ten features (60%). Consequently, there could have been three additional children with CP±L included in the CAS group had we used the 50% cut-off. Thus, as many as 26% of children with CP±L could potentially have cooccurring CAS, or at least several speech features indicating difficulties with speech motor planning and control.

Replicating the use of just one occurrence of a specific feature as evidence of the presence of that feature, was questioned by the two raters. Research on the development of speech motor control has shown that boys until age 5 experience a slower maturational course of speech motor development. After a plateau between the ages of 7 to 12, adultlike speech motor processes are used from age 14 and upwards (Smith & Zelaznik, 2004). This knowledge about typically later maturation of speech abilities makes it questionable to apply just one incorrect production as an indicator for presence of a CAS speech feature, especially in 5-year-olds. However, different diagnostic procedures have used different speech tasks and cut-offs for the number of CAS features needed for a diagnosis (e.g. Shriberg et al., 2011). The specific aim of this project was to evaluate a checklist, constructed for speakers of another language (Iuzzini-Seigel & Murray, 2017) and parameters thus had to be replicated as closely as possible.

6 CONCLUSIONS

- Swedish SLPs had relevant theoretical and/or clinical knowledge about CAS, but often reported a need for further education (Study I).
- Findings suggested cross-linguistic applicability of CAS speech feature definition and operationalization between English and Swedish speakers (Studies I and III).
- Swedish-speaking 5-year-olds with CAS shared a distinct speech profile including the five features: speech sound inconsistency of consonants and vowels, vowel error, voicing error, difficulty achieving initial articulatory configurations or transitionary movement gestures and stress errors (Study III).
- Prosodic impairment was seen almost exclusively in children with CAS but not in children of the same age with other SSDs (Study III).
- In children with CP±L and SSD, a hightened cooccurrence of CAS should be anticipated (Study III).
- There was a consistent gap between worse expressive and better receptive language ability in children with CAS, not seen in children with non-CAS SSD. Expressive language disorder should be expected in more than half of children with CAS (Study IV).
- Poor articulation proficiency in children with CP±L, was not related to orofacial dysfunction. The high prevalence of orofacial dysfunction was related to drooling and impaired sensory function (Study II).
- Parental ratings of communication abilities in everyday life both added ecological validity to formal assessment and confirmed formal findings (Studies II and IV).

7 CLINICAL IMPLICATIONS

The goal of clinical research is to accelerate and improve the development and delivery of services provided after implementing research findings into clinical practice. How this is best accomplished within the field of communication sciences and disorders has recently been addressed in a tutorial by Douglas and Burshnic (2019). The proposed means are within the framework of implementation science, focusing on the direct collaboration between clinicians and researchers to lessen the gap between research and practice. In this project I transferred from the role of curious and frustrated clinician to researcher and am now obligated and determined to find ways to further clinical implementation. Having one foot in research and one within clinical practice could facilitate collaboration and exploring different means for implementation. Results from study I indicated that the majority of SLPs (83%) had actively been searching for information on their own, acknowledging the need for lifelong learning as part of their professional development. Possibly, an implementation workshop with SLPs, in analogy to the one described by Shrubsole and colleagues (2018), could influence practice change in a positive way. Targeting different domains including knowledge, beliefs about own capabilities and consequences as well as addressing barriers for the implementation such as lack of time and leadership, could raise awareness of potential difficulties and facilitate implementation of differential diagnosis of SSDs and diagnosis of CAS in particular.

Identifying children in need for SLP assessment and/or intervention could be aided by using the quick ICS screening tool, in study II shown to be reliable for rating a child's intelligibility (for more information about the ICS validity and reliability, see McLeod, 2020). Children born with CP±L are enrolled in a cleft palate team in Sweden, with scheduled routine visits to a SLP at ages 1.5, 3, 5, 7, 10, 16 and 19 years. Perhaps, regularly distributing a screening tool such as the ICS between visit-years during the preschool and early school years, could engage parents continuously reflecting over their child's communicative ability and be profitable for both clinicians and parents. This has already been suggested and included in the International Consortium for Health Outcomes Measurement (ICHOM) standard set at ages 5, 12 and at final visit (Allori et al., 2017). Another way to make use of the ICS is in bilingual children. The ICS has been translated into over 60 languages (https://www.csu.edu.au/research/multilingual-speech/ics) and could be used to compare a child's intelligibility in both spoken languages before engaging an interpreter, for further assessment, if needed.

Including the orofacial screening tool (NOT-S, Bakke et al., 2007), used in study II, into routine visits at age 5 could be a time effective and easy way to identify the higher proportion of children with orofacial dysfunction and guide interventions focusing on difficulties with breathing, drooling, chewing and swallowing.

For children with CP±L, awareness about possible cooccurrence of speech difficulties including CAS should be anticipated in children with severe disorder at age 5 years.

The cooccurrence of expressive language disorder in more than half of children with CAS and several with CP±L, stresses the need for language assessment for all children with suspected CAS and severe SSD. Assessment of children with difficulties to cooperate could be aided by using information from a parental checklist, such as the CCC-2 (Bishop, 2011).

8 FUTURE STUDIES

Larger scale and longitudinal research approaches, including several age-groups and participants with mild to severe CAS or SSD, are needed to corroborate the speech and language profiles found in this study. Research collaborations and cross-linguistic studies, using the same protocols to expand participant numbers, could be profitable. Research collaborations within Sweden could do the same, working towards a standard set and national guidelines for diagnosis of children with CAS.

Developing a comprehensive screening instrument, combining the speech and language feature profiles found for CAS in this project, could help bridging the gap between research and clinic. In addition, parental ratings of intelligibility and communication in everyday life could be part of the screening procedure. Parental ratings in this project were found to be in line with SLP assessment, and to be both time effective and adding ecological validity. The goal of such a screening instrument could be twofold, both to assist in the identification of suspected CAS patients and patients difficult to assess or classify, in need for referral to a specialized SLP.

Vowel inconsistency, and the inconsistency severity percentage of vowels (ISPv) proposed in this project, may have potential as an exclusive marker of CAS. However, this needs to be explored further. Future studies should also include languages with less complex vowel systems compared to Swedish.

Another line of future research should focus on severity of CAS and an increased understanding of the relative contribution of different speech features influence on intelligibility. To explore which one of the CAS speech features influences speech intelligibility the most could be of great value with direct clinical implications, aiding decisions about which treatment plan goals to prioritize.

9 ACKNOWLEDGEMENTS

This work would not have been possible without the support and contributions from a great number of people. I wish to express my sincere gratitude to:

Anette Lohmander, who agreed to be my main supervisor 'if there were children with cleft palate involved'. Thank you for your professional supervision and guidance; for being inspiring, reliable, brilliant, patient and frank. You made me grow and I am so glad you have grown some interest in childhood apraxia of speech as I have had the privilege to discover and appreciate the cleft area.

Anita McAllister, co-supervisor with vast knowledge and experience within multiple areas. Thank you for being supportive, inspiring and believing in me.

Per Östberg, who became my main supervisor after the half-time. Thank you for your guidance and sharing knowledge about theoretical frameworks, methodology and statistics.

Sofia Strömbergsson, co-author and valuable reviewer of the thesis, thank you for your brilliant yet unpresuming comments and suggestions.

Elisabeth Lundström, my employer at the Medical unit, Speech and Language Pathology, Karolinska University Hospital. Thank you for your supportive and friendly advice and enabling me to combine research with clinical work.

Liv Thalén, friend, former fellow PhD student and colleague. Thank you for sharing all ups and downs during the PhD-journey. I am so grateful for our discussions about methodology, statistics and ethics – not to forget our 'Tea for two'-breaks and your loyal support at all times.

Åsa Mogren and *Susanne Rex,* fellow PhD students and friends, for sharing significant methodological discussions and headaches within our common area of research and for all geeky good times. Looking forward to future collaborations! *Susanne,* thank you for time-consuming consensus judgements.

Emilie Hagberg for participation in both assessment and time-consuming transcriptions and in addition, for your interest and handling the clinical work with CAS patients. Hoping for future collaborations!

Jill Nyberg, Emilie Hagberg, Tove Movérare, Liisi Raud Westberg and *Katrin Stabel-Svensson,* dear former colleagues at the Craniofacial team at Karolinska University Hospital. Thank you for the splendid collaboration, making space for me and my project and helping to combine and facilitate clinical work with research interests. A special thanks to you, *Liisi,* for the fine illustrations.

All fellow PhD students for conversations and especially research seminars, HÖST-retreats and the instructive journey to Canada and Illinois in 2016: *Anna Nyman, Anna Persson, Annika Szabo Portela, Ineke Samson, Marion Lieberman, Jill Nyberg, Joakim Körner Gustafsson, Susanne Rex, Åsa Mogren, Helena Hybbinette* and *Liv Thalén.*

All colleagues at the Division of Speech and Language Pathology, at Karolinska Institutet. Thank you for showing interest in my work: *Kerstin Johansson, Päivikki Aarne, Ellika Schalling, Anna Eva Hallin, Ulrika Nygren, Maria Södersten* and *Svante Granqvist*.

A special thanks to *Kicki Hedestedt*, *Anna Peterson* and *Agneta Wittlock* for always rapidly and kindly helping with the numerous challenges of administration.

All my friends and/or *colleagues*, near and far away, none mentioned, and none forgotten!

My family, always on my mind and surrounding me with love:

Jan, my husband and best friend since 1985. This project has consumed a lot of time and occupied my thoughts, yet you have been my greatest supporter, tack älskling!

My son *Henrik* and wife *Evelina,* grandsons *Benjamin* and *Alexander*. You have opened your home and welcomed me, thank you! Spending time with the boys is the most rewarding and lovely experience and relaxation.

My daughter, *Charlott,* thank you for being close and truly understanding my urge for research.

My parents, *Mutter* and *Vater*, thank you for choosing me, adopting and loving me and letting me grow. Ich liebe Euch!

This research was financially supported by Majblommans Riksförbund, the Aina Börjeson Foundation for Speech Language Pathology Research and Treatment, the Foundation Frimurare Barnhuset, Stockholm, the Stockholm County Council and Karolinska Institutet

10 REFERENCES

Allori, A. C., Kelley, T., Meara, J. G., Albert, A., Bonanthaya, K., Chapman, K., . . . Wong, K. W. (2017). A standard set of outcome measures for the comprehensive appraisal of cleft care. *Cleft Palate Craniofac J, 54*(5), 540-554. doi:10.1597/15-292

American Speech-Language Hearing Association. Technical Report. *Childhood apraxia of speech*. (2007). Available at: https://www.asha.org/policy/TR2007-00278/

Atkinson, M. E., & Howard, S. J. (2011). Physical structure and function and speech production associated with cleft palate. In S. Howard & A. Lohmander (Eds.), *Cleft Palate Speech* (p. 5-22). Chichester: UK: John Wiley & Sons, Ltd.

Bakke, M., Bergendal, B., McAllister, A., Sjögreen, L., & Åsten, P. (2007). Development and evaluation of a comprehensive screening for orofacial dysfunction. *Swed Dent J, 31*(2), 75-84.

Ball, M., Müller, N., Klopfenstein, M., & Rutter, B. (2009). The importance of narrow phonetic transcription for highly unintelligible speech: some examples. *Logoped Phoniatr Vocol, 34*(2), 84-90. doi:10.1080/14015430902913535

Ballard, K. J., Granier, J. P., & Robin, D. A. (2000). Understanding the nature of apraxia of speech. Theory, analysis, and treatment. *Aphasiology, 14*(10), 969-995.

Bishop, D. V. (2011). *The Children's Communication Checklist-CCC-2.* (Second ed.) Stockholm, Sweden: Pearson Education.

Bishop, D. V., Snowling, M. J., Thompson, P. A., Greenhalgh, T., & CATALISE consortium. (2016). CATALISE: A multinational and multidisciplinary Delphi consensus study. Identifying language impairments in children. *PLoS One, 11*(7), e0158753. doi:10.1371/journal.pone.0158753

Blumenthal, C., & Lundeborg Hammarström, I. (2014). LINUS LINköpingsUnderSökningen: Ett fonologiskt testmaterial från 3 år, *Skriftserie i logopedi [LINUS The Linköping investigation: A phonological test-battery*] Linköping: Linköping University Electronic Press. Available at: https://www.diva-portal.org/smash/get/diva2:737467/FULLTEXT01.pdf

Boyce, J. O., Kilpatrick, N., Reilly, S., Da Costa, A., & Morgan, A. T. (2018). Receptive and expressive language characteristics of school-aged children with non-syndromic cleft lip and/or palate. *Int J Lang Commun Disord, 53*(5), 959-968. doi:10.1111/1460-6984.12406

Boyce, J. O., Sanchez, K., Amor, D. J., Reilly, S., Da Costa, A., Kilpatrick, N., & Morgan, A. T. (2019). Exploring the speech and language of individuals with non-syndromic submucous cleft palate: a preliminary report. *Int J Lang Commun Disord, 54*(5), 767-778. doi:10.1111/1460-6984.12474

Britton, L., Albery, L., Bowden, M., Harding-Bell, A., Phippen, G., & Sell, D. (2014). A cross-sectional cohort study of speech in five-year-olds with cleft palate +/- lip to support development of national audit standards: Benchmarking speech standards in the United Kingdom. *Cleft Palate Craniofac J, 51*(4), 431-451. doi:10.1597/13-121

Centanni, T. M., Green, J. R., Iuzzini-Seigel, J., Bartlett, C. W., & Hogan, T. P. (2015). Evidence for the multiple hits genetic theory for inherited language impairment: A case study. *Front Genet, 6*, 272. doi:10.3389/fgene.2015.00272

Chapman, K., Dixon, A., Wilson, K., Dobbelsteyn, C., Cordero, K., Trost-Cardamone, J., . . . Baylis, A. (2017). *Benchmarking speech outcomes of kindergarteners with cleft palate*. Paper presented at the 74th Annual Meeting of the American Cleft palate - Craniofacial Association, The Broadmoor, Colorado Springs, CO.

Chetpakdeechit, W., Mohlin, B., Persson, C., & Hagberg, C. (2010). Cleft extension and risks of other birth defects in children with isolated cleft palate. *Acta Odontol Scand, 68*(2), 86-90. doi:10.3109/00016350903258003

Cleland, J., Wood, S., Hardcastle, W., Wishart, J., & Timmins, C. (2010). Relationship between speech, oromotor, language and cognitive abilities in children with Down's syndrome. *Int J Lang Commun Disord, 45*(1), 83-95. doi:10.3109/13682820902745453

Cloutman, L. L. (2013). Interaction between dorsal and ventral processing streams: where, when and how? *Brain Lang, 127*(2), 251-263. doi:10.1016/j.bandl.2012.08.003

Collett, B. R., Leroux, B. L., & Speltz, M. L. (2010). Language and early reading among children with orofacial clefts. *Cleft Palate Craniofac J, 47*, 284-292.

Crary, M. A., Landess, S., & Towne, R. (1984). Phonological error patterns in developmental verbal dyspraxia. *J Clin Neuropsychol, 6*(2), 157-170. doi:10.1080/01688638408401206

D'Antonio, L. L., Scherer, N. J., Miller, L. L., Kalbfleisch, J. H., & Bartley, J. A. (2001). Analysis of speech characteristics in children with velocardiofacial syndrome (VCFS) and children with phenotypic overlap without VCFS. *Cleft Palate Craniofac J, 38*(5), 455-467. doi:10.1597/1545-1569_2001_038_0455_aoscic_2.0.co_2

Darley, F. L. (1982). *Aphasia*. Philadelphia: W.B. Saunders Co.

DiDonato Brumbach, A. C., & Goffman, L. (2014). Interaction of language processing and motor skill in children with specific language impairment. *J Speech Lang Hear Res, 57*(1), 158-171. doi:10.1044/1092-4388(2013/12-0215)

Douglas, N. F., & Burshnic, V. L. (2019). Implementation Science: Tackling the research to practice gap in communication sciences and disorders. *Perspectives of the ASHA Special Interest Groups, 4*(February 2019), 3-7. doi:https://doi.org/10.1044/2018_PERS-ST-2018-0000

Duffy, J. R. (2020). *Motor speech disorders: Substrates, differential diagnosis, and management* (Fourth ed.). St. Louis, MO: Elsevier Mosby.

Fey, M. E. (1992). Clinical forum: articulation and phonology treatment. Articulation and phonology: inextricable constructs in speech pathology. *Lang Speech Hear Serv Sch*, (23), 225-232.

Fiori, S., Guzzetta, A., Mitra, J., Pannek, K., Pasquariello, R., Cipriani, P., . . . Chilosi, A. (2016). Neuroanatomical correlates of childhood apraxia of speech: A connectomic approach. *Neuroimage Clin, 12*, 894-901. doi:10.1016/j.nicl.2016.11.003

Forrest, K. (2003). Diagnostic criteria of developmental apraxia of speech used by clinical speech-language pathologists. *Am J Speech Lang Pathol, 12*(3), 376-380. doi:10.1044/1058-0360(2003/083)

Gibbon, F. E. (2004). Abnormal patterns of tongue-palate contact in the speech of individuals with cleft palate. *Clin Linguist Phon, 18*(4-5), 285-311.

Gibbon, F., Smeaton-Ewins, P., & Crampin, L. (2005). Tongue-palate contact during selected vowels in children with cleft palate. *Folia Phoniatr Logop, 57*(4), 181-192. doi:10.1159/000085186

Gierut, J. A., & Morrisette, M. L. (2005). The clinical significance of optimality theory for phonological disorders. *Top Lang Disord,* (25), 266-280.

Guyette, T., & Diedrich, W. (1981). A critical review of developmental apraxia of speech. In N. J. Lass (Ed.), *Speech and language: Advances in basic research and practice* (Vol. 5, pp. 1-49). New York, NY: Academic Press.

Hadden, W. B. (1891). On certain defects of articulations in children, with cases illustrating the results of education on the oral system. *J Ment Sci*, 96-105.

Hagberg, C., Larson, O., & Milerad, J. (1998). Incidence of cleft lip and palate and risks of additional malformations. *Cleft Palate Craniofac J, 35*(1), 40-45. doi:10.1597/1545-1569_1998_035_0040_ioclap_2.3.co_2

Hagoort, P. (2017). The core and beyond in the language-ready brain. *Neurosci Biobehav Rev, 81*(Pt B), 194-204. doi:10.1016/j.neubiorev.2017.01.048

Hall, K. P., Jordan, L.S., Robin, D.A. (1993). *Developmental Apraxia of Speech*. Austin, TX: Pro-ed.

Hardin-Jones, M., & Chapman, K. L. (2011). Cognitive and language issues associated with cleft lip and palate. *Semin Speech Lang, 32*(2), 127-140. doi:10.1055/s-0031-1277715

Harding, A., & Grunwell, P. (1996). Characteristics of cleft palate speech. *Eur J Disord Commun, 31*(4), 331-357. doi:10.3109/13682829609031326

Harding, A., & Grunwell, P. (1998). Active versus passive cleft-type speech characteristics. *Int J Lang Commun Disord, 33*(3), 329-352. doi:10.1080/136828298247776

Heselwood, B., & Howard, S. (2008). Clinical phonetic transcription. In M. J. Ball, M. Perkins, N. Müller & S. Howard (Eds.), *The Handbook of Clinical Linguistics* (p. 381–399) Oxford, UK: Whiley-Blackwell

Hickok, G. (2012). The cortical organization of speech processing: feedback control and predictive coding the context of a dual-stream model. *J Commun Disord, 45*(6), 393-402. doi:10.1016/j.jcomdis.2012.06.004

Hickok, G., & Poeppel, D. (2004). Dorsal and ventral streams: A framework for understanding aspects of the functional anatomy of language. *Cognition, 92*(1-2), 67-99. doi:10.1016/j.cognition.2003.10.011

Hickok, G., & Poeppel, D. (2007). The cortical organization of speech processing. *Nat Rev Neurosci, 8*(5), 393-402. doi:10.1038/nrn2113

Hill, E. L. (2001). Non-specific nature of specific language impairment: A review of the literature with regard to concomitant motor impairments. *Int J Lang Commun Disord, 36*(2), 149-171. doi:10.1080/13682820010019874

Howard, S. (2004). Compensatory articulatory behaviours in adolescents with cleft palate: Comparing the perceptual and instrumental evidence. *Clin Linguist Phon, 18*(4-5), 313-340. doi:10.1080/02699200410001701314

Hutters, B., & Brøndsted, K. (1987). Strategies in cleft palate speech - with special reference to Danish. *Cleft Palate J, 24*(2), 126-136.

Impellizzeri, A., Giannantoni, I., Polimeni, A., Barbato, E., & Galluccio, G. (2019). Epidemiological characteristic of Orofacial clefts and its associated congenital anomalies: retrospective study. *BMC Oral Health, 19*(1), 290. doi:10.1186/s12903-019-0980-5

Institute of Medicine, National Academies of Sciences, Engineering, Medicine. (2016). *Speech and Language Disorders in Children: Implications for the Social Security Administration's Supplemental Security Income Program*. Washington, DC: The National Academies Press.

IPA The International Phonetic Alphabet. (2005). Available at: https://www.internationalphoneticassociation.org/content/full-ipa-chart#ipachartpng

IPA The International Phonetic Alphabet, extIPA Symbols for disordered speech. (2008). Available at: https://www.internationalphoneticassociation.org/sites/default/files/extIPAChart2008.pdf.

Iuzzini, J. (2012). Inconsistency of speech in children with childhood apraxia of speech, phonological disorders and typically developing speech *[Unpublished doctoral dissertation]*. Available at: https://www.researchgate.net/profile/Jenya_Iuzzini-Seigel/publication/258693515_Inconsistency_of_speech_in_children_with_childhood_apraxia_of_speech_phonological_disorders_and_typical_speech/links/5808ded508ae993dc0507db5/Inconsistency-of-speech-in-children-with-childhood-apraxia-of-speech-phonological-disorders-and-typical-speech.pdf

Iuzzini-Seigel, J. (2019). Motor performance in children with childhood apraxia of speech and speech sound disorders. *J Speech Lang Hear Res, 62*(9), 3220-3233. doi:10.1044/2019_JSLHR-S-18-0380

Iuzzini, J., & Forrest, K. (2010). Evaluation of a combined treatment approach for childhood apraxia of speech. *Clin Linguist Phon, 24*(4-5), 335-345. doi:10.3109/02699200903581083

Iuzzini-Seigel, J., Hogan, T. P., & Green, J. R. (2017). Speech inconsistency in children with childhood apraxia of speech, language impairment, and speech delay: Depends on the stimuli. *J Speech Lang Hear Res, 60*(5), 1194-1210. doi:10.1044/2016_JSLHR-S-15-0184

Iuzzini-Seigel, J., Hogan, T. P., Guarino, A. J., & Green, J. R. (2015). Reliance on auditory feedback in children with childhood apraxia of speech. *J Commun Disord, 54*, 32-42. doi:10.1016/j.jcomdis.2015.01.002

Iuzzini-Seigel, J., & Murray, E. (2017). Speech assessment in children with childhood apraxia of speech. *Perspectives of the ASHA Special Interest Groups, 2*(2), 47-60. doi:10.1044/persp2.SIG2.47

Joffe, V., & Pring, T. (2008). Children with phonological problems: A survey of clinical practice. *Int J Lang Commun Disord, 43*(2), 154-164. doi:10.1080/13682820701660259

Josephs, K. A., Duffy, J. R., Strand, E. A., Machulda, M. M., Senjem, M. L., Master, A. V., . . . Whitwell, J. L. (2012). Characterizing a neurodegenerative syndrome: Primary progressive apraxia of speech. *Brain, 135*(Pt 5), 1522-1536. doi:10.1093/brain/aws032

Klintö, K., Brunnegård, K., Havstam, C., Appelqvist, M., Hagberg, E., Taleman, A. S., & Lohmander, A. (2019). Speech in 5-year-olds born with unilateral cleft lip and palate: A prospective Swedish intercenter study. *J Plast Surg Hand Surg, 53*(5), 309-315. doi:10.1080/2000656X.2019.1615929

Klintö, K., Salameh, E. K., & Lohmander, A. (2016). Phonology in Swedish-speaking 5-year-olds born with unilateral cleft lip and palate and the relationship with consonant production at 3 years of age. *Int J Speech Lang Pathol, 18*(2), 147-156. doi:10.3109/17549507.2015.1081287

Kuehn, D. P., & Moller, K. T. (2000). Speech and language issues in the cleft palate population: The state of the art. *Cleft Palate Craniofac Journal, 37*(4), 1-35. doi:10.1597/1545-1569_2000_037_0348_saliit_2.3.co_2

Kummer, A. W., Lee, L., Stutz, L. S., Maroney, A., & Brandt, J. W. (2007). The prevalence of apraxia characteristics in patients with velocardiofacial syndrome as compared with other cleft populations. *Cleft Palate Craniofac J, 44*(2), 175-181. doi:10.1597/05-170.1

Laffin, J. J., Raca, G., Jackson, C. A., Strand, E. A., Jakielski, K. J., & Shriberg, L. D. (2012). Novel candidate genes and regions for childhood apraxia of speech identified by array comparative genomic hybridization. *Genet Med, 14*(11), 928-936. doi:10.1038/gim.2012.72

Lagerberg, T. B., Hellstrom, A., Lundberg, E., & Hartelius, L. (2019). An investigation of the clinical use of a single-word procedure to assess intelligibility (Swedish test of intelligibility for children) and an evaluation of the validity and reliability of the intelligibility in context scale. *J Speech Lang Hear Res, 62*(3), 668-681. doi:10.1044/2018_JSLHR-S-18-0018

Lai, C. S., Fisher, S. E., Hurst, J. A., Vargha-Khadem, F., & Monaco, A. P. (2001). A forkhead-domain gene is mutated in a severe speech and language disorder. *Nature, 413*(6855), 519-523. doi:10.1038/35097076

Lancaster, H. S., Lien, K. M., Chow, J. C., Frey, J. R., Scherer, N. J., & Kaiser, A. P. (2020). Early speech and language development in children with nonsyndromic cleft lip and/or palate: A meta-analysis. *J Speech Lang Hear Res, 63*(1), 14-31. doi:10.1044/2019_JSLHR-19-00162

Law, J., Boyle, J., Harris, F., Harkness, A., & Nye, C. (2000). Prevalence and natural history of primary speech and language delay: Findings from a systematic review of the literature. *Int J Lang Commun Disord, 35*(2), 165-188. doi:10.1080/136828200247133

Lee, J. C., Dick, A. S., & Tomblin, J. B. (in press). Altered brain structures in the dorsal and ventral language pathways in individuals with and without developmental language disorder (DLD). *Brain Imaging Behav*. doi:10.1007/s11682-019-00209-1

Leow, A. M., & Lo, L. J. (2008). Palatoplasty: evolution and controversies. *Chang Gung Med J, 31*(4), 335-345.

Lewis, B. A., Freebairn, L. A., Hansen, A. J., Iyengar, S. K., & Taylor, H. G. (2004). School-age follow-up of children with childhood apraxia of speech. *Lang Speech Hear Serv Sch, 35*(2), 122-140. doi:10.1044/0161-1461(2004/014)

Liégeois, F., Mayes, A., & Morgan, A. (2014). Neural correlates of developmental speech and language disorders: Evidence from neuroimaging. *Curr Dev Disord Rep, 1*, 215-227. doi:10.1007/s40474-014-0019-1

Liégeois, F. J., Turner, S. J., Mayes, A., Bonthrone, A. F., Boys, A., Smith, L., . . . Morgan, A. T. (2019). Dorsal language stream anomalies in an inherited speech disorder. *Brain, 142*(4), 966-977. doi:10.1093/brain/awz018

Liepmann, H. (1900). Das Krankheitsbild der Apraxie (motorischen Asymbolie) auf Grund eines Falles von einseitiger Apraxie. [The disease profile of apraxia (motor asymbolia) in a case of unilateral apraxia] *Monatsschrift für Psychiatrie und Neurologie*, (8), 15-44, 102-132, 182-197.

Lohmander A. (2011) Surgical intervention and speech outcomes in cleft lip and palate. In S. Howard & A. Lohmander (Eds.). *Cleft Palate Speech: Assessment and Intervention.* Chichester: UK: John Wiley & Sons, Ltd.

Lohmander, A., Borell, E., Henningsson, G., Havstam, C., Lundeborg, I., & Persson, C. (2005). *SVANTE - SVenskt Artikulations- och Nasalitets-Test [SVANTE – The Swedish articulation and nasality test]*. Lund, Sweden: Pedagogisk Design.

Lohmander, A., Lundeborg, I., & Persson, C. (2017). SVANTE - The Swedish articulation and nasality test - Normative data and a minimum standard set for cross-linguistic comparison. *Clin Linguist Phon, 31*(2), 137-154. doi:10.1080/02699206.2016.1205666

Lohmander, A., & Persson, C. (2008). A longitudinal study of speech production in Swedish children with unilateral cleft lip and palate and two-stage palatal repair. *Cleft Palate Craniofac J, 45*(1), 32-41. doi:10.1597/06-123.1

Lohmander, A., Persson, C., Willadsen, E., Lundeborg, I., Alaluusua, S., Aukner, R., . . . Semb, G. (2017). Scandcleft randomised trials of primary surgery for unilateral cleft lip and palate: 4. Speech outcomes in 5-year-olds - velopharyngeal competency and hypernasality. *J Plast Surg Hand Surg, 51*(1), 27-37. doi:10.1080/2000656X.2016.1254645

Lundeborg I, McAllister A, Samuelsson C, Ericsson E, Hultcrantz E. (2009). Phonological development in children with obstructive sleep-disordered breathing. *Clin Linguist Phon,* 23(10), 751-61.

Márquez-Ávila, C. S., Vizcaíno-Alarcón, A., García-Delgado, C., Núñez-Martínez, P. M., Flores-Ramírez, F., Reyes-de la Rosa A del, P., . . . Morán-Barroso, V. F. (2015). Velocardiofacial syndrome in Mexican patients: Unusually high prevalence of congenital heart disease. *Int J Pediatr Otorhinolaryngol, 79*(11), 1886-1891. doi:10.1016/j.ijporl.2015.08.038

Mars, M., Sell, D., & Habel, A. (2008). Introduction. In M. Mars, D. Sell, & A. Habel, (Eds.), *Management of cleft lip and palate in the developing world*. Chichester, UK: John Wiley & Sons Ltd.

McAllister, A., & Lundeborg Hammarström, I. (2014). Oral sensorimotor functions in typically developing children 3 to 8 years old, assessed by the Nordic orofacial test, NOT-S. *J Med Speech-Lang Pathol, 21(1),* 51-59.

McCormack, J., McLeod, S., McAllister, L., & Harrison, L. J. (2010). My speech problem, your listening problem, and my frustration: The experience of living with childhood speech impairment. *Lang Speech Hear Serv Sch, 41*(4), 379-392. doi:10.1044/0161-1461(2009/08-0129)

McLeod, S. (2020). Intelligibility in context scale: Cross-linguistic use, validity, and reliability. *Speech. Language and Hearing, 23*(1), 9-16. doi:10.1080/2050571X.2020.1718837

McLeod, S., & Harrison, L. J. (2009). Epidemiology of speech and language impairment in a nationally representative sample of 4- to 5-year-old children. *J Speech Lang Hear Res, 52*(5), 1213-1229. doi:10.1044/1092-4388(2009/08-0085)

McLeod, S., Harrison, L. J., & McCormack, J. (2012a). The intelligibility in context scale: Validity and reliability of a subjective rating measure. *J Speech Lang Hear Res, 55*(2), 648-656. doi:10.1044/1092-4388(2011/10-0130)

McLeod, S., Harrison, L. J., & McCormack, J. (2012b). Skattning av Förståelighet i Kontext: Svenska [Intelligibility in Context Scale: Swedish]. In T. Lagerberg (Trans.). Bathurst, NSW, Australia: Charles Sturt University. Available at http://www.csu.edu.au/research/multilingual-speech/ics

McNeil, M. R., Robin, D. A., & Schmidt, R. A. (2009). Apraxia of speech: Theory and differential diagnosis. In M. R. McNeil (Ed.), *Clinical Management of sensorimotor speech disorders* (Second ed.). New York, NY: Thieme Medical Publishers.

McNeill, B. C., & Gillon, G. T. (2013). Expressive morphosyntactic development in three children with childhood apraxia of speech. *Speech, Language and Hearing*, 16(1), 9–17. doi:10.1179/2050571X12Z.0000000005

Meredith, A., & Potter. N. (2011). *Diagnostic criteria for childhood apraxia of speech: a survey study*. Poster presented at the ASHA convention, San Diego, CA. Poster retrieved from www.asha.org

Milerad, J., Larson, O., Hagberg, C., & Ideberg, M. (1997). Associated malformations in infants with cleft lip and palate: a prospective, population-based study. *Pediatrics, 100*(2 Pt 1), 180-186. doi:10.1542/peds.100.2.180

Morgan, A. T., Bellucci, C. C., Coppersmith, J., Linde, S. B., Curtis, A., Albert, M., . . . Kapp-Simon, K. (2017). Language development in children with cleft palate with or without cleft lip adopted from non-English-speaking countries. *Am J Speech Lang Pathol, 26*(2), 342-354. doi:10.1044/2016_AJSLP-16-0030

Morgan, A. T., & Liégeois, F. (2010). Re-thinking diagnostic classification of the dysarthrias: A developmental perspective. *Folia Phoniatr Logop, 62*(3), 120-126. doi:10.1159/000287210

Morgan, A. T., Su, M., Reilly, S., Conti-Ramsden, G., Connelly, A., & Liégeois, F. J. (2018). A brain marker for developmental speech disorders. *J Pediatr, 198*, 234-239 e231. doi:10.1016/j.jpeds.2018.02.043

Morgan, A. T., & Webster, R. (2018). Aetiology of childhood apraxia of speech: A clinical practice update for paediatricians. *J Paediatr Child Health, 54*(10), 1090-1095. doi:10.1111/jpc.14150

Morley, M. (1957). Developmental articulatory apraxia. *The development and disorders of speech in childhood* (First ed., p. 217-231). Edinburgh, UK: E. & S. Livingstone Ltd.

Morley, M. (1970). *Cleft Palate and Speech*. Edinburgh, UK: E. & S. Livingstone Ltd.

Morley, M., Court, D., & Miller, H. (1954). Developmental dysarthria. *Br Med J, 1*(4852), 8-10. doi:10.1136/bmj.1.4852.8

Moser, D., Basilakos, A., Fillmore, P., & Fridriksson, J. (2016). Brain damage associated with apraxia of speech: Evidence from case studies. *Neurocase, 22*(4), 346-356. doi:10.1080/13554794.2016.1172645

Murray, E., McCabe, P., Heard, R., & Ballard, K. J. (2015). Differential diagnosis of children with suspected childhood apraxia of speech. *J Speech Lang Hear Res, 58*(1), 43-60. doi:10.1044/2014_JSLHR-S-12-0358

Murray, E., Thomas, D., & McKechnie, J. (2019). Comorbid morphological disorder apparent in some children aged 4-5 years with childhood apraxia of speech: Findings from standardised testing. *Clin Linguist Phon, 33*(1-2), 42-59. doi:10.1080/02699206.2018.1513565

Norbury, C. F., Gooch, D., Wray, C., Baird, G., Charman, T., Simonoff, E., . . . Pickles, A. (2016). The impact of nonverbal ability on prevalence and clinical presentation of language disorder: Evidence from a population study. *J Child Psychol Psychiatry, 57*(11), 1247-1257. doi:10.1111/jcpp.12573

Nyberg, J., Peterson, P., & Lohmander, A. (2014). Speech outcomes at age 5 and 10 years in unilateral cleft lip and palate after one-stage palatal repair with minimal incision technique - a longitudinal perspective. *Int J Pediatr Otorhinolaryngol, 78*(10), 1662-1670. doi:10.1016/j.ijporl.2014.07.016

Pannbacker, M. (1988). Management strategies for developmental apraxia of speech: A review of literature. *J Commun Disord, 21*(5), 363-371. doi:10.1016/0021-9924(88)90021-4

Persson, C., Lohmander, A., Jonsson, R., Óskarsdóttir, S., & Söderpalm, E. (2003). A prospective cross-sectional study of speech in patients with the 22q11 deletion syndrome. *J Commun Disord, 36*(1), 13-47. doi:10.1016/s0021-9924(02)00133-8

Peter, B., Button, L., Stoel-Gammon, C., Chapman, K., & Raskind, W. H. (2013). Deficits in sequential processing manifest in motor and linguistic tasks in a multigenerational family with childhood apraxia of speech. *Clin Linguist Phon, 27*(3), 163-191. doi:10.3109/02699206.2012.736011

Peterson-Falzone, S., Hardin-Jones, M., Karnell, M. (2010). *Cleft Palate Speech* (Fourth ed.) St. Louis, MO: Mosby.

Poeppel, D., Emmorey, K., Hickok, G., & Pylkkanen, L. (2012). Towards a new neurobiology of language. *J Neurosci, 32*(41), 14125-14131. doi:10.1523/JNEUROSCI.3244-12.2012

Preston, J. L., Molfese, P. J., Mencl, W. E., Frost, S. J., Hoeft, F., Fulbright, R. K., . . . Pugh, K. R. (2014). Structural brain differences in school-age children with residual speech sound errors. *Brain Lang, 128*(1), 25-33. doi:10.1016/j.bandl.2013.11.001

Programs to examine phonetic and phonologic evaluation records (PEPPER). The Phonology Project. Available at https://phonology.waisman.wisc.edu/

Reddy, R. R., Gosla Reddy, S., Vaidhyanathan, A., Berge, S. J., & Kuijpers-Jagtman, A. M. (2017). Maxillofacial growth and speech outcome after one-stage or two-stage palatoplasty in unilateral cleft lip and palate. A systematic review. *J Craniomaxillofac Surg, 45*(6), 995-1003. doi:10.1016/j.jcms.2017.03.006

Rex, S., McAllister, A., Hansson, K. (2016). *Dynamisk motorisk talbedömning (DYMTA) [Dynamic evaluation of motor speech skills]*. Lund, Sweden: Kunskapsutveckling i Lund AB.

Rice, M. L., & Hoffman, L. (2015). Predicting vocabulary growth in children with and without specific language impairment: a longitudinal study from 2;6 to 21 years of age. *J Speech Lang Hear Res, 58*(2), 345-359. doi:10.1044/2015_JSLHR-L-14-0150

Rolheiser, T., Stamatakis, E. A., & Tyler, L. K. (2011). Dynamic processing in the human language system: synergy between the arcuate fascicle and extreme capsule. *J Neurosci, 31*(47), 16949-16957. doi:10.1523/JNEUROSCI.2725-11.2011

Rosenbek, J. (1978). Treating apraxia of speech In D. Johns (Ed.), *Clinical Management of Neurogenic Communication Disorders* (pp. 191-241). Boston, MA: Little Brown.

Rosenbek, J., & Wertz, R. (1972). A review of 50 cases of developmental apraxia of speech. *Lang Speech Hear Serv Sch* (3), 23-33.

Rutjens, C. A., Spauwen, P. H., & van Lieshout, P. H. (2001). Lip movement in patients with a history of unilateral cleft lip. *Cleft Palate Craniofac J, 38*(5), 468-475. doi:10.1597/1545-1569_2001_038_0468_lmipwa_2.0.co_2

Sell, D., Mildinhall, S., Albery, L., Wills, A. K., Sandy, J. R., & Ness, A. R. (2015). The cleft care UK study. Part 4: Perceptual speech outcomes. *Orthod Craniofac Res, 18 Suppl 2*, 36-46. doi:10.1111/ocr.12112

Semb, G., Enemark, H., Friede, H., Paulin, G., Lilja, J., Rautio, J., . . . Worthington, H. (2017). A Scandcleft randomised trials of primary surgery for unilateral cleft lip and palate: 1. Planning and management. *J Plast Surg Hand Surg, 51*(1), 2-13. doi:10.1080/2000656X.2016.1263202

Semel, E., Wiig, E. H., & Secord, W. A. (2013). *Clinical evaluation of language fundamentals-Forth Edition (CELF-4), [Swedish version]* Stockholm, Sweden: Pearson Assessment.

Shriberg, L. D. (1993). Four new speech and prosody-voice measures for genetics research and other studies in developmental phonological disorders. *J Speech Hear Res, 36*(1), 105-140. doi:10.1044/jshr.3601.105

Shriberg, L. D. (2010a). Childhood speech sound disorders: From postbehaviorism to the postgenomic era. In R. Paul & P. Flipsen (Eds.), *Speech Sound Disorders in Children* (pp. 1-33). San Diego, CA: Plural Publishing.

Shriberg, L. D. (2010b). A neurodevelopmental framework for research in childhood apraxia of speech. In B. Maassen, & P. van Lieshout (Eds.), *Speech motor control: New developments in basic and applied research* (pp. 259-270). Oxford, UK: Oxford University Press.

Shriberg, L. D., Aram, D. M., & Kwiatkowski, J. (1997). Developmental apraxia of speech: I. Descriptive and theoretical perspectives. *J Speech Lang Hear Res, 40*(2), 273-285.

Shriberg, L. D., Campbell, T. F., Karlsson, H. B., Brown, R. L., McSweeny, J. L., & Nadler, C. J. (2003). A diagnostic marker for childhood apraxia of speech: The lexical stress ratio. *Clin Linguist Phon, 17*(7), 549-574.

Shriberg, L. D., Fourakis, M., Hall, S. D., Karlsson, H. B., Lohmeier, H. L., McSweeny, J. L., . . . Wilson, D. L. (2010). Extensions to the speech disorders classification system (SDCS). *Clin Linguist Phon, 24*(10), 795-824. doi:10.3109/02699206.2010.503006

Shriberg, L. D., & Kwiatkowski, J. (1982). Phonological disorders III: A procedure for assessing severity of involvement. *J Speech Hear Disord, 47*(3), 256-270.

Shriberg, L. D., Lohmeier, H. L., Strand, E. A., & Jakielski, K. J. (2012). Encoding, memory, and transcoding deficits in childhood apraxia of speech. *Clin Linguist Phon, 26*(5), 445-482. doi:10.3109/02699206.2012.655841

Shriberg, L. D., Potter, N. L., & Strand, E. A. (2011). Prevalence and phenotype of childhood apraxia of speech in youth with galactosemia. *J Speech Lang Hear Res, 54*(2), 487-519. doi:10.1044/1092-4388(2010/10-0068)

Shriberg, L. D., Strand, E. A., Fourakis, M., Jakielski, K. J., Hall, S. D., Karlsson, H. B., . . . Wilson, D. L. (2017a). A diagnostic marker to discriminate childhood apraxia of speech from speech delay: I. Development and description of the pause marker. *J Speech Lang Hear Res, 60*(4), S1096-S1117. doi:10.1044/2016_JSLHR-S-15-0296

Shriberg, L. D., Strand, E. A., Fourakis, M., Jakielski, K. J., Hall, S. D., Karlsson, H. B., . . . Wilson, D. L. (2017b). A diagnostic marker to discriminate childhood apraxia of speech from speech delay: II. Validity studies of the pause marker. *J Speech Lang Hear Res, 60*(4), S1118-S1134. doi:10.1044/2016_JSLHR-S-15-0297

Shriberg, L. D., Strand, E. A., Fourakis, M., Jakielski, K. J., Hall, S. D., Karlsson, H. B., . . . Wilson, D. L. (2017c). A diagnostic marker to discriminate childhood apraxia of speech from speech delay: III. Theoretical coherence of the pause marker with speech processing deficits in childhood apraxia of speech. *J Speech Lang Hear Res, 60*(4), S1135-S1152. doi:10.1044/2016_JSLHR-S-15-0298

Shriberg, L. D., Strand, E. A., Fourakis, M., Jakielski, K. J., Hall, S. D., Karlsson, H. B., . . . Wilson, D. L. (2017d). A diagnostic marker to discriminate childhood apraxia of speech from speech delay: IV. The pause marker index. *J Speech Lang Hear Res, 60*(4), S1153-S1169. doi:10.1044/2016_JSLHR-S-16-0149

Shriberg, L. D., Strand, E. A., Jakielski, K. J., & Mabie, H. L. (2019). Estimates of the prevalence of speech and motor speech disorders in persons with complex neurodevelopmental disorders. *Clin Linguist Phon, 33*(8), 707-736. doi:10.1080/02699206.2019.1595732

Shriberg, L. D. & McSweeny, J. L. (2002). Classification and misclassification of childhood apraxia of speech. (Tech. Rep. No. 11). Phonology Project, Waisman Center, University of Wisconsin-Madison. Available at: https://phonology.waisman.wisc.edu/wp-content/uploads/sites/532/2018/05/TREP11.pdf

Shrubsole, K., Worrall, L., Power, E., & O'Connor, D. A. (2018). The acute aphasia implementation study (AAIMS): A pilot cluster randomized controlled trial. *Int J Lang Commun Disord, 53*(5), 1021-1056. doi:10.1111/1460-6984.12419

Smith, A., & Zelaznik, H. N. (2004). Development of functional synergies for speech motor coordination in childhood and adolescence. *Dev Psychobiol, 45*(1), 22-33. doi:10.1002/dev.20009

Solot, C. B., Sell, D., Mayne, A., Baylis, A. L., Persson, C., Jackson, O., & McDonald-McGinn, D. M. (2019). Speech-language disorders in 22q11.2 deletion syndrome: Best practices for diagnosis and management. *Am J Speech Lang Pathol, 28*(3), 984-999. doi:10.1044/2019_AJSLP-16-0147

Spiteri, E., Konopka, G., Coppola, G., Bomar, J., Oldham, M., Ou, J., . . . Geschwind, D. H. (2007). Identification of the transcriptional targets of FOXP2, a gene linked to speech and language, in developing human brain. *Am J Hum Genet, 81*(6), 1144-1157. doi:10.1086/522237

Stone, M., Shawker, T. H., Talbot, T. L., & Rich, A. H. (1988). Cross-sectional tongue shape during the production of vowels. *J Acoust Soc Am, 83*(4), 1586-1596. doi:10.1121/1.395913

Stothard, S. E., Snowling, M. J., Bishop, D. V., Chipchase, B. B., & Kaplan, C. A. (1998). Language-impaired preschoolers: a follow-up into adolescence. *J Speech Lang Hear Res, 41*(2), 407-418. doi:10.1044/jslhr.4102.407

Strand, E. A. (2020). Dynamic temporal and tactile cueing: A treatment strategy for childhood apraxia of speech. *Am J Speech Lang Pathol, 29*(1), 30-48. doi:10.1044/2019_AJSLP-19-0005

Strand, E. A. & McCauley, R. J. (2019). *Dynamic evaluation of motor speech skill (DEMS)*. Baltimore, MD: Brookes

Thoonen, G., Maassen, B., Gabreels, F., Schreuder, R., & de Swart, B. (1997). Towards a standardised assessment procedure for developmental apraxia of speech. *Eur J Disord Commun, 32*(1), 37-60. doi:10.3109/13682829709021455

Tillman, K. K., Hakelius, M., Hoijer, J., Ramklint, M., Ekselius, L., Nowinski, D., & Papadopoulos, F. C. (2018). Increased risk for neurodevelopmental disorders in children with orofacial clefts. *J Am Acad Child Adolesc Psychiatry, 57*(11), 876-883. doi:10.1016/j.jaac.2018.06.024

Van Lierde, K. M., Bettens, K., Luyten, A., Plettinck, J., Bonte, K., Vermeersch, H., & Roche, N. (2014). Oral strength in subjects with a unilateral cleft lip and palate. *Int J Pediatr Otorhinolaryngol, 78*(8), 1306-1310. doi:10.1016/j.ijporl.2014.05.017

Vargha-Khadem, F., Gadian, D. G., Copp, A., & Mishkin, M. (2005). FOXP2 and the neuroanatomy of speech and language. *Nat Rev Neurosci, 6*(2), 131-138. doi:10.1038/nrn1605

Vargha-Khadem, F., Watkins, K. E., Price, C. J., Ashburner, J., Alcock, K. J., Connelly, A., . . . Passingham, R. E. (1998). Neural basis of an inherited speech and language disorder. *Proc Natl Acad Sci U S A, 95*(21), 12695-12700. doi:10.1073/pnas.95.21.12695

Watkins, K. E., Dronkers, N. F., & Vargha-Khadem, F. (2002). Behavioural analysis of an inherited speech and language disorder: comparison with acquired aphasia. *Brain, 125*(Pt 3), 452-464. doi:10.1093/brain/awf058

Willadsen, E., Lohmander, A., Persson, C., Lundeborg, I., Alaluusua, S., Aukner, R., . . . Semb, G. (2017). Scandcleft randomised trials of primary surgery for unilateral cleft lip and palate: 5. Speech outcomes in 5-year-olds - consonant proficiency and errors. *J Plast Surg Hand Surg, 51*(1), 38-51. doi:10.1080/2000656X.2016.1254647

Williams, R., Ingham, R. J., & Rosenthal, J. (1981). A further analysis for developmental apraxia of speech in children with defective articulation. *J Speech Hear Res, 24*(4), 496-505. doi:10.1044/jshr.2404.496

Vuolo, J., & Goffman, L. (2018). Language skill mediates the relationship between language load and articulatory variability in children with language and speech sound disorders. *J Speech Lang Hear Res, 61*(12), 3010-3022. doi:10.1044/2018_JSLHR-L-18-0055

Yoss, K. A., & Darley, F. L. (1974). Developmental apraxia of speech in children with defective articulation. *J Speech Hear Res, 17*(3), 399-416. doi:10.1044/jshr.1703.399

Zelaznik, H. N., & Goffman, L. (2010). Generalized motor abilities and timing behavior in children with specific language impairment. *J Speech Lang Hear Res, 53*(2), 383-393. doi:10.1044/1092-4388(2009/08-0204)

Zuk, J., Iuzzini-Seigel, J., Cabbage, K., Green, J. R., & Hogan, T. P. (2018). Poor speech perception is not a core deficit of childhood apraxia of speech: Preliminary findings. *J Speech Lang Hear Res, 61*(3), 583-592. doi:10.1044/2017_JSLHR-S-16-0106

Zwaan, R. A., Etz, A., Lucas, R. E., & Donnellan, M. B. (2018). Improving social and behavioral science by making replication mainstream: A response to commentaries. *Behav Brain Sci, 41*, e157. doi:10.1017/S0140525X18000961