Supplemental Material S1. CAS in special populations.

The capsule descriptions below highlight select populations in which CAS has been reported. Here we describe communication and motor deficits evidenced by some of the complex genetic, metabolic, and neurobehavioral populations that have been previously associated with CAS. The occurrence of CAS in different disorder groups may hold clues regarding its nature and origin.

Genetic Disorders

Galactosemia

Galactosemia is a metabolic disorder that affects the processing of the milk sugar, galactose, and affects 1/53,000 infants in the United States (National Newborn Screening and Genetics Resource Center). All subtypes of galactosemia are associated with cognitive-linguistic and speech disorders and although severity may be impacted by postnatal exposure to milk, even children with no postnatal exposure are at risk due to intrauterine exposure. A survey of 243 individuals with galactosemia revealed that 60% reported a history of speech disorders (Waggoner, Buist, & Donnell, 1990). Nelson and colleagues (Nelson, Waggoner, Tuerck, Donnell, & Buist, 1991) performed speech evaluations on 24 individuals with galactosemia and found that 54% evidenced "verbal dyspraxia." Webb and colleagues (Webb, Singh, Kennedy, & Elsas, 2003) conducted speech evaluations in 24 individuals with galactosemia and similarly found that 15 out of 24 (63%) patients evidenced "verbal dyspraxia." More recent prevalence estimates suggest that CAS is observed in 18% of children with galactosemia (Shriberg, Potter, & Strand, 2011). Discrepancies between the earlier studies and Shriberg et al.'s (2011) investigation are likely due to differences in diagnostic criteria across studies.

All of the studies that investigated the communication profiles of children with galactosemia also reported language impairments and low cognition in a large percentage of participants. Potter and colleagues (Potter, Lazarus, Johnson, Steiner, & Shriberg, 2008) reported that 15 of out 17 participants with borderline-low cognition had receptive and expressive language impairments and 9 out of 16 participants with typical cognition had language impairment, most often affecting only expressive language. Likewise, Waggoner and colleagues found that 45% of children with galactosemia evidenced low cognition with IQs below the normal limit. In addition, they found that 52% displayed language impairments (Nelson et al., 1991; Waggoner et al., 1990). It is clear that even at the low end of the prevalence estimates, CAS occurs 180 times more frequently in children with galactosemia than in the general population and comes with cognitive-linguistic deficits that will also impact learning and response to treatment.

Down Syndrome

Individuals with Down syndrome have a third copy of chromosome 21 (hence the name Trisomy 21) and are known to have challenges in speech and cognitive-linguistic skills as well as craniofacial dysmorphologies such as hard palate anomalies and macroglossia (Kent & Vorperian, 2013). Dysarthria frequently occurs in this population, resulting in decreased precision of consonants and vowels (Kent & Vorperian, 2013). In addition, a subset of children are thought to have oral motor apraxia and/or CAS (Kumin, 2006; Rupela, Velleman, & Andrianopoulos, 2016). Historically, children with Down syndrome have often been excluded from studies on CAS due to frequent co-occurrence of muscle weakness, craniofacial dysmorphology, hearing loss, and low IQ scores as the presence of these conditions complicates the diagnosis of CAS. However, CAS is reported to be present in a substantial number of children in this population. In a survey of 1620 parents of children with Down syndrome, 15% reported that their child had a diagnosis of CAS (Kumin, 2006). Kumin found that those with CAS showed a later onset of speech and lower speech intelligibility ratings relative to children with Down syndrome without CAS. In addition, some parents also reported that their child evidenced signs of CAS (e.g., inconsistent

errors, vowel errors) but did not have a formal CAS diagnosis. Rupela et al. (2016) investigated motor speech skills in 7 children with Down syndrome. Findings showed that over 50% of participants with Down syndrome met nearly all CAS diagnostic criteria, suggesting a higher prevalence of CAS in this population than previously reported. Overall, participants tended to display a mixed profile of CAS and dysarthria, showing within-group variability and overlapping symptoms of the disorder types.

Fragile X

Fragile X syndrome occurs when there is a single-gene mutation on the X chromosome and is considered the most common inherited cause of cognitive impairments (Abbeduto & Hagerman, 1997). This disorder is associated with a range of oromotor, generalized motor and communication deficits including word finding difficulties, cluttering, and CAS (Hanson, Jackson, Hagerman, Opitz, & Reynolds, 1986; Spinelli, Rocha, Ana Clelia De Oliveira, Giacheti, & Richieri-Costa, 1995). Spinelli and colleagues (Spinelli et al., 1995) examined speech and language abilities in 10 Brazilian participants with Fragile X and found that nearly half of participants demonstrated word-finding challenges and signs of CAS. Other research shows that males are affected more severely than females and that males with Fragile X are more likely to have hearing loss associated with recurrent ear infections, low intelligibility, rate variability, stuttering-like sound repetitions, and features of CAS such as vowel errors (Abbeduto & Hagerman, 1997; Vilkman, Niemi, & Ikonen, 1988). In addition, males tend to show perseveration of words, phrases and even topics (Abbeduto & Hagerman, 1997). In contrast, females tend to demonstrate tangential language, which may be associated with frontal lobe dysfunction rather than speech deficits.

Neurodevelopmental Diagnoses

Seizure Disorders

There are many etiologies for seizures in children including high fevers, genetic anomalies, metabolic disorders, and hypoxic ischemic encephalopathy as could occur following a birth injury (National Center for Chronic Disease Prevention and Health Promotion, 2019). Whereas some children will experience a single seizure in their lifetime, such as an infantile febrile seizure, others will experience recurrent unprovoked seizures throughout childhood and beyond. Recurrent unprovoked seizures (i.e., epilepsy), affect .6% of children younger than 17 years amounting to 470,000 children in the United States with a diagnosis of epilepsy (National Center for Chronic Disease Prevention and Health Promotion, 2019). Some children with seizures may experience a wide range of deficits related to the disorder that underlies the seizure activity, or to the seizure activity itself. Deficits include cognitive and other developmental delays (Bellinger et al., 1999). CAS has been noted to occur with several forms of epilepsy (Caspari, Strand, Kotagal, & Bergqvist, 2008; Roll et al., 2006) including autosomal dominant rolandic epilepsy, which is a rare form associated with severe and long-term communicative disorders (Scheffer et al., 1995). Scheffer and colleagues (1995) investigated a family with benign rolandic epilepsy and found that all five members with this diagnosis evidenced signs of oral and speech apraxia. In some cases, speech deficits and apraxic symptoms may occur during seizure activity but will resolve after the seizure has ended or following treatment with antiepileptic medication, whereas others will evidence persistent communication disorders.

Autism Spectrum Disorder

The autism diagnosis is commonly associated with speech, language and oromotor deficits, and in some cases, with CAS (Boyar et al., 2001). The literature reports that children with autism evidence a range of verbal output from nonverbal or single word output to children with advanced vocabulary and language abilities (Smith, Mirenda, & Zaidman-Zait, 2007; Tager-Flusberg, Paul, & Lord, 2005; Tager-Flusberg et al., 2009) and frequently evidence prosodic variations wherein atypical stress or a 'sing song' intonation is used (Van Santen, Prud'Hommeaux, Black, & Mitchell, 2010). The extant research on the

comorbidity of CAS and autism is equivocal (Boyar et al., 2001; Shriberg, Paul, Black, & Van Santen, 2011) with some studies showing a high rate of comorbid CAS in families with heritable genetic diagnoses associated with autism (e.g., 15q11-q13 (Boyar et al., 2001) and other studies showing no association (Shriberg et al., 2011). Shriberg and colleagues (2011) examined speech in 46 children aged 4-7 years of age with autism. Participants were part of a larger study investigating prosody in children with autism and consequently, they were required to have fluent language production. Because of this, study results have limited external validity as children with CAS can have highly limited verbal output and therefore would not meet this verbal fluency inclusionary criterion. Shriberg and colleagues found that 15% of participants evidenced signs of speech delay and 32% evidenced speech errors of sibilants or rhotics. In contrast, none of their participants demonstrated features of CAS. It is possible that if a more severe group of children with autism were investigated, the findings could reveal comorbid CAS.

Attention-Deficit/Hyperactivity Disorder

Attention-deficit/hyperactivity disorder (ADHD) is characterized by low attention, high impulsivity, and difficulty with self-regulation and modulation of activity level (Rappley, 2005); together, this constellation of symptoms leads to social and academic difficulties (Redmond, 2011). Underlying mechanisms of ADHD include the dopamine and norepinephrine transmitter systems in the frontostriatal circuitry (Rappley, 2005). Genetics, low birthweight, head injury, and exposure to toxins (e.g., lead) are also associated with increased risk of ADHD. While there are three types of ADHD, 80% of patients are diagnosed with the combined inattentive, hyperactive and impulsive variant (Rappley, 2005). ADHD occurs more often in males than females (2.5-9:1 depending on the study) and affects 3-7% of all children (Rappley, 2005). In addition to the challenging symptoms associated with ADHD, this diagnosis often co-occurs with language impairment, learning disabilities, dyslexia (Cohen et al., 2000; Tirosh & Cohen, 1998), and motor impairments like developmental coordination disorder (Blondis, 1999); consequently, these comorbidities further compound the difficulties these children experience in achieving success in academic and social environments. A parent survey (n = 201) of functional characteristics of children with CAS (Teverovsky, Bickel, & Feldman, 2009) revealed that poor focus and difficulty maintaining attention were among the most prevalent functional issues reported for children with CAS. The Procedural Deficit Hypothesis (Ullman & Pierpont, 2005) has been used to explain the co-occurrence of disorders such as ADHD, dyslexia, language impairment and developmental coordination disorder. The procedural learning system is the mechanism by which we learn patterns without being explicitly taught. Practice and multiple repetitions help patterns to become stored in the procedural memory and lead to automaticity of production. We use the procedural learning system to acquire the patterns needed to produce speech sounds, grammatical rules, and motor acts. Consequently, a procedural learning deficit can lead to impairments in both cognitive-linguistic and motor domains, including comorbidity of speech, language, and motor impairments in children with CAS.

Hypotonia and Dysarthria

CAS is a problem of motor planning or programming that occurs in the *absence* of neuromuscular deficits such as abnormal reflexes or tone (American Speech-Language-Hearing Association, 2007). By definition, hypotonia and dysarthria are not part of the CAS diagnosis, but it is not uncommon for children with CAS to evidence dysarthria or generalized hypotonia as a comorbidity (Laffin et al., 2012). Some of the medical diagnoses (e.g., Down syndrome, galactosemia) that are associated with CAS, are also associated with low tone and dysarthria (Ridel, Leslie, & Gilbert, 2005). For children with galactosemia, those who fail to receive immediate treatment at birth are at greater risk for developing neurological issues including hypotonia (Ridel et al., 2005). When hypotonia--and specifically dysarthria associated with hypotonia--is concurrent with CAS, we could expect a compounded effect on speech production.

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