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3 **Rhythm and timing as vulnerabilities in neurodevelopmental**
4 **disorders**

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1 **Abstract**

2 Millions of children are impacted by neurodevelopmental disorders, which unfold early in life, have
3 varying genetic etiologies, and can involve a variety of specific or generalized impairments in social,
4 cognitive, and motor functioning requiring potentially life-long specialized supports. While specific
5 disorders vary in their domain of primary deficit (e.g., autism spectrum disorder (social), attention-
6 deficit/hyperactivity disorder (attention), developmental coordination disorder (motor), developmental
7 language disorder (language)), comorbidities between neurodevelopmental disorders are common.
8 Intriguingly, many neurodevelopmental disorders are associated with difficulties in skills related to
9 rhythm, timing, and synchrony though specific profiles of rhythm and timing impairments vary across
10 disorders. Impairments in rhythm and timing may instantiate vulnerabilities for a variety of
11 neurodevelopmental disorders and may contribute to both the primary symptoms of each disorder as
12 well as the high levels of comorbidities across disorders. Drawing upon genetic, neural, behavioural, and
13 interpersonal constructs across disorders, we consider how disrupted rhythm and timing skills early in
14 life may contribute to atypical developmental cascades that involve overlapping symptoms within the
15 context of a disorder's primary deficits. Consideration of the developmental context, as well as common
16 and unique aspects of the phenotypes of different neurodevelopmental disorders, will inform
17 experimental designs to test this hypothesis including via potential mechanistic intervention approaches.

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20 **Keywords:** neurodevelopmental disorders, rhythm, synchrony, language disorders, autism spectrum
21 disorder, developmental coordination disorder

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1 **Introduction**

2 Rhythm and timing are essential to successful development. Beginning in the neonatal period,
3 infants are sensitive to rhythmic regularities present in music and speech, with EEG studies indicating
4 detection of auditory changes occurring at rhythmically salient moments[1,2]. According to some
5 theories, humans’ sensitivity to rhythm to coordinate behavior is essential to the forming of social bonds
6 critical for survival[3]. The importance of rhythm is exemplified by its prominence in infant-directed
7 communication, which provides a predictable, temporal structure to facilitate coordinated interaction
8 between infant and caregiver (e.g., modulation of attention, turn-taking vocal exchanges)[4]. Rhythm is
9 also salient to infants in part because it crosses modalities[5]: for example, a mother singing a nursery
10 rhyme to her child provides integrated rhythmic information across auditory (vocal acoustics), visual
11 (facial and body movements), vestibular (rocking/bouncing motion) and haptic (patting child)
12 modalities. By supporting temporal predictions regarding when and what will occur across modalities,
13 rhythm provides a foundation for individuals to attend to the world around them and plan and execute
14 behaviors. Indeed, success in early temporal coordination such as measured, e.g., by the relative
15 durations of interpersonal pauses during an adult-infant vocal interaction, predicts an array of socio-
16 cognitive outcomes in language, cognition, and attachment (e.g., 4).

17 Given the fundamental role of rhythm in typical development, it is perhaps not surprising that
18 impairments in rhythm, timing, and synchrony / coordination occur across a variety of
19 neurodevelopmental disorders (NDDs)[6–8]. NDDs, which impact millions of children and include both
20 relatively common (e.g., attention-deficit/hyperactivity disorder (ADHD); autism spectrum disorder
21 (ASD); developmental coordination disorder (DCD); language disorders) and rare (e.g., specific genetic
22 syndromes) disorders, begin early in life and may require life-long, specialized supports. NDDs are
23 characterized by specific constellations of strengths and weaknesses that involve cognitive, sensory,
24 motor, and social functioning (Table 1). While the etiology and primary diagnostic deficit(s) of specific
25 disorders vary, overlapping behavioral symptoms occur across NDDs and comorbidities between
26 disorders are common[9]. Here we explore an emerging framework that suggests that impairments in
27 rhythm and time processing may be associated with comorbidities and common areas of divergence from
28 typical development across different NDDs; moreover, individual differences in rhythm processing could
29 explain heterogeneity of skill development within disorders. In the current paper, we integrate
30 knowledge from genetic, neuroscientific, behavioral and clinical perspectives to examine the
31 development of rhythm in its phenotypic correlations and biological underpinnings across NDDs. We
32 review cross-domain rhythm skills in a variety of NDDs and propose future directions that include
33 rhythm in models of typical and atypical human development.

34
35 **Genetic and Neural Perspectives in Rhythm/Timing Impairments: It’s Time for a Transdiagnostic**
36 **Approach**

37 Human rhythm and timing sensitivities emerge very early in development and contribute to
38 adaptive behaviors including language and social communication. If (impaired) rhythm processing plays
39 a role in the manifestation of NDDs, we must consider what genetic factors might play a role in the
40 development of rhythm processing. Similar to most cognitive traits that vary across the population, there
41 is a continuous, normal distribution of rhythm sensitivity / skill in the population, and these individual
42 differences can provide a lens into the underlying biology. Rhythm-related skills such as rhythm
43 discrimination and sensorimotor tapping show moderate *heritability* (i.e., a proportion of the variance in
44 rhythm skills are due to genetic factors), as demonstrated by twin studies (e.g. [10]). The molecular
45 genetics underlying rhythm ability have also been recently investigated in a large-scale genome-wide
46 association study (GWAS)[11]. Genetic associations with self-reported beat synchronization were
47 examined in N=606,825 (the phenotype was responses to the item “*Can you clap in time with a musical*
48 *beat?*”, validated in relation to task-based synchronization to a musical beat in a separate sample).
49 Findings indicated a highly polygenic genetic architecture, i.e., beat synchronization is associated with
50 genetic variation at a large number of genomic loci occurring widely across the genome. These genetic
51 associations showed enrichment for regions of the genome that regulate gene expression in the central

1 nervous system, both in fetal and adult brain tissue, highlighting potential early neurodevelopmental
2 processes. The study also uncovered genetic *pleiotropy* (shared genetic architecture among distinct
3 traits[12]) between beat synchronization and two types of biological rhythms: respiration and circadian
4 chronotypes.

5 These initial GWAS results for rhythm align with conceptual frameworks of ongoing work in the
6 psychiatric genetics field showing that widespread pleiotropy among cognitive / neurological traits is the
7 rule rather than exception[13]. Not only is there emerging evidence of pleiotropy between neurological
8 and psychiatric traits[14,15], but recent work analyzing the relationship between over 500 GWAS's shows
9 that 90% of genomic loci were linked to multiple traits[16]. Indeed, pleiotropic genetic effects span
10 clinical / developmental boundaries[13] and are reported for a growing number of clinically distinct
11 disorders (see for example shared genetic liability of reading disability with several other NDD
12 traits[17,18]). The Atypical Rhythm Risk Hypothesis (ARRH) predicts that genetic liability for atypical
13 rhythm increases the risk of diverse developmental speech and language problems in part through
14 genetic pleiotropy[6]. As evidence for this, ARRH points to atypical rhythm as a frequent feature among
15 developmental speech and language disorders, with converging evidence of atypical rhythm in motor
16 and attentional disorders that are often co-morbid with speech and language disorders[6]. Many different
17 aspects of atypical rhythm task performance (e.g., rhythm discrimination, beat perception and
18 synchronization) have been linked to these disorders (see below and Supplemental Table 1); there is not a
19 clear, consistent pattern of a specific type of atypical rhythm being systemically linked only to a specific
20 disorder. Indeed, performance on different rhythm tasks tends to be correlated[19], which may reflect
21 some degree of underlying pleiotropy[12]. Per ARRH, some shared variance among genetics of atypical
22 rhythm skills is expected to also overlap with developmental speech and language problems.
23 Furthermore, frameworks such as ARRH are consistent with the development of transdiagnostic criteria
24 [20], which focus on identifying behavioral and biological features co-occurring across diagnostically
25 distinct conditions as an alternative to identifying single "core deficits" of each diagnosis, (see [21] for
26 discussion of the limitations of core-deficit hypotheses in NDDs, and Table 1 for examples of cross-
27 disorder comorbidities).

28 Genetic liabilities may link to impairments across disorders through neural endophenotypes for
29 rhythm and time processing[6]. Rhythm and time perception and production involve interactions
30 between the auditory and motor systems. Auditory rhythm processing involves a network of cortical and
31 subcortical motor areas including basal ganglia, cerebellum, premotor cortex, and supplementary motor
32 area (see [22] for a review). Neurologically, listening to auditory rhythms without movement activates
33 motor regions of the brain (e.g.,[22,23]) and both transient brain stimulation and neurological disorders
34 affecting motor regions impair time perception (e.g.,[24,25]). People's rhythm perception is impacted by
35 how they move to the music[26] – or, in the case of infants, how the infants are moved to the music[27] --
36 as by vestibular stimulation[28]. Rhythm processing is subserved by neural oscillatory activity that
37 synchronizes to external stimuli. Under frameworks such as Dynamic Attending Theory [29], neural
38 entrainment to rhythmic stimuli involves extracting regularities from incoming sensory input to develop
39 expectancies (predictions) regarding timing and content of upcoming events. Neural entrainment to
40 rhythmic signals such as music and speech is also modulated by attention and experience[30,31].
41 Structural abnormalities and atypical functional activity for rhythm and time processing are observed
42 across a variety of NDDs including speech / language disorders, developmental coordination disorder,
43 ASD, and rare genetic syndromes (see below).

44 **Rhythm and Timing Profiles in NDDs**

45 We next review profiles of NDDs with a focus on the common theme of atypical rhythm skills
46 and their association with a variety of functional impairments on tasks targeting attention, language,
47 communication, and social functioning. We included disorders for which extant research has considered
48 multiple aspects of rhythm and timing skills and because of their patterns of comorbidity with each other
49 in these different domains of functioning.
50

1 **Speech/Language Disorders**

2 Speech/language disorders are common in childhood (3-16%) though many children are not
3 formally diagnosed or treated[32]. As summarized in the Atypical Rhythm Risk Hypothesis (ARRH)[6],
4 accumulating evidence demonstrates impaired timing skills across a variety of speech/language
5 disorders, which exhibit frequent comorbidities among each other and with other disorders such as
6 ADHD and DCD. The majority of rhythm research in speech/language disorders thus far has focused on
7 dyslexia, a developmental disorder affecting ~3-10% of children with characteristic difficulties in word
8 decoding, which impacts individuals' spelling performance and the development of reading fluency[33].
9 A few studies have investigated timing skills in children with developmental language disorder
10 (previously known as specific language impairment), a similarly common developmental disorder with a
11 ~3-7% prevalence rate, that is characterized by weak language abilities in one or multiple domains that
12 cannot be explained by a known biomedical condition[34] (such as a brain injury, hearing loss or
13 intellectual disability or autism spectrum disorder). Timing skills have also been examined in individuals
14 with stuttering, which is a speech disorder appearing in ~0.3-5.6% of children[35]. The speech of children
15 who stutter shows frequent occurrences of repetitions or prolongations of sounds, syllables, or words that
16 disrupt the rhythmic flow of speech[9].

17 Rhythm skills are often assessed with tapping tasks and rhythm discrimination tasks. Tapping
18 tasks measure the ability to temporally coordinate with a predictable event by asking participants to tap
19 to the beat of music or together with an isochronous metronome[36]. Performance is typically described
20 by the consistency/variability of the taps, the difference between the expected and the actual tapping
21 rate, or the difference between the expected and the actual times of the taps. In rhythm discrimination
22 tasks, participants are typically presented with two rhythms that are either the same or different as a
23 result of changing the duration of one or more tones or the interval between two tones. Compared to age-
24 matched typically developing peers, tapping rates of children with DLD and with dyslexia have been
25 reported to deviate more from the expected tapping rate, and taps of children who stutter to occur
26 significantly earlier than the expected time according to the stimulus [37–39]. There is some inconsistency
27 across studies in regard to behavioral performance, however, and between behavioral and neural
28 measures (e.g., some studies report reduced tapping consistency in dyslexia[37,40] while others observe
29 intact consistency of synchronized tapping [41,42] but atypical neural responses[41]). Rhythm
30 discrimination has been found to be impaired in dyslexia, DLD and stuttering [38,43,44]. Processing of
31 low-level cues related to rhythm processing, such as amplitude rise time or duration, has also frequently
32 been found to be weaker in individuals with DLD [45] and dyslexia [37,40,46,47] compared to their
33 typically developing peers, though one study did not observe differences in duration discrimination in
34 dyslexia [46].

35 Impairments appear in processing of timing-related aspects of spoken language as well. Children
36 with dyslexia and DLD demonstrate impaired performance on tasks measuring word stress or sentence-
37 level prosody processing [48,49]. In [48], word stress sensitivity was measured with two tasks in children
38 with dyslexia and TD peers. At 9 years of age, children were presented with stimuli that had the same
39 segmental information (the syllable *dee* presented repeatedly) but differed in their stress pattern, and had
40 to choose the stimulus that matched a picture (e.g., the matching stimulus for a picture of Harry Potter
41 was DEE-dee DEE-dee). Children with dyslexia demonstrated reduced sensitivity to word stress
42 compared to age-matched and younger, reading-matched peers. At 13 years, stress sensitivity was
43 measured with a stress discrimination task in which the same word was presented twice either with the
44 same stress pattern or with different stress patterns (e.g., DIfficulty (SWWW) and diFFiculty (WSWW)),
45 and children had to decide if they are the same or different; children with dyslexia performed worse than
46 age-matched peers [48]. Sentence-level prosody processing was found to be impaired in children with
47 DLD in an artificial language learning task with and without prosodic cues (i.e., frequency, intensity and
48 duration) to the underlying language structure. In contrast to children with TD, children with DLD could
49 not take advantage of the prosodic cues in acquiring the rules of the artificial language [49].

50 Some of the structural and functional brain characteristics of children with speech/language
51 disorders have been proposed to underlie atypical timing skills in these populations. Functional

1 connectivity measured with resting state fMRI in brain areas associated with rhythm processing (basal
2 ganglia-thalamocortical network) as well as structural connectivity in areas supporting internal timing
3 (putamen, SMA) appear to be weaker in individuals who stutter [50]. Interestingly, stuttering is
4 significantly reduced if individuals are exposed to a regular external rhythm like a metronome and
5 otherwise atypical brain activation patterns become similar to those in individuals who do not stutter in
6 parallel with improved speech fluency [51]. Oscillatory activity in beta frequency band, which has been
7 proposed to reflect functional coordination between auditory and motor systems and involved in timing,
8 has also been found to be atypical in adults who stutter [50]. In dyslexia, the degree of neural entrainment
9 to the speech envelope [52] as well as to non-speech stimuli [53] is less when compared to TD children.
10 Neural entrainment to the regularities of auditory stimuli has been proposed to be impaired in DLD as
11 well, but to our knowledge, this hypothesis has not been tested yet, nor have other neural correlates of
12 impaired timing skills in DLD.

13 Performance on various measures of rhythm as described above (speech rhythm, rhythm
14 discrimination, tapping to the beat) has been associated with language skills in children with language
15 impairments in multiple studies (e.g., [54]) indicating that a common mechanism underlies the
16 development of both rhythm and language processing. This idea is supported by a recent meta-analysis
17 of neuroimaging studies showing that shared neural structures underlying temporal hierarchical
18 processing and predictive coding are involved in both rhythm and spoken language processing [55].

19 Motivated by findings on 1) weak timing skills in children with speech/language disorders and
20 2) their associations with speech/language skills, it has been proposed that improving rhythm processing
21 with music training could also benefit speech/language skills. In a randomized controlled trial, children
22 with dyslexia performed better on rhythm reproduction, phonological awareness, and reading tasks
23 following 30 weeks of music training focusing on rhythm skills, compared to a control group that
24 completed a painting training[56]. Improvements in rhythm skills and phonological awareness were
25 associated suggesting that mechanisms involved in rhythm-based processing support language
26 acquisition and phonological development.

27 The short-term effect of rhythm on subsequent speech/language processing of children with
28 DLD and/or dyslexia has also been investigated with rhythmic priming paradigms: for instance,
29 Przybylski et al. [57] found that children with dyslexia and DLD (as well as children with TD) perform
30 better on a grammaticality judgment task following an exposure to a rhythm with a regular vs. an
31 irregular beat, indicating shared mechanisms underlying rhythm and speech/language processing.
32

33 **Attention-Deficit/Hyperactivity Disorder (ADHD)**

34 ADHD is a common neurodevelopmental disorder (~4-7% of children) characterized by
35 inattention and/or hyperactivity-impulsivity, which interferes with everyday functioning[9]. Children
36 may exhibit ADHD symptoms independent of other disorders though ADHD also occurs comorbidly
37 with other NDDs (e.g., language disorders, DCD, ASD)[58–61]. Children with ADHD have difficulties
38 with perceiving, reproducing or comparing durations [62] as well as with beat perception in music that
39 cannot be accounted for by duration coding problems [63]. Beat perception is, however, comparable to
40 TD children's performance when stimuli consist of simple sound patterns instead of music with a
41 complex structure[63].

42 A recent study [63] found lower synchronization consistency in children with ADHD than in TD
43 children in a finger tapping task, both when children were asked to synchronize their taps with tones and
44 with the beat of music. Children with ADHD had more difficulty tapping to real music than simple tonal
45 stimuli. Children with comorbid ADHD and DCD demonstrated even lower performance than children
46 with only ADHD. The authors suggest that the greater difficulty with synchronizing to music may
47 indicate difficulties with internal generation and maintenance of the beat in ADHD because the beat in
48 music must be inferred based on the rhythmic patterns (versus it being provided by a periodic, acoustic
49 cue as with a metronomic tone series) [63]. Interestingly, children with ADHD showing better beat
50 tracking abilities also performed better on tasks measuring flexibility and inhibition, which are
51 characteristic impairments in ADHD [63]

1 Structural brain abnormalities described in ADHD appear to be associated with these timing
2 deficits. Duration discrimination impairments were related to atypical function of corticocerebellar and
3 cortico-striatal pathways [64]. The basal ganglia and their connectivity with cortical areas (e.g.,
4 supplementary motor area, premotor cortex, auditory cortex) have been suggested to be associated with
5 internal beat generation and maintenance (i.e., perceiving and maintaining the beat from the hierarchical
6 rhythmic structure even without the onset of a physical acoustic cue at each beat time) [65]; abnormalities
7 in these areas and pathways may underlie rhythmic difficulties with this process in individuals with
8 ADHD, who often show structural basal ganglia abnormalities. In addition, research has revealed
9 atypical resting state oscillatory activity in children with ADHD, which is proposed to play a crucial role
10 in temporal processing according to several theories (see [66] for a review).

11 While several studies have found impaired timing skills as well as structural/ functional
12 abnormalities in timing-related brain areas/ functions in children with ADHD on the group level, these
13 characteristics are not general across all children with ADHD. These results highlight individual
14 differences within an NDD and suggest that timing impairments may be a feature of a subgroup of
15 children with ADHD (see [66][63]).

16 **Developmental Coordination Disorder**

17 Developmental coordination disorder (DCD) is a neurodevelopmental disorder with a prevalence
18 of around 5-6% that involves deficits in fine and/or gross motor skills, postural control, balance, and
19 motor learning that are significant enough to affect self-care and activities of daily living. While different
20 criteria for diagnosis have been used (see [67]), the Diagnostic and Statistical Manual of Mental Disorders,
21 Fifth edition[9], definition of DCD includes early-developing very poor coordinated motor skills for age
22 (e.g., scores < 16th percentile on the Motor Assessment Battery for Children, MACB-2) that affect activities
23 of leisure and play, impact academic and vocation performance, and that cannot be explained by
24 intellectual impairment or other neurological conditions affecting motor function. DCD is heterogenous,
25 involving fine and/or gross motor skills. Children with DCD may have trouble with tasks from running
26 to throwing and catching a ball to tying their shoes to using pencils and scissors. For more than half of
27 children diagnosed with DCD, the impairments continue into adolescence, suggesting that it is not
28 simply a question of delayed motor development[68].

29 DCD has high co-morbidity with other developmental disorders involving difficulties with
30 timing and rhythm[8]. It has been estimated that 50% of children with DCD also have a diagnosis of
31 ADHD, and vice versa[58,59]. DCD has also been linked to language disorders, including DLD and
32 dyslexia[69,70]. While children with ASD frequently exhibit DCD symptoms (up to 79%; [71]), less than
33 10% of children with DCD have ASD [72]. There are few genetic studies to date, but heritability estimates
34 for DCD have been as high as 70%[73].

35 There is relatively little research in general on DCD compared to other developmental disorders,
36 and the majority of studies have focused on motor or visuo-motor impairments. However, several studies
37 using questionnaires indicate that children with DCD also have general sensory processing difficulties,
38 including in the domains of audition, balance (vestibular) and body awareness[74].

39 Motor deficits in DCD critically involve deficits in motor and sensorimotor timing[75], and poor
40 timing (often conceptualized as poor predictive internal modeling) can explain their less accurate, slower,
41 and more variable performance on a number of motor tasks[8,76], including rhythmic multi-joint
42 coordination, motor sequencing, motor learning, use of feedback, automatization and anticipation[75,76],
43 as well as visual tracking of objects[77], visual-motor coincident timing[78] and tapping along to
44 rhythmic sequences of visual[79] or auditory[80] events. Neuroimaging studies show general
45 abnormalities including reduced cortical thickness, reduced white matter in sensorimotor tracts, and
46 compromised connectome distributed networks (for a review, see [75]). The timing and rhythm deficits in
47 DCD are particularly consistent with reported abnormalities in cerebellar function [75,81].

48 While the auditory and motor systems are intimately connected, little research has investigated
49 auditory time and rhythm perception in DCD in the absence of a motor task. Chang et al. [82]
50 hypothesized that children with DCD would show deficits in both auditory duration perception and
51

1 auditory rhythm perception given evidence that the auditory system connects with the motor system to
2 accomplish time perception. Using psychophysical methods, they found that, compared to typically
3 developing children, those with DCD had poorer discrimination thresholds for detecting changes in the
4 duration of single time intervals, and detecting the presence of non-isochrony in an otherwise
5 isochronous tone sequence, while their pitch discrimination thresholds were relatively unaffected.
6 Furthermore, electroencephalography (EEG) showed delayed event-related potential responses in the
7 DCD children in response to change detection for duration and rhythm, but not pitch.

8 9 **Autism Spectrum Disorder (ASD)**

10 Individuals with Autism spectrum disorder (ASD), a heterogeneous but highly heritable
11 NDD[73], constitute approximately 1.5% of the general population, and exhibit impairments in social
12 engagement, communication, and restricted/repetitive behaviors, which includes sensory atypicalities[9].
13 Individuals with ASD often exhibit comorbidities with various other psychiatric disorders and
14 conditions, including epilepsy, ADHD, motor coordination deficits, anxiety, and cognitive
15 impairment[60]. Speech and language problems may also occur with some individuals not developing
16 spoken language and others exhibiting fluent speech[83]. As for motor development and function,
17 children and adults with ASD often show poor lower-limb coordination during tasks requiring balance,
18 agility, and speed, and poor upper-limb coordination during visuomotor and manual dexterity tasks[84].
19 Sensory and motor difficulties may contribute to and/or reflect social communication impairments in
20 ASD[85] including in regard to rhythm and timing[86].

21 Attention problems are commonly observed in individuals with ASD[73]. Challenges in
22 modulating attention to others (e.g., joint attention) may contribute to language impairments in
23 individuals with ASD[87]. Reduced attention to social audio-visual speech synchrony is observed in
24 children with ASD compared to children without ASD[88] and sensitivity to audiovisual synchrony is
25 associated with language skills in children with ASD[89]. In regard to speech skills, some individuals
26 exhibit repetitive, stereotyped language and/or atypical speech prosody[9,90]. Impairments in vocal
27 turn-taking occur beginning in infancy[91] while difficulties maintaining appropriate conversational
28 turn-taking are observed in some older children and adults[92].

29 In regard to nonverbal social coordination, children with ASD exhibit different and less stable
30 forms of social synchronization, or the ability to synchronize one's body together with a partner[93]. For
31 example, individuals with ASD show reduced synchronization to others during rhythm interaction
32 activities such as swinging a pendulum[94], rocking in a rocking chair[95], and rhythmic clapping or
33 drumming games[93,96,97]. Difficulties with behavioral imitation are also common[98]. Some studies
34 relate social synchronization difficulties to performance on other social tasks though findings are
35 somewhat mixed at this time perhaps due to task and population heterogeneity[93,96,97]. A growing
36 body of research seeks to enhance social-emotional capacities such as joint attention, eye contact, emotion
37 inference and empathy via supporting interpersonal coordination and synchrony in both children and
38 adults with ASD[99–101].

39 A few studies have investigated musical rhythm skills in ASD. Studies indicate age-appropriate
40 musical rhythm perception (same/difference judgments of musical rhythm patterns)[102] and rhythm
41 production (tapping rhythmic patterns with an example)[103], with performance increasing with age and
42 degree of metric structure (i.e., better performance for strongly metrical vs. weakly metric rhythms). In
43 contrast, impairments are observed for rhythmic sensorimotor synchronization on tasks requiring
44 speaking or tapping to a beat, particularly in regard to lower consistency of synchronization in
45 individuals with ASD[42,86,104]. Impairments are also observed in discriminating auditory durations,
46 especially for shorter (subsecond) intervals[105]. Neuroimaging studies in individuals with ASD reveal
47 reduced connectivity of fronto-temporal and cortical-subcortical networks[106,107], as well as structural
48 abnormalities in the cerebellum and basal ganglia[107,108]. Children with ASD who participated in a
49 music therapy intervention demonstrated increased resting state functional connectivity between
50 auditory, striatal, and motor regions post-intervention compared to children in a non-music control
51 intervention, which was related to children's communication skills on a parent questionnaire[109].

Williams syndrome

In comparison to the previously reviewed disorders, Williams syndrome (WS) is a rare (~1/10,000) neurodevelopmental disorder with a known genetic etiology, the deletion of ~26-28 genes on chromosome 7 [110]. Nevertheless, WS is included here because of its unique cognitive-behavioral phenotype, which presents both overlaps with, and differences from, several of the disorders discussed above, as well as the existence of a robust literature into musical and rhythm processing in WS.

The WS phenotype includes mild to moderate cognitive impairment with deficits in visuospatial construction skills[111]. Common comorbidities include ADHD (~65%; particularly in childhood), as well as anxiety and phobias (~50%)[112]. While initial profiles of WS focused on their strengths in verbal and social skills, more recent research from the last decade highlights a more nuanced profile of strengths and difficulties within these domains[111].

Language development is delayed in WS, though areas such as concrete vocabulary, verbal short-term memory, and grammatical skills become relative strengths later in development (at mental-age expected levels)[111]. Of relevance to rhythm and timing skills, reduced sensitivity to word stress patterns are observed, as well as atypical speech prosody (such as observed in ASD)[113–115]. While WS is associated with hypersociability, difficulties with social pragmatics are common and ASD-related symptomatology is elevated in WS even compared to other non-ASD developmental disabilities[116]. Social coordination difficulties are observed in WS across the lifespan such as impairments in joint attention and integrating social gaze during the early years (before verbal skills develop), and impairments in initiating and maintaining conversations in older (verbal) individuals[111,114,115].

Rhythm and timing skills have also been assessed in WS through music perception and production tasks. Many individuals with WS experience auditory sensitivities and heightened emotional responsiveness to music, but there are substantial individual differences in musical skills. In general, rhythm skills in WS are reduced compared to chronological-age matched peers but commensurate with mental-age abilities. For example, individuals with WS perform worse than age-matched peers on tasks involving same/difference judgments of rhythmic patterns, detecting beat alignment to real music, and reproducing rhythmic patterns by clapping or singing[117–120]. Motor difficulties are often common including coordination of rhythmic motor movements and disrupted perception-action coupling[121,122].

Only one study has assessed neural correlates of rhythm skills in WS using EEG [123]. During passive listening to rhythmic patterns, adults with WS exhibited the canonical oscillatory activity in beta and gamma bands in response to beat onsets. However, individuals with WS also exhibited greater alpha activity, as well as increased amplitude of auditory evoked potentials. This suggests that rhythm and beat processing may connect with their atypical auditory attention profile (e.g., increased responsiveness, poor inhibition and attention disengagement). Neuroimaging studies in WS also reveal differences in brain structure and connectivity in areas important for beat and rhythm processing (e.g., reduced basal ganglia volume)[124].

Summary and Future Directions

Rhythm is an early-emerging and essential component of human development and interactions; yet, as reviewed here, impairments in rhythm are associated with a variety of NDDs including relatively common disorders with complex and varying genetic etiologies (e.g., ADHD, language disorders, DCD, ASD) as well as rare genetic syndromes of known etiology (e.g., WS). Indeed, as reviewed above, the available research finds that many types of rhythm impairments are evident across multiple NDDs (see Supplemental Table 1). Rhythm impairments may be associated with particular facets of individual NDDs, the common comorbidities across NDDs, and broader social-emotional/behavioral difficulties frequently observed (Figure 1). Indeed, regardless of the “primary” domain of a given disorder, profiles of impairments that include increased timing and rhythm deficits in children with various NDDs increase the risk of mental health problems, social problems, and poor academic performance [60,112,125,126].

1 In this summary section, we consider how transdiagnostic investigations into rhythm and timing
2 skills across domains may be fruitful for elucidating underlying biology, characterizing
3 psychological/behavioral sequelae, and designing effective interventions for individuals with various
4 NDDs. Frameworks that consider heterogeneity within and across NDDs dovetail with ongoing efforts to
5 identify the etiology of features and function that are common across multiple mental traits and
6 disorders[127], leveraging phenotypic heterogeneity and comorbidities as an important source of
7 biological covariation (e.g., as in the National Institutes of Mental Health Research Domain Criteria
8 (RDoC) Project). Although rhythm is not currently formally included as an RDoC domain, motor
9 processes and sensory domains (important components of rhythm processing) have recently been
10 incorporated into RDoC [128,129]. Increasing evidence suggests that transdiagnostic investigations across
11 NDDs may be more powerful for revealing links between underlying mechanisms and functional
12 outcomes than comparisons of specific NDDs and typical controls[21,130].

13 Critical to NDDs is the focus on *development*; these are disorders that unfold over time and reflect
14 interactions among genetic vulnerabilities, neural development, and a variety of environmental factors
15 (Figure 1). Overlapping difficulties as well as the degree to which different domains are impacted across
16 different NDDs may reflect similarities and differences in the timing, amount, and how widespread (e.g.,
17 across neural systems) are the instantiation of atypical developmental processes[131]. Additionally,
18 development is a dynamic process and any vulnerabilities in rhythm processing will both impact and be
19 shaped by other (common and unique) vulnerabilities as well as experiences (e.g., as in
20 neuroconstructivist approaches[131]). For example, rhythm is integrally connected with the motor system
21 suggesting potential feedback loops between vulnerabilities in rhythm perception and motor skills; as
22 summarized above, motor impairments of varying degrees commonly occur across NDDs [6,58,69,71].
23 Another example comes from rhythms in social contexts. Rhythm and timing deficits may impair
24 attention shifting and modulation that contribute to successful social interactions; at the same time,
25 atypical (decreased or increased) interest in social information may reduce opportunities to develop and
26 refine rhythm and timing skills needed for social coordination[132].

27 Given the developmental context of NDDs, one important and growing direction for future
28 research includes longitudinal designs of rhythm sensitivity early in life in children with or at risk for
29 various NDDs (due to family risk status or other health risk factors) in order to investigate trajectories of
30 rhythm sensitivity development, as well as relationships between early rhythm sensitivity and later
31 functional language, social, emotional, and motor skills. While some studies with infants at risk for
32 ADHD, ASD, and/or language disorders, as well as children with genetic syndromes such as WS, have
33 investigated early motor, language, sensory, or attentional functioning, rhythm processing has generally
34 not been a focus of these studies [61,131]. Yet the evidence presented in the current paper suggests
35 theoretical support for such future work. One recent study reported associations between infants'
36 temporal sensitivity (amplitude envelope rise time discrimination, important for synchronization of
37 neural oscillatory activity to the temporal signal and reflective of the speech rhythm) and later vocabulary
38 development[133]. Ladányi and colleagues suggest that rhythm may be a powerful means of early
39 identification of children at risk for language disorders due to shared underlying biology[6]. Large-scale
40 population-wide epidemiological studies are needed to test the prediction that atypical rhythm increases
41 the risk of presence of developmental speech and language problems, as well as DCD and ADHD.
42 Furthermore, specific familial influences (genetic and environment factors) accounting for the
43 hypothesized shared risk will need to be disentangled and may point to specific convergent or divergent
44 biological pathways.

45 From an assessment standpoint, in order to better conceptualize common and unique rhythm
46 difficulties across different NDDs, transdiagnostic approaches should thoroughly assess participants for
47 comorbid conditions in order to appropriately characterize their samples (e.g., DCD+DLI vs DCD alone).
48 Additionally, studies should utilize task batteries that incorporate a variety of rhythm and temporal
49 processing activities (e.g., beat perception and production, interval timing, simple vs. complex rhythms).
50 Tasks must also consider different domains (e.g., visual, auditory, tactile, multisensory) and consider
51 tasks with and without motor components, as well as tasks with and without social contexts. Parsing

1 specific rhythm and timing skills across domains may reveal rhythm profiles across different disorders
2 and/or profiles of comorbidities. For example, some children may be particularly impaired in tasks that
3 involve explicit motor components (i.e., rhythm production) while others may perform similarly across
4 perception and production tasks; some children may be supported by rhythm tasks embedded in
5 linguistic/speech or social stimuli while others may be particularly impaired in such contexts. More
6 nuanced studies of the processes underlying tasks would also clarify profiles across disorders or
7 comorbidities. For example, impairments in rhythmic synchronization to beat-based stimuli are observed
8 across nearly all NDD disorders (see Supplemental Table 1). However, it is unknown if difficulties across
9 disorders involve the same or overlapping components (e.g., beat finding, beat maintenance, beat
10 adjustment, error correction). Comparisons across disorders with different types of beat synchronization
11 tasks may be informative for parsing specific impairment profiles (e.g., tapping at different tempi, fixed
12 vs. variable tempi, manipulating the metrical strength, specific acoustic characteristics of stimuli).

13 It is also critical to identify mechanisms by which rhythm processing contributes to individual
14 differences in phenotypic expressions across NDDs and whether overlapping behavioral difficulties are
15 subserved by the same neural mechanisms across different NDDs or if different (potentially
16 compensatory) profiles are observed. Rhythmic processing involves temporal predictability (e.g.,
17 Dynamic Attending Theory[29]), impairments in which are associated with multiple downstream effects
18 including attention to (or attentional disengagement from) sensory stimuli. For example, the Temporal
19 Sampling Framework proposes that impairments in processing slow rhythms (caused by inefficient
20 phase-locking of neural oscillatory activity at low frequencies) are predictive of reduced phonological
21 development in language disorders[134]. Another potential mechanism may involve reward processing,
22 which is impacted in multiple NDDs[135]. Reward processing shares neural pathways (e.g., caudate)
23 with rhythmic sensorimotor synchronization and connects synchrony with subsequent prosocial
24 behavior[136]. In addition to assessing neural activity (e.g., EEG, MEG), other methodological approaches
25 that allow for assessing how behaviors unfold over time (e.g., movement tracking, eye-tracking) may
26 elucidate mechanistic processes underlying rhythm skills across NDDs, as well as links to functional
27 skills across domains.

28 As noted in the reviews of different NDDs, there is substantial interest and growing research in
29 rhythm-based interventions for children with NDDs [56,100,101]. Rhythm-based intervention studies take
30 a variety of forms and target a range of outcomes measures. The general principle of these interventions
31 is that providing structured, predictable, rhythmic stimuli increases relevant neural activity to support
32 behavioral task performance (e.g., increasing oscillatory power at the stimulus frequency). As proof-of-
33 concept designs, several studies have used rhythmic priming activities, in which regular rhythmic stimuli
34 precede or co-occur with target stimuli (e.g., hearing or reading sentences, completing a motor task), to
35 investigate rhythm facilitation of task performance [57]. Other studies involve single or multi-session
36 auditory-motor training activities, often using music/music and movement activities or interventions
37 [100,109]. While there is promising evidence from several studies, larger studies with appropriate
38 comparison conditions are needed, as well as a broadening of the types of symptoms and NDDs being
39 targeted. As with all interventions, clearly elucidated theories of change are needed in order to optimize
40 intervention design; indeed, intervention studies can be used to test connections between proposed
41 mechanisms and outcomes behaviors. Mechanistic intervention research across and within NDDs will
42 support intervention development and help determine for whom interventions are most appropriate and
43 for what target outcomes.

44

45 **Conclusion**

46 Rhythm and timing underlie a variety of human behaviors including attentional, sensory, motor,
47 linguistic, and social domains. There is considerable evidence that rhythm and timing deficits are
48 common across a variety of NDDs with overlapping profiles of rhythm impairments. The presence of
49 timing and rhythm processing deficits across NDDs suggests there may be overlapping genetic and
50 neural vulnerabilities for developing NDDs and potentially explains one facet of the high comorbidity
51 across disorders. Individual differences in rhythm skills in different domains may also help to explain

1 heterogeneity within disorders in regard to magnitude and scope of co-occurring challenges.
2 Transdiagnostic approaches that include rhythm impairments in models of NDDs may point to novel
3 mechanisms of action for characterizing NDDs and in the design of intervention strategies to support
4 children with NDDs.

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20 **References**

- 21 1. Suppanen E, Huotilainen M, Ylinen S. 2019 Rhythmic structure facilitates learning from auditory
22 input in newborn infants. *Infant Behav. Dev.* **57**, 101346. (doi:10.1016/j.infbeh.2019.101346)
- 23 2. Winkler I, Háden GP, Ladinig O, Sziller I, Honing H. 2009 Newborn infants detect the beat in
24 music. *Proc. Natl. Acad. Sci. U. S. A.* **106**, 2468–2471. (doi:10.1073/pnas.0809035106)
- 25 3. Savage PE, Loui P, Tarr B, Schachner A, Glowacki L, Mithen S, Fitch WT. In press. Music as a
26 coevolved system for social bonding. *Behav. Brain Sci.*
- 27 4. Jaffe J, Beebe B, Feldstein S, Crown CL, Jasnow MD. 2001 Rhythms of dialogue in infancy:
28 coordinated timing in development. *Monogr. Soc. Res. Child Dev.* **66**, i–viii, 1–132.
29 (doi:10.2307/3181589)
- 30 5. Lewkowicz DJ. 2003 Learning and Discrimination of Audiovisual Events in Human Infants: The
31 Hierarchical Relation Between Intersensory Temporal Synchrony and Rhythmic Pattern Cues.
32 *Dev. Psychol.* **39**, 795–804. (doi:10.1037/0012-1649.39.5.795)
- 33 6. Ladányi E, Persici V, Fiveash A, Tillmann B, Gordon RL. 2020 Is atypical rhythm a risk factor for
34 developmental speech and language disorders? *Wiley Interdiscip. Rev. Cogn. Sci.*
35 (doi:10.1002/wcs.1528)
- 36 7. Peretz I, Vuvan DT. 2017 Prevalence of congenital amusia. *Eur. J. Hum. Genet.* **25**, 625–630.
37 (doi:10.1038/ejhg.2017.15)
- 38 8. Trainor L, Chang A, Cairney J, Li Y-C. 2018 Is auditory perceptual timing a core deficit of
39 developmental coordination disorder? *Ann. N. Y. Acad. Sci.* **1423**, 30–39.
- 40 9. American Psychiatric Association. 2013 *Diagnostic and Statistical Manual of Mental Disorders, fifth*
41 *edition: DSM-5*. 5th edn. American Psychiatric Pub.
42 (doi:10.1176/appi.books.9780890425596.744053)
- 43 10. Mosing MA, Verweij KJH, Madison G, Ullén F. 2016 The genetic architecture of correlations
44 between perceptual timing, motor timing, and intelligence. *Intelligence* **57**, 33–40.
- 45 11. Niarchou M *et al.* 2019 Unravelling the genetic architecture of musical rhythm.
46 (doi:10.1101/836197)
- 47 12. Solovieff N, Cotsapas C, Lee PH, Purcell SM, Smoller JW. 2013 Pleiotropy in complex traits:
48 challenges and strategies. *Nat. Rev. Genet.* **14**, 483–495. (doi:10.1038/nrg3461)
- 49 13. Smoller JW. 2019 Psychiatric genetics begins to find its footing. *Am. J. Psychiatry.*
50 (doi:10.1176/appi.ajp.2019.19060643)
- 51 14. Anttila V *et al.* 2018 Analysis of shared heritability in common disorders of the brain. *Science (80-*
52 *).* **360**. (doi:10.1126/science.aap8757)
- 53 15. Lee PH *et al.* 2019 Genomic Relationships, Novel Loci, and Pleiotropic Mechanisms across Eight
54 Psychiatric Disorders. *Cell* **179**, 1469–1482.e11. (doi:10.1016/j.cell.2019.11.020)
- 55 16. Watanabe K *et al.* 2019 A global overview of pleiotropy and genetic architecture in complex traits.

- 1 *Nat. Genet.* **51**, 1339–1348. (doi:10.1038/s41588-019-0481-0)
- 2 17. Willcutt EG, McGrath LM, Pennington BF, Keenan JM, DeFries JC, Olson RK, Wadsworth SJ. 2019
- 3 Understanding Comorbidity Between Specific Learning Disabilities. *New Dir. Child Adolesc. Dev.*
- 4 **2019**, 91–109. (doi:10.1002/cad.20291)
- 5 18. Gialluisi A *et al.* 2020 Genome-wide association study reveals new insights into the heritability
- 6 and genetic correlates of developmental dyslexia. *Mol. Psychiatry* (doi:10.1038/s41380-020-00898-x)
- 7 19. Tierney A, White-Schwoch T, MacLean J, Kraus N. 2017 Individual differences in rhythm skills:
- 8 Links with neural consistency and linguistic ability. *J. Cogn. Neurosci.* **29**, 855–868.
- 9 (doi:10.1162/jocn_a_01092)
- 10 20. Sauer-Zavala S, Gutner CA, Farchione TJ, Boettcher HT, Bullis JR, Barlow DH. 2017 Current
- 11 Definitions of “Transdiagnostic” in Treatment Development: A Search for Consensus. *Behav. Ther.*
- 12 (doi:10.1016/j.beth.2016.09.004)
- 13 21. Astle DE, Fletcher-Watson S. 2020 Beyond the Core-Deficit Hypothesis in Developmental
- 14 Disorders. *Curr. Dir. Psychol. Sci.* , 1–7. (doi:10.1177/0963721420925518)
- 15 22. Grahn JA. 2012 Neural Mechanisms of Rhythm Perception: Current Findings and Future
- 16 Perspectives. *Top. Cogn. Sci.* **4**, 585–606. (doi:10.1111/j.1756-8765.2012.01213.x)
- 17 23. Fujioka T, Trainor LJ, Large EW, Ross B. 2012 Internalized Timing of Isochronous Sounds Is
- 18 Represented in Neuromagnetic Beta Oscillations. *J. Neurosci.* **32**, 1791–1802.
- 19 (doi:10.1523/JNEUROSCI.4107-11.2012)
- 20 24. Cope T, Grube M, Singh B, Burn D, Griffiths T. 2014 The basal ganglia in perceptual timing:
- 21 Timing performance in Multiple System Atrophy and Huntington’s disease. *Neuropsychologia* **52**,
- 22 73–81.
- 23 25. Ross JM, Iversen JR, Balasubramaniam R. 2018 The role of posterior parietal cortex in beat-based
- 24 timing perception: A continuous theta burst stimulation study. *J. Cogn. Neurosci.* **30**, 633–643.
- 25 (doi:10.1162/jocn_a_01237)
- 26 26. Phillips-Silver J, Trainor LJ. 2007 Hearing what the body feels: Auditory encoding of rhythmic
- 27 movement. *Cognition* **105**, 533–546. (doi:10.1016/j.cognition.2006.11.006)
- 28 27. Phillips-Silver J, Trainor LJ. 2005 Feeling the Beat : Movement Influences Infant Rhythm
- 29 Perception. *Science (80-.)*. **308**, 1430. (doi:10.1126/science.1110922)
- 30 28. Trainor L, Gao X, Lei J, Lehtovaara K, Harris L. 2009 The primal role of the vestibular system in
- 31 determining musical rhythm. *Elsevier* **45**, 35–43.
- 32 29. Large EW, Jones MR. 1999 The dynamics of attending: How People Track Time-Varying Events.
- 33 *Psychol. Res.* **106**, 119–159. (doi:10.1037/0033-295X.106.1.119)
- 34 30. Herrojo Ruiz M, Maess B, Altenmüller E, Curio G, Nikulin V V. 2017 Cingulate and cerebellar beta
- 35 oscillations are engaged in the acquisition of auditory-motor sequences. *Hum. Brain Mapp.* **38**,
- 36 5161–5179. (doi:10.1002/hbm.23722)
- 37 31. Cirelli LK, Spinelli C, Nozaradan S, Trainor LJ. 2016 Measuring neural entrainment to beat and
- 38 meter in infants: Effects of music background. *Front. Neurosci.* **10**, 1–11.
- 39 (doi:10.3389/fnins.2016.00229)
- 40 32. National Academies of Sciences, Engineering and M. 2016 *Speech and Language Disorders in*
- 41 *Children: Implications for the Social Security Administration’s Supplemental Security Income Program.*
- 42 Washington, DC: National Academic Press. (doi:https://doi.org/10.17226/21872)
- 43 33. Snowling MJ. 2013 Early identification and interventions for dyslexia: A contemporary view. *J.*
- 44 *Res. Spec. Educ. Needs* **13**, 7–14. (doi:10.1111/j.1471-3802.2012.01262.x)
- 45 34. Bishop DVM *et al.* 2017 Phase 2 of CATALISE: a multinational and multidisciplinary Delphi
- 46 consensus study of problems with language development: Terminology. *J. Child Psychol. Psychiatry*
- 47 *Allied Discip.* **58**, 1068–1080. (doi:10.1111/jcpp.12721)
- 48 35. Yairi E, Ambrose N. 2013 Epidemiology of stuttering: 21st century advances. *J. Fluency Disord.* **38**,
- 49 66–87. (doi:10.1016/j.jfludis.2012.11.002)
- 50 36. Repp BH. 2005 Sensorimotor synchronization: A review of the tapping literature. *Psychon. Bull.*
- 51 *Rev.* **12**, 969–992. (doi:10.3758/BF03206433)
- 52 37. Thomson JM, Goswami U. 2008 Rhythmic processing in children with developmental dyslexia:
- 53 Auditory and motor rhythms link to reading and spelling. *J. Physiol. Paris* **102**, 120–129.
- 54 (doi:10.1016/j.jphysparis.2008.03.007)
- 55 38. Cumming R, Wilson A, Leong V, Colling LJ, Goswami U. 2015 Awareness of Rhythm Patterns in
- 56 Speech and Music in Children with Specific Language Impairments. *Front. Hum. Neurosci.* **9**, 672.
- 57 (doi:10.3389/fnhum.2015.00672)
- 58 39. Falk S, Müller T, Dalla Bella S. 2015 Non-verbal sensorimotor timing deficits in children and

- 1 adolescents who stutter. *Front. Psychol.* **6**, 847. (doi:10.3389/fpsyg.2015.00847)
- 2 40. Thomson JM, Fryer B, Maltby J, Goswami U. 2006 Auditory and motor rhythm awareness in
3 adults with dyslexia. *J. Res. Read.* **29**, 334–348. (doi:10.1111/j.1467-9817.2006.00312.x)
- 4 41. Colling LJ, Noble HL, Goswami U. 2017 Neural Entrainment and Sensorimotor Synchronization to
5 the Beat in Children with Developmental Dyslexia: An EEG Study. *Front. Neurosci.* **11**, 360.
6 (doi:10.3389/fnins.2017.00360)
- 7 42. Vishne G, Jacoby N, Malinovitch T, Epstein T, Frenkel O, Ahissar M. 2020 Impaired online error-
8 correction disrupts synchronization to external events in autism. *bioRxiv.* , 2020.09.28.316828.
9 (doi:10.1101/2020.09.28.316828)
- 10 43. Overy K, Nicolson RI, Fawcett AJ, Clarke EF. 2003 Dyslexia and music: Measuring musical timing
11 skills. *Dyslexia* **9**, 18–36. (doi:10.1002/dys.233)
- 12 44. Chang S-E, Chow HM, Wieland EA, McAuley JD. 2016 Relation between functional connectivity
13 and rhythm discrimination in children who do and do not stutter. *NeuroImage Clin.* **12**, 442–450.
14 (doi:10.1016/j.nicl.2016.08.021)
- 15 45. Corriveau K, Pasquini E, Goswami U. 2007 Basic Auditory Processing Skills and Specific
16 Language Impairment: A New Look at an Old Hypothesis. *J. Speech, Lang. Hear. Res.* **50**, 647–666.
17 (doi:10.1044/1092-4388(2007/046))
- 18 46. Huss M, Verney JP, Fosker T, Mead N, Goswami U. 2011 Music, rhythm, rise time perception and
19 developmental dyslexia: Perception of musical meter predicts reading and phonology. *Cortex* **47**,
20 674–689. (doi:10.1016/J.CORTEX.2010.07.010)
- 21 47. Wang HLS, Huss M, Hämäläinen JA, Goswami U. 2012 Basic auditory processing and
22 developmental dyslexia in Chinese. *Read. Writ.* **25**, 509–536. (doi:10.1007/s11145-010-9284-5)
- 23 48. Goswami U, Mead N, Fosker T, Huss M, Barnes L, Leong V. 2013 Impaired perception of syllable
24 stress in children with dyslexia: A longitudinal study. *J. Mem. Lang.* **69**, 1–17.
25 (doi:10.1016/j.jml.2013.03.001)
- 26 49. Weinert S. 1992 Deficits in acquiring language structure: The importance of using prosodic cues.
27 *Appl. Cogn. Psychol.* **6**, 545–571. (doi:10.1002/acp.2350060607)
- 28 50. Chang S-E, Garnett EO, Etchell A, Chow HM. 2019 Functional and Neuroanatomical Bases of
29 Developmental Stuttering: Current Insights. *Neuroscientist* **25**, 566–582.
30 (doi:10.1177/1073858418803594)
- 31 51. Toyomura A, Fujii T, Kuriki S. 2015 Effect of an 8-week practice of externally triggered speech on
32 basal ganglia activity of stuttering and fluent speakers. *Neuroimage* **109**, 458–468.
33 (doi:10.1016/j.neuroimage.2015.01.024)
- 34 52. Power AJ, Colling LJ, Mead N, Barnes L, Goswami U. 2016 Neural encoding of the speech
35 envelope by children with developmental dyslexia. *Brain Lang.* **160**.
36 (doi:10.1016/j.bandl.2016.06.006)
- 37 53. Cutini S, Szucs D, Mead N, Huss M, Goswami U. 2016 Atypical right hemisphere response to slow
38 temporal modulations in children with developmental dyslexia. *Neuroimage* **143**, 40–49.
39 (doi:10.1016/j.neuroimage.2016.08.012)
- 40 54. Corriveau KH, Goswami U. 2009 Rhythmic motor entrainment in children with speech and
41 language impairments: Tapping to the beat. *Cortex* **45**, 119–130. (doi:10.1016/j.cortex.2007.09.008)
- 42 55. Heard M, Lee YS. 2020 Shared neural resources of rhythm and syntax: An ALE meta-analysis.
43 *Neuropsychologia* **137**, 107284. (doi:10.1016/j.neuropsychologia.2019.107284)
- 44 56. Flaugnacco E, Lopez L, Terribili C, Montico M, Zoia S, Schön D. 2015 Music training increases
45 phonological awareness and reading skills in developmental dyslexia: A randomized control trial.
46 *PLoS One* **10**, 1–17. (doi:10.1371/journal.pone.0138715)
- 47 57. Przybylski L, Bedoin N, Krifi-Papoz S, Herbillon V, Roch D, Léculier L, Kotz S a, Tillmann B. 2013
48 Rhythmic auditory stimulation influences syntactic processing in children with developmental
49 language disorders. *Neuropsychology* **27**, 121–31. (doi:10.1037/a0031277)
- 50 58. Piek JP, Pitcher TM, Hay DA. 2007 Motor coordination and kinaesthesia in boys with attention
51 deficit-hyperactivity disorder. *Dev. Med. Child Neurol.* **41**, 159–165. (doi:10.1111/j.1469-
52 8749.1999.tb00575.x)
- 53 59. Kadesjo B, Gillberg C. 2001 The Comorbidity of ADHD in the General Population of Swedish
54 School-age Children. *J. Child Psychol. Psychiatry* **42**, 487–492. (doi:10.1111/1469-7610.00742)
- 55 60. Hawks Z, Constantino J. 2020 Neuropsychiatric “Comorbidity” as Causal Influence in Autism. *J.*
56 *Am. Acad. Child Adolesc. Psychiatry* **59**, 229–235.
- 57 61. Johnson MH, Gliga T, Jones E, Charman T. 2015 Annual research review: Infant development,
58 autism, and ADHD - Early pathways to emerging disorders. *J. Child Psychol. Psychiatry Allied*

- 1 *Discip.* **56**, 228–247. (doi:10.1111/jcpp.12328)
- 2 62. Noreika V, Falter CM, Rubia K. 2013 Timing deficits in attention-deficit/hyperactivity disorder
3 (ADHD): Evidence from neurocognitive and neuroimaging studies. *Neuropsychologia* **51**, 235–266.
4 (doi:10.1016/j.neuropsychologia.2012.09.036)
- 5 63. Puyjarinet F, Bégel V, Lopez R, Dellacherie D, Dalla Bella S. 2017 Children and adults with
6 Attention-Deficit/Hyperactivity Disorder cannot move to the beat. *Sci. Rep.* **7**, 11550.
7 (doi:10.1038/s41598-017-11295-w)
- 8 64. Valera EM, Spencer RMC, Zeffiro TA, Makris N, Spencer TJ, Faraone S V., Biederman J, Seidman
9 LJ. 2010 Neural Substrates of Impaired Sensorimotor Timing in Adult Attention-
10 Deficit/Hyperactivity Disorder. *Biol. Psychiatry* **68**, 359–367. (doi:10.1016/j.biopsych.2010.05.012)
- 11 65. Grahn JA, Rowe JB. 2013 Finding and feeling the musical beat: Striatal dissociations between
12 detection and prediction of regularity. *Cereb. Cortex* **23**, 913–921. (doi:10.1093/cercor/bhs083)
- 13 66. Slater JL, Tate MC. 2018 Timing Deficits in ADHD: Insights From the Neuroscience of Musical
14 Rhythm. *Front. Comput. Neurosci.* **12**. (doi:10.3389/fncom.2018.00051)
- 15 67. Blank R *et al.* 2019 International clinical practice recommendations on the definition, diagnosis,
16 assessment, intervention, and psychosocial aspects of developmental coordination disorder. *Dev.*
17 *Med. Child Neurol.* **61**, 242–285. (doi:10.1111/dmcn.14132)
- 18 68. Visser J, Geuze R, Kalverboer A. 1998 The relationship between physical growth, the level of
19 activity and the development of motor skills in adolescence: Differences between children with
20 DCD. *Hum. Mov. Sci.* **17**, 573–608.
- 21 69. Visscher C, Houwen S, Scherder E, Moolenaar B, Hartman E. 2007 Motor profile of children with
22 developmental speech and language disorders. *Pediatrics* **120**, e158–e163.
- 23 70. Gomez A, Sirigu A. 2015 Developmental coordination disorder: core sensori-motor deficits,
24 neurobiology and etiology. *Neuropsychologia* **79**, 272–287.
- 25 71. Green D, Charman T, Pickles A, Chandler S, Loucas T, Simonoff E, Baird G. 2009 Impairment in
26 movement skills of children with autistic spectrum disorders. *Dev. Med. Child Neurol.* **51**, 311–316.
27 (doi:10.1111/j.1469-8749.2008.03242.x)
- 28 72. Lingam R, Hunt L, Golding J, Jongmans M, Emond A. 2009 Prevalence of developmental
29 coordination disorder using the DSM-IV at 7 years of age: a UK population-based study. *Pediatrics*
30 **123**, e693–e700.
- 31 73. Lichtenstein P, Carlström E, Råstam M, Gillberg C, Anckarsäter H. 2010 The genetics of autism
32 spectrum disorders and related neuropsychiatric disorders in childhood. *Am. J. Psychiatry* **167**,
33 1357–1363. (doi:10.1176/appi.ajp.2010.10020223)
- 34 74. Allen S, Casey J. 2017 Developmental coordination disorders and sensory processing and
35 integration: Incidence, associations and co-morbidities. *Br. J. Occup. Ther.* **80**, 549–557.
36 (doi:10.1177/0308022617709183)
- 37 75. Wilson PH, Smits-Engelsman B, Caeyenberghs K, Steenbergen B, Sugden D, Clark J, Mumford N,
38 Blank R. 2017 Cognitive and neuroimaging findings in developmental coordination disorder: new
39 insights from a systematic review of recent research. *Dev. Med. Child Neurol.* **59**, 1117–1129.
40 (doi:10.1111/dmcn.13530)
- 41 76. Debrabant J, Gheysen F, Caeyenberghs K, Van Waelvelde H, Vingerhoets G. 2013 Neural
42 underpinnings of impaired predictive motor timing in children with Developmental Coordination
43 Disorder. *Res. Dev. Disabil.* **34**, 1478–1487.
- 44 77. Adams ILJ, Lust JM, Wilson PH, Steenbergen B. 2014 Compromised motor control in children
45 with DCD: A deficit in the internal model?-A systematic review. *Neurosci. Biobehav. Rev.* **47**, 225–
46 244. (doi:10.1016/j.neubiorev.2014.08.011)
- 47 78. Çaçola P, Ibane M, Ricard M, Gabbard C. 2016 Children with developmental coordination
48 disorder demonstrate a spatial mismatch when estimating coincident-timing ability with tools.
49 *Res. Dev. Disabil.* **48**, 124–131.
- 50 79. Castelnaud P de, Albaret J, Chaix Y, Zanone P-G. 2007 Developmental coordination disorder
51 pertains to a deficit in perceptuo-motor synchronization independent of attentional capacities.
52 *Hum. Mov. Sci.* **26**, 477–490.
- 53 80. Whitall J, Chang T-Y, Horn C, Jung-Potter J, McMenamim S, Wilms-Floet A, Clark JE. 2008
54 Auditory-motor coupling of bilateral finger tapping in children with and without DCD compared
55 to adults. *Hum. Mov. Sci.* **27**, 914–931.
- 56 81. Zwicker JG, Missiuna C, Harris SR, Boyd LA. 2011 Brain activation associated with motor skill
57 practice in children with developmental coordination disorder: An fMRI study. *Int. J. Dev.*
58 *Neurosci.* **29**, 145–152. (doi:10.1016/j.ijdevneu.2010.12.002)

- 1 82. Chang A, Li Y-C, Chan J, Dotov D, Cairney J, Trainor L. 2020 Inferior auditory time perception in
2 children with motor difficulties. *Child Dev.*
- 3 83. Brignell A, Williams K, Jachno K, Prior M, Reilly S, Morgan AT. 2018 Patterns and Predictors of
4 Language Development from 4 to 7 Years in Verbal Children With and Without Autism Spectrum
5 Disorder. *J. Autism Dev. Disord.* **48**, 3282–3295. (doi:10.1007/s10803-018-3565-2)
- 6 84. Bhat A, Landa R, therapy JG-P, 2011 undefined. 2011 Current perspectives on motor functioning
7 in infants, children, and adults with autism spectrum disorders. *Phys. Ther.* **91**, 1116–11129.
- 8 85. Thye MD, Bednarz HM, Herringshaw AJ, Sartin EB, Kana RK. 2018 The impact of atypical sensory
9 processing on social impairments in autism spectrum disorder. *Dev. Cogn. Neurosci.* **29**, 151–167.
10 (doi:10.1016/j.dcn.2017.04.010)
- 11 86. Franich K, Wong HY, Yu ACL, To CKS. 2020 Temporal Coordination and Prosodic Structure in
12 Autism Spectrum Disorder: Timing Across Speech and Non-speech Motor Domains. *J. Autism
13 Dev. Disord.* , 1–21. (doi:10.1007/s10803-020-04758-z)
- 14 87. Bruinsma Y, Koegel RL, Koegel LK. 2004 Joint attention and children with autism: A review of the
15 literature. *Ment. Retard. Dev. Disabil. Res. Rev.* **10**, 169–175. (doi:10.1002/mrdd.20036)
- 16 88. Grossman RB, Steinhart E, Mitchell T, Mcilvane W. 2015 ‘Look who’s talking!’ Gaze Patterns for
17 Implicit and Explicit Audio-Visual Speech Synchrony Detection in Children With High-
18 Functioning Autism. *Autism Res.* **8**, 307–316. (doi:10.1002/aur.1447)
- 19 89. Patten E, Watson LR, Baranek GT. 2014 Temporal Synchrony Detection and Associations with
20 Language in Young Children with ASD. *Autism Res. Treat.* **2014**, 1–8. (doi:10.1155/2014/678346)
- 21 90. Paul R, Augustyn A, Klin A, Volkmar FR. 2005 Perception and production of prosody by speakers
22 with autism spectrum disorders. *J. Autism Dev. Disord.* **35**, 205–220. (doi:10.1007/s10803-004-1999-
23 1)
- 24 91. Northrup JB, Iverson JM. 2015 Vocal Coordination During Early Parent – Infant Interactions
25 Predicts Language Outcome in Infant Siblings of Children with Autism Spectrum Disorder.
26 *Infancy* **20**, 1–25. (doi:10.1111/inf.12090)
- 27 92. Charlop MH, Milstein JP. 1989 Teaching autistic children conversational speech using video
28 modeling. *J. Appl. Behav. Anal.* **22**, 275–285. (doi:10.1901/jaba.1989.22-275)
- 29 93. Fitzpatrick P, Romero V, Amaral JL, Duncan A, Barnard H, Richardson MJ, Schmidt RC. 2017
30 Social Motor Synchronization: Insights for Understanding Social Behavior in Autism. *J. Autism
31 Dev. Disord.* **47**, 2092–2107. (doi:10.1007/s10803-017-3124-2)
- 32 94. Fitzpatrick P, Frazier JA, Cochran DM, Mitchell T, Coleman C, Schmidt RC. 2016 Impairments of
33 social motor synchrony evident in autism spectrum disorder. *Front. Psychol.* **7**.
34 (doi:10.3389/fpsyg.2016.01323)
- 35 95. Marsh KL, Isenhower RW, Richardson MJ, Helt M, Verbalis AD, Schmidt RC, Fein D. 2013 Autism
36 and social disconnection in interpersonal rocking. *Front. Integr. Neurosci.* **7**, 4.
37 (doi:10.3389/fnint.2013.00004)
- 38 96. Fitzpatrick P, Romero V, Amaral JL, Duncan A, Barnard H, Richardson MJ, Schmidt RC. 2017
39 Evaluating the importance of social motor synchronization and motor skill for understanding
40 autism. *Autism Res.* **10**, 1687–1699. (doi:10.1002/aur.1808)
- 41 97. Kaur M, M. Srinivasan S, N. Bhat A. 2018 Comparing motor performance, praxis, coordination,
42 and interpersonal synchrony between children with and without Autism Spectrum Disorder
43 (ASD). *Res. Dev. Disabil.* **72**, 79–95. (doi:10.1016/j.ridd.2017.10.025)
- 44 98. Ingersoll B. 2008 The Social Role of Imitation in Autism: Implications for the Treatment of
45 Imitation Deficits. *Infants Young Child.* **21**, 107–119.
- 46 99. Landa RJ, Holman KC, O’Neill AH, Stuart EA. 2011 Intervention targeting development of
47 socially synchronous engagement in toddlers with autism spectrum disorder: a randomized
48 controlled trial. *J. Child Psychol. Psychiatry* **52**, 13–21. (doi:10.1111/j.1469-7610.2010.02288.x)
- 49 100. Srinivasan SM, Kaur M, Park IK, Gifford TD, Marsh KL, Bhat AN. 2015 The Effects of Rhythm and
50 Robotic Interventions on the Imitation/Praxis, Interpersonal Synchrony, and Motor Performance
51 of Children with Autism Spectrum Disorder (ASD): A Pilot Randomized Controlled Trial. *Autism
52 Res. Treat.* **2015**, 1–18. (doi:10.1155/2015/736516)
- 53 101. Srinivasan SM, Bhat AN. 2013 A review of ‘music and movement’ therapies for children with
54 autism: embodied interventions for multisystem development. *Front. Integr. Neurosci.* **7**, 22.
55 (doi:10.3389/fnint.2013.00022)
- 56 102. Jamey K, Foster NEV, Sharda M, Tuerk C, Nadig A, Hyde KL. 2019 Evidence for intact melodic
57 and rhythmic perception in children with Autism Spectrum Disorder. *Res. Autism Spectr. Disord.*
58 **64**, 1–12. (doi:10.1016/j.rasd.2018.11.013)

- 1 103. Tryfon A, Foster NE, Ouimet T, Doyle-Thomas K, Anagnostou E, Sharda M, Hyde KL. 2017
2 Auditory-motor rhythm synchronization in children with autism spectrum disorder. *Res. Autism*
3 *Spectr. Disord.* **35**, 51–61. (doi:10.1016/j.rasd.2016.12.004)
- 4 104. Morimoto C, Hida E, Shima K, Okamura H. 2018 Temporal Processing Instability with
5 Millisecond Accuracy is a Cardinal Feature of Sensorimotor Impairments in Autism Spectrum
6 Disorder: Analysis Using the Synchronized Finger-Tapping Task. *J. Autism Dev. Disord.* **48**, 351–
7 360. (doi:10.1007/s10803-017-3334-7)
- 8 105. Isaksson S, Salomäki S, Tuominen J, Arstila V, Falter-Wagner CM, Noreika V. 2018 Is there a
9 generalized timing impairment in Autism Spectrum Disorders across time scales and paradigms?
10 *J. Psychiatr. Res.* **99**, 111–121. (doi:10.1016/j.jpsychires.2018.01.017)
- 11 106. Hahamy A, Behrmann M, Malach R. 2015 The idiosyncratic brain: Distortion of spontaneous
12 connectivity patterns in autism spectrum disorder. *Nat. Neurosci.* **18**, 302–309.
13 (doi:10.1038/nn.3919)
- 14 107. Langen M, Leemans A, Johnston P, Ecker C, Daly E, Murphy CM, dell’Acqua F, Durston S,
15 Murphy DGM. 2012 Fronto-striatal circuitry and inhibitory control in autism: Findings from
16 diffusion tensor imaging tractography. *Cortex* **48**, 183–193. (doi:10.1016/j.cortex.2011.05.018)
- 17 108. Sussman D *et al.* 2015 The autism puzzle: Diffuse but not pervasive neuroanatomical abnormalities
18 in children with ASD. *NeuroImage Clin.* **8**, 170–179. (doi:10.1016/j.nicl.2015.04.008)
- 19 109. Sharda M, Tuerk C, Chowdhury R, Jamey K, Foster N, Custo-Blanch M, Tan M, Nadig A, Hyde K.
20 2018 Music improves social communication and auditory-motor connectivity in children with
21 autism. *Transl. Psychiatry* **8**, 231. (doi:10.1038/s41398-018-0287-3)
- 22 110. Martens MA, Wilson SJ, Reutens DC. 2008 Research Review: Williams syndrome: A critical review
23 of the cognitive, behavioral, and neuroanatomical phenotype. *J. Child Psychol. Psychiatry Allied*
24 *Discip.* **49**, 576–608. (doi:10.1111/j.1469-7610.2008.01887.x)
- 25 111. Mervis CB, John AE. 2010 Cognitive and behavioral characteristics of children with Williams
26 syndrome: Implications for intervention approaches. *Am. J. Med. Genet. Part C Semin. Med. Genet.*
27 **154**, 229–248. (doi:10.1002/ajmg.c.30263)
- 28 112. Leyfer OT, Woodruff-Borden J, Klein-Tasman BP, Fricke JS, Mervis CB. 2006 Prevalence of
29 psychiatric disorders in 4 to 16-year-olds with Williams syndrome. *Am. J. Med. Genet. Part B*
30 *Neuropsychiatr. Genet.* **141**, 615–622. (doi:10.1002/ajmg.b.30344)
- 31 113. Nazzi, T., Paterson, S., & Karmiloff-Smith, A. 2003 Early word segmentation by infants and
32 toddlers with Williams Syndrome. **4**, 251–271.
- 33 114. Klein-Tasman BP, Mervis CB, Lord C, Phillips KD. 2007 Socio-communicative deficits in young
34 children with Williams syndrome: Performance on the autism diagnostic observation schedule.
35 *Child Neuropsychol.* **13**, 444–467. (doi:10.1080/09297040601033680)
- 36 115. Klein-Tasman BP, van der Fluitt F, Mervis CB. 2018 Autism Spectrum Symptomatology in
37 Children with Williams Syndrome Who Have Phrase Speech or Fluent Language. *J. Autism Dev.*
38 *Disord.* **48**, 3037–3050. (doi:10.1007/s10803-018-3555-4)
- 39 116. Klein-Tasman BP, Phillips KD, Lord C, Mervis CB, Gallo FJ. 2009 Overlap with the autism
40 spectrum in young children with Williams syndrome. *J. Dev. Behav. Pediatr.* **30**, 289–299.
41 (doi:10.1097/DBP.0b013e3181ad1f9a)
- 42 117. Lense MD, Dykens EM. 2016 Beat perception and sociability: Evidence from Williams syndrome.
43 *Front. Psychol.* **7**. (doi:10.3389/fpsyg.2016.00886)
- 44 118. Don A, Schellenberg G, Rourke B. 1999 Music and language skills of children with Williams
45 syndrome. *Child Neuropsychol.* **5**, 154–170.
- 46 119. Martens MA, Reutens DC, Wilson SJ. 2010 Auditory cortical volumes and musical ability in
47 Williams syndrome. *Neuropsychologia* **48**, 2602–2609. (doi:10.1016/j.neuropsychologia.2010.05.007)
- 48 120. Hopyan T, Dennis M, Weksberg R, Cyrtrynbaum C. 2001 Music skills and the expressive
49 interpretation of music in children with Williams–Beuren syndrome: Pitch, rhythm, melodic
50 imagery, phrasing, and musical affect. *Child Neuropsychol.* **7**, 42–53.
- 51 121. Mayall LA, D’Souza H, Hill EL, Karmiloff-Smith A, Tolmie A, Farran EK. 2020 Motor Abilities and
52 the Motor Profile in Individuals with Williams Syndrome. *Adv. Neurodev. Disord.* , 1–15.
53 (doi:10.1007/s41252-020-00173-8)
- 54 122. Vivanti G, Dissanayake C, Fanning PAJ, Hocking DR. 2018 Reduced Motor Interference in
55 Preschoolers with Autism Spectrum Disorder and Williams Syndrome. *Dev. Neuropsychol.* **43**, 751–
56 763. (doi:10.1080/87565641.2018.1531289)
- 57 123. Kasdan A, Gordon RL, Lense MD. 2020 Neurophysiological correlates of dynamic beat tracking in
58 individuals with Williams syndrome. *Biol. Psychiatry Cogn. Neurosci. Neuroimaging* **0**.

- (doi:10.1016/j.bpsc.2020.10.003)
124. Campbell LE, Daly E, Toal F, Stevens A, Azuma R, Karmiloff-Smith A, Murphy DGM, Murphy KC. 2009 Brain structural differences associated with the behavioural phenotype in children with Williams syndrome. *Brain Res.* **1258**, 96–107. (doi:10.1016/j.brainres.2008.11.101)
125. Cairney J. 2015 Developmental coordination disorder and its consequences: an introduction to the problem. In *Developmental Coordination Disorder and its Consequences*, pp. 5–32. Toronto: Toronto Press.
126. Law J, Rush R, Schoon I, Parsons S. 2009 Modeling developmental language difficulties from school entry into adulthood: Literacy, mental health, and employment outcomes. *J. Speech, Lang. Hear. Res.* **52**, 1401–1416. (doi:10.1044/1092-4388(2009/08-0142))
127. Simmons JM, Quinn KJ. 2014 The NIMH Research Domain Criteria (RDoC) Project: Implications for genetics research. *Mamm. Genome.* (doi:10.1007/s00335-013-9476-9)
128. Garvey MA, Cuthbert BN. 2017 Developing a motor systems domain for the NIMH RDoC program. *Schizophr. Bull.* (doi:10.1093/schbul/sbx095)
129. Harrison LA, Kats A, Williams ME, Aziz-Zadeh L. 2019 The importance of sensory processing in mental health: A proposed addition to the research domain criteria (RDoC) and suggestions for RDoC 2.0. *Front. Psychol.* (doi:10.3389/fpsyg.2019.00103)
130. Choi EJ *et al.* 2020 Beyond diagnosis: Cross-diagnostic features in canonical resting-state networks in children with neurodevelopmental disorders. *NeuroImage Clin.* **28**, 102476. (doi:10.1016/j.nicl.2020.102476)
131. Karmiloff-Smith A. 2015 An alternative to domain-general or domain-specific frameworks for theorizing about human evolution and ontogenesis. *AIMS Neurosci.* **2**, 91–104. (doi:10.3934/Neuroscience.2015.2.91)
132. Lense MD, Jones WR. 2016 Beat-based entrainment during infant-directed singing supports social engagement. In *Proceedings of the 14th International Conference on Music Perception & Cognition (ICMPC14)*,
133. Kalashnikova M, Goswami U, Burnham D. 2019 Sensitivity to amplitude envelope rise time in infancy and vocabulary development at 3 years: A significant relationship. *Dev. Sci.* **22**. (doi:10.1111/desc.12836)
134. Goswami U. 2011 A temporal sampling framework for developmental dyslexia. *Trends Cogn. Sci.* **15**, 3–10. (doi:10.1016/j.tics.2010.10.001)
135. Dichter GS, Damiano CA, Allen JA. 2012 Reward circuitry dysfunction in psychiatric and neurodevelopmental disorders and genetic syndromes: Animal models and clinical findings. *J. Neurodev. Disord.* **4**, 19. (doi:10.1186/1866-1955-4-19)
136. Kokal I, Engel A, Kirschner S, Keysers C. 2011 Synchronized drumming enhances activity in the caudate and facilitates prosocial commitment - If the rhythm comes easily. *PLoS One* **6**, 1–12. (doi:10.1371/journal.pone.0027272)
137. Germanò E, Gagliano A, Curatolo P. 2010 Comorbidity of ADHD and dyslexia. *Dev. Neuropsychol.* **35**, 475–493. (doi:10.1080/87565641.2010.494748)
138. Tirosh E, Cohen A. 1998 Language deficit with attention-deficit disorder: A prevalent comorbidity. *J. Child Neurol.* **13**, 493–497. (doi:10.1177/088307389801301005)
139. Gillberg C, Gillberg IC, Rasmussen P, Kadesjö B, Söderström H, Råstam M, Johnson M, Rothenberger A, Niklasson L. 2004 Co-existing disorders in ADHD - Implications for diagnosis and intervention. *Eur. Child Adolesc. Psychiatry, Suppl.* **13**, 80–92. (doi:10.1007/s00787-004-1008-4)
140. Stevens T, Peng L, Barnard-Brak L. 2016 The comorbidity of ADHD in children diagnosed with autism spectrum disorder. *Res. Autism Spectr. Disord.* **31**, 11–18. (doi:10.1016/j.rasd.2016.07.003)
141. Lai MC, Kasseh C, Besney R, Bonato S, Hull L, Mandy W, Szatmari P, Ameis SH. 2019 Prevalence of co-occurring mental health diagnoses in the autism population: a systematic review and meta-analysis. *The Lancet Psychiatry* **6**, 819–829. (doi:10.1016/S2215-0366(19)30289-5)
142. Baio J *et al.* 2018 Prevalence of Autism Spectrum Disorder Among Children Aged 8 Years — Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2014. *MMWR. Surveill. Summ.* **67**, 1–23. (doi:10.15585/mmwr.ss6706a1)
143. Blank R, Smits-Engelsman B, Polatajko H, Wilson P. 2012 European Academy for Childhood Disability (EACD): Recommendations on the definition, diagnosis and intervention of developmental coordination disorder (long version). *Dev. Med. Child Neurol.* **54**, 54–93. (doi:10.1111/j.1469-8749.2011.04171.x)
144. Harris SR, Mickelson ECR, Zwicker JG. 2015 Diagnosis and management of developmental coordination disorder. *CMAJ* **187**, 659–665. (doi:10.1503/cmaj.140994)

- 1 145. Missiuna C *et al.* 2014 Psychological distress in children with developmental coordination disorder
2 and attention-deficit hyperactivity disorder. *Res. Dev. Disabil.* **35**, 1198–1207.
3 (doi:10.1016/j.ridd.2014.01.007)
- 4 146. Cohen NJ, Vallance DD, Barwick M, Im N, Menna R, Horodezky NB, Isaacson L. 2000 The
5 Interface between ADHD and Language Impairment: An Examination of Language, Achievement,
6 and Cognitive Processing. *J. Child Psychol. Psychiatry* **41**, 353–362. (doi:10.1111/1469-7610.00619)
- 7 147. Flapper BCT, Schoemaker MM. 2013 Developmental Coordination Disorder in children with
8 specific language impairment: Co-morbidity and impact on quality of life. *Res. Dev. Disabil.* **34**,
9 756–763. (doi:10.1016/j.ridd.2012.10.014)
- 10 148. Catts HW, Adlof SM, Hogan TP, Weismer SE. 2005 Are specific language impairment and dyslexia
11 distinct disorders? *J. Speech, Lang. Hear. Res.* **48**, 1378–1396. (doi:10.1044/1092-4388(2005/096))
- 12 149. Chaix Y, Albaret JM, Brassard C, Cheuret E, de Castelnau P, Benesteau J, Karsenty C, Démonet JF.
13 2007 Motor impairment in dyslexia: The influence of attention disorders. *Eur. J. Paediatr. Neurol.*
14 **11**, 368–374. (doi:10.1016/j.ejpn.2007.03.006)
- 15 150. Druker K, Hennessey N, Mazzucchelli T, Beilby J. 2019 Elevated attention deficit hyperactivity
16 disorder symptoms in children who stutter. *J. Fluency Disord.* **59**, 80–90.
17 (doi:10.1016/j.jfludis.2018.11.002)
- 18 151. Arndt J, Schools AP, Healey EC. 2001 School-Age Children Who Stutter. *Lang. Speech. Hear. Serv.*
19 *Sch.* **32**, 68–78.
- 20 152. Pitts CH, Mervis CB. 2016 Performance on the kaufman brief intelligence test-2 by children with
21 Williams syndrome. *Am. J. Intellect. Dev. Disabil.* **121**, 33–47. (doi:10.1352/1944-7558-121.1.33)
- 22 153. Problovski HZG, Lavi D, Yozevitch R, Sherman M, Hagay Y, Dahan A. 2021 Impairments of
23 interpersonal synchrony evident in attention deficit hyperactivity disorder (ADHD). *Acta Psychol.*
24 *(Amst)*. **212**, 103210. (doi:10.1016/j.actpsy.2020.103210)
- 25
26

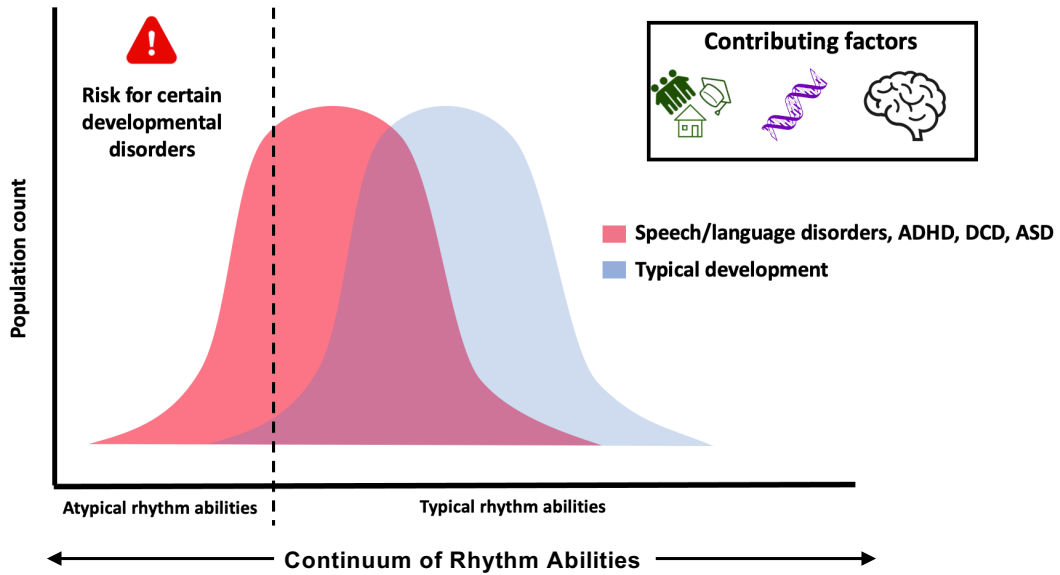
1 **Table 1.** NDDs associated with impairments in rhythm/timing skills. NDDs emerge early in
 2 development and involve impairments/ delays in one or more functional domains.
 3

NDD	Primary Characterization	Estimated Prevalence	Common Comorbidities (examples)*
Attention-Deficit/Hyperactivity Disorder (ADHD)	Persistent pattern of inattention and / or hyperactivity-impulsivity that interferes with functioning or development[9].	~4-7 %	Learning disorders including dyslexia (18-45%)[137], DLD (45%)[138], other externalizing disorders (e.g., oppositional defiant disorder; 50-60%)[139], DCD (50%) [139]
Autism spectrum disorder (ASD)	Early emerging and persistent deficits in social communication and interaction and restricted, repetitive patterns of behavior[9].	~1.5%	ADHD (20-59%)[140,141], anxiety (20-40%)[141], intellectual disability (33%)[142]
Developmental coordination disorder (DCD)	Impairments in motor skills and coordination (e.g., clumsiness, slowness and inaccuracy of motor skills) that significantly and persistently interfere with everyday activities[9].	~5-6%	ADHD (50%)[143,144], learning disorders including dyslexia, DLD [140,141], anxiety (16-48%)[145]
Developmental language disorder (DLD)	Difficulties in understanding and / or using language in one or multiple domains (e.g., expressive grammar) that cannot be explained by a known biomedical condition (such as a brain injury, hearing loss, intellectual disability, or autism spectrum disorder)[34].	~3-7%	ADHD (46%)[146], DCD (20-75%)[147], dyslexia (17-67%)[148]
Dyslexia	Learning disorder involving difficulties in word decoding and identifying speech sounds, which impact the development of reading and spelling skills [33].	~3-10%	ADHD (18-42%)[137], DLD (15-55%)[148], DCD (40-57%)[149]
Stuttering	Speech disorder characterized by frequent occurrences of repetitions or prolongations of sounds,	~0.3-5.6%	ADHD (6%), subclinical ADHD symptoms (~50%)[150],

	syllables, or words that disrupt the rhythmic flow of speech[9].		language disorder (35%)[151]
Williams syndrome (WS)	Neurodevelopmental disorder caused by the deletion of ~26 genes on chromosome 7; associated with mild to moderate intellectual deficits, attention problems, hypersociability, and auditory sensitivities[110].	~0.01%	ADHD (65%)[112], anxiety / phobias (50%)[112], intellectual disability (43%)[152], ASD (10-20%)[114,115]

1 * Prevalence rates of comorbidities may vary across studies in part due to study design (e.g., population
2 sample vs. clinical cohort; screening surveys vs. clinical interviews; self- vs. parent-report) and changes in
3 diagnostic criteria across time (including whether or not diagnosis of specific separate comorbid
4 disorders was permitted)
5

1 **Figure 1.** Impaired rhythm processing skills may be a risk factor for developing a variety of
2 neurodevelopmental disorders (NDDs) and may help explain high levels of comorbidities across
3 disorders and broader patterns of behavioral/emotional problems. Genetic vulnerabilities, environmental
4 factors (e.g., education, training, social interactions), and neural processing contribute to rhythm skills,
5 development of NDDs and profiles within and across NDDs.
6
7



8
9

supplemental Table 1. Summary of performance on different types of rhythm and timing tasks across NDDs

	Interval (Duration) Timing	Rhythm Perception and Production	Beat Perception and Synchronization	Speech Rhythm/Prosody	Interpersonal Movement Coordination
ADHD	↓ perceiving or copying event durations; ↓ duration discrimination [62,64]	--	↓ beat alignment perception in real music; ↓ sensorimotor synchrony to beat (tapping consistency) especially for real music; ↓ detection of non-isochrony in music but ~ in tones[63]	--	↓ intentional interpersonal movement synchrony[153]
ASD	↓ duration discrimination [105]	~ rhythm pattern perception[102]; ~ repeating precise rhythm patterns[103]	↓ sensorimotor synchrony to beat (tapping consistency) [42,86,104]; reduced error correction for tempo changes [42]	↓ word stress production; atypical prosody[9,90]	↓ spontaneous and intentional interpersonal movement synchrony [93–97]
DCD	↓ duration discrimination [82]	--	↓ sensorimotor synchrony to beat (tapping consistency, tap alignment, tapping rate at slow tempi) [80]; ↓ detection of non-isochrony [82]; delayed ERP response to non-isochrony[82]	--	--
DLD	↓ duration discrimination [45]	↓ rhythm pattern perception [38]	↓ sensorimotor synchrony to beat (tapping rate) [38,54]	↓ sentence-level prosody perception [49]	--
Dyslexia	↓ duration discrimination [37,40,47] or ~duration discrimination[46]	↓ rhythm pattern perception [43]	↓ or ~ sensorimotor synchrony (tapping consistency, rate) to beat across studies[37,40–42]	↓ word stress perception [48]; ↓ neural entrainment to speech envelope[52]	--
Stuttering	--	↓ rhythm pattern perception[44]	↓ sensorimotor synchrony to beat (tap alignment) [39]	Speech repetitions and sound prolongation [9]	--
WS	--	↓ rhythm pattern perception*[118–120]; ↓ repeating precise rhythm patterns* [118–120] *may compare to mental-age level	↓ beat alignment perception in real music[117]; ↓ meter recognition[117]; ~clapping in time to simple music [119]; ~beat and gamma activity, ↑ alpha activity and ERP amplitude during beat perception [123]	↓ word stress perception[113]; atypical prosody[114,115]	--

Note: Summaries reflect general trends across multiple studies when available; there is heterogeneity across individuals within all studies

- = poorer performance compared to chronological age-matched peers
- = similar performance to chronological age-matched peers
- = increased response compared to chronological age-matched peers
- = not enough data available in category