nature portfolio

Peer Review File

Musical rhythm abilities and risk for developmental speech-language problems and disorders: epidemiological and polygenic associations.

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This file contains all reviewer reports in order by version, followed by all author rebuttals in order by version.

Version 0:

Reviewer comments:

Reviewer #1

(Remarks to the Author)
In this study, the authors conducted an epidemiological investigation and explored polygenic associations related to musical rhythm abilities and risk for developmental speech-language problems and disorders, using the largest samples to date. They found that rhythm impairment would be a significant risk factor for speech-language disorders in the general adult population. Furthermore, this study revealed a shared genetic architecture between musical rhythm and reading abilities. While the manuscript is well-crafted, a few comments require the attention of the authors.

1. The introduction section is quite lengthy; I would suggest improving this paragraph, making it more concise and focused.

2. The authors found that a 1 SD decrease in rhythm scores were significantly associated with a 7% lower likelihood of having a stutter. This finding was inconsistent with previous studies. If the authors have information about the history of rhythm-based therapies, it should be provided. Moreover, in the meta-analysis, significant heterogeneity was found across data cohorts. Considering the inconsistent result for stuttering, I would suggest performing an additional meta-analysis that does not include the stuttering dataset and comparing the results from these two analyses.

3. The statistical estimation of the difference in medians and distributions of beat synchronization PGS across the Yes and No categories for speech-language therapy history should be provided. Additionally, since the history of speech-language therapy may influence the oral reading score, why not separate these two groups for analysis? Something special may be obscured by it.

4. The authors performed two independent studies; however, a lack of connection was made between these two. Were there any causal or mediation associations between PGS, lower musical rhythm, and higher communication problems or disorders?

5. The limitations of this study should be discussed in an appropriate paragraph, maybe in the discussion part. Similarly, I would suggest improving the discussion section, making it more refined.

6. The significant estimates (p-value) should be provided in figure 2.

Reviewer #2

(Remarks to the Author)
The authors report analyses of four large-scale datasets to examine the relationship between musical rhythm and speech/language/reading abilities. They find that musical rhythm (e.g. tapping to a rhythm, identifying isochronous tempos, self-reported rhythm abilities) is a significant risk factor in speech/language/reading deficits. There was evidence for a genetic component to the risk factor as well. These results further support many other studies that have found evidence for the role of rhythm in speech and language.

The paper is well-written, and the sheer amount and diversity of data seems worth publishing—epidemiological investigations are new in this domain, and as the authors say, this is the largest to date (by far I imagine). Investigations into the role of rhythm in speech and language have been increasing in recent years, so many researchers across several communities are likely to be interested in the work. I noted two issues in reviewing the study.

For one, the study used a “retrospective” design where adults were asked about deficits and interventions in the past, and reports were used to estimate risk factors and effects in adulthood. It seems important to consider the possible effects that some kind of speech, language, or reading intervention might have on results. In one case, lower rhythm scores correlated with a lower chance of stuttering, which the authors suggest may have been due to rhythm-based treatments of stuttering. Do they have any data or evidence to support this conjecture? Is it possible that any effective treatment of stuttering might improve rhythm scores? In another case, they found that lower scores correlated with support for learning disabilities. Does that mean whatever support was received did not help with the disability? Or did it help, but not improve rhythm scores? I think the authors should address the question of how interventions might affect correlations, with analyses if the data would allow (through discussion if not).

The PGS correlations were understandably modest but interesting, nonetheless. The authors note that correlation of oral reading scores with beat synchronization PSG scores appeared to hold only for high scores on both variables. This restriction of effect seems to suggest that beat synchronization may help with advanced reading, but not cause a deficit. Given that the authors interpret their results in terms of deficits and possible interventions, they should further address this restriction of effect.

Reviewer #3

(Remarks to the Author)
This large-scale study investigates the link between musical rhythm abilities and developmental speech-language related disorders.
Compared with previous literature the large N (39,092) constitutes the main advance of the study. With a retrospective design, the study shows that rhythmic impairments (including beat synchronization and rhythm discrimination) are a modest and constant factor in the likelihood of having developed speech language disorders across several independent datasets. This finding is consistent with the predictions of the Atypical Rhythm Risk Hypothesis. Importantly, the authors show that the polygenic architecture of rhythm predicts reading scores over and above the predictive value of known polygenic architecture of reading. This suggests that reading skills draw upon biology shared with musical rhythm skills.

The study is interesting, original, and the methods is sound. There are a few considerations/limitations of the approach that should be addressed in the paper.

1) The study is clearly grounded on the MAPLE framework / Atypical Rhythm Risk Hypothesis. In line with the hypothesis, it establishes an association between rhythm impairment and speech-language disorders. However, the retrospective correlational approach is not sufficient to exclude alternative explanations for the observed comorbidity of rhythm and language impairments. Could other variables play a role in both rhythm perception and language development? For example, these could be the socio-economic status/the richness of sensory-cognitive inputs experienced during development, musical engagement, or general musical abilities. Potential confounding variables that might influence the rhythm and language relationship should emerge more clearly or be discussed in the paper. It seems that socio-economic status and musical engagement information are available for some of the cohorts and could be tested here.

2) The effect size was modest. How clinically relevant is this effect size? The authors could mention alternative hypotheses, and consequently consider/mention factors, if any, that could be stronger predictors, hence have a larger impact, on speech-language disorders.

3) The general statement on p. 17 that rhythm impairments were associated with increased likelihood of a series of speech-language disorders should not include stuttering (as reported on p. 12, stuttering yielded the opposite effect).

4) p. 11: “Poor rhythmic skills are associated with the likelihood to have received therapies as child.” If rhythmic deficits persist, does it mean that traditional language therapies haven’t been successful after all? And that rhythmic-based therapies might be more specific and effective? This for example was hypothesised on the unexpected effect of high rhythmic abilities in individuals who stuttered, perhaps as an effect of targeted rhythmic therapies.

5) The statistical analyses could be clearer. To enhance transparency and reproducibility, the authors should describe in detail the statistical models (sample, variable selection, software packages) that have been run to produce all the reported results.

Minor issues:
1) p.18: This could be clearer “Last, based on current referral practices in the US and other countries, our large-scale findings about rhythm and history of speech-language therapy may serve as a proxy for developmental speech-language delays, which are known to hinder educational and socioeconomic trajectories.” How can these large-scale findings be a proxy? It might make more sense to say that the current findings suggest that rhythmic skills and rhythm related PGSs can be used as a proxy/predictor of language delays.

2) It would be helpful to provide the age range of all the subgroups from the various studies analysed for the current work. For example, in the ABCD cohort individuals were monitored from about 10 years old up to 10 years later. Were the reading score data included in this study sampled from the latest year of monitoring? This would offer insights into the life stages during which participants were tested.

3) There is a number or writing/grammatical typos. Please check the manuscript throughout:
p. 4: “are sensitive to early intervention.25–28” should be “are sensitive to early intervention25–28.”

p. 7: “whether lower performance on musical rhythm measures are associated with higher” should be “whether lower performance on musical rhythm measures is associated with a higher …”

p.12: ““Results showed that a 1 SD decrease in rhythm scores were significantly” should be “Results showed that a 1 SD decrease in rhythm scores was significantly … with a lower likelihood ….”

p. 16 “sychronization” should be “synchronization”.

Version 1:

Reviewer comments:

Reviewer #1

(Remarks to the Author)
The authors have addressed my previous concerns, I have no further comments.

Reviewer #2

(Remarks to the Author)
The authors have done a very thorough job of responding to reviewer comments and making good revisions wherever needed. I endorse publication.

Reviewer #3

(Remarks to the Author)
The authors appear to have addressed the concerns raised by myself and, as far as I can tell, other reviewers. I have no further concerns with this nice work.

We thank the reviewers for their detailed and constructive feedback, and respond to comments point-by-point below:

Reviewer #1 comments

In this study, the authors conducted an epidemiological investigation and explored polygenic associations related to musical rhythm abilities and risk for developmental speech-language problems and disorders, using the largest samples to date. They found that rhythm impairment would be a significant risk factor for speech-language disorders in the general adult population. Furthermore, this study revealed a shared genetic architecture between musical rhythm and reading abilities. While the manuscript is well-crafted, a few comments require the attention of the authors.

We thank reviewer 1 for their thoughtful comments which we address below.

1. The introduction section is quite lengthy; I would suggest improving this paragraph, making it more concise and focused.

Thank you for this feedback, which has strengthened the manuscript. We have now made the Introduction section much more efficient in conveying the background literature and study motivations, and have reduced the word count by ~25%.

2. The authors found that a 1 SD decrease in rhythm scores were significantly associated with a 7% lower likelihood of having a stutter. This finding was inconsistent with previous studies. If the authors have information about the history of rhythm-based therapies, it should be provided.

Thank you for bringing to our attention that the result and statement need clarification. We have now cited a review of the rhythm-based therapies used for stuttering, in response to Reviewer 2's request, clarifying that we do not have information on the therapy history of individuals who stutter in our sample:

> "Our results diverge from previous studies in that rhythm and stuttering were not associated in the direction expected based on the literature. This could be due to our focus on individual variability in rhythm skills *within* individuals who stutter(ed), in contrast with case/control designs[27,40,41]; or because individuals who stutter(ed) may be exposed to rhythm-focused therapies, improving their rhythm abilities. While we cannot test this conjecture in the present data, we suggest it as a potential explanation that should be tested systematically in future research, as there is a substantial history of "rhythmic speech" or singing and other music therapies being used to treat stuttering[56,57]**"**

3. Moreover, in the meta-analysis, significant heterogeneity was found across data cohorts. Considering the inconsistent result for stuttering, I would suggest performing an additional meta-analysis that does not include the stuttering dataset and comparing the results from these two analyses.

We appreciate this helpful suggestion. As Reviewer 1 suggests, we have now conducted an additional meta-analysis excluding the stuttering result. We have revised the Results section accordingly to add:

"Since lower rhythm scores were associated with lower risk of stuttering (compared to other speech-language disorders, where lower rhythm scores were associated with higher risk), we conducted an additional meta-analysis without stuttering included. Meta-analysis results were virtually unchanged without stuttering included in the model (OR = 1.34 [1.18 – 1.48], p <.0001; Table S.1.2)."

4. The statistical estimation of the difference in medians and distributions of beat synchronization PGS across the Yes and No categories for speech-language therapy history should be provided.

Thank you for the suggestion to add these statistical estimations. As it is highly unconventional to test differences between medians and distributions for PGSs, (because PRSs are usually normalized and standardized, and computed for the whole group rather than separately for cases and controls) they are more suitable for testing mean differences (e.g. using t-tests). We have revised to add information about statistical estimation of differences between PGS means in speech-language therapy history cases compared to controls as follows:

"A two-tailed Independent samples t-test showed significantly lower beat synchronization PGS means in the cases ("Yes": N = 214) compared to controls ("No": N = 1,388), $t(df = 280) = -2.62$, $p = .00916$."

5. Additionally, since the history of speech-language therapy may influence the oral reading score, why not separate these two groups for analysis? Something special may be obscured by it.

We tested associations between word reading PGS and musical rhythm discrimination scores, controlling for age, sex, and population substructure (5 genetic ancestry PCs) separately in speech-language therapy cases and controls, in the *Vanderbilt Online Musicality Study (OM)* dataset (we believe Reviewer 1 was specifically referring to the ABCD data which contains oral reading scores, however it was not possible to test this model due to a lack of data on speech-language therapy available for that cohort). Results in the OM cohort showed that the model for speech-language therapy <u>controls</u> was nearly identical to the overall model reported in the manuscript (and in fact the model fit statistics showed that the model fit the data slightly less well: *Full sample:* model R2 = 0.016, model p = 0.00038, Beta = 0.09 compared with *Controls only:* N = 1,452; model R = 0.016, p = 0.00264, beta = 0.10, p = 0.00058). On the other hand, word reading PGS were not significantly associated with musical rhythm perception in the <u>cases-only</u> model (N = 217, model R2 = 0.08134, model p = 0.022, Beta = 0.103, p = 0.13). In theory, it is possible that the genetics of reading, and rhythm perception abilities, are differentially associated in subsets of individuals who did or did not have developmental speech-language problems. However, note that we only had access to N = 217 cases in this particular model, and post-hoc power analyses show that the model is underpowered to detect small effects (power achieved = 0.66). Further, PGS analyses are not recommended in such small sample sizes. Therefore, we have chosen not to currently include these results in the manuscript due to lack of robustness and interpretability. However, we now address the reviewer's broader question briefly in our Discussion as such:

"Given the present study design, which yielded case Ns consistent with the population prevalence for developmental speech-language disorders, we could not systematically tease

apart whether genetic associations between rhythm and reading play out differently in individuals with a history of developmental speech-language problems compared to others. This remains a question for future studies that target the enrollment of individuals with a developmental history of speech-language problems into genomics studies."

6. The authors performed two independent studies; however, a lack of connection was made between these two. Were there any causal or mediation associations between PGS, lower musical rhythm, and higher communication problems or disorders?

We appreciate the suggestion to connect the designs and findings from the two studies. In our view, the Study 2 (polygenic score prediction) design reinforces the results found in Study 1 (epidemiological associations). For example, from Study 1 we see that rhythm and reading problems are associated, and then in Study 2 we theorize based on existing frameworks that their phenotypic associations will also be reflected in shared genetic associations, and that those might operate bidirectionally (rhythm genetics as a predictor of reading phenotypes and vice versa). We have now clarified the connection between Study 1 and 2 briefly in the manuscript's Discussion as follows:

Discussion: "Study 2 (*N* = 7,180) tested theories of genetic pleiotropy (shared genetic influences) between musicality and language traits[24,25,47] as a partial explanation of associations found in Study 1."

As for the specific question about causal or mediating effects between PGS for musical rhythm, musical rhythm scores, and language disorders, we have now analyzed this in the *Vanderbilt Online Musicality Study* cohort. Based on the results, we have added text to the Results and Discussion sections, and added a new figure in the Results section.

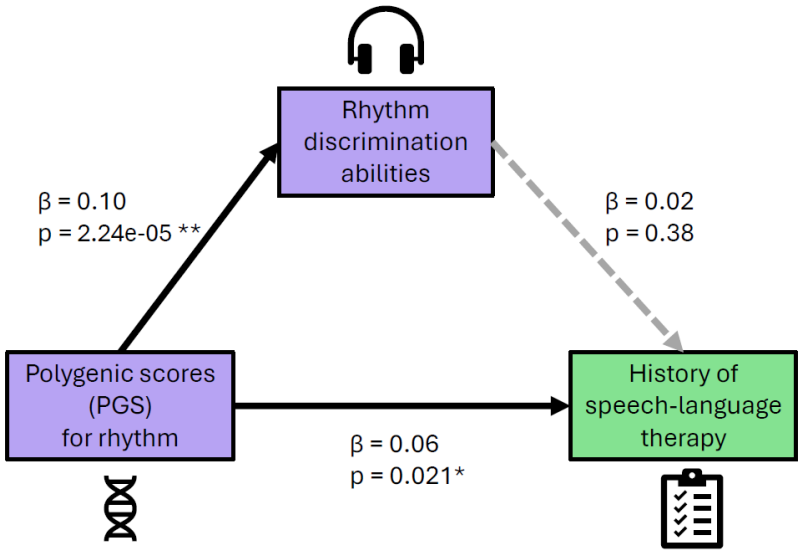
Results: "To clarify whether genetic associations between musical rhythm abilities and speech-language problems played out through horizontal (direct) or vertical (mediated) pleiotropy, we tested a mediation model in the *Vanderbilt Online Musicality Study* cohort (*N* = 1,787 [N_{Female} = 1,326]; see *Methods: Data Processing and Analyses*). Path analysis showed significant direct effects of rhythm PGS on speech-language therapy history (i.e. history of speech-language problems), but this relationship was not mediated by rhythm discrimination abilities (*chi-sq* = 24.43, *p* = .000013, *CLI* = 1.0; *TLI* = 1.0). These results further clarify our cross-trait PGS findings, providing evidence that the genetic pleiotropy underlying rhythm and language traits is of the horizontal and not vertical variety (i.e., not mediated) (see [25] for further discussion on possible unmediated and mediated genetic pleiotropy between rhythm and speech-language disorders). Figure 4 shows all beta and p-values for the mediation model. See Tables S.8.1. - S.8.2 for model details."

Mediation model details are as follows (given in *Data Processing and Analyses* section):

"***Rhythm-Language Mediation Model.*** The model (in OM cohort data) was tested using the *lavaan* package (Rosseel, 2012) with default model specification, with beat synchronization PGSs as the predictor, musical rhythm discrimination scores as potential mediators, and speech-language therapy history status as the outcome variable (see Tables S.8.1 and S.8.2 for

further details on the model). Residuals for musical rhythm discrimination scores were extracted from a linear model. Covariates were age, sex, and 5 genetic ancestry PCs."

For your reference, Fig 4 is below:



Discussion: "Mediation analyses showed direct effects of genetic predispositions for musical rhythm abilities on clinical speech-language outcomes (consistent with horizontal pleiotropy), which were not mediated by phenotypic musical rhythm scores. Thus, associations between rhythm and language during development are not necessarily due to cognitive transfer effects from sequence and timing processing and learning to linguistic domains (e.g. phonological and reading development), rather may be driven by other complex gene-brain-environment interplays. These findings further characterize the details of genetic associations found between rhythm and speech-language disorders, complementing recent findings about shared genetic architecture[32]."

7. The limitations of this study should be discussed in an appropriate paragraph, maybe in the discussion part.

Thank you for this suggestion. We have now discussed some limitations of the study in a paragraph in the discussion section, as follows:

"The current study has a few limitations. First, case *N*s were modest in certain cohorts and models (e.g., 10-13 Dyslexia cases in RPS models; 43 late talkers in the RP model), making these models statistically underpowered. Conversely, cases were very well represented in several other models (e.g. 2713 Dyslexia cases and 2424 DLD cases in LL models). Second, the present data do not allow us to systematically investigate whether a history of particular therapies or interventions (e.g. for stuttering, or related to the "history of speech-language therapy" item) influenced the phenotypic and genetic relationships found here. Future studies should examine whether childhood speech-language therapy can have lasting effects on

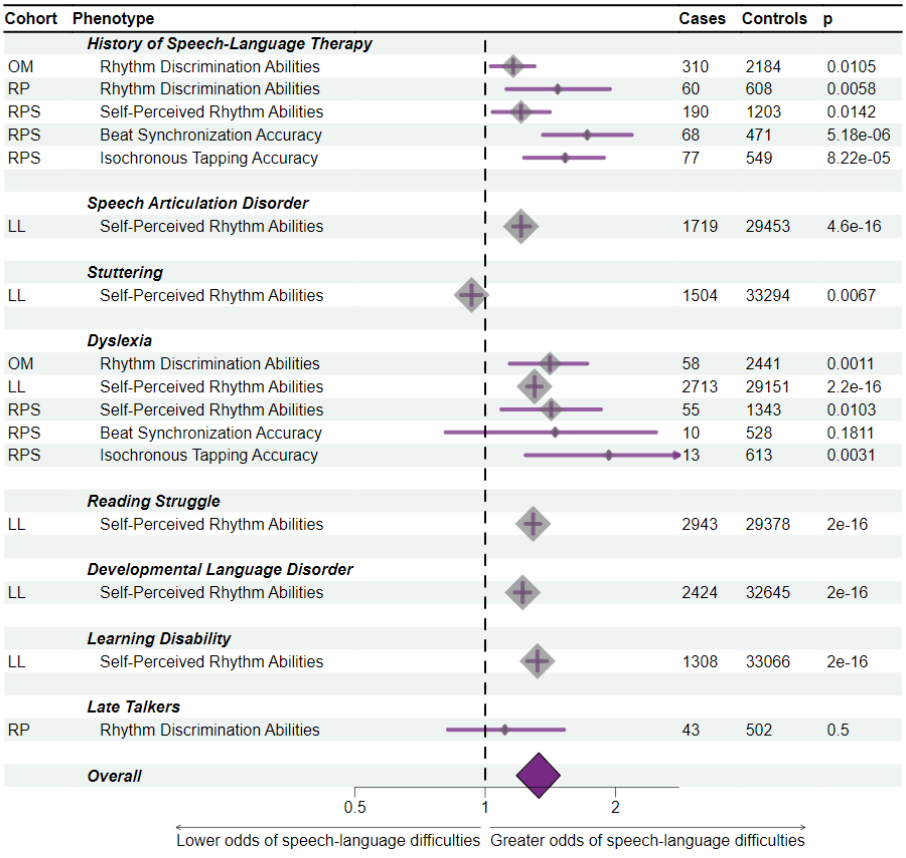
musicality-language associations. As is common in the literature, PGS models were derived from currently existing GWAS summary statistics from studies in individuals with European genetic ancestry, potentially limiting their overall generalizability. Future work should include more diverse genetic ancestries[59,60], and musicality phenotypes across diverse cultural groups[61]."

8. Similarly, I would suggest improving the discussion section, making it more refined.

Thank you for this suggestion. We have now refined and focused the manuscript's Discussion section, reducing its total word count by 25%.

9. The significant estimates (p-value) should be provided in figure 2.

Thank you for this comment. We agree that this makes the figure more useful to readers and have now revised Figure 2 to include p-values. For your reference, Fig. 2 is given below:



Reviewer #2 comments

The authors report analyses of four large-scale datasets to examine the relationship between musical rhythm and speech/language/reading abilities. They find that musical rhythm (e.g. tapping to a rhythm, identifying isochronous tempos, self-reported rhythm abilities) is a significant risk factor in speech/language/reading deficits. There was evidence for a genetic component to the risk factor as well. These results further support many other studies that have found evidence for the role of rhythm in speech and language.

The paper is well-written, and the sheer amount and diversity of data seems worth publishing—epidemiological investigations are new in this domain, and as the authors say, this is the largest to date (by far I imagine). Investigations into the role of rhythm in speech and language have been increasing in recent years, so many researchers across several communities are likely to be interested in the work. I noted two issues in reviewing the study.

Thank you for your positive evaluation and for your suggestions we provide a detailed response below:

1. For one, the study used a "retrospective" design where adults were asked about deficits and interventions in the past, and reports were used to estimate risk factors and effects in adulthood. It seems important to consider the possible effects that some kind of speech, language, or reading intervention might have on results. In one case, lower rhythm scores correlated with a lower chance of stuttering, which the authors suggest may have been due to rhythm-based treatments of stuttering. Do they have any data or evidence to support this conjecture? Is it possible that any effective treatment of stuttering might improve rhythm scores? In another case, they found that lower scores correlated with support for learning disabilities. Does that mean whatever support was received did not help with the disability? Or did it help, but not improve rhythm scores? I think the authors should address the question of how interventions might affect correlations, with analyses if the data would allow (through discussion if not).

Reviewer 2 raises very interesting questions that are both scientifically and clinically relevant. The revised manuscript addresses these questions in two places:

First, a new paragraph about the stuttering results in the Discussion section (see response to *Reviewer 1, Comment 2*)

We also now discuss this alongside other study limitations in the Discussion section:

> "…the present data do not allow us to systematically investigate whether a history of particular therapies or interventions (e.g. for stuttering, or related to the "history of speech-language therapy" item) influenced the phenotypic and genetic relationships found here. Future studies should examine whether childhood speech-language therapy can have lasting effects on musicality-language associations."

2. The PGS correlations were understandably modest but interesting, nonetheless. The authors note that correlation of oral reading scores with beat synchronization PGS scores appeared to hold only for high scores on both variables. This restriction of effect seems to

suggest that beat synchronization may help with advanced reading, but not cause a deficit. Given that the authors interpret their results in terms of deficits and possible interventions, they should further address this restriction of effect.

Upon revisiting this part of the manuscript, we realize that the way we had framed the interpretation of results would be confusing to readers. For example, we did not mean to imply that there is a *restriction* of effect, or that the correlation *only holds* for high scores on both variables. From the data, we cannot conclude that "beat synchronization may help with advanced reading, but not cause a deficit," and did not intend to imply this. It is common for PGS deciles to be most informative at the tail ends, so we have now revised to emphasize this expected and found pattern. We now show that individuals in the lowest and highest PGS deciles show significantly different scores on the phenotypes, e.g. in Fig. 3A and 3B. Similarly, we also show that mean beat synchronization PGSs differ across individuals who did or did not report developmental problems with speech and language, e.g. Fig. 3C. We clarify this in the Results section as follows (Fig 3 is below for your reference):

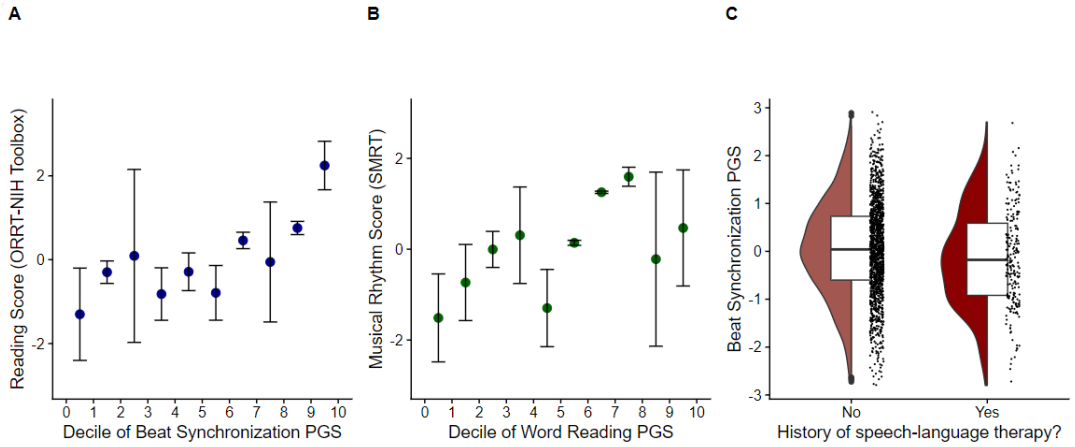


Figure 3A Results:

> "The tails of the beat synchronization PGS distribution are informative (Fig. 3A), with individuals in the highest PGS decile showing significantly better oral reading scores than those in the lowest decile (t (df = 1077) = -3.69, p = .000232); see *Methods: Data Processing and Analyses*."

Figure 3B Results:

> "Again, the tails of the word reading PGS distribution are informative (Fig. 3B), with individuals in the highest PGS decile showing significantly better rhythm discrimination scores than those in the lowest decile (t (df = 350) = -2.56, p = .011; see *Methods: Data Processing and Analyses*)."

Figure 3C Results:

> "A two-tailed independent samples t-test showed significantly lower beat synchronization PGS means in the cases ("Yes": N = 218) compared to controls ("No": N = 1,456), t (df = 280) = -2.56, p = .0109); see *Methods: Data Processing and Analyses*."

Reviewer #3 Comments

This large-scale study investigates the link between musical rhythm abilities and developmental speech-language related disorders. Compared with previous literature the large N (39,092) constitutes the main advance of the study. With a retrospective design, the study shows that rhythmic impairments (including beat synchronization and rhythm discrimination) are a modest and constant factor in the likelihood of having developed speech language disorders across several independent datasets. This finding is consistent with the predictions of the Atypical Rhythm Risk Hypothesis. Importantly, the authors show that the polygenic architecture of rhythm predicts reading scores over and above the predictive value of known polygenic architecture of reading. This suggests that reading skills draw upon biology shared with musical rhythm skills.

The study is interesting, original, and the methods is sound. There are a few considerations/limitations of the approach that should be addressed in the paper.

Thank you for the positive evaluation. We provide a detailed response below.

1. The study is clearly grounded on the MAPLE framework / Atypical Rhythm Risk Hypothesis. In line with the hypothesis, it establishes an association between rhythm impairment and speech-language disorders. However, the retrospective correlational approach is not sufficient to exclude alternative explanations for the observed comorbidity of rhythm and language impairments. Could other variables play a role in both rhythm perception and language development? For example, these could be the socio-economic status/the richness of sensory-cognitive inputs experienced during development, musical engagement, or general musical abilities. Potential confounding variables that might influence the rhythm and language relationship should emerge more clearly or be discussed in the paper. It seems that socio-economic status and musical engagement information are available for some of the cohorts and could be tested here.

We of course agree that many variables are at play here in both rhythm abilities and language development, including the ones that reviewer 3 mentions. Our focus here is to emphasize that one of the important risk factors for language impairments is likely rhythm impairments (partially driven by genetic individual differences). While the main models in Study 1 control for Age and Sex, all reported associations hold when educational attainment levels are included as additional covariate in models. Education is a commonly used proxy for socio-economic status (SES), suggesting that SES is likely not confounding the relationships found here. We also show in two different datasets that the associations found in Study 1 are still significant over and above the effects of music engagement and training (measured 3 different ways across cohorts where this information was available) and educational attainment. We now report additional models in the supplement, and have revised the Results section to include the following:

> "To investigate whether other relevant factors such as socioeconomic status (SES) and music engagement or training explain the relationship between musical rhythm and a history of speech-language problems and disorders, we also conducted regression analyses with music engagement and educational attainment (a proxy for SES) included as covariates, in two cohorts (Tables S.9.1 - S.9.5). In brief, associations between musical

rhythm abilities and speech-language disorders were robust over and above the effects of socioeconomic and music training factors."

2) The effect size was modest. How clinically relevant is this effect size? The authors could mention alternative hypotheses, and consequently consider/mention factors, if any, that could be stronger predictors, hence have a larger impact, on speech-language disorders.

The central goal of this work is to emphasize, with large samples, that rhythm abilities are a widely overlooked factor in our understanding of developmental speech-language disorders. We argue throughout that perceptual-motor rhythm abilities - and individual *predispositions* for such abilities – are a useful *dimension* for continued examination in clinical-translational research for multiple developmental speech-language disorders, going beyond a core-deficit model of individual disorders. Towards this goal, our results show that on average, every 1 standard deviation decrease in rhythm scores on a wide variety of musical rhythm measures is associated with an approximately 1.3 times increase in the odds of having developmental speech-language difficulties or disorders, across a variety of conditions. We believe these are clinically impactful findings in that they emphasize the importance and potential usefulness of rhythm skills in future screening tools for speech and language, which in turn could result in improved identification of individuals at-risk for these disorders. Additionally, our results suggest potentially shared genetic and neurobiological mechanisms, aligning with previous theoretical work. These insights could have future clinical implications beyond the observed correlation, such as improving our understanding of developmental speech-language disorders and their (neuro)biological correlates. We certainly agree that many factors other than rhythm abilities have a likely greater clinically relevant effect on speech-language disorders, however we believe that discussion about all of the other specific factors is beyond the scope of this work. We do briefly mention other transdiagnostic dimensions that we think are important for speech-language disorders:

"Other relevant domains for speech-language disorders may include sensorimotor, cognitive, or social processes that overlap to some extent with each other, and with rhythm abilities."

More directly to the reviewer's point, we have now added additional text to our discussion section in its final paragraph:

"Based on the current data, we cannot directly assess how clinically impactful these insights about rhythm skills as a correlate or risk factor for developmental speech-language disorders will be, relative to other known predictors and dimensions. Our results suggest shared genetic influences, with potential downstream effects on shared neurobiology, aligning with previous theoretical work. These insights could have future clinical value beyond the correlations observed here, including for precision medicine approaches which rely on better understanding individual differences. Therefore, future efforts in building and sharing large-scale epidemiological and genomic data focused on communication-related traits are important to expand the current evidence base."

3) The general statement on p. 17 that rhythm impairments were associated with increased likelihood of a series of speech-language disorders should not include stuttering (as reported on p. 12, stuttering yielded the opposite effect).

Thank you for noticing this oversight, we have now removed stuttering from the list in the general statement that was previously on p.17 (in the Discussion section). This paragraph now emphasizes the converging evidence across many disorders, while clarifying that this does not apply to the stuttering findings. This revision also explicitly discusses stuttering findings (see also our responses to *Reviewer #1's Comment #2* and *Comment #3*).

> "Consistent with the predictions of the *Atypical Rhythm Risk Hypothesis*[25], our epidemiological investigations (Study 1; *N* = 39,358) found substantial converging evidence that rhythm impairments are a transdiagnostic risk factor for developmental communication-related disorders. We showed this using unprecedented sample sizes, and across four independent cohorts, with rhythm abilities (perception, production, and synchronization) measured in several different ways. Specifically, greater rhythm impairments were associated with increased odds of childhood history of speech-language therapy, speech or articulation disorders, dyslexia, reading struggles, DLD, and learning disabilities."

4) p. 11: "Poor rhythmic skills are associated with the likelihood to have received therapies as child." If rhythmic deficits persist, does it mean that traditional language therapies haven't been successful after all? And that rhythmic-based therapies might be more specific and effective? This for example was hypothesized on the unexpected effect of high rhythmic abilities in individuals who stuttered, perhaps as an effect of targeted rhythmic therapies.

Thank you for this clarifying question. We did not mean to imply that rhythmic therapies are more specific or effective than traditional language therapies, or that childhood speech-language therapy for those who received it was not effective. We believe the revisions we made in response to reviewers' comments now address this concern (see our more detailed response to *Reviewer 1 (Comment #2* and *#7)*.

5) The statistical analyses could be clearer. To enhance transparency and reproducibility, the authors should describe in detail the statistical models (sample, variable selection, software packages) that have been run to produce all the reported results.

We appreciate this comment and are committed to transparency and reproducibility. Additional details about samples, data processing, analyses, and software packages have been included in this revision, in two new subsections with the Methods: (1) "Data Processing and Analyses"; (2) "Cohort Details". The manuscript's Introduction and Results sections now refer readers to this new section throughout. Further, our code is now shared on an OSF repository (currently accessible at: https://osf.io/jc87w/?view_only=312c13e7646440648ed46441baf0182e), which will be made public upon publication. We have also shared source data (where allowable within data use agreements), to ensure transparency, and reproducibility by other researchers.

We also now clarify where readers can find these details early in the Results section:

> "Details of phenotypic measures related to musical rhythm abilities, and speech-language difficulties/disorders are given in *Methods: Cohort Details*. Variable selection for models was theory driven throughout. Rhythm measures were included as predictors and speech-language measures were included as outcome, to test our central hypotheses (see *Methods: Data*

Processing and Analyses). All Study 1 statistical models controlled for age and sex (Tables S.2.1 - S.5.6)."

Minor issues:

6) p.18: This could be clearer "Last, based on current referral practices in the US and other countries, our large-scale findings about rhythm and history of speech-language therapy may serve as a proxy for developmental speech-language delays, which are known to hinder educational and socioeconomic trajectories." How can these large-scale findings be a proxy? It might make more sense to say that the current findings suggest that rhythmic skills and rhythm related PGSs can be used as a proxy/predictor of language delays.

Thank you for noticing that oversight. That statement was unclear, and has been removed altogether in this revision.

7) It would be helpful to provide the age range of all the subgroups from the various studies analysed for the current work. For example, in the ABCD cohort individuals were monitored from about 10 years old up to 10 years later. Were the reading score data included in this study sampled from the latest year of monitoring? This would offer insights into the life stages during which participants were tested.

We agree with the reviewer here that providing age ranges will be helpful for lifespan insights when considering the results of the study. To be consistent across all datasets, we now include age ranges, mean ages, and SDs of ages, for each dataset in the Methods section. For example, we now specify for the ABCD cohort:

> "*N* = 5,460 participants … (2,571 females; $Mean_{Age}$ = 9.46 years; *SD* = 0.54 years) were included in the study"

and for the OM cohort:

> "The present study analyses included *N* = 2,535 participants (1,833 females); aged 18 - 88 ($Mean_{Age}$ = 42.27 years; *SD* = 15.81 years) of the original study cohort for phenotypic analyses; and N = 1,792 participants for genetic analyses (1326 females); aged 18 - 88 ($Mean_{Age}$ = 44.96 years; *SD* = 16.23 years).

8) There is *(sic)* **a number or writing/grammatical typos. Please check the manuscript throughout:**

p. 4: "are sensitive to early intervention.25–28" should be "are sensitive to early intervention25–28."

Thank you for the correction. Here and elsewhere in the manuscript, we have moved all superscript references to before the period, as suggested.

p. 7: "whether lower performance on musical rhythm measures are associated with higher" should be "whether lower performance on musical rhythm measures is associated with a higher …"

We have now corrected this, as suggested.

p.12: ““Results showed that a 1 SD decrease in rhythm scores were significantly” should be “Results showed that a 1 SD decrease in rhythm scores was significantly … with a lower likelihood ….”

We have now corrected this, as suggested.

p. 16 “sychronization” should be “synchronization”.

We have now corrected this typo, as suggested, and copy edited the rest of the manuscript.