

Investigating the genetic relationship between motor traits and music training.

Henechowitz T.L., ^{1,2} ; Gordon, R.L., ^{2,3,4} ; Tan, D., ¹ ; Thaut, M.H., ¹

1 .Music and Health Science Research Collaboratory, Faculty of Music, University of Toronto

2. Vanderbilt Genetics Institute, Vanderbilt University Medical Center, Nashville, TN, USA

3. Department of Otolaryngology – Head and Neck Surgery, Vanderbilt University Medical Center, Nashville, TN, USA

4. Vanderbilt Brain Institute, Vanderbilt University, Nashville, TN, USA

Vanderbilt Genetics Institute

VANDERBILT UNIVERSITY
MEDICAL CENTER

Introduction

Evidence for phenotypic associations between **music training** and **motor traits**.

Musicians compared to non-musicians show:

- enhanced sensorimotor skills, manual dexterity, and bimanual and spatial motor learning^{1–6}.
- structural changes in the corpus callosum, internal capsule, sensorimotor, and subcortical areas⁷.
- greater auditory-motor network connectivity⁷.

Evidence for genetic basis (heritability) of **music training**.

Trait	Heritability (h^2)
Musical instrument engagement	0.78
Musical aptitude	0.30–0.66
Musical talent	0.26–0.92
Music practice	0.78

Table 1. adapted from Nayak et al. (2022), *Neurobiology of Language*

Evidence for genetic predispositions for **motor traits**.

- behavioural motor traits** ($h^2=0.29–0.75$)^{8–10}
- subcortical brain volumes implicated in motor control** ($h^2=0.75$)¹¹
- Parkinson's disease** ($h^2=0.16–0.36$)¹²

Is there a relationship between genetic predispositions for motor traits and music training?

Hypothesis

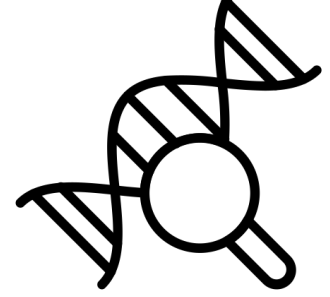
Predict shared genetic architecture between **motor traits** (behavioural, clinical, and neuromotor) and **music training**.

Methods - Data

- Music training** – individual genotyped data, phenotyped for Musician status (N=1492 musicians and N=4893 matched controls of European ancestry)¹³



1. Algorithmic search of Vanderbilt's electronic health records



2. Search for genotyped records in BioVU repository

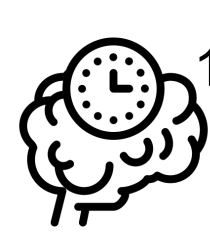


3. N=1492 musicians and N=4893 matched controls

- Motor traits:** Results from previous discovery Genome wide association studies (GWAS)^{15–17}

Behavioural Traits

Neuromotor Clinical



Processing speed



Neuromuscular strength



Locomotion



Putamen volume

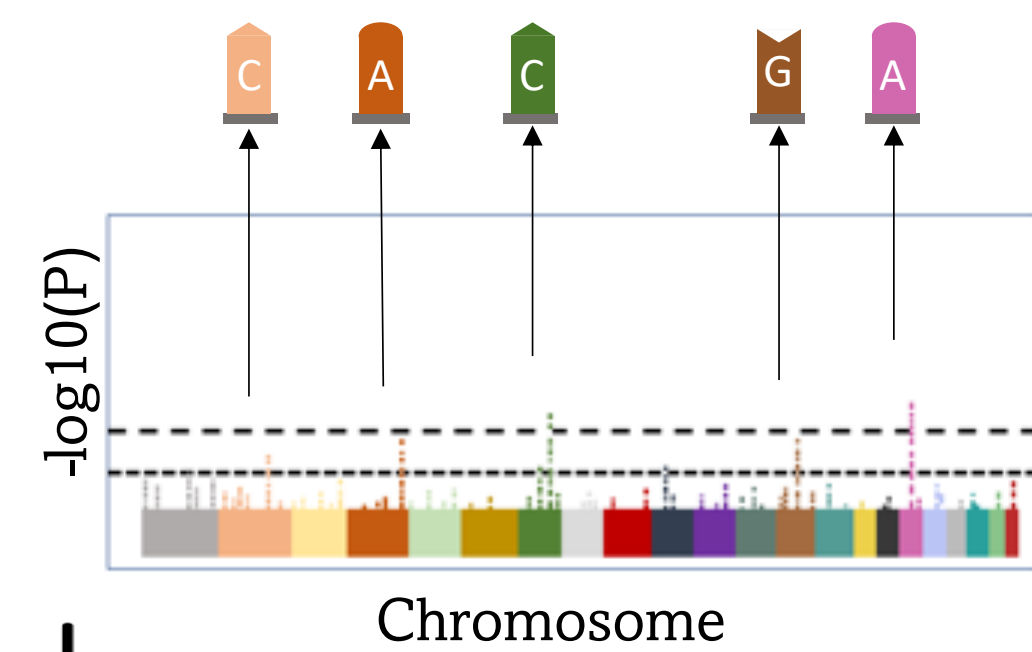


Parkinson's disease

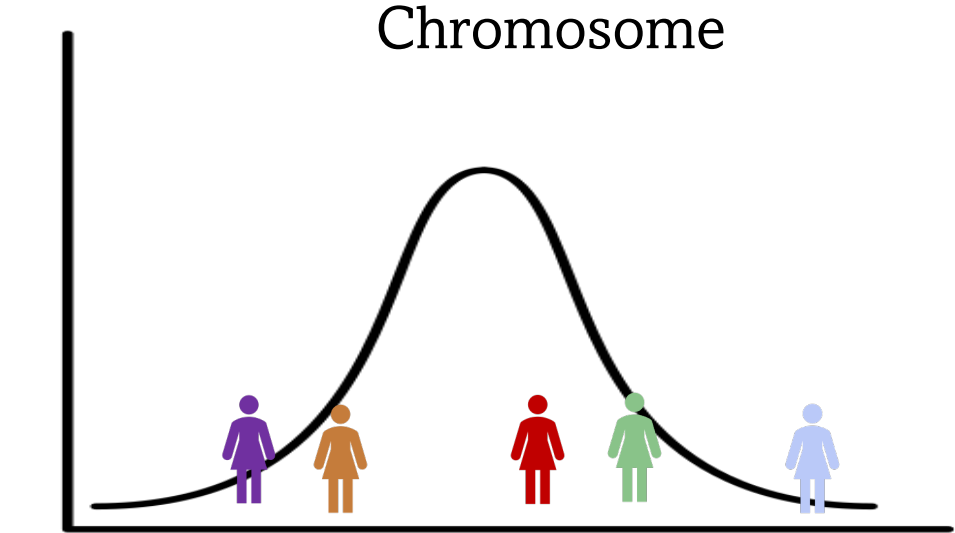
GWAS Reaction time N= 384081 Hand grip strength N= 359729 Walking Pace N=358695 N=29984 ICD20 diagnosis N= 361194

Methods – Genetic Analyses

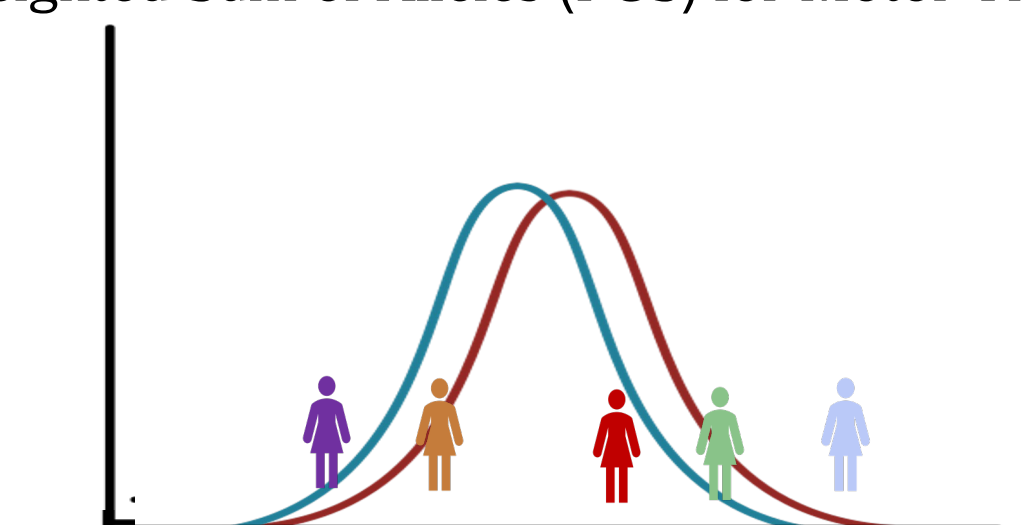
Polygenic scores (PGS) were generated to test the association between **music training** and five **motor traits** using prs-cs software¹⁶.



A. Extract the weighted sum of alleles from Discovery GWAS of a **motor trait** (i.e., locomotion)



B. Weights are applied to a **new genotyped sample of musicians and controls** to get polygenic scores



C. Relate the **polygenic scores for motor trait** to the measured **music training trait** (musician or control)

Weighted Sum of Alleles (PGS) for Motor Trait

Figure 1. Explanation of Polygenic scores adapted from Gustavson and Coleman et al. (under review)

D. 5 Logistic Regression models fitted (one for each motor trait)

Hypothesis: $\log\text{-odds}(\text{musician}=1, \text{control}=0) \sim \text{Motor-PGS} + \text{covariates} + e$

Results

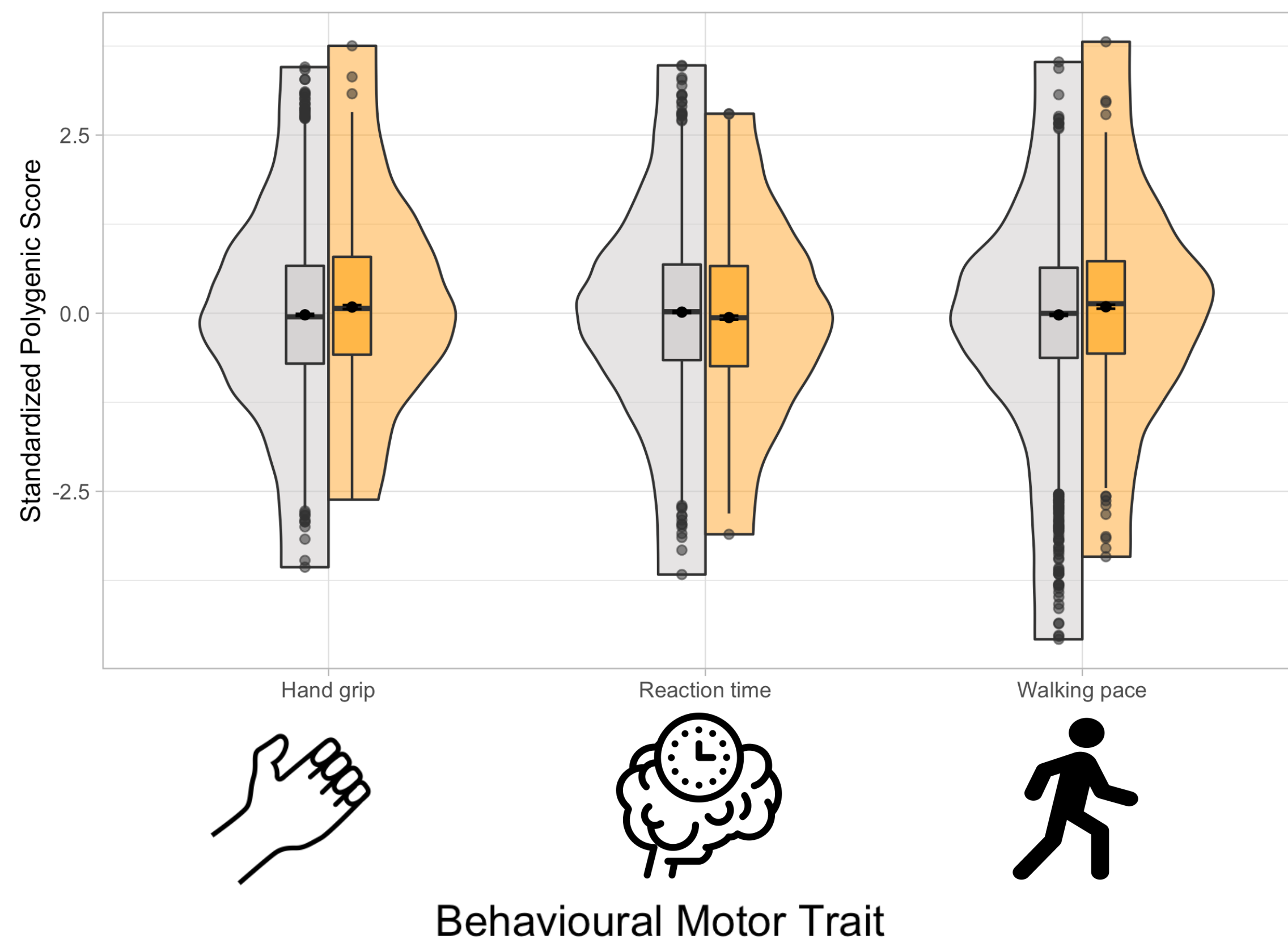
- Evidence for genetic associations **between motor behaviour traits** and **music training**.

- Processing speed PGS** predicts musician status, when controlling for gender and ancestry principal components, **$p=0.0136$** .
 - On average, a 1-point increase in standardized PGS for longer reaction time was associated with an 8% decrease in the odds of being a musician (vs. control).
 - OR = 0.92 (95% CI of 0.891 to 0.98), *Nagelkerke pseudo-R²* = 0.014.

- Neuromuscular strength PGS** predicts musician status, when controlling for gender and ancestry principal components, **$p=0.0023$** .
 - On average, a 1-point increase in standardized PGS for hand grip strength was associated with a 10% increase in the odds of being a musician (vs. control).
 - OR = 1.10 (95% CI of 1.04 to 1.17), *Nagelkerke pseudoR²* = 0.015.

- Locomotion strength PGS** predicts musician status, when controlling for gender and ancestry principal components, **$p<0.0001$** .
 - On average, a 1-point increase in standardized PGS for usual walking pace was associated with an 18% increase in the odds of being a musician (vs. control).
 - OR = 1.18 (95% CI of 1.01 to 1.26), *Nagelkerke pseudoR²* = 0.018.

Figure 2. Distributions of Behavioural Motor Trait Polygenic Scores by Musician Status

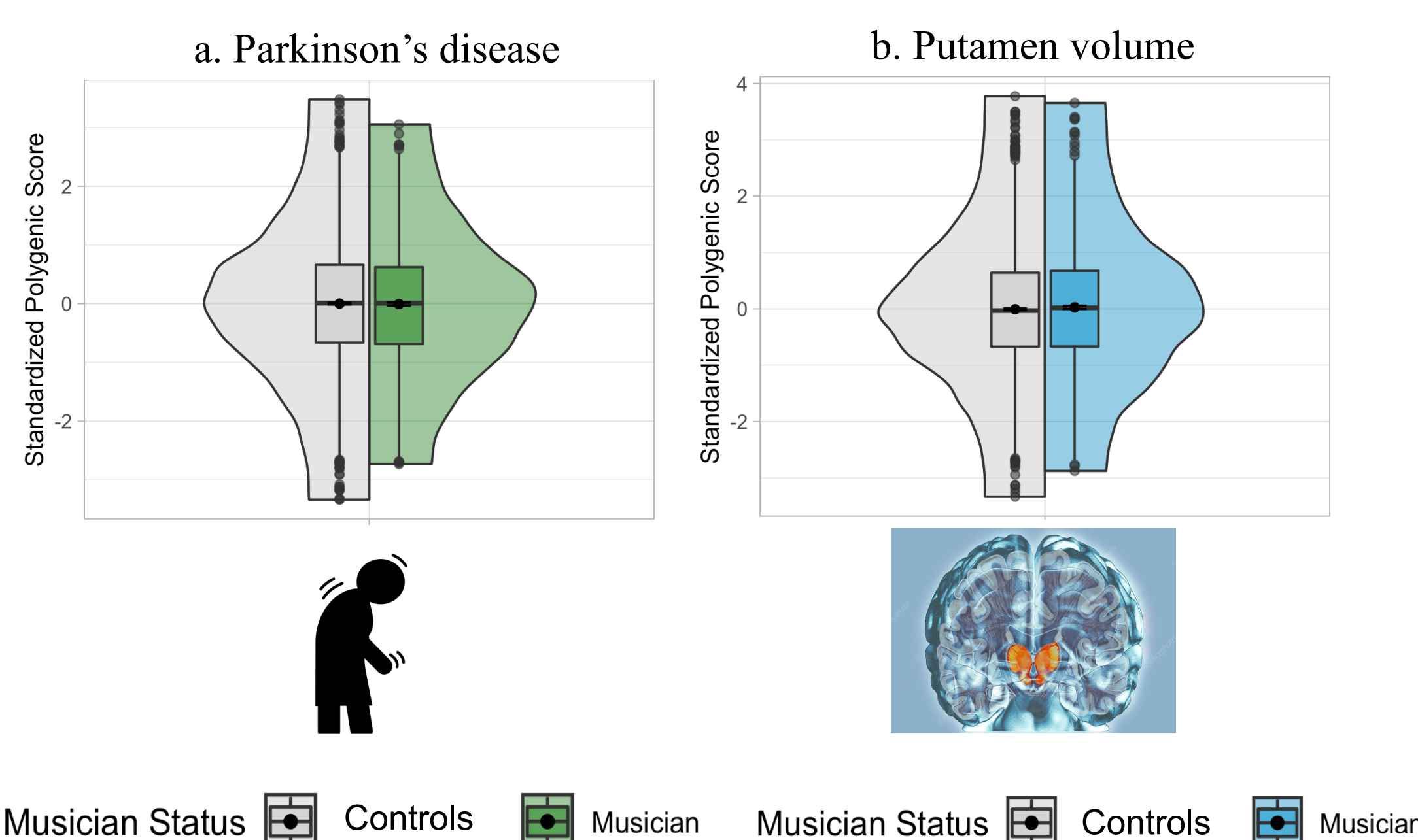


- Genetic associations between **music training** and **clinical motor trait** or **neuromotor trait** and **music training** are non-significant.

a. PRS of **clinical motor trait** (Parkinson's disease) does not predict Musician status, $p=0.79683$, *Nagelkerke pseudo-R²* = 0.01250194.

b. PRS of **neuromotor trait** (subcortical volume of Putamen) does not predict Musician status, $p=0.77983$, *Nagelkerke pseudo-R²* = 0.01249931.

Figure 3. Distribution of Polygenic Scores by Musician Status



Discussion

Genetic association of motor behaviour traits and music training indicates potential shared biology.

- Walking Pace PGS with largest effect is genetically correlated with rhythm and several health traits¹⁷
- Future planned **Neuromotor** analyses include volume of the caudate, cingulate, and cortical volumes
- Predict the genetic predispositions to caudate volume** in musicians to volume of the caudate in musicians due to importance for motor control and music training⁷
- Predict genetic variation in longitudinal change in brain area volumes** across the lifespan are important for music training¹¹
- Future studies may investigate other **clinical traits**

Limitations and Future Directions

- BioVU musician-control data is limited to Europeans Data collection is underway for more diverse samples with deeper phenotyping of musicians
- Findings will be replicated in larger cohorts

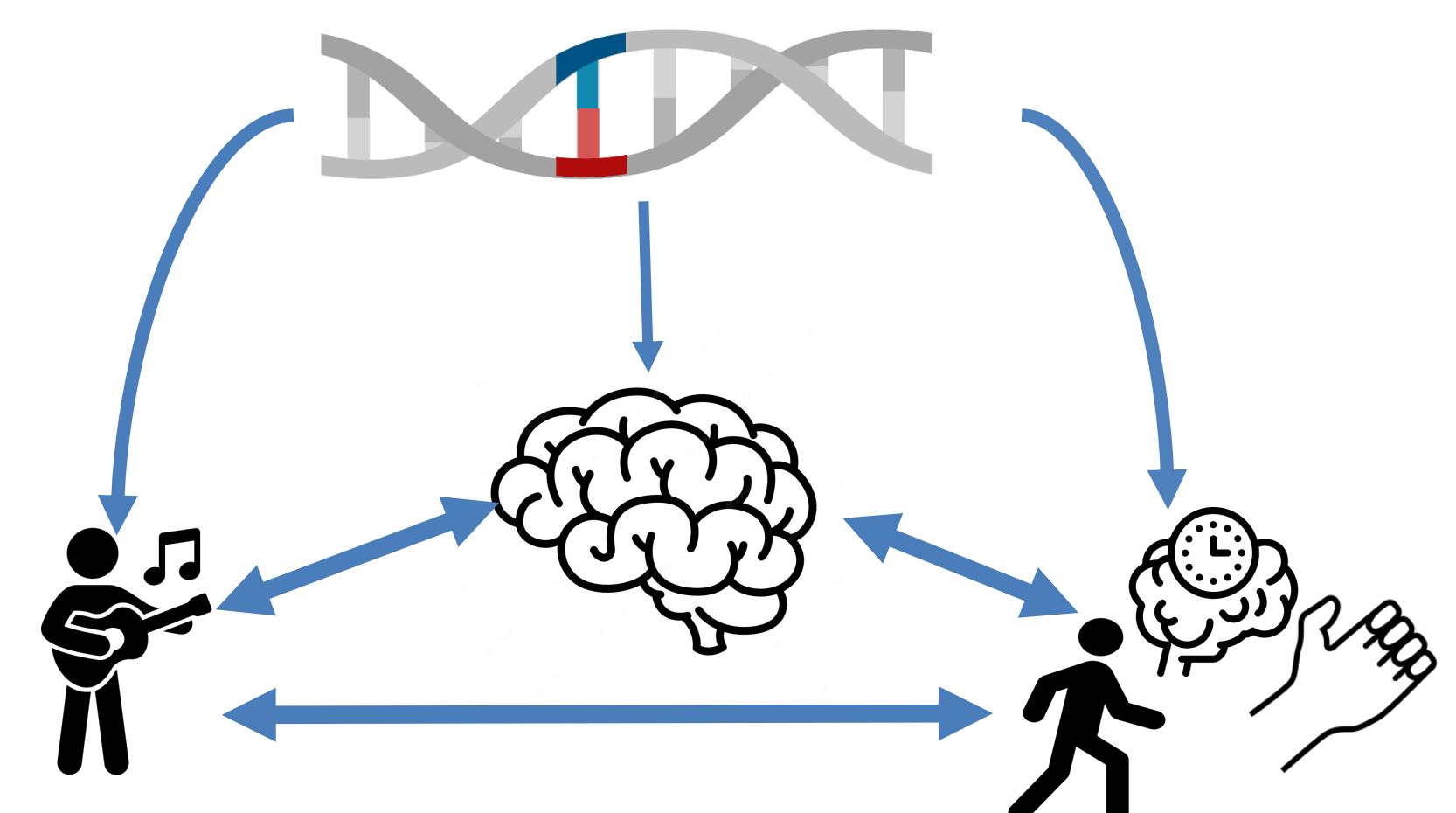
- Future direction: examining genetically regulated gene expression¹⁸

Current level of Analysis → Future Analyses



- Modelling the genetic relationship between motor behaviour, brain, and music training.

Mediation? Causality?



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Connect with Me!

Tara Henechowitz, BMus.Hons, M.A.

Ph.D. Candidate in Neuroscience at the University of Toronto

Visiting Ph.D. Candidate at Vanderbilt Music Cognition Laboratory,

Vanderbilt Genetics Institute, Vanderbilt University Medical Centre

tara.henechowitz@mail.utoronto.ca

I'm on Twitter!

