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Music and Genetics

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ABSTRACT

The first part of this review provides a brief historical background of behavior genetic research and how twin and genotype data can be utilized to study genetic influences on individual differences in human behavior. We then review the field of music genetics, from its emergence to large scale twin studies and the recent, first molecular genetic studies of music-related traits. In the second part of the review, we discuss the wider utility of twin and genotype data beyond estimating heritability and gene-finding. We present four examples of music studies that utilized genetically informative samples to analyze causality and gene-environmental interplay for music skills. Overall, research in the field of music genetics has gained much momentum over the last decade and its findings highlight the importance of studying both environmental and genetic factors and particularly their interplay, paving the way for exciting and fruitful times to come.

1. Behavior genetic research

To analyze genetic influences on a behavior of interest, behavior genetics research has made use of *twin data* and *genotype data*. Since the early 1900s, twin studies have been used to estimate the relative importance of genetic and environmental factors on individual differences in behavior. Monozygotic (MZ) twins are derived from a single fertilized egg cell and share ~100% of their segregating genes, whereas dizygotic (DZ) twins are derived from two distinct zygotes and share on average 50% of their segregating genes. In addition, both types of twins share their common (or family) environment, which includes their home environment, their prenatal environment (i.e., their mother's womb), and many other family-related factors (such as the neighborhood) that make the two twins of a pair more similar to each other. Pairs of neither type share their unique environment, which are all influences making the twins different from one another, e.g., different teachers, friends or idiosyncratic experiences. Therefore, when the resemblance in the behavior of interest is higher within MZ twin pairs than within DZ twin pairs, we can conclude that genetic factors influence variation in the behavior. As common environmental factors make both types of twins more similar to each other, a DZ twin correlation larger than half the MZ twin correlation suggests common environmental influences. Differences between MZ twins are attributed to unique environmental influences. With the use of structural equation modeling, estimates of genetic, common environmental and unique environmental influences can be calculated, where the unique environment term will also include measurement error (Neale and Cardon, 1992). In addition to allowing estimations of genetic influences on traits (the heritability) and their covariation, twin studies can also be utilized to strengthen causal inferences by controlling for familial confounding and investigate more complex gene-environment interplay. We will discuss some examples of designs used for such purposes at the end of the review.

Collectively, decades of twin studies show that phenotypic variability in essentially all human complex traits partly reflects genetic variability (Polderman et al., 2015). Molecular genetic research, evolving after the discovery of the deoxyribonucleic acid (DNA) helix in 1953, offered the opportunity to investigate exactly which genetic variants in the genome are involved with certain human traits or behavior. The human DNA contains four to five million single-nucleotide polymorphisms (SNPs), or genetic variants. In the 1980s, family linkage studies were firstly used to link genetic regions to heritable human behavior at the molecular level. However, this approach turned out to be successful only in exceptional cases, namely for phenotypes that are influenced by genes with very large effect sizes, such as single-gene

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disorders. In the early 2000s, the first whole human genome was sequenced. At first, researchers tried to test hypotheses about associations between behavior and specific genetic variants based on ideas of possible underlying biological mechanisms. This was the era of so-called candidate gene studies. However, it soon became apparent that there was not enough understanding of the genetic architecture of human diseases and particularly complex behavior to come up with good enough a priori hypotheses. Since then, candidate gene studies have been shown to be extremely prone to false-positive findings and have encountered severe replication problems (Duncan and Keller, 2011). Over time, as more human genomes were sequenced, more insight into the underlying human genetic architecture was gained. Most importantly, it became clear that most human behavior is polygenic, meaning that is it influenced by more than one genetic variant. Likewise, genetic variants are typically pleiotropic and influence more than one trait (Abdellaoui and Verweij, 2021). An important step was the emergence of genome reference datasets that make it possible to impute missing SNPs. This allowed measuring more genetic variants in individuals, for less money, and resulted in the first genome-wide association study (GWAS) in 2005. In a GWAS, each measured and imputed genetic variant (or SNP) is tested for its association with a behavior of interest in an exploratory manner. As this leads to huge numbers of tests being conducted and most human traits are influenced by many genetic variants with very small effects, GWASs require extremely large samples and rigid adjustment for multiple testing. Nevertheless, this hypothesis-free design has resulted in many new and replicable associations between genetic variants and human diseases or behavior (Abdellaoui and Verweij, 2021). It also gave rise to post-GWAS approaches to further study genetic variants discovered by the GWAS and their associations. For example, in the polygenic score approach, the estimated effect sizes of the genetic variants as identified in the GWAS are used as weights to calculate a score for each individual, representing his or her genetic propensity for the behavior studied in the GWAS (Wray et al., 2020). Polygenic scores offer the possibility to investigate, among other things, phenomena such as gene-environment correlation, gene-environment interaction and within-family causality (Willoughby et al., 2023). Overall, in the last decades, the field of molecular genetics has made impressive strides forward, with innovative methodologies that facilitate the exploration of the genetic basis of human traits and new gene-finding techniques developing at a fast rate. Notably, the synthesis of the world of twin research and molecular genetics is being hailed as the most important development in behavior genetic research in the 21st century (Plomin, 2023).

2. Music and genetics

While much research on music-related traits and behavior has focused on environmental factors, the underlying genetic architecture has only more recently gained attention. The first evidence for a genetic basis for music-related traits comes from the fact that music is, since ancient times, present in all populations and cultures around the world (Morley, 2018). If people from all around the world engage in music, it seems that music engagement is a human behavioral tendency that is part of our biology, and not only dependent on a particular environment or culture. Another reason to suspect genetic influences on music-related traits comes from the observation that music skills aggregate within families (Bruton, 2021). One of the most famous examples is the Bach family, which consisted of more than fifty highly accomplished and well-known musicians. The fact that music abilities cluster in families does not tell us exactly how important genetic influences are, because family members share both part of their genes and common environment. Nevertheless, it does suggest that there might be a heritable component to music-related traits. Lastly, we know about at least two genetically determined syndromes that cause cognitive impairments, but also alter individuals' music skills. The Williams-Beuren syndrome, caused by a heterozygous gene deletion on chromosome 7, causes serious cognitive deficits. Music skills, however, are relatively retained and the affected individuals often show a strong interest in music (Thakur et al., 2018). On the other hand, a different condition, caused by a rare mutation on the same chromosome, is characterized by severe language problems and reduced music skills (Fisher and Scharff, 2009). The fact that gene mutations can alter music abilities suggests that music-related traits are at least to some degree influenced by genetic factors.

2.1. *Twin studies on music skills and music-related traits*

An overview of heritability estimates derived by twin studies on self-reported and objectively measured music skills, music achievement and other music-related traits is given in Fig. 1.

One of the first twin studies that investigated to what degree music abilities were influenced by genetic and environmental influences was conducted by Coon and Carey (1989), who studied young twins' resemblance for an interest in a profession in music, instrumental performance in school, instrumental performance outside of school, and receiving honors in music. Although common family environmental influences explained most variation in music abilities, they also found evidence for a significant influence of genetic factors, though to a lesser extent. However, this study was based on a relatively small sample of children and today we know that for most human behaviors, influences of the common environment, if present, are stronger during childhood and decrease in adulthood, while the influence of genetic factors in contrast increase with age (Knopik et al., 2017). In line with this, Gustavson et al. (2023) found instrument engagement in 10-year old children (including singing) rated by their parents to be mostly influenced by common environmental influences (92%) (Gustavson et al., 2023), while adolescent instrument engagement and singing was highly heritable (78% and 43% respectively) (Gustavson et al., 2021). Importantly, using parental reports can introduce so-called 'rater bias', which can lead to an overestimation of common environmental influences and an underestimation of genetic influences, possibly explaining some of the variation we see between child- and parent rated measures (Wesseldijk et al., 2017). Another study by (Vinkhuyzen et al., 2009) explored the heritability of self-rated aptitude in the music domain in adulthood ranging from less competent than most people, to exceptionally skilled (four response alternatives). Heritability estimates for music aptitude were moderate (30–66%), with significant common environmental influences. Exceptional skill showed an even higher heritability (86%). All these studies relied on either parental- or self-reported questionnaire responses that were not objectively measuring music ability.

The first study that objectively measured music skills in twins, was conducted by Drayna et al., (2001), who administered a test requiring the participant to identify incorrect pitches in familiar melodic stimuli in 136 MZ and 148 DZ twin pairs. The authors found genetic factors to explain 70–80% of individual differences in music pitch recognition. The largest twin study until now using objectively measured music skills looked at music discrimination skills for melodies, rhythms, and single pitches in around 10,500 adult Swedish twin individuals (Mosing et al., 2014; Ullén et al., 2014). All were moderately heritable (melodies 50%, rhythms 59% and pitches 12% in males and 30% in females). Only variation in pitch discrimination ability in males was partly influenced by the common environment (38%). A recent study by Yeom et al. (2022) investigated objectively measured singing ability across five performance measures of pitch and interval accuracy and found a moderate heritability of 40.7%, and a similar influence of the common environment (37.1%). Lastly, there are three small Finnish family pedigree studies (that in contrast to twin studies compare resemblance between multiple family members instead of twins) (Oikkonen et al., 2015; Pulli et al., 2008; Ukkola, Onkamo, Raijas, Karma, and Järvelä, 2009), which reported moderate heritably estimates for performance on the Karma Music Test (Karma, 2007) and pitch and time discrimination tests (Seashore et al., 1940). The Karma Music Test measures recognition

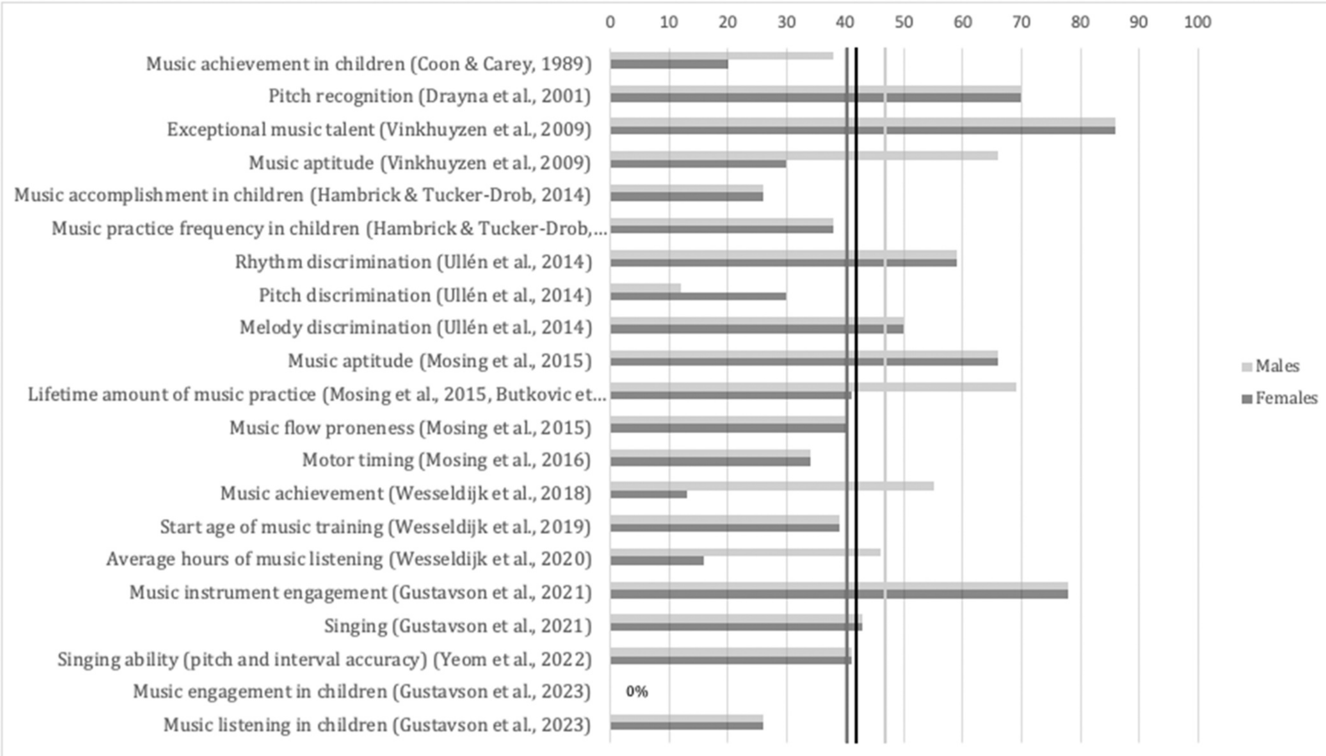

Fig. 1. Overview of heritability estimates for music-related traits and behavior derived by twin studies. Studies included adult participants unless indicated otherwise. Average heritability estimates for males, females and the total mean average (in black) are indicated by the vertical lines.

of melodic contour, grouping, relational pitch processing, and Gestalt principles. The Seashore tests and the Swedish Musical Discrimination Test measure the ability to discriminate between small differences in basic musical elements, such as melodies, single pitches, or rhythmic patterns. Clearly, musical ability is multifaceted, and complex and subjective musical skills, such as the ability to perform in a musically expressive way, or to improvise, remain challenging to measure.

Beside studies on music skills, there are also twin studies investigating genetic and environmental influences on self-reported music achievement. A study by Hambrick and Tucker-Drob (2015) looked at whether participants received a high ranking in a music contest, and reported a heritability of 26% for music accomplishment, while common environmental influences explained 61% of the variation. A more recent twin study in 6500 twins showed that genetic factors are particularly important in men (55%) for lifetime music achievement, while genetic influences were much smaller (13%) in women (Wesseldijk et al., 2019). In women, 40% of the variance in music achievement was explained by common environmental influences, compared to 14% in men. These discrepancies between the sexes are in agreement with the studies by Coon and Carey (1989) and Vinkhuyzen et al. (2009), who also found that common family environmental factors are more important for self-reported music skills in women than in men. One possible explanation for such sex-differences is that in the Western culture, girls are more often encouraged to engage in music playing independent of their talent or interest, while boys are more likely encouraged to pursue sports (and possibly discouraged to play a music instrument), unless they show specific talent or interest in music (i.e., genetic predisposition) in the first place.

There are twin studies on other music-related phenotypes that are worth mentioning. Two twin studies to date investigated absolute pitch, i.e., the ability to identify pitches without relying on an external reference note, and found a significantly higher concordance rate of absolute pitch for monozygotic than for dizygotic twins, suggesting genetic influences (Theusch and Gitschier, 2011). Genetic influences have also been found for music specialization, namely instrument choice, instrument category, and the type of music individuals engage in (Mosing and Ullén, 2018, Fig. 1 does not include this study due to the lack of one heritability estimate). In line with these results, also the time which people spend listening to music has been shown to be influenced by genetic factors in adults (16–46%) (Wesseldijk et al., 2020) and in 10-year old children (26%) (Gustavson, Nayak et al., 2023). One of the most exciting and surprising findings in this field of research came from two twin studies which found that the time spent on music practice itself, which traditionally has been regarded as a solely environmental influence on music skill, is also partly influenced by genetic factors (40%–70%) (Hambrick and Tucker-Drob, 2015; Mosing et al., 2014). In addition, the latter study (Mosing et al., 2014) demonstrated that the relationship between music practice and musical aptitude was entirely explained by familial factors, with no evidence for a causal effect of music practice on aptitude (as measured by the Swedish Music Discrimination Test), a finding which provides a serious challenge for the deliberate practice theory (Ericsson et al., 1993). Similarly, a twin study investigating the positive association between music practice and general intelligence – commonly interpreted as reflecting a transfer effect from practice to intelligence – also found the association to be mostly explained by shared genetic factors (Mosing et al., 2016). This suggests that voluntary music practice in the general population though associated with intelligence is not likely to have any causal influence on intelligence. Lastly, even the age at which children start music training, often considered a purely environmental decision taken by the parents and regarded as a potential causal predictor of good music skills in adulthood, was partly influenced by genetic factors (39%) (Wesseldijk et al., 2020). Results from these studies show that genetics plays a substantial role for almost all music-related traits and behaviors and have led to a shift in understanding the etiology of expertise, away from the deliberate practice theory, and towards the development of the multifactorial gene-environment interaction model (MGIM) (Ullén et al., 2016). Central features of this model are that expertise in music and other domains depend on many factors apart from practice at the phenotypic level, and that gene-environment interplay plays a crucial role for expertise acquisition. Overall, the research findings reviewed have not only led to a paradigm shift within the field of music and expertise research, but also has informed research in other fields, including neuroscience and psychology.

To summarize, even though the exact amount of genetic influence differs depending on the aspect of music measured, subjectivity of the measure and the rater, the age range of the twin sample, and the sex distribution, twin studies consistently show that a broad range of music skills and music-related behaviors have a considerable genetic basis (ranging from 0% to 86%, with an average of 42% for all studies, see Fig. 1). Further, genetic influences seem to be higher for music skills or aptitude than for music achievement or engagement, higher for men than for women and tend to increase with age.

2.2. Molecular genetic studies on music-related traits

Although the field is still in its infancy, the first studies aiming to reveal specific genes relevant for music-related traits and behavior have also emerged. Just as in most research fields, the earliest molecular genetic studies on music skills focused on linkage and candidate gene studies, which are known to suffer from replication problems and are hampered by small sample sizes. The most consistent findings are associations between genetic variants (SNPs) on chromosome 8q and absolute pitch and music perception as well as between chromosome 4 and music aptitude, accuracy of pitch perception, and pitch accuracy during singing and composing in Finnish and Mongolian populations (Park et al., 2012; Pulli et al., 2008). In addition, the gene AVPR1A on chromosome 12 has been associated with music perception, dance performance and music listening (Ukkola-Vuoti et al., 2011), whereas gene SLC6A4 on chromosome 17 showed associations with dance performance, music memory and choral singing (Granot et al., 2007). Lastly, music aptitude has also been found to be related to several copy number variations in the genome. For a detailed review of candidate and genome-wide linkage studies on music skills, see Tan et al., (2014); Beccacece et al., (2021).

Recently, the first large-scale GWAS was performed on a music-related phenotype using data from the personal genetics company 23andMe. In this GWAS, the authors compared the genomes of individuals who reported that they can clap in time with a music beat ($N = 555{,}660$) to those that reported they cannot ($N = 51{,}165$) (Niarchou et al., 2022). To date this is the only large scale GWAS on a music-related phenotype. Although this single question is obviously limited as a measure of music skills, the authors performed extensive validations of the item, showing that it was correlated with accuracy in tapping to the beat of music excerpts and associated with several other music-related phenotypes. The GWAS identified sixty-nine genetic loci that influence variation in self-reported music beat synchronization ability. Overall, this study revealed that the underlying genetic architecture of humans' capacity to synchronize to a music beat is highly polygenic, meaning that many genetic loci are involved, as well as pleiotropic, with the genetic loci being involved in several human traits. As a follow-up study, the effect sizes from this GWAS were used to calculate polygenic scores in the Swedish twin sample (described above) that was extensively phenotyped on music skills and music-related traits (Wesseldijk et al., 2022). The resulting polygenic scores, which represent each individual's genetic propensity for their (self-perceived) capacity to synchronize to a music beat, could significantly predict objectively measured rhythm discrimination as well as other music skills, like melody discrimination, pitch discrimination and overall music aptitude. Interestingly, the genetic variants underlying self-reported beat synchronization ability also significantly and to a similar degree predicted other music-related behaviors such as total amount of music practice, music listening, achievement in music, and flow proneness in the music domain and even dance achievement. In contrast, the polygenic score was not significantly associated with any non-music related control variables such as intelligence, sport engagement or flow proneness in other domains. This suggests, that the self-reported beat synchronization GWAS and as such the polygenic score may tap into the genetic architecture underlying broader music-related traits with good discriminant validity and can be utilized for further research into gene-environmental interplay underlying music-related traits. This finding was replicated by a recent study that found the polygenic score for beat synchronization ability to predict both rhythm perception and music engagement in ~1800 American individuals, confirming that genetic influences underlying self-reported beat synchronization ability also influence individuals' rhythmic discrimination aptitude and the degree to which they engage in music. In addition, using genome-wide complex trait analyses (GCTA or GREML), the authors were able to calculate a SNP-based heritability of 31% for rhythmic perception and 12% for self-reported music engagement (Gustavson et al., 2023).

To summarize, even though early results from molecular genetic studies on music-related traits are encouraging, they are hampered by replication problems and small effect sizes. Recently the first well-powered GWAS and post-GWAS genetic analyses were conducted on a music-related phenotype. Given the complexity of music-related traits and their many facets, it is likely that there will be many genetic variants of small effect relevant for music-related traits. As has been seen for other complex traits in the field of human genetics, to unravel the underlying genetic architecture of music, collaborative efforts are needed. The recently founded Musicality Genomics Consortium aims to find ways to (1) define minimal but reliable measures of music-related traits to administer in large genotyped samples, and (2) to harmonize and combine different music-related phenotypes measured in genotyped samples across the world, to maximize sample size. See 'www.mcg.uva.nl/musicgens' for more information. (Fig. 2).

3. The utility of twin and genotype data beyond heritability and gene-finding

That genetics play a role in music-related traits and behavior is well-established by now, and it will only be a matter of time until large-scale GWAS and post-GWAS approaches reveal additional genetic variants relevant for music. However, as for almost all human behavior, genetic and environmental factors work together in a complex interplay in the development of music skills. It is therefore important, when studying the etiology of music-related behavior and its relation to other traits, to take into account both genetic and environmental factors as well as interactions (G×E) and correlations (*r*GE) between them. *G×E interaction* refers to when the magnitude of genetic influence varies as a function of an environmental exposure or when the effect of a given environment depends on an individual's genotype. *r*GE is when genetic and environmental factors correlate with each other, i.e., in a passive, reactive or active way (Knopik et al., 2017). *Passive r*GE refers to the association between the genotype a child inherits and the environment in which the child is raised. For example, musically inclined parents will not only inherit their musical talent to their children but may also create a more musical environment for themselves and their children resulting in a correlation between the child's musical talent and musical family environment. This is also often referred to as genetic nurture. *Reactive r*GE is when environmental conditions are provided to an individual as a reaction to genetically influenced phenotypes expressed by the individual (e.g., a child may be invited to enroll to a special music class in reaction to the child displaying musical talent). Lastly, *active r*GE, also referred to as 'niche-picking' occurs when genetic factors influence an individual to actively search out or create specific environments, i.e., someone with musical interest may be likely to seek out an environment suitable and supportive of music playing (a music college). Genetically informative samples can be utilized to explore such different forms of gene-environment interplay. Further, because MZ twins are genetically

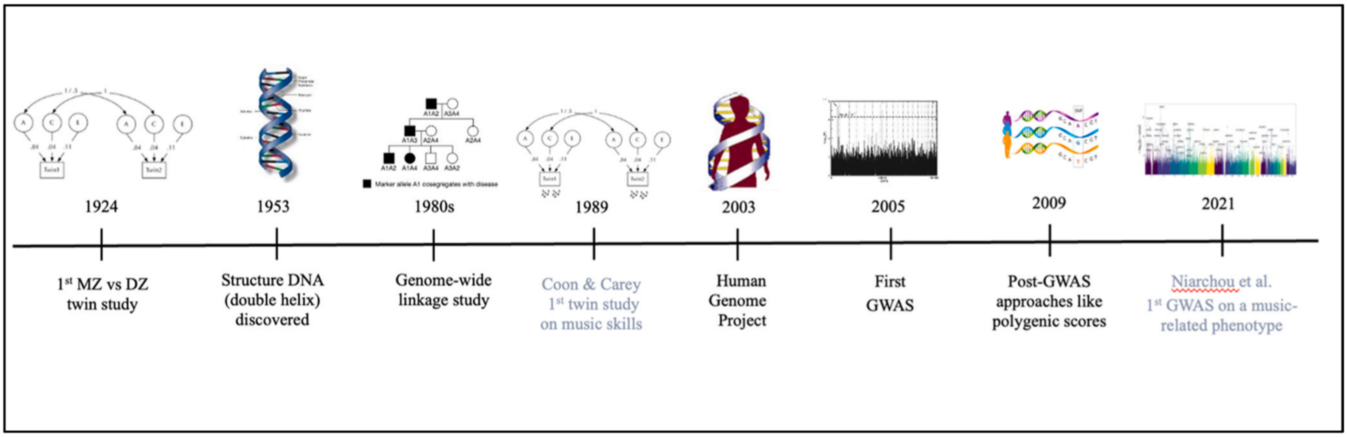

Fig. 2. Timeline of developments in behavior genetic research in relation to milestones in music genetic research.

identical and share their common environment, they are perfect case-controls for each other. Therefore, comparing within-pair effects in MZ twins who differ in their exposure and outcome can estimate associations free from familial confounding and strengthen causal inferences (the co-twin control design; McGue et al., 2010). Below we discuss four examples of studies using twin and genotype data or a combination of both to explore *causality* and *gene-environmental interplay* (G×E and *r*GE) underlying music-related traits. These studies have also been chosen to illustrate how studies using music as a model domain allow researchers to analyze phenomena of broad interest for behavior genetics and indeed the behavioral and neurosciences in general, i.e. sensitive periods in skill acquisition, the importance of the childhood environment for adult achievement, and the relations between leisure activities and health.

3.1. Is there a sensitive period in childhood for music practice? Testing causality with the co-twin control design

A common observation is that successful musicians often start their music training early. One explanation for this is that there may be a sensitive period in early childhood, during which the brain is particularly susceptible to music stimulation. However, it could also be the case that children with greater music skills start music training at an earlier age, as this is more rewarding for them or they are more encouraged. In this scenario, genetic factors would contribute both to starting age of training and level of music skills in adulthood. On the other hand, childhood music training may often be initiated by parents, who share genes with their children. This would imply a role for common familial influences. Importantly, if starting age of training has a causal effect on later skills, we would expect the association to be independent of familial factors. By studying twins, it is possible to estimate genetic and environmental influences on age of onset of music training and analyze discordant MZ twin pairs. If an earlier age of onset for music training truly causes higher music skills, it would be expected that the MZ twins who started at a younger age than their co-twins have, on average, higher music skills. A recent study in 310 professional musicians and 7786 twins found that an earlier age of onset is indeed associated with higher music skills and music achievement in adulthood (Wesseldijk et al., 2020). Even when controlling for lifetime practice, an earlier age of onset of music training predicted higher levels of music skills, but not music achievement, in adulthood. However, the twin analyses showed that the association was fully explained by familial factors, where familial factors influence both the age someone starts training and their music skills in adulthood. In line with that, there was no difference in music skills between twins that started earlier and their later-starting MZ co-twins. Thus, these findings provide little support for a direct causal effect of age of practice onset and music skills and highlight the importance of taking familial influences into account when studying effects of early training on expertise.

3.2. What is the importance of a stimulating childhood environment for adult achievement? Analyses of G×E interaction using a moderator twin model

To gain a better understanding of why most musically active people typically perform at a modest level while a few reach extraordinarily high levels of skill, a study in 6610 twins investigated whether the musical enrichment of the childhood environment moderated the influence of genetic factors on levels of music achievement in adulthood (Wesseldijk et al., 2019). This is a form of *G×E interaction*, when the magnitude of genetic influence varies as a function of an environmental exposure, and can be tested using a so-called moderator twin model (Purcell, 2002). In the study, genetic, common, and unique environmental factors affecting music achievement were estimated, conditional on the level of musical enrichment in the childhood environment, namely, an index derived from the number of music records in the family home, the number of individuals in the family environment playing an instrument, the frequency of concert visits, and music education before the age of 12. The results showed that not only is a more enriched childhood environment associated with higher levels of music achievement in adulthood, it also was associated with higher variation in music achievement, as well as higher heritability. In other words, a musically enriched childhood environment increased the importance of genetic factors on levels of music achievement in adulthood, leading to even higher music achievements in individuals with a genetic predisposition for music.

3.3. Music engagement and mental health – Analyses of G × E interaction with polygenic scores

An example using genotype data to investigate *G×E interaction* comes from a recent study investigating the relationship between music engagement and mental health. While intuitively people commonly believe that making music is good for their mental health and positive effects of music therapy have been established, some studies find more self-reported mood symptoms among musicians (see Gustavson et al., 2021 for a review). To explain these contrasting findings, a recent study investigated whether the association between music engagement and mental health varied depending on an individual's genetic risk for mental health problems, in the form of a polygenic score for major depressive disorder or bipolar disorder (Wesseldijk et al., 2023). Analyses of 5648 individuals showed that people who play music and practice more reported more self-reported depressive symptoms. Effects of music engagement on self-reported depressive symptoms did not differ depending on the individual's polygenic score for either major depressive or bipolar disorder meaning there was no evidence for G×E interaction. It is important to note that polygenic scores as yet explain little genetic variance as they are based on GWASs that capture only a fraction of the genetic variation underlying traits. With sample sizes of the discovery GWASs increasing, prediction accuracy of polygenic scores increase (Abdellaoui and Verweij, 2021). Additionally, detection of interaction effects requires large samples; 80% of power for a moderate effect requires samples larger than 10,000 individuals, while detecting large effects requires only around 600 individuals (Duncan and Keller, 2011; Plomin et al., 2022). Therefore, replication of findings from G×E research is warranted.

3.4. The predictive validity of the first polygenic score for a musical phenotype – Combining genotype and twin data in a within-family design

Lastly, an example of how twin and genotype data can be combined to study *r*GE comes from a recent study using the polygenic score for an individual's capacity to synchronize to a music beat. As explained above, genetic and environmental factors can correlate and this can happen in different forms, i.e., passive, reactive or active. In 5648 genotyped individuals, it was found that the rhythm polygenic score did not only predict other music-related outcomes including music aptitude, practice hours, music achievement etc., but also the level of musical enrichment of the childhood environment (calculated as described in the example before; $r = 0.05$, $p < .001$, CI.02–0.08) (Wesseldijk et al., 2022). This shows that there is some form of *r*GE at play for music-related behavior, as individuals with higher genetic predisposition for music tend to more often grow up in a musically enriched family environment than individuals with a lower genetic propensity for music. Whether this is due to passive, reactive or active *r*GE cannot easily be disentangled, but with a within-family design in complete dizygotic twin-pairs (Selzam et al., 2019), the authors showed that the predictive value of the rhythm polygenic score did not deteriorate within dizygotic twin-pairs (when controlling for common family environmental influences) compared to between unrelated individuals. This suggests that passive *r*GE did not inflate effects of the rhythm polygenic score and that the correlation between the level of music enrichment of the family childhood environment and individuals' genetic predisposition for music could reflect active or reactive *r*GE. Altogether this suggests that when studying the relationship between family environments and its associations with individuals' music skills or other outcomes, effects are likely confounded by familial factors including genetic factors, common family environment and their interplay.

4. Conclusion

Twin studies consistently show that music skills and music-related behaviors have a considerable genetic basis (ranging from 0% to 86%, with an average around 42%). Additionally, genetic influences seem to be more important for individual differences in music skills or aptitude than for variation in music achievement or engagement, higher for men than women and tend to increase with age. Molecular genetic research has only just started to reveal specific genes relevant for music-related traits, and many of the gene-finding studies are limited by small samples and replication problems. However, the first well-powered GWAS identified sixty-nine genetic loci associated with the self-reported ability to synchronize to a music beat. Given the complexity of music-related traits, larger GWASs are needed to provide a better understanding of the genetic variants relevant for different music-related traits and behavior. We concluded this review with four examples which show how studies of music can shed light on questions of broad scientific interest and illustrate how we can utilize genetically informative samples in music research beyond just estimating heritability or identifying genetic loci. Overall, genetic research to date highlights its importance for research on music and, indeed, any culturally acquired behavior, to consider both environmental and genetic factors, as well as their complex patterns of interaction and covariation.

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