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The genetic aspect of musicality, perfect pitch and congenital Amusia

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Abstract

As one of the most important aspects of art, music is also a part of human biology and has had a significant influence on human evolution and development. In addition, it is an essential component of cultural heritage. Both hereditary and environmental variables are thought to play a role in developing and manifesting musical talent. Although environmental variables affecting musical ability have been extensively studied, genetic influences are less well understood. The genetic influence was strongly supported in studies of a random population, twins, and families of talented musicians. Linkage analysis, variation in gene copy number, and scanning for whole-genome expression were among the modern biomolecular methods used to discover genes or chromosomal areas linked to musical ability. Singing and music perception have been linked to many loci on chromosome 4, while absolute pitch and music perception have been linked to specific loci on chromosome 8q. Music perception, memory, and listening have all been linked to the AVPR1A gene on chromosome 12q, while SLC6A4 on chromosome 17q has been linked to music memory and choir involvement.

Keywords: Amusia, music genetics, music perception, music production.

Introduction

Music is a universal language. The ability to perceive, create and reproduce music is recognized as a ubiquitous communication process that involves rhythm, pitch and timbre. However, music competency is diverse across individuals and that adds a driving force to the long-standing debate of whether musical reception and performance are of genetic or environmental background or both.

Compared to more comprehensive research done in the language domain, few studies have focused on the genetic foundation of musical skills (Newbury and Monaco, 2010; Carrion-Castillo et al., 2013). Furthermore, prior behavioural genetic studies of musical aptitude often lacked scientific accuracy or sample numbers (Coon and Carey, 1989). The advent of genetic research in the post-

genomic age offers much potential for this area, which is yet largely unexplored (Tan et al., 2014). Except for a few advances, such as individual variations in musicality explained by genetic background, the present level of knowledge of the genetic foundation of music talent has not been examined much since the development of molecular genetic research (Stewart, 2008; Peretz, 2016; Gingras et al., 2015). It was discovered via the showing of microRNA fraction overexpression in peripheral blood as soon as two hours after a classical music performance. has-miR-3909, has-miR-30d-5p, has-miR-92a-3p, has-miR-222-3p, and has-miR-30a-5p are the five microRNAs that were shown to be significant (Nair et al., 2019). Genes influencing auditory and creative involvement in music have recently been identified using genome-wide linkage and association scanning. The primary instruments for detecting gene copy number changes and estimating gene expression are now gene copy number changes and gene expression estimates, and the findings of this research will be given later on (Szyfter et al., 2020).

The goal of this review is to describe findings of the genetic background of musical ability, as well as new and previously established molecular techniques, to help music and genetic researchers gain a better understanding of this relatively new field, and to encourage increased research effort into uncovering the genetic basis of musical ability.

Inheritance of musical talent in renowned artists' families

The well-known truth is that musical talent runs in families. The family of Johann Sebastian Bach (1685–1750), one of the greatest musical geniuses of all time, is one of the most remarkable instances in music history. There has been a characteristic of hereditary musical talents for over 200 years, spanning six generations of artists. Out of 35 musicians, Johann Sebastian and at least six of his close relatives have left an indelible mark on the history of music: in the generation before Johan Sebastian, the flautist Johann Ambrosius and organist Johann Christoph, and two generations later, four sons, all outstanding composers—Wilhelm Friedemann, Carl Philip Emanuel, Johann Christian Friedr (Wolff, 1983). In reality, the Bach family only received training in the profession of musician, which was handed down from father to son and therefore provided a source of income. However, its difficult to explain the existence of seven famous musicians in one family, across generations, one of whom is an acknowledged genius, and at least two more who are extremely well-known, as the result of family practice alone (Szyfter et al., 2020).

Human genetic method

Various genetic analytical techniques may be used to examine the connection between genes and phenotypes. This section gives an overview of the behavioural and molecular genetic methods frequently utilized in human genetic research.

Behavioural genetic approaches

Familial aggregation

Family aggregation is the clustering of a few traits, behaviors, or syndromes in a given family. Family aggregation may arise thanks to genetic or environmental similarities. This issue may be addressed via familial aggregation, which compares

whether the prevalence of a characteristic is higher in a proband's family than in the general population (Naj et al., 2012). Families and controls are only asked to provide phenotypic evidence. The sibling recurrence-risk ratio (s), which estimates the percentage of proband siblings who also show the investigated feature compared to the population prevalence, is a typical metric resulting from familial aggregation. The size and shape of family associations discovered in domestic aggregation research may provide valuable information about genes and the environment's roles (Naj et al., 2012). A score as low as 1 indicates that genetic effects are negligible, while a value greater than 5 suggests that a genetic theory is worth investigating (Mitry et al., 2011).

The phrase musical aptitude was coined to describe the capacity to approximate rhythm, timbre, tone length, pitch, and music assembly to make the findings on musicality measurable and quantitative. Karma music test (KMT) is a measuring instrument that uses small abstract sound patterns that are repeated to create hierarchic structures (Karma, 1994). The Gaussian distribution of musical aptitude was discovered in the population, which corresponds to conclusions made from observations of brilliant musicians' families.

Ascertainment bias may exaggerate family aggregation measures, which are solely used to assess the presence of familial grouping (Guo, 1998). It does not say how much of the family grouping is caused by genetic or environmental factors. Follow-up research, such as twin and adoption studies, may provide answers to such questions.

Twin studies

Tests on identical or fraternal twins are known as twin studies. The goal is to highlight the significance of environmental and genetic influences on characteristics, phenotypes, and diseases. In behavioural genetics, twin research is regarded as a critical tool. Twin studies aid separates the relative importance of genetic and environmental variables in trait variation (Verweij et al., 2012). Identical or monozygotic (MZ) twins share almost all of their DNA, while fraternal or dizygotic (DZ) twins share just approximately half of their genes, just like any other sibling. As a result, if concordance for a trait is much more significant in the MZ twins, the trait is likely to be heritable.

Twin studies may be used to assess the effects of genetic influence, unique and shared environment on a characteristic using structural equation modelling and statistical tools like Mx (Neale et al., 2006).

Twin studies backed up the importance of genetic variables in the development of personal musicality (Oikkonen and Järvelä, 2014). The participants, who were monozygotic and dizygotic twin pairs of Caucasian ancestry, were instructed to distinguish between right and wrong sounds in well-known tunes (Drayna et al., 2001). The research was conducted using a distorted tunes test based on note identification, a famous melody with an erroneous pitch. Heritability was evaluated for 71% of the data (all data) and 80% once a specific limit value was presented. The scientists concluded that differences in musical pitch identification are primarily due to highly heritable differences in auditory processes. Separate research of Dutch twin pairs looked at music, arts, language, mathematics, chess, and sports

skills. It was shown that shared surroundings had a negligible impact on musical aptitude and talent abilities and that genetic factors play a significant role in musical diversity (Vinkhuyzen et al., 2009).

Family pedigree analysis

Family pedigrees may also be used to estimate heritability. The ratio of additive genetic variation to a total phenotypic variable variance is known as heritability in the narrow sense (h^2). Heritability estimate is a valuable prelude to molecular genetic research since the magnitude of h^2 may suggest the statistical power for finding the causative genes of a characteristic (Bochud, 2012). When several related characteristics' h^2 estimations are available, the trait with the best h^2 estimate may be selected for gene mapping. In human research, h^2 analyses below 0.2 are regarded low, those between 0.2 and 0.5 are considered moderate, and those over 0.5 are called high heritability (Tan et al., 2014). High h^2 values indicate that the genotype is tightly linked to the trait phenotype, but this does not mean that every gene linked to the trait significantly impacts the phenotype (Visscher et al., 2008).

Analysis of segregation

Segregation analysis is used to determine whether familial data for a specific disorder or other traits are compatible with particular inheritance methods. Modes of inheritance tried in segregation analyses contain Mendelian, digenic or polygenic models. The family data are fitted with several segregation models reflecting various attribute heritage patterns. Using maximum probability methods, the best suited genetic model is identifiable (i.e., the pattern of inheritance that best describes how the characteristic is passed down the family line). The segregation ratio is an essential measurement of the percentage of offspring that inherits that specific characteristic from a parent (Strachan and Read, 1999). For autosomal recessive and autosomal dominant inheritance, the expected segregation ratio is 0.5 and 0.25 correspondingly. These proportions are for Mendelian characteristics; a difference between these numbers shows that the trait may potentially have partial penetration, may be predisposed to various genes, or both environmental and genetic variables influence the quality. For example, in research, the absolute pitch had a segregation ratio of 0.089 (Theusch and Gitschier, 2011). This implies that the feature was not taken from the Mendelian pattern. The separation analysis often acts as a precursor to parametric connection analysis, which requires specifying the heritage pattern of the stated characteristic (Schnell and Sun, 2012).

Genetic-molecular methods

Analysis of linkages

Linkage analysis is a genetic technique that identifies chromosomal segments which co-segregate through families with the disease phenotype and is an analytical tool used to detect most lipodystrophic genes. Analysis of the link may be parametric or non-parametric.

Linkage analysis involves using single-nucleotide polymorphism (SNP) arrays for every family member of a big family or multiple family pedigrees. If it is thought that a genetic locus predisposes a characteristic, members with the same

markers should have a higher similarity to those who do not share the markers. The linkage analysis is thus intended to identify features in the SNP array which are frequently prevalent within and across pedigrees with interest (Tan et al., 2014). The non-parametric or model-free linking checks if relative characteristics share more alone than was mistakenly anticipated (Xu et al., 2012). Parametric (model-based) link analysis requires the inheritance mode specification provided by segregation analysis. Linkage is then evaluated by comparing the likelihood that the test data is obtained if a marker locus & trait locus are associated with the probability of the test data obtained if the 2 loci are not connected (Schnell and Sun, 2012). Computerized LOD analysis is an easy method to analyse complicated family pedigrees to determine the connection between Mendelian characteristics (or between a trait and a marker, or two markers). The LOD score (logarithm (base 10) of the odds) established by Newton Morton is a statistical measure often used in human, animal and plant linking. The LOD data compares the probability of obtaining the test data if the 2 loci are connected to the potential of simply by chance seeing the same data. Positive LOD values support the existence of a connection, whereas low LOD ratings suggest that the connection is not so probable. A LOD score for every three is generally seen as an essential indication of the connection, since it shows that the chances of the two loci being connected and legacy together exceed 1000–1. Alternatively, substantial evidence to deny the connection is taken into consideration as a LOD score −2. Generally, results within the range of $-2 < x < 3$ are considered to be nonconclusive evidence for connection with results between $2 < x < 3$, justifying further research (Tan et al., 2014).

Analysis of Association

Relationship analysis is a statistical technique used for determining the association between a genetic variation and a characteristic (Carey, 2003b). An association study may either use a population-based approach or a family-based design in which relatives control cases. Statistical analyses are conducted to evaluate whether a specific allele in the candidate gene approach has a greater frequency.

In this method, only specific allele variants are studied, which is a major drawback of the candidate gene approach. If multiple genes are involved or the trait under study is complex, this approach is unsuitable. This method relies heavily on the researcher's "educated guess".

Instead, genome-wide association study (GWAS) can be applied even without prior knowledge of potential candidate genes. It involves an agnostic search of the entire human genome, generally using SNP arrays with many common markers (Sun and Dimitromanolakis, 2012).

Exome sequencing

Exome sequencing is a genetic method for the sequencing of a genome's entire protein coding region. The first stage is only to choose the DNA subset that encodes proteins known as exons. It comprises two phases. The second stage involves sequencing exonic DNA with any high-performance DNA sequence technique.

Exome accounts for about 1.5% of the whole genome. Thus, exome sequencing,

like GWAS, may be carried out without previous knowledge of possible applicant genes or genetic variations. In addition, it can detect unusual causative variants with unique metabolic characteristics, which cannot be found by linking studies because of insufficient research power (Singleton, 2011).

CNV analysis

Copy number variations (CNVs) are genomic alterations that lead to abnormal copies of 1 or more genes. Structural genomic rearrangements like duplications, deletions, translocations, and inversions can cause CNVs. Microarray-based CNV analysis techniques generally use SNP arrays or aCGH (array comparative genomic hybridization) platforms to detect gains or losses of copy numbers within the test sample compared with a reference sample (Alkan et al., 2011).

Music perception abilities

Absolute pitch ability

Absolute pitch, often known as the perfect pitch, is unique music for identifying or producing pits without external reference. The prevalence estimated is less than 1 in 10,000 (Bachem, 1955; Profita and Bidder, 1988). In 1500, this estimate was updated to 1 (Gingras et al., 2015)

Various scholars via family studies have investigated the genetic basis of absolute pitch. Profita and Bidder (1988) performed one of the first segregation investigations with 35 AP probes in 19 families and found substantial family occurrence. In females of this sample, the absolute pitch was more frequent and vertical transmission was found. The segregation ratio was estimated to be between 0,24 and 0,37 and indicates an incomplete autosomal dominant gene. However, since no control participant was recruited, they were unable to establish any recurrence risk ratios.

A further family aggregation research generated an estimated sibling recurrence risk ratio of 20, which indicates that siblings with absolute pitch have an estimated 20 times higher probability of having final pitch than the general population (Gregersen and Kumar, 1996). Gregersen's team subsequently performed two more family aggregation studies which generated an estimated 8.3 and 12.2 relative sibling risk (sib RR) correspondingly (Gregersen et al., 1999 & 2001). Thus, Sib RR offers a more cautious approach than μs (Naj et al., 2012).

Gregersen's team also compared the occurrence of AP in Asian (n=36) and non-Asian (n=50) conservatory students and calculated it as 49.3% and 18.1%, respectively. This finding was reflected later in subsequent studies by Deutsch et al. 2006, Hove et al. 2010, Miyazaki et al. 2012. It was hypothesized that the differences in absolute pitch could be connected with speech development because of deep tonality in East-Asian languages (Deutsch et al., 2006). This impact on AP performance was also discussed in the study on 37 AP possessors of mixed ethnicity (Van Hedger and Nusbaum, 2019).

Studies on large samples of musicians presented that almost all displaying Absolute Pitch started their musical education by 7. It was also recommended that it is somewhat unlikely that an individual can develop Absolute Pitch if musical training has been created after the age of 11 (Sergeant, 1969). However, this view does not hold precisely in the face of

the most current information since Van Hedger et al., (2019) showed that Adults could learn absolute Pitch and the learned Absolute Pitch is indistinguishable from an inborn ability. In view of this, Baharloo et al., (1998) controlled for early music training by only examining families where the contributors & one or more of their siblings had received music training before 6 years of age. The λs was estimated to be approximately 7.5 (Gregersen, 1998). In a subsequent study, Baharloo and colleagues estimated λs for the most severe form of AP, termed "AP-1" (Baharloo et al., 2000). The AP-1 phenotype was defined by a reliably high level of pitch naming ability, falling at least three standard errors above the mean score of a randomized cluster of AP and non-AP musicians. Also controlling for early music training, the λs for AP-1 was estimated to fall within 7.8–15.1, with a greater likelihood of the true value being found near the upper end of this range. However, it is possible that even after controlling for early music training, the estimated λs may still be influenced by other shared environmental factors experienced by the AP-1 probands and their concordant siblings. The authors hence noted that the λs approximation might not wholly reflect genetic factors. Nonetheless, the high estimates of λs from various familial aggregation studies suggest a significant role for genetic influences on the development of AP and the possibility of a major-gene effect (Tan et al., 2014).

Morphometric brain structure investigations have discovered another factor that may influence AP development. AP musicians have left-hand asymmetry of a portion of the temporal lobe known as planum timescale (PT), an area traditionally linked to language and auditory processing.

Non-parametric multi-point linking analysis indicated the potential linking of the European/Ashkenazi Jewish/Indian Combined Dataset with chromosomes 8q24.21 (LOD = 2.330) and 8q21.11 (LOD = 2.069) (Table 1). One of the four genes identified in the neighbourhood of the linkage peak of 8q24.21 was ADCY8 (Adenylate cyclase 8), expressed nearly exclusively in the brain (Wong et al., 1999; Ludwig and Seuwen, 2002; De Quervain and Papassotiropoulos, 2006). Other peaks were observed in European families at loci 8q21.11 (LOD = 2.236), 7q22.3 (LOD = 2.074) and 9p21.3 (LOD = 2.048). Linkage area on 7q22.3 was also seen in a sub-set of 19 East Asian AP families, with a smaller connection point (LOD between 1 and 1.5).

AP segregation study was conducted in monozygous twins (78.6%), dizygous twins (45.2%) and their families by Theusch and Gitschier (2011). He also found that AP is likely to be genetically heterogeneous, not just mendelian inherited. Environmental, epigenetic, & stochastic variables probably contribute to the expression of Absolute Pitch.

Smith et al. investigated pitch discrimination in multiethnic ancestry people in 2017. The better presentation was linked to greater intelligence, East Asian background, male sex, younger age, and appropriate music instruction (especially before age 6). GWAS & gene-based analyses of collapse have examined a limited sample volume. While chromosomal areas (4q22, 4q23-4q26, chromosome 3) have previously demonstrated in connection with pitch perception, no significant correlations have been found.

Studies on huge samples of artists showed that nearly everyone with

Absolute Pitch began their musical instruction at seven. Furthermore, it was suggested that it is relatively improbable that someone would be able to acquire Absolute Pitch beyond the age of 11. (Sergeant, 1969). This concept does not exist in the face of the latest facts. Van Hedger et al., (2019) showed that certain adults can acquire absolute pitch, and that the taught final pitch is distinct from the innate ability.

Congenital Amusia

Congenital amus or tone deafness, despite its normal cognition, language and hearing skills, is a fine-grained perceptual impairment defined by an inability to identify incorrect notes in melodies (Peretz and Hyde, 2003). Congenital amus has an estimated frequency of 4% of the population (Kalmus and Fry, 1980). Although, however, a comprehensive investigation of the neurological foundation of congenital amusia was made (Peretz and Hyde, 2003; Hyde et al., 2007; Mandell et al., 2007; Loui et al., 2009; Mignault Goulet et al., 2012), there was little exploration of its genetic origin.

In the first congenital amusia family aggregation study, Peretz et al., (2007) conducted an online amusic diagnostic exam with 13 amusic probands and 17 controls, as well as 58 proband families (out of 9 prominent families) and 58 control family members (from 10 families). The findings have shown that 39% of first-degree relatives have congenitally amused, whereas only 3% of controls have been equally identified. Notably, the μs was 10.8 for amusia congenital, whereas the risk of recurrence of offspring was considerably lower at 2.3. While the high μs indicates a likely hereditary foundation for congenital amusa, Peretz et al., hypothesised that exposure to a musical environment created may reduce the risk of offspring of amusing evidence. However, Mignault Goulet et al. (2012) found that the music perception and electrophysiological measurements of seven amusing youngsters (ages 10–12) did not change basically after four weeks of daily listening to the music. This promotes that listening to everyday music is insufficient to enhance pitches' perception or stimulate brain plasticity in amusing progenies. Another study conducted in the same research group with a large cohort of Canadian participants found that 46% of first-degree proband family members had a prevalence of congenital amusia. Other associated problems such as dyslexia, speech dysfunction, memory problems or spatial placement problems have been identified in just a few amusing minorities. The scientists concluded that many interacting genes might affect congenital amus (Peretz & Vuvan, 2017). Deregulations of the aforementioned genes such as AVPR1A (12q), SLC6A4 (17q) and the loci identified on 8q and Chromosome 4 are suggested for the cause of the disease (Tan et al., 2014).

Gingras et al., (2015) focused on musical extremes such as congenital amusia and absolute pitch. The amusia genes FOXP2 (7q31.2) (Gingras et al., 2015) and locus 22q11 are particular genes (Gao et al., 2018). Previous gene mutations in humans produce serious speech and language impairments, such as developing verbal dyspraxia (Lai et al., 2001). In birds singing, his orthology is essential for song learning & the adult recital (Adam et al., 2016), and echolocation in bats (Li et al., 2007).

Table 1. Summary of molecular genetic studies investigating absolute pitch.

Study type	Participants	Ancestry	Locus implicated	Genetic variant(s) implicated	Gene implicated	Possible function(s) of the gene
Genome-wide linkage study (Theusch et al., 2009)	73 AP families	European, Ashkenazi Jewish, Indian, East Asian	8q24.21	SNP rs3057 LOD= 2.330 Eu/AJ/I LOD= 3.464 EU	ADCY8	Learning and memory
			7q22.3	SNP rs2028030 LOD = 2.074 Eu LOD~1–1.5 E Asian		
			8q21.11	SNP rs1007750 LOD = 2.069 Eu/AJ/I LOD = 2.236 for Eu		
			9p21.3	SNP rs2169325 LOD = 2.048 Eu		
Genome-wide linkage study: exome sequencing (Gregersen et al., 2013)	53 AP multiplex families	Caucasian, Asian	6q14.1-16.1		EPHA7	Neural connectivity and development
	36 synesthesia multiplex families		Peak LOD= 4.68			
		2q	SNP rs1482308 HLOD = 4.7 (combined data set) SNP rs6759330 HLOD = 3.93			

ADCY8: adenylate cyclase 8; AJ: Ashkenazi Jewish ancestry; E Asian: East Asian ancestry; EPHA7: ephrin type-A receptor 7; Eu: European ancestry; HLOD: heterogeneity logarithm of odds score; I: Indian ancestry; LOD: logarithm of odds score; SNP: single nucleotide polymorphism.

Source: Tan et al., 2014

Music perception

Studies of child musical behaviour have revealed that children may identify melodic or rhythmic changes in musical patterns and notice changes in pitch & rhythm (Trehub et al., 1984, 1987, 1999; Trainor and Trehub, 1992, 1993; Trainor and Heinmiller, 1998; Trainor et al., 2002, Trehub, 2006; Honing et al., 2009; Winkler et al., 2009). These findings and the omnipresent aspect of music across all civilizations (McDermott and Hauser, 2005) indicate that all people are endowed with an inherent form of musicality and that genetic components may be part of their expression.

Individual changes in ease of auditory ability indicate that auditory capacity is prone to change. Gaab et al. (2006) noted that fast learners engaged the supramarginal left gyrus and left Heschl's gyrus more often in the post-training period in conjunction with their slow learners (participants were designated as slow or fast learners in an auditory differentiation training task). Jäncke et al. (2001) revealed various short term functional activation patterns compared to those who had shown no progress in the frequency discrimination test. Zatorre et al. (2012) showed that individuals who had learned a micro-melody task faster had steeper fMRI BOLD responses, even before they trained on the task, to alter their auditive cortex. These findings indicate that inherent variations in brain function may affect the ability of the person to perceive music and develop musical talents.

Foster and Zatorre (2010) found that Heschl's sulcus & bilateral sulcus intraparietal performance with a relatively pitched test includes grey matter content and cortical thickness even after music instruction. These results are compatible with Relative Pitch processing genetic effects since substantial heritability (650–97%) for total brain volume and grey and white matter volumes have been repeatedly reported in behavioural genetics studies (Peper et al., 2007).

In one large twin study performed in 2001, 136 monozygotic twin pairs and 148 dizygotic twin pairs went through the Distorted Tunes Test (DTT), where they judged whether simple well-known melodies had incorrect pitches that could have rendered them “out-of-tune” (Drayna et al., 2001). Twin structural modeling revealed a very high heritability estimate of 71–80% with no effect of shared environment, thus indicating a substantial genetic component influencing melodic perception ability.

A study on 15 musical Finnish families investigated the genetic basis of music aptitude using: The Karma Music Test, and Seashore's pitch and rhythm discrimination tests (Pulli et al., 2008). The Seashore tasks use paired discrimination to measure pitch & rhythm perception (Radocy and Boyle, 2012), while the Karma Music Test evaluates the ability to distinguish patterns in sound sequences (Karma, 2007). Heritability estimates of 42, 57, 21, and 48% were obtained for the Karma Music Test, Seashore's pitch and rhythm discrimination tests, and the combined score on all three tests.

Genome-wide linkage analysis revealed proof of linkage on chromosome 4q22 (LOD = 3.33 near markers D4S423 and D4S2460) and linkage evidence on chromosome region 8q13-21 (LOD = 2.29) for the combined score. Interestingly, the linkage peak at 8q13-21 was close to the

linkage on chromosome 8q21.11 identified in the AP study by Theusch et al., (2009), pointing to a possible convergence of AP and general music perception abilities. UNC5C, netrin receptor, is the candidate gene at the tallest linkage peak of chromosome 4q22.

A follow-up candidate gene study involving 19 Finnish musical families found that the AVPR1A (arginine vasopressin 1a) haplotype RS1+RS3 on chromosome 12q has significant associations with performance on the Karma Music Test & the combined score on the Karma & Seashore music tasks (Ukkola et al., 2009). Analysis on the polymorphisms of other candidate genes such as SLC6A4, TPH1, & DRD2 produced weak and inconclusive results. Prior studies have revealed that arginine vasopressin (AVP) plays a key role in social cognition & behaviour (Ferguson et al., 2002; Bielsky et al., 2004; Depue and Morrone-Strupinsky, 2005; Hammock and Young, 2005) and in social & spatial memory (Aarde & Jentsch, 2006). In this research, its association with auditory pattern perception proposes a potential link between music perception & human social functioning.

In the rhythm domain, one study has described that mutation of the FOXP2 (Forkhead box protein P2) gene on chromosome 7q31 impairs rhythm perception & production while leaving pitch perception & production abilities intact (Alcock et al., 2000).

Music memory

Granot et al., (2007) investigated the potential connection between phonological and musical memory with the AVPR1A & SLC6A4 genes (solute carrier family VII [neurotransmitter transporter serotonin], member IV). A previously documented connection between arginine vasopressin (AVP) and spatial and social memory was provided to justify targeting these two genes (Ferguson et al., 2002; Aarde & Jentsch, 2006). Furthermore, Serotonin also interacts with AVP in the hypothalamus (Albers et al., 2002) and serotonin enhances arginine vasopressin production (Gálfi et al., 2005). This leads to a possible epistatic connection between the AVPR1A gene, which provides the blueprint for synthesising the arginine vasopressin receptor and the SLC6 A4 gene, the transporter of serotonin which is essential for serotonin receptor supplies. Granot et al. have generalised 82 individuals from its institution with little musical training for the AVPR1A (RS1 & RS3 haplotypes) & SLC6A4 (HTTLPR) versatility using population and family association studies. The participants' phonological and music memory performance was assessed using a broad range of tests. Results generated significant genes for two melodic memory tasks, 1 rhythmic memory task and1 phonological memory task, even after using stringent Bonferroni adjustments for many tests, via epistatic gene interactions between AVPR1A and SLC6A4 polymorphisms. This offers early evidence of an epistatic connection between AVPR1A and SLC6A4 polymorphisms that is likely associated with short-term music memory, or more often, phonological memory.

Music listening

Ukkola-Vuoti et al., (2011) investigated the behaviour of 31 Finnish households in listening to music using questionnaires. A family-based investigation of relationships has shown favourable correlations

between haplotypes of AVPR1A and active music listening. The RS1+AVR haplotype and the present active musical listening and the RS1+RS3 haplotype and lifetime activity listening were the most significant correlations. No notable connection between listening and the polymorphisms of the SLC6A4 has been found. In this research, active listening refers to concentrated listening, such as attending concerts. Since Ukkola et al., (2009) have demonstrated that the same AVPR1A promotor area (RS1+RS3) is connected with music perception, these results indicate a similar genetical foundation for active listening frequency and perception.

Singing

In 1008 individuals from 73 extended Mongolian families, Park et al., (2012) examined the genetic variables that underlie vocabulary via family-based linkages and association testing. They performed a pitch production accuracy test and discovered that the target pitches with variations under a semitone were precisely matched by 357 participants (35.4 percent). The heritability of singing accuracy was found at 40% with the use of pedigree data. A study was conducted on genome-wide linkages, the most significant linkage peak found on 4q23 (LOD = 3.1 at marker D4S2986). The results coincide with chromosome 4q areas, which show links for the perception of music (Pulli et al., 2008; Oikkonen et al., 2014). A familial association study at the hypothesised connection site showed that SNP rs12510781 on 4q26 was most closely linked with singing precision. The authors also used an exotic sequence to search for additional likely SNP candidates and discovered in UGT8 a non-synonymous SNP (rs4148254) on 4q26. Furthermore, CNV study employing a comparative genomic hybridization (aCGH) array showed that a loss copy number upstream of the UGT8 might be related to singing accurately at 5.6 kb (5600 base pairs).

Discussion

As discussed in this article, much research has started to provide insights into music's genetic basis. Several promising and convergent findings have begun to emerge to date. Several chromosomal locations 8q were involved with two or more musical features. For example, loci 8q21 and locus 8q24 were involved with Absolute Pitch and perception of music (Pulli et al., 2008; Theusch et al., 2009; Ukkola-Vuoti et al., 2013). Similarly, loci 4p14 and 4q22 on chromosome 4 were linked with perception of music, especially with pitch identification (Pulli et al., 2008; Oikkonen et al., 2014), while the nearby locus 4q23 was associated with the precision of the pitch of singing ability (Park et al., 2012).

To date, several genes have been very significant in music genetics research. For example, the AVPR1A gene on chromosome 12q has been linked with music listening and music memory (Ukkola-Vuoti et al., 2011), perception of music (Ukkola et al., 2009). (Granot et al., 2007). On the other hand, the SLC6A4 gene was linked with the recollection of music (Granot et al., 2007) (Morley et al., 2012).

It is essential to reproduce the current research findings to validate the obtained data, particularly in small sample size studies (e.g., Granot et al., 2007, Pulli et al., 2008; Ukkola-Vuoti et al., 2013). For example, an existing big genome study (Oikkonen et al., 2014) failed to identify

the linkages between AVPR1A and music perception, which the same research group had previously revealed during another candidate gene analysis (Ukkola et al., 2009). The polymorphisms of genes such as AVPR1A & SLC6A4 were selected for many candidate-gene association studies based on the results of previous music studies. However, the multi-faceted character of musical ability may make a candidate gene, along with one musical function, a poor candidate for another musical function. This is shown by Morley et al. (2012), who discovered, despite their statistical power, no relationship between AVPR1A polymorphisms with involvement in choruses. Researchers may thus be more sensitive to choose potential genes based on supporting evidence from linkage analyses or GWAS of linked musical capacity.

For future researchers, it will be essential to utilise other populations and more extensive samples to reproduce the findings of the present investigations. In addition, many molecular genetic investigations have been conducted in different Finnish multigenerational families. Therefore, extending the findings of these families to other ethnic groups will help substantiate the connections mentioned.

Since molecular genes are still new, many of the studies here utilise older molecular genetic techniques, such as mapping the linkage or the candidate gene approach. Researchers in music genetics may explore combining CNV, SNP methods and results from CNV analysis may supplement the findings from SNP analysis (Stranger et al., 2007). Other recent procedures include exom sequencing as well as methylation studies to explore the possible role of epigenetic effects and the underlying molecular and biological processes (Rowe and Tenesa, 2012).

The possible impact of epistasis, gene-environmental interactions and epigenetic effects on music abilities are another major route in music genetic research. These factors may illustrate why many of the genetic variations involved in complex characteristics can only explain a small proportion of family study heritage predicted (Stranger et al., 2011). Therefore, researchers should increase awareness and concentrate on gene-environment interaction. For example, apparent environmental processes such as brain plasticity caused by training may be influenced by genetics (Brans et al., 2010; Vinkhuyzen et al., 2010). Likewise, environmental factors may change genetic expression via epigenetic processes (Fagiolini et al., 2009; Sweatt, 2013).

While the collected results to far seem encouraging, a more detailed study is needed. Most research has utilised assessments of music's capacity to work on music, giving unfair relevance to some perceptional skills, such as detecting pitch and rhythm while disregarding others.

Music impairments, such as tonal deafness (Peretz et al., 2007) & beat deafness (Phillips-Silver et al., 2011), may offer fruitful paths for future research since deficiencies are often more distinct than capacities to phenotype. However, at now, relatively few genetic studies based on music impairments have been conducted.

Our present understanding is restricted to the conclusion that FOXP2 may play a part in the processing of music rhythms, language and speech (Alcock et al., 2000; Lai et al., 2001). Thus, comparative

genomic study between music and language skills may help us understand the common and un-common genetic and neurological processes for music and language and can help to address important issues regarding music & language origins (Peretz, 2009).

To conclude, research into the genetics of music has produced encouraging findings, which emphasise the necessity for further study in this area. Enlightenment of musical talent's genetic foundation may be difficult because many natural elements need thorough identification, classification, and genetic research. In conjunction with the successful pace at which molecular genetics and statistical designs advance, an ever more precise picture of genetic processes underlying the genesis of musical characteristics are beginning to emerge. These mechanisms may then be linked with neuroscientific findings of the neurological basis of certain musical functions and behaviour. This will eventually enable us to understand better how interactions between nature and nutrition influence the development of human musical capabilities throughout our lifetime.

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References

Aarde, S. M. and Jentsch, J. D. (2006). Haploinsufficiency of the arginine-vasopressin gene is associated with poor spatial working memory performance in rats. *Horm. Behav*. 49: 501–508.

Adam, I., Mendoza, E., Kobalz, U., Wohlgemuth, S. and Scharff, C. (2016). FoxP2 directly regulates the reelin receptor VLDLR developmentally and by singing. *Molecular and Cellular Neuroscience.* 74: 96–105.

Albers, H. E., Karom, M. and Smith, D. (2002). Serotonin and vasopressin interact in the hypothalamus to control communicative behavior. *Neuroreport.* 13: 931–933.

Alcock, K. J., Passingham, R. E., Watkins, K. and Vargha, K. F. (2000). Pitch and timing abilities in inherited speech and language impairment. *Brain Lang*. 75: 34–46.

Alkan, C., Coe, B. P. and Eichler, E. E. (2011). Genome structural variation discovery and genotyping. *Nat. Rev. Genet*. 12: 363–376.

Bachner-Melman, R., Dina, C., Zohar, A. H., Constantini, N., Lerer, E., Hoch, S., Sella, S., Nemanov, L., Gritsenko, I., Lichtenberg, P., Granot, R. and Ebstein, R. P. (2005). AVPR1a and SLC6A4 gene polymorphisms are associated with creative dance performance. *PLoS Genet.* 1: e42.

Baharloo, S., Johnston, P. A., Service, S. K., Gitschier, J. and Freimer, N. B. (1998). Absolute pitch: an approach for identification of genetic and nongenetic components. *Am. J. Human. Genet.* 62: 224–231.

Baharloo, S., Service, S. K., Risch, N., Gitschier, J. and Freimer, N. B. (2000). Familial aggregation of absolute pitch. *Am. J. Hum. Genet.* 67: 755–758.

Bielsky, I. F., Hu, S. B., Szegda, K. L., Westphal, H. and Young, L. J. (2004). Profound impairment in social recognition and reduction in anxiety-like behavior in vasopressin V1a receptor knockout mice. *Neuropsychopharmacology.* 29: 483–493.

Bochud, M. (2012). Estimating heritability from nuclear family and pedigree data. In: Elston R. C., Satagopan J. M., Sun S. (eds) (New York, NY: Humana Press; Springer). *Statistical Human Genetics: Methods and Protocols*. Pp. 171–186.

Brauchli, C., Leipold, S. and Jäncke, L. (2019). Univariate and multivariate analyses of functional networks in absolute pitch. *Neuroimage.* 189:241–247.

Brans, R. G. H., Kahn, R., Schnack, H. G., Van, Baal, G. C. M., Posthuma, D. and Van, H. N. E. M. (2010). Brain plasticity and intellectual ability are influenced by shared genes. *J. Neurosci.* 30: 5519–5524.

Carrion-Castillo, A., Franke, B. and Fisher, S. E. (2013). Molecular genetics of dyslexia: an overview. *Dyslexia.* 19: 214–240.

Coon, H. and Carey, G. (1989). Genetic and environmental determinants of musical ability in twins. *Behav. Genet.* 19: 183–193.

Depue, R. A. and Morrone-Strupinsky, J. V. (2005). A neurobehavioral model of affiliative bonding: implications for conceptualizing a human trait of affiliation. *Behav. Brain Sci.* 28: 313–350.

De-Quervain, D. J. F. and Papassotiropoulos, A. (2006). Identification of a genetic cluster influencing memory performance and hippocampal activity in humans. *Proc. Natl. Acad. Sci. U.S.A.* 103: 4270–4274.

Deutsch, D., Henthorn, T., Marvin, E. and Xu, H. (2006). Absolute pitch among American and Chinese conservatory studentsd: prevalence differences, and evidence for a speech-related critical period. *J. Acoust. Soc. Am.* 119719-119722.

Dovern, A., Fink, G. R., Fromme, A. C. B., Wohlschläger, A. M., Weiss, P. H. and Riedl, V. (2012). Intrinsic network connectivity reflects consistency of synesthetic experiences. *J. Neurosci.* 32: 7614–7621.

Drayna, D., Manichaikul, A., De, Lange, M., Snieder, H. and Spector, T. (2001). Genetic correlates of musical pitch recognition in humans. *Science.* 291: 1969–1972.

Foster, N. E. V. and Zatorre, R. J. (2010). Cortical structure predicts success in performing musical transformation judgments. *Neuroimage.* 53: 26–36.

Gaab, N., Gaser, C. and Schlaug, G. (2006). Improvement-related functional plasticity following pitch memory training. *Neuroimage.* 31: 255–263.

Gao, L., Tang, S. X. and Yi, J. J. (2018). Musical auditory processing, cognition, and psychopathology in 22q11.2 deletion syndrome. *Am. J. Med. Genet. B. Neuropsychiatr. Genet*. 177: 765–773.

Gingras, B., Honing, H., Peretz, I., Trainor, L. J. and Fisher, S. E. (2015). Defining the biological bases of individual differences in musicality. *Philosoph. Transact. B.* 370: e20140092.

Goycoolea, M. V., Mena, I., Neubauer, S. G., Levy, R. G., Grez, M. F. and Berger, C. G. (2007). Musical brains: a study of spontaneous and evoked musical sensations without external auditory stimuli. *Acta Otolaryngol.* 127: 711–721.

Granot, R. Y., Frankel, Y., Gritsenko, V., Lerer, E., Gritsenko, I. and Bachner-Melman, R. (2007). Provisional evidence that the arginine vasopressin 1a receptor gene is associated with musical memory. *Evolut. Hum. Behav.* 28: 313–318.

Grayton, H. M., Fernandes, C., Rujescu, D. and Collier, D. A. (2012). Copy number variations in neurodevelopmental disorders. *Prog. Neurobiol.* 99: 81–91.

Gregersen, P. K. (1998). Instant recognition: the genetics of pitch perception. *Am. J. Hum. Genet.* 62: 221–223.

Gregersen, P. K., Kowalsky, E., Kohn, N. and Marvin, E. W. (1999). Absolute pitch: prevalence, ethnic variation, and estimation of the genetic component. *Am. J. Hum. Genet.* 65: 911–913.

Gregersen, P. K., Kowalsky, E., Kohn, N. and Marvin, E. W. (2001). Early childhood music education and predisposition to absolute pitch: teasing apart genes and environment. *Am. J. Med. Genet.* 98: 280–282.

Gregersen, P. K., Kowalsky, E., Lee, A., Baron-Cohen, S., Fisher, S. R., Asher, J. E., Ballard, D., Freudenberg, J. and Li, W. (2013). Absolute pitch exhibits phenotypic and genetics overlap with synesthesia. *Human Molec. Genet.* 22: 2097–2104.

Gregersen, P. K. and Kumar, S. (1996). The genetics of perfect pitch. *Am. J. Hum. Genet.* 59 (Suppl.): A179.

Guo, S. W. (1998). Inflation of sibling recurrence-risk ratio, due to ascertainment bias and/or overreporting. *Am. J. Hum. Genet.* 63: 252–258.

Henthorn, T. and Deutsch, D. (2007). Ethnicity versus early environment: comment on 'Early childhood music education and predisposition to absolute pitch: teasing apart genes and environment' by Peter K. Gregersen, Elena Kowalsky, Nina Kohn, and Elizabeth West Marvin [2000]. *Am. J. Med. Genet.* A143: 102–103.

Honing, H., Ladinig, O., Háden, G. P. and Winkler, I. (2009). Is beat induction innate or learned: probing emergent meter perception in adults and newborns using event-related brain potentials. *Ann. N.Y. Acad. Sci.* 1169: 93–96.

Hove, M. J., Sutherland, M. E. and Krumhansi, C. L. (2010). Ethnicity effects in relative pitch. *Psychon. Bull. Rev.* 17: 310–316.

Hyde, K. L., Lerch, J. P., Zatorre, R. J., Griffiths, T. D., Evans, A. C. and Peretz, I. (2007). Cortical thickness in congenital amusia: when less is better than more. *J. Neurosci.* 27: 13028–13032.

Järvelä, I. (2018). Genomics studies on musical aptitude, music perception, and practice. *Ann. N. Y. Acad. Sci*. 1423: 82–91.

Kalmus, H. and Fry, D. B. (1980). On tune deafness (dysmelodia): frequency, development, genetics and musical

background. *Ann. Hum. Genet.* 43: 369–382.

Karma, K. (1994). Auditory and visual temporal structuring: how important is sound to musical thinking. *Psychol. Music.* 22: 20–30.

Keenan, J. P., Thangaraj, V., Halpern, A. R. and Sclaug, G. (2001). Absolute pitch and planum temporale. *NeuroImage.* 14: 1402–1408.

Ku, C. S., Cooper, D. N., Polychronakos, C., Naidoo, N., Wu, M. and Soong, R. (2012). Exome sequencing: dual role as a discovery and diagnostic tool. *Ann. Neurol.* 71: 5–14.

Lai, C. S. L., Fisher, S. E., Hurst, J. A., Vargha-Khadem, F. and Monaco, A. P. (2001). A forkhead-domain gene is mutated in a severe speech and language disorder. *Nature.* 413: 519–523.

Lathrop, G. M., Lalouel, J. M., Julier, C. and Ott, J. (1984). Strategies for multilocus linkage analysis in humans. *Proc. Natl. Acad. Sci. U.S.A.* 81: 3443–3446.

Levitin, D. J. (2012). What does it mean to be musical? *Neuron.* 73: 633–637.

Lewis, C. M. and Knight, J. (2012). Introduction to genetic association studies. *Cold Spring Harb. Protoc.* 7: 297–306.

Li, C. C., Chakravarti, A. and Halloran, S. L. (1987). Estimation of segregation and ascertainment probabilities by discarding the single probands. *Genet. Epidemiol.* 4: 185–191.

Li, C. C. and Mantel, N. (1968). A simple method of estimating the segregation ratio under complete ascertainment. *Am. J. Hum. Genet.* 20: 61–81.

Li, G., Wang, J., Rossiter, S. J., Jones, G., Cotton, J. A. and Zhang, S. (2008). The hearing gene Prestin reunites echolocating bats. *Proceedings of the National Academy of Sciences.* 105 (37): 13959–13964.

Liu, X., Kanduri, C. and Oikkonen, J. (2016). Detecting signatures of positive selection associated with musical aptitude in the human genome. *Sci. Rep.* 6: 21198.

Loui, P., Alsop, D. and Schlaug, G. (2009). Tone deafness: a new disconnection syndrome? *J. Neurosci.* 29: 10215–10220.

Mariath, L. M., Silva, A. M., Kowalski, T. W., Gattino, G. S., Araujo, G. A., Figueiredo, F. G., Tagliani-Ribeiro, A., Roman, T., Vianna, F. S. L., Schuler-Faccini, L. and Schuch, J. B. (2017). Music genetics research: association with musicality of a polymorphism in the AVPR1A gene. *Genet. Molec. Biol.* 40: 421–429.

Mandell, J., Schulze, K. and Schlaug, G. (2007). Congenital amusia: an auditory-motor feedback disorder? *Restor. Neurol. Neurosci.* 25: 323–334.

McDermott, J. and Hauser, M. (2005). The origins of music: innateness, uniqueness, and evolution. *Music Percept.* 23: 29–59.

Mignault, G. G., Moreau, P., Robitaille, N. and Peretz, I. (2012). Congenital amusia persists in the developing brain after daily music listening. *PLoS ONE.* 7: e36860.

Mitry, D., Williams, L., Charteris, D. G., Fleck, B. W., Wright, A. F. and Campbell, H. (2011). Population-based estimate of the sibling recurrence risk ratio for

rhegmatogenous retinal detachment. *Invest. Ophthalmol. Vis. Sci.* 52: 2551–2555.

Morgan and Linkage. (2003a). In: Carey G. (ed.). Thousand Oaks, CA: Sage Publications, Inc. Chapter 10: *Human Genetics for the Social Sciences.* Pp. 161–180.

Morley, A. P., Narayanan, M., Mines, R., Molokhia, A., Baxter, S. and Craig, G. (2012). AVPR1A and SLC6A4 polymorphisms in choral singers and non-musicians: a gene association study. *PLoS ONE.* 7: e31763.

Naj, A. C., Park, Y. S. and Beaty, T. H. (2012). Detecting familial aggregation. In: Elston R. C., Satagopan J. M., Sun S. (eds.) (New York, NY: Humana Press; Springer). *Statistical Human Genetics: Methods and Protocols*. Pp. 119–150.

Nandram, B., Jai-Won, C. and Hongyan, X. (2011). Maximum likelihood estimation for ascertainment bias in sampling siblings. *J. Data Sci.* 9: 23.

Neale, M. C., Boker, S. M., Xie, G. and Maes, H. H. (2006). *Mx: Statistical Modeling*. Richmond, VA: Department of Psychiatry.

Newbury, D. F. and Monaco, A. P. (2010). Genetic advances in the study of speech and language disorders. *Neuron.* 68: 309–320.

Oikkonen, J., Huang, Y., Onkamo, P., Ukkola-Vuoti, L., Raijas, P. and Karma, K. (2015). A genome-wide linkage and association study of musical aptitude identifies loci containing genes related to inner ear development and neurocognitive functions. *Mol. Psychiatry*. 20(2): 275-282.

Oikkonen, J. and Järvelä, I. (2014). Genomics approaches to study musical aptitude. *Bioessays.* 36: 1102–1108.

Park, H., Lee, S., Kim, H. J., Ju, Y. S., Shin, J. Y., Hong, D., von, Grotthuss, M., Lee, D. S., Park, C., Kim, J. H., Kim, B., Yoo, Y. J., Cho, S. I., Sung, J., Lee, C., Kim, J. I. and Seo, J. S. (2012). Comprehensive genome analyses associate UGT8 variants with musical ability in a Mongolian population. *J. Med. Genet.* 49: 747–752.

Peretz, I. (2009). Music, language and modularity framed in action. *Psychol. Belg.* 49: 157–175.

Peretz, I., Cummings, S. and Dubé, M. P. (2007). The genetics of congenital amusia (tone deafness): a family-aggregation study. *Am. J. Hum. Genet.* 81: 582–588.

Peretz, I. and Vuvan, D. T. (2017). Prevalence of congenital amusia. *Eur. J. Human Genet.* 25: 625–630.

Profita, J. and Bidder, T. G. (1988). Perfect pitch. *Am. J. Med. Genet.* 29: 763–771.

Pulli, K., Karma, K., Norio, R., Sistonen, P., Göring, H. H. H. and Järvelä, I. (2008). Genome-wide linkage scan for loci of musical aptitude in Finnish families: evidence for a major locus at 4q22. *J. Med. Genet.* 45: 451–456.

Ross, D. A., Olson, I. R. and Gore, J. C. (2003). Absolute pitch does not depend on early musical training. *Ann. N.Y. Acad. Sci.* 999: 522–526.

Schnell, A. H. and Sun, X. (2012). Model-based linkage analysis of a quantitative trait. In: Elston R. C., Satagopan J. M., Sun S. (eds.) (New York, NY: Humana Press; Springer).

Statistical Human Genetics: Methods and Protocols. Pp. 263–284.

Sergeant, D. (1969). Experimental investigation of absolute pitch. *J. Res. Music Educ.* 17: 135–143.

Singleton, A. B. (2011). Exome sequencing: a transformative technology. *Lancet Neurol.* 10: 942–946.

Spencer, C. C. A., Su, Z., Donnelly, P. and Marchini, J. (2009). Designing genome-wide association studies: sample size, power, imputation, and the choice of genotyping chip. *PLoS Genet.* 5: e1000477.

Strachan, T. and Read, A. P. (1999). Complex diseases: theory and results. In: New York, NY: Wiley-Liss *Human Molecular Genetics*, 2nd edn.

Sun, L. and Dimitromanolakis, A. (2012). Identifying cryptic relationships. In: Elston R. C., Satagopan J. M., Sun S. (eds.) (New York, NY: Humana Press; Springer). *Statistical Human Genetics: Methods and Protocols*. Pp. 47–58.

Szyfter, K. and Witt, M. P. (2020). How far musicality and perfect pitch are derived from genetic factors? *J. Appl. Genet. Sep*. 61(3): 407-414.

Tan, Y. T., McPherson, G. E., Peretz, I., Berkovic, S. F. and Wilson, S. J. (2014). The genetic basis of music ability. *Front. Psychol.* 5: Art. 658.

The association study. (2003b). In: Carey G. (ed.). Thousand Oaks, CA: Sage Publications, Inc. Chapter 11: *Human Genetics for the Social Sciences.* Pp. 181–192.

Theusch, E., Basu, A. and Gitschier, J. (2009). Genome-wide study of families with absolute pitch reveals linkage to 8q24.21 and locus heterogeneity. *Am. J. Hum. Genet.* 85: 112–119.

Theusch, E. and Gitschier, J. (2011). Absolute pitch twin study and segregation analysis. *Twin Res. Hum. Genet.* 14: 173–178.

Trainor, L. J. and Heinmiller, B. M. (1998). The development of evaluative responses to music: infants prefer to listen to consonance over dissonance. *Infant Behav. Dev.* 21: 77–88.

Trainor, L. J. and Trehub, S. E. (1992). A comparison of infants' and adults' sensitivity to Western musical structure. *J. Exp. Psychol. Hum. Percept. Perform.* 18: 394–402.

Trainor, L. J. and Trehub, S. E. (1993). What mediates infants' and adults' superior processing of the major over the augmented triad? *Music Percept.* 11: 185–196.

Trainor, L. J., Tsang, C. D. and Cheung, V. H. W. (2002). Preference for sensory consonance in 2- and 4-month-old infants. *Music Percept.* 20: 187–194.

Trehub, S. E. (2003). The developmental origins of musicality. *Nat. Neurosci.* 6: 669–673.

Trehub, S. E. (2006). Infants as musical connoisseurs. In: McPherson G. E. (ed.) (New York, NY: Oxford University Press). *The Child as Musician: A Handbook of Musical Development*. Pp. 33–49.

Trehub, S. E., Bull, D. and Thorpe, L. A. (1984). Infants' perception of melodies: the role of melodic contour. *Child Dev.* 55: 821–830.

Trehub, S. E., Schellenberg, E. G. and Kamenetsky, S. B. (1999). Infants' and adults' perception of scale

structure. *J. Exp. Psychol. Hum. Percept. Perform.* 25: 965–975.

Trehub, S. E., Thorpe, L. A. and Morrongiello, B. A. (1987). Organizational processes in infants' perception of auditory patterns. *Child Dev.* 58: 741–749.

Ukkola, L. T., Onkamo, P., Raijas, P., Karma, K. and Järvelä, I. (2009). Musical aptitude is associated with AVPR1A-haplotypes. *PLoS ONE* 4: e5534.

Ukkola-Vuoti, L., Kanduri, C., Oikkonen, J., Buck, G., Blancher, C. and Raijas, P. (2013). Genome-wide copy number variation analysis in extended families and unrelated individuals characterized for musical aptitude and creativity in music. *PLoS ONE* 8: e56356.

Ukkola-Vuoti, L., Oikkonen, J., Onkamo, P., Karma, K., Raijas, P. and Järvelä, I. (2011). Association of the arginine vasopressin receptor 1A (AVPR1A) haplotypes with listening to music. *J. Hum. Genet.* 56: 324–329.

Verweij, K. J. H., Mosing, M. A., Zietsch, B. P. and Medland, S. E. (2012). Estimating heritability from twin studies. In: Elston R. C., Satagopan J. M., Sun S. (eds.) (New York, NY: Humana Press; Springer). *Statistical Human Genetics: Methods and Protocols*. Pp. 151–170.

Vinkhuyzen, A. A. E., Van-Der, S. S., De-Geus, E. J. C., Boomsma, D. I. and Posthuma, D. (2010). Genetic influences on "environmental" factors. *Genes Brain Behav.* 9: 276–287.

Vinkhuyzen, A. A. E., Van-Der, Sluis, S., Posthuma, D. and Boomsma, D. I. (2009). The heritability of aptitude and exceptional talent across different domains in adolescents and young adults. *Behav. Genet.* 39: 380–392.

Visscher, P. M., Hill, W. G. and Wray, N. R. (2008). Heritability in the genomics era-concepts and misconceptions. *Nat. Rev. Genet.* 9: 255–266.

Watts, C., Murphy, J. and Barnes, B. K. (2003). Pitch matching accuracy of trained singers, untrained subjects with talented singing voices, and untrained subjects with nontalented singing voices in conditions of varying feedback. *J. Voice.* 17: 185–194.

Weeks, D. E., Lehner, T., Squires, W. E., Kaufmann, C. and Ott, J. (1990). Measuring the inflation of the LOD score due to its maximization over model parameter values in human linkage analysis. *Genet. Epidemiol.* 7: 237–243.

Winkler, I., Háden, G. P., Ladinig, O., Sziller, I. and Honing, H. (2009). Newborn infants detect the beat in music. *Proc. Natl. Acad. Sci. U.S.A.* 106: 2468–2471.

Xu, W., Bull, S. B., Mirea, L. and Greenwood, C. M. T. (2012). Model-free linkage analysis of a binary trait. In: Elston R. C., Satagopan J. M., Sun S. (eds.) (New York, NY: Humana Press; Springer). *Statistical Human Genetics: Methods and Protocols*. Pp. 317–345.