

# Genes, brain dynamics and art: the genetic underpinnings of creativity in dancing, musicality and visual arts

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Creativity, art and artistic creation in music, dance and visual arts are brain activities specific to humans. Their genetic background remained unexplored for years, but many recent studies have uncovered significant associations with cognition-related genes and loci. These studies are summarized in the present article. Creativity is a trait with heavy genetic influences, which are also associated with mental disorders and altruism. Associated genes include dopaminergic, serotonergic and other genes (a1-antitrypsin, neuregulin, Brain-derived neurotrophic factor). Music is another complex phenotype with important genetic background. Studies in musicians and their families have highlighted the contribution of loci (e.g., 4q22) and specific genes (vasopressin receptor 1 $\alpha$  and serotonin transporter). The latter two are also associated with dancing. Although few studies have investigated visual arts, they appear to be influenced by genetic differences, which could explain the increased prevalence of synesthesia in artists and individuals with autism. Lastly, although genes play an important role in creativity and art, epigenetics and the environment should not be overlooked. The genetic exploration of artistic creativity may provide useful knowledge on cognition, behavior and brain function. It may also enable targeted and personalized art therapy in health and disease.

## Keywords

Genetics; Behavior; Cognition; Artists; Psychosis; Creativity; Neuroesthetics

## 1. Introduction

Creativity and artistic creation are inherent components of human nature and, more specifically, human behavior. Art as a human creation is as old as 40,000 BC [1] and evolved in line with human genetic, social and cultural co-evolution [2], with visual art masterpieces occupying museums and musical or dance performances filling theaters and stages worldwide. This universal phenomenon of art and artistic creativity intrigued philosophical thinking from antiquity, with philosophers such as Plato and Aristotle initiating a quest for the meaning of art and esthetics [3]. In the 19th century, interest in the biological roots of this complex human behavior led it from philosophy to psychological experiments, leading to a neuroscientific approach in the latter half of the 20th century, when the neurobiologist Semir Zeki identified distinct brain

areas involved in perceiving visual elements, such as form, color and movement, as well as beauty [3]. In 1994, in the middle of the “Decade of the Brain” (1990–2000), he introduced the term neuroesthetics [3], positing that, since esthetics and artistic expression are a product of brain function, a theory of esthetics needs to have a neurobiological basis [4]. In discussing the substrate of this neurobiological basis, we are certainly guided towards behavioral neurochemistry and the human genome.

This progress was made possible due to technological achievements in imaging and genetics. Functional neuroimaging, initially using electroencephalography, Positron Emission Tomography, magnetoencephalography and, more recently, functional Magnetic Resonance-Imaging (fMRI), can identify brain regions activated during cognitive activity or behavior. These techniques, along with advanced, large-scale genetic and genomic analytical methods such as Genome-Wide Association Studies (GWAS), have paved the way to unique discoveries in neurology, psychiatry and cognitive neuroscience. These techniques can elucidate the missing links between the phenotype of creativity and artistic expression, the endophenotype of brain circuitry, and the human genome [5].

The neuroanatomy and neurochemistry of creativity are complex, and creation is rooted in spatiotemporal brain dynamics [6]. Genetic, pharmacologic and other experiments have implicated dopaminergic (nigrostriatal and mesocortical), serotonergic and noradrenergic circuits, which affect the cognitive processes of resistance, flexibility and reward [7]. Involved brain areas include the right thalamus, fusiform gyrus and prefrontal cortex [8]. The identification of the genes and loci mediating artistic creation will not only improve our understanding of the mystery of artistry. It will also lead to a more comprehensive understanding of brain dynamics, cognitive functions, behaviors and associated disorders, and the role of art in daily life and various disease states, making evidence-based applications of art-based therapeutic approaches more feasible.

Prior research in the genetics of cognition and behavior has shown that the association of gene polymorphisms with cognitive processes is challenging, with the results often consisting of weak associations [9]. Creativity is a complex, metacognitive phenomenon, which cannot be simply and robustly accounted for by a small group of genes or brain areas [10, 11]. Added to that, the elusive nature of art and its multifaceted characters render associations of genes with art-related phenotypes even more difficult. However, many groups have performed studies examining the genetic background of creativity or artistic expression, producing interesting significant associations that can shed light on both brain function and art itself. In this narrative review, we summarize relevant studies examining how genetics underlie brain functions involved in the creation and perception of art.

## 2. Methods

Relevant published scientific articles were searched on the Medline database via PubMed and Embase until May 2021, using the following combination of terms: (gene OR genes OR genetic\* OR polymorphism) AND (creativity OR artist) AND brain. Potentially eligible studies spanned from 1968 to 2021. No restrictions on language and publication year were applied. Reference lists of the included studies and relevant reviews were additionally hand-searched for potentially eligible studies (snowball method). The authors summarize the results of genetic linkage and association studies in Tables 1,2,3.

## 3. Creativity, mental illness and art

*"A writer is someone who has taught his mind to misbehave."*

—Oscar Wilde

Creativity is the ability to produce work that is original and novel, but at the same time meaningful and useful [12]. It is an attribute of the human brain that contributes to its adaptability and differentiates it from other animals [5]. Creativity can guide the creation of art or find an expression in different professional and social fields, including biomedical research [13]. In all of its expressions, creativity entails the ability to perceive incoming signals and devise seemingly random combinations between them, generating novel, meaningful ideas [14]. This was recently demonstrated in a study employing both electroencephalographic monitoring and transcranial alternating current stimulation: alpha oscillations in the right temporal lobe were associated with the ability to suppress obvious associations to allow the drawing of remote connections, and thus engage in the abstract thinking required in a creative process [15].

The twin study is a key methodology in behavioral genetics: it compares the similarity of different traits between monozygotic (identical) with dizygotic (nonidentical) twins to reveal the importance of environmental and genetic influences. Twin studies, both in 4-year-old British twins and 18–77-year-old US twins reared apart, have shown that ap-

plied creativity and figure drawing have heavy genetic influences, sometimes greater than the environmental effect [16, 17]. In toddlers, performance in divergent thinking tests is moderately to highly correlated to the parents' performance, demonstrating that, from early neurodevelopmental stages, the background for creativity is present, either due to genetic influences or the impact of social learning [18]. A common genetic substrate has also been proposed for homosexuality and creativity in theater and writing, as this association was found in Swedish twins [19]. Convergent thinking, the ability to make associations between concepts, is another important but overlooked component of the creative process.

Interestingly, the genetic background appears to differ between convergent and divergent thinking. Whereas in a study of Chinese college students, divergent thinking was associated with KATNAL2 polymorphisms, convergent thinking was associated with polymorphisms in Catechol-O-methyltransferase (COMT) and Synaptosomal nerve-associated protein 25 (SNAP-25), which in turn have been implicated in neuroplasticity and cognition [20]. This points to convergent and divergent thinking as two distinct creative processes, not two extremes of one common process. Besides a different genetic background, differences between convergent and divergent thinkers can be observed in the underlying memory processing, personality, and neurochemistry (involving noradrenergic and dopaminergic pathways, respectively) [21].

Since antiquity, creativity has been associated with mental disorders, even with inappropriate terms such as "mad genius" [22]. This appears to be a true association, as patients with schizophrenia or bipolar disorder exhibit high creativity and may work in more artistic and creative professions, respectively, whereas, according to registry studies, their siblings are also more likely to have a creative occupation, working as designers, scientists, artists, musicians or authors [22–24]. A polygenic risk score analysis showed that the genetic risk for schizophrenia and bipolar disorder could predict a creative occupation regardless of familial relations, implicating that these disorders share a genetic background with creative employment [23]. The heritability of working in a creative profession, such as architecture, art teaching, design, curating, writing, reporting or performing, has been calculated at 70%, pointing to a strong genetic influence [25]. The preservation of genetic polymorphisms related to mental disorders in the gene pool could signify they also carry positive effects, namely creativity and altruism [26, 27]. Genes participating in this shared vulnerability model include *Taq1A*, *DRD2*, *COMT*, *5-HTR2A*, *SCL6A4* and *TPH1* [28]. As described above, these genes participate in dopaminergic and serotonergic pathways and convergent thinking, which are all associated with creativity. Underlying endophenotypes include decreased latent inhibition and increased novelty-seeking [28]. Attention deficit-hyperactivity disorder is also associated with higher creative achievement [29]. In contrast, COMT polymorphisms play a role in increased brain

connectivity within and between the default mode and dorsal attention networks in children with the disorder [30].

The dopaminergic system appears to be at the forefront of creativity association studies due to its role in creative thought and behavior [31]. It has been proposed that striatal dopamine allows flexibility, whereas prefrontal dopamine is associated with persistence, with changes in this fine balance accounting for both creativity and psychiatric disorders [32]. Parkinson's disease has also been associated with increased creativity, preoccupation with art and artistic output, either due to dopaminergic treatment or directly due to damage in the nigrostriatal, prefrontal and mesolimbic pathways [33]. A groundbreaking pilot study in 2006 found significant associations of creativity with the A1 allele of the D2 dopamine receptor (*DRD2*) gene locus, which, combined with a serotonergic gene locus, could account for 9% of the variance in creativity between subjects [34]. Performance in divergent thinking tests is negatively associated with D2 receptor density in the thalamus [31]. This lower firing threshold could reduce the filtering capacity of the thalamus and thus increase information flow and pre-frontal cortical excitation, possibly resulting in wide associations and stimulus perceptions, but also a higher liability for psychotic disorders. A common finding in these studies is that creativity is unrelated to intelligence [31, 34].

Another study associated *DRD2* with emotional intelligence, which increased divergent thinking, particularly in female subjects [35]. Besides *DRD2*, the D4 dopamine receptor gene has also been studied as a candidate "creativity gene". Another study found an association of the 7-repeat allele with low levels of divergent thinking, as well as low flexibility and impulsivity [36]. Additionally, subjects with the 5-repeat *DRD4* allele have higher impulsivity, lower focus, and thus higher creativity levels on testing [9]. They also exhibit higher mean diffusivity in the cortex and subcortical areas on functional imaging, possibly signifying that creative individuals are inattentive and cannot suppress irrelevant information. Zabelina *et al.* [11] confirm the importance of dopaminergic genes for creativity, namely the Dopamine transporter in the striatum and COMT in the PFC, contradicting Reuter *et al.* [34] who found no association with COMT. COMT polymorphisms have also been associated with insight problem solving (i.e., the "aha" moment when realizing a solution to a problem) [37]. The importance of COMT in both dopamine and norepinephrine metabolism also reinforces the importance of norepinephrine in creative cognition, although other noradrenergic "creative" genes have not been identified [7, 21].

The serotonergic system is related to memory, cognition and mood, and has projections in the prefrontal cortex [38]. One study associated polymorphisms in the serotonin transporter, encoded by *SLC6A4*, with verbal and figural creative ability (creating sentences and pictures, respectively): the 5HTTLPR short/short haplotype, leading to decreased expression, thus higher serotonin availability, was significantly

associated with more original ideas [38]. Additionally, the A allele of Tryptophan hydroxylase 1, a gene participating in serotonin synthesis, is significantly associated with creativity and, together with the *DRD2* dopamine receptor gene described above, has been found to account for 9% of the variance in creativity [34]. It has been proposed that the two systems interact, with dopamine being more involved in left hemisphere functions (verbal creativity). At the same time, serotonin acts more in the right hemisphere (figural and numeric creativity) [34].

Genes outside these neurotransmitter families have also been associated with creativity. Interestingly, silent carriers of alpha-1 antitrypsin mutations, who do not exhibit pulmonary emphysema or liver disease, are significantly more likely to have an "intense creative energy" phenotype, and to be creative artists, working in music, dancing, visual arts, writing, photography or acting, whether professionally or not [39]. They also exhibit higher anxiety, bipolar disorder and post-traumatic stress disorder [39, 40]. This has been associated with alpha-1 antitrypsin's role in inflammation, copper homeostasis and neurodevelopment [40]. It has also been proposed that these individuals exhibit higher signal flow in subcortical circuits [40]. A polymorphism in the neuregulin 1 promoter is also associated with higher creativity in individuals with high Intelligence Quotients [26]. This gene is also related to PFC activation and has been linked to psychosis, affecting neuronal development, neuroplasticity and the glutamatergic system [26].

Interestingly, a study found that patients with bipolar disorder in the manic phase only exhibited higher creativity if they had a high-functioning allele in the *BDNF* gene. In contrast, this effect was not present in patients without mania or healthy controls and is possibly related to an increase in dopaminergic activity [41]. *BDNF* is involved in neurogenesis, memory and cognition and implicated in depression and bipolar disorder. Creative cognition also correlates with plasma oxytocin levels, and single nucleotide polymorphisms in the oxytocin receptor gene can predict creative imagination and other creative traits. Oxytocin decreases anxiety and potentiates dopaminergic stimulation. Interestingly, intranasal administration can increase creativity but decrease analytical reasoning [42, 43].

Published in 2018, the first genome-wide association study on creativity employed whole-genome analysis and fMRI whole-brain connectivity measures in fMRI to identify genes and circuits underlying figural creativity [44]. The model combining the two approaches (neural and genetic) could predict creativity at a rate of 78.4%. The results validated the importance of genes in creativity (genetic data yielded predictability of 77.5%) and uncovered the importance of new neurotransmitter systems, pointing to glutamatergic and *GABAergic* genes, as well as strong top-down control networks and weak bottom-up sensory processes (contradicting previous studies [9, 31, 40], Table 1, Ref. [9, 11, 20, 26, 31, 34–36, 38, 40, 41]), and areas such as the vi-

**Table 1. Summary of published studies examining the genetic background of creativity.**

Study type	Outcome or phenotype measured	Creativity		Country	Reference
		Gene or locus associated	Neurotransmitter/process involved		
Association	creativity tests	<i>DRD2, TPH1</i>	dopamine, serotonin	Germany	[34]
Association	artistic occupation or vocation	alpha-1 antitrypsin	neurodevelopment, inflammation, copper	USA	[40]
Association	creativity tests (verbal and figural)	<i>SLC6A4</i> (serotonin transporter)	serotonin	Russia	[38]
Association	self-reported creativity	neuregulin 1	neurodevelopment, neuroplasticity, glutamate	Hungary	[26]
PET/MRI	divergent thinking test	<i>DRD2</i>	dopamine	Sweden	[31]
Association	creativity tests (in patients with mania)	<i>BDNF</i>	dopamine	Brazil	[41]
Association	divergent thinking test	<i>DRD4</i>	dopamine	Israel	[36]
Association	emotional intelligence, divergent thinking test	<i>DRD2</i>	dopamine	Japan	[35]
Association	divergent thinking test, DTI	<i>DRD4</i>	dopamine	Japan	[9]
Association	divergent thinking test, real-world creative achievement	dopamine transporter, COMT	dopamine	USA	[11]
Genome-wide association	figural creativity tests	<i>GABRG3, SHANK2, FGF12</i>	glutamate, GABA	China	[44]
Association	divergent and convergent thinking tests	<i>KATNAL</i> and COMT, respectively	microtubule function, dopamine respectively	China	[20]

sual association cortex and areas near Broca's and Wernicke's areas [44]. A more recent Genome-Wide Association Study of creativity test performance in China found that creativity was a polygenic trait not associated with a single locus, controlled by numerous genes with small effects and showing an overlap with schizophrenia, depression, and risk tolerance and risky behavior [45].

It should be noted that the external validity of divergent thinking tools that are used in most of the studies above is questionable: like all neuropsychologic batteries, creativity tests may not capture the same effects, cognitive processes or endophenotypes as real-world, perceived or subjective creativity. Test scores may even be associated with different dopaminergic circuits than real-world creativity [11], and genetic associations may also be different [46]. As a result, the findings discussed here (summarized in Table 1) should be interpreted with caution, as the generalizability of test performance to real-life traits is not perfect.

#### 4. Dancing to the tune of serotonin and vasopressin?

*"Dance is the hidden language of the soul."*

—Martha Graham

The phenotype of a good dancer is complex, entailing a wide range of mental abilities, including music perception, coordination, creativity and physical competence. An association study in dancers, athletes and subjects who were neither dancers nor athletes revealed a significant association of dancing with polymorphisms of the arginine vasopressin 1a receptor (*AVPR1a*) and the serotonin transporter (*SLC6A4*)

genes. The dancers' characteristics associated with the haplotypes included spirituality, altered consciousness, social contact and communication. Using a robust family-based test, the authors validated this association (Table 2, Ref. [47–56]) [47].

Also called arginine vasopressin and antidiuretic hormone, vasopressin is important in higher cognitive functions [50]. Vasopressin -particularly the *AVPR1a* genotype- has also been associated with affiliative behavior, courtship and social communication [47]. The human serotonin transporter gene (*SLC6A4*; *5-HTT*) is expressed in the brain, particularly in areas participating in emotion [50]. Serotonin has been associated with spiritual experiences, which often incorporate dancing. It is hypothesized that decreased *SLC6A4* promoter function, which results in higher serotonin levels, could result in higher creativity and attention to music. Another possible association was with the dopamine D4 receptor (*DRD4*) [47].

Interestingly, *SLC6A4* polymorphisms also modulate cognitive flexibility under psychosocial stress, such as a public performance [57]. Although these initial associations are revealing, they cannot adequately to explain the wide differences in dancing abilities between people, which could be affected by numerous other genes, epigenetic changes and other environmental effects. Dancing is a complex phenotype whose background warrants further exploration with well-designed genetic and genomic studies including subjects with diverse, well-documented relationships with dance: different training, culture, perceived talent or ability, dance types, musical training, dancing solo, with a partner or in a group etc.



**Table 2. Summary of published studies examining the genetic background of musicality and dancing.**

Music and dancing					
Study type	Outcome or phenotype measured	Gene or locus associated	Neurotransmitter/process involved	Country	Reference
Association	professional dance	<i>AVPR1a, SLC6A4</i>	vasopressin, serotonin	Israel	[47]
Linkage	music perception tests	4q22, 8q13-q21	neurogenesis, inner ear transduction	Finland	[48]
Genome-wide linkage	absolute pitch	8q24.21, 7q22.3, 8q21.11, 9p21.3	unknown, possibly adenylate cyclase	USA	[49]
Association	music perception tests	<i>AVPR1a, SLC6A4, TPH1</i>	vasopressin, serotonin	Finland	[50]
Association	active music listening	<i>AVPR1a</i> (vasopressin receptor)	vasopressin	Finland	[51]
Genome-wide linkage and association	pitch-production accuracy test	4q23, UGT8	myelin lipid synthesis and clearance	Mongolia	[52]
Association	choir participation	<i>SLC6A4</i> (serotonin transporter)	serotonin	UK	[53]
Genome-wide CNV	music perception tests, self-reported musical creativity	5q31.1 (protocadherin- $\alpha$ ), 2p22 (GALM), 8q24	neurodevelopment, serotonin, synaptic function	Finland	[54]
Genome-wide linkage	music perception tests	3q21.3 (GATA2), 4p14 (protocadherin 7)	auditory pathway development, cochlea, amygdala	Finland	[55]
Genome-wide linkage	arranging and composing music, non-musical creativity	16p12.1-q12.1, 4q22.1, Xp11.23, 18q21	cerebellar LTD, hearing, synaptogenesis, neurogenesis	Finland	[56]

## 5. Is musical expression based on gene expression?

*"It really is a very odd business that all of us, to varying degrees, have music in our heads."*

—Oliver Sacks, *Musophilia: Tales of Music and the Brain*

It is common knowledge that musical talent is not equally distributed among all individuals [58]. Certain "musical" families, such as the Bach family, which produced over 50 prominent musicians over 200 years, dominate music history. While cultural factors, exposure to music and professional or amateur training are all important environmental determinants of each individual's relationship with music [59], primary evidence has shown that musicality, like other creative attributes, has a biological basis [54, 60]. An interesting observation is that universal musical rules formed independently in different cultures that did not interact, indicating that these rules were determined by the organization of the human brain rather than cultural factors [48]. These musical rules, guided by neural, genetic, cognitive or even mathematic principles, were not known to the first human creators of music, and were only studied, understood and defined retrospectively by scholars and scientists. In this sense, the cognitive functions underlying music closely resemble language [60, 61].

Although music is also a very complex phenotype, its two extreme forms have a clear definition and exhibit significant heritability (Table 2). Congenital amusia (tone deafness), where subjects cannot recognize melodies and out-of-key-notes while their rhythm perception is intact, is a familial condition, appearing in 39% of first-degree relatives of affected individuals compared to 3% in the general population [62]. In general, perceiving pitch has a heritability of 71–80%, while the shared environment within families does not

significantly affect pitch perception [63]. On the other end of the spectrum, absolute pitch (AP), the ability to name a pitch without a reference, also has a genetic component [64], which has been localized to 8q24.21 and, less robustly, to 7q22.3, 8q21.11, and 9p21.3 [49]. Interestingly, a study has identified a phenotypic and genetic overlap between AP and synesthesia. These two "artistic extreme" cognitive phenotypes tend to coexist in individuals and share a linkage with chromosomes 6p and 2, possibly pointing to a common neurodevelopmental background [65].

A research group from Finland has been performing genetic analyses in a cohort of families of musicians and non-musicians, using music perception tests that minimize the effect of training and culture (Table 2) [48]. Initially, they demonstrated a substantial heritability of 47% in combined test performance. Linkage analysis showed significant linkage on 4q22, which contains the netrin receptor *UNC5C* (important during neurogenesis), and suggestive linkage on 8q13-q21. This area contains the *TRPA1* gene (transient receptor potential ankyrin 1, possibly a transduction channel in inner ear hair cells) [48]. A research group in Mongolia also corroborated the importance of this locus in their population, finding a linkage for musicality at 4q23, with an overlapping supporting interval [52]. This finding confirms that, while music and the corresponding musical phenotype varies significantly across different cultures, musicality is an inherent human trait with common genetic roots regardless of cultural expression.

Besides test performance, self-reported creativity and musicality are also associated with copy number variations in loci containing genes involved in neurodevelopment, serotonin metabolism, learning, memory, synaptic function and schizophrenia (e.g., galactose mutarotase, protocadherin- $\alpha$  1–9, *MCTP2*) [54].

The serotonin and vasopressin systems appear to be involved in various aspects of the musical phenotype. Besides playing an instrument, composing, improvising or arranging are different cerebral functions associated with activation in prefrontal, sensory and motor areas and deactivation of limbic areas [66]. Genetic determinants have been found in this population as well, with self-reported musical creation correlating with test performance, which in turn was strongly associated with *AVPR1A* haplotypes (RS1 and RS3), and weakly with *SCL6A4* polymorphisms (variable number tandem repeat). These are the same polymorphisms found in dancers and are involved in social and affective behavior [47]. Significant differences in *AVPR1* haplotypes have also been found in individuals who actively listen to music [51]. *SLC6A4* has been associated with choir participation [53], while both genes have also been associated with memory [67]. Interestingly, administration of intranasal vasopressin was shown to improve participants' mood, increase alertness and decrease working memory for musical tasks only in a complex fashion [68].

However, a genome-wide linkage analysis performed in a larger sample in the Finland cohort yielded lower heritability estimates, between 23 and 34% for composing and arranging and only 11% for improvising [56]. Concerning arranging, the analysis revealed a significant linkage with an area containing the *GSG1L* AMPA receptor gene, which is important in cerebellar long-term depression and hearing. The cerebellum—and its synaptic plasticity—has previously been associated with musical ability, improvisation and rhythm working memory. It also revealed a suggestive link with an area near the *MYCN* gene, mutations of which cause Feingold syndrome type 1 (microcephaly, intellectual disability, digital malformations and deafness) [56]. Composing was linked to 4q22.1, containing the netrin receptor *UNC5C*, which is implicated in neurodevelopment, and *UGT8*, which had also been found in Mongolian musical families [52]. The “neither composing nor arranging” phenotype was linked to an area previously associated with cognition, which contains the cadherin genes associated with schizophrenia. Finally, non-musical creativity was linked to an area containing several genes involved in synaptogenesis and neurogenesis (synapsin 1), as well as the memory, reward and emotion systems (*ELK1*, *KCND1* and *SYP*) [56].

Besides executive mental functions, a GWAS on the same cohort focused on the sensory, auditory component of music perception. The strongest linkage was found near the *GATA binding protein 2* (*GATA2*) gene, which regulates the development of cochlear hair cells and the inferior colliculi, which are important in a tonotopic organization. Another region linked to music perception contained the protocadherin 7 genes, which have been linked to the function of the cochlea and the amygdala. Regions of the absolute pitch were not present in the linkage, indicating that AP is a cerebral “gift” rather than an auditory property [55].

The limitations of most published studies are the small sample sizes and the possibly low accuracy of self-reporting or standardized testing, which may not perfectly capture real-world ability [69]. However, the findings remain significant and provide useful insights into the genetics of musicality. Although most of the findings stem from the same cohort in Finland, other cohorts from the UK and Mongolia seem to validate the involvement of these genes and loci. Musicality is not only genetically determined, and the interactions between genetic and environmental components, such as growing up in a musical environment and receiving professional training, are also worth exploring [70]. The importance of environmental exposure is discussed in Section 7.

## 6. Visual arts and synesthesia

*“It took me four years to paint like Raphael, but a lifetime to paint like a child.”*

—Pablo Picasso

Besides performing arts, visual arts are also important components of artistic creation. Using magnetoencephalographic and functional MRI studies, Semir Zeki has studied the neuroanatomy behind viewing forms, colors, faces and moving objects, uncovering a parallel processing system, whereby each stimulus is individually processed in a dedicated area of the visual cortex [71, 72]. Interestingly, if it exists, the neuroanatomical substrate that mediates the integration of all these attributes (form, color, movement) into a whole (e.g., a painting) has not been discovered yet.

Patients with Parkinson's disease exhibit increased interest in visual arts, either producing or admiring it. Although the dopaminergic disruption may be important, the precise physiological and neurochemical correlations of this nuanced behavioral change have not been identified [33]. In certain studies discussed above, such as in the British and US studies in monozygotic or dizygotic twins, children and adults, applied creativity was tested by asking the participants to draw human figures or houses. Creative talent in these drawings carried a heavy genetic component, sometimes greater than the environmental effect [16, 17]. However, very few studies have associated visual arts with specific genes or loci. As discussed above, silent alpha-1 antitrypsin mutation carriers are more likely to be creative and work in visual arts or photography [39]. In the genome-wide association study on creativity discussed before, the phenotype measured was figural creativity, which had a heavy genetic component associated with areas such as the visual association cortex and areas near Broca's and Wernicke's areas [44].

Synesthesia, where stimulation of one sensory or cognitive pathway (e.g., letters or sounds) is associated with experiences in a second pathway (e.g., colors), is a heritable, polygenic phenomenon present in 2–4% of the population [73, 74]. As a different way of “seeing the world”, it has been hypothesized to “predispose” to artistic creation and is indeed more frequent in art students [75]. Synesthesia, in particular seeing colors when listening to sounds, appears to have a

**Table 3. Summary of published studies examining the genetic background of synesthesia.**

Study type	Outcome or phenotype measured	Synesthesia			
		Gene or locus associated	Neurotransmitter/process involved	Country	Reference
Genome-wide linkage	sound-color synesthesia	2q24, 5q33, 6p12, 12p12	neurodevelopment, neuroplasticity autism	UK	[76]
Association	sound-color synesthesia	COL4A1, ITGA2, MYO10, ROBO3, SLC9A6, and SLIT2	axonogenesis	Netherlands	[77]

genetic component. A linkage study found a significant linkage with chromosome 2q24 and suggestive linkage with other areas (5q33, 6p12, and 12p12) [76]. An association study for the same trait found associations with genes involved in the process of axonogenesis (SLIT2, MYO10, ROBO3, ITGA2, COL4A1, and SLC9A6), whereby a disruption could result in atypical, increased structural and functional neural connections between different cortical areas, leading to synesthesia (Table 3, Ref. [76, 77]) [77, 78]. According to some studies, synesthesia may genetically overlap with schizophrenia and absolute pitch, the latter relationship localizing to chromosomes 6q and 2 [65, 79].

Interestingly, synesthesia is more prevalent in patients with autism with savant traits [80]. Latent savant-like skills can be uncovered in healthy individuals without autism or savant traits by suppressing left frontotemporal lobe activity, indicating that the dynamics for such cognitive functionality exist in all brains but are suppressed [81]. Children with autism, who have no significant environmental exposure to art, but can create magnificent works of art, are especially thought-provoking examples of the cerebral and genetic determinants of artistic creativity. A characteristic example is Iris Grace Halmshaw, a British artist with autism who started painting at age 5: her paintings not only allowed her to communicate her thoughts and emotions but are also coveted by art galleries worldwide for their immense artistic value.

## 7. Not just genes

Creativity and artistry are multifaceted traits, determined by multiple components of behavior and personality, each having its own genetic and environmental determinants. Although this work attempted to concentrate the available evidence on the genetic differences in artistic individuals, it is clear that environmental factors are also important. For instance, psychological factors such as birth order or exposure to an artistic household can affect artistic expression, creativity, and even mental illness [82]. Identifying these factors is important since they can be modified with appropriate interventions [83]. For example, a recent study showed that *DRD2* and *COMT* polymorphisms interact with the parenting style the individual was exposed to, such as mother authoritative-ness, to explain variance in creativity. More specifically, a high genetic susceptibility (“creative genes”) leads to a greater environmental susceptibility (being more or less creative depending on positive or negative parenting) in an interesting genetic-environmental interaction [84].

In exploring the effect of environmental factors, epigenetics may prove to be an important connecting link. Although there have been no studies on the epigenetics correlating with creativity and artistic cognition, it has been hypothesized that the methylation status of the dopamine transporter 1 [85] or the estrogen receptor type  $\alpha$  [86] could be associated with creativity and artistic perception [87]. Additionally, epigenetic effects related to Alzheimer’s disease may influence artistic output [88], which is known to be affected by the disease [89]. Epigenetics may also underlie the positive effect of art on mental and somatic health [87]. This entire field remains unexplored but could answer many questions about early life experiences, exposure to art, professional training and rehearsing, and their relationship with creative and artistic cognition. Epigenetic inheritance may also play an important role and should be explored [90].

## 8. Conclusions

From antiquity until now, artistic creativity has been supposed to have significant genetic elements and social and environmental influences. Many genes and genetic loci are associated with creativity or artistry, a subset of them also exhibiting correlations with neurodevelopmental or psychiatric disorders. Further genetic exploration of human artistic creativity will uncover essential knowledge regarding cognition, behavior and general brain functionality, enabling a more targeted and personalized use of art therapy in health and disease.

## Abbreviations

AP, absolute pitch; COMT, Catechol-O-methyltransferase; fMRI, functional Magnetic Resonance-Imaging; GWAS, Genome-Wide Association Studies; SBNAP-25, Synaptosomal nerve-associated protein 25; *DRD2*, D2 dopamine receptor; *BDNF*, Brain-derived neurotrophic factor; 5-HTT, serotonin transporter gene; TRPA1, transient receptor potential ankyrin 1.

## Author contributions

MA conceived, guided and supervised the project and provided additional articles. MGS designed the search and conducted the literature review and data extraction. Both authors participated in drafting the manuscript, revised it critically, and approved the final version.

## Ethics approval and consent to participate

Not applicable.

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