Review

American Journal of Alzheimer's Disease & Other Dementias®
Volume 38: 1–15

DOI: 10.1177/15333175231214833
journals.sagepub.com/home/aja
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Music Engagement as a Source of Cognitive Reserve

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Abstract

Music engagement is a ubiquitous activity that is thought to have cognitive benefits for the rapidly aging population. In the absence of robust treatment approaches for many age-related and neuropathological health issues, interest has emerged surrounding lifestyle-enriching activities, like exercise and music engagement, to build cognitive reserve across the lifespan and preserve neurocognitive function in older adults. The present review evaluates evidence of neurocognitive preservation arising from lifelong music engagement with respect to the cognitive reserve hypothesis. We collated a body of neuroimaging, behavioral and epidemiological evidence to adjudicate the benefits of music engagement for cognitive reserve. The findings suggest that music engagement should be considered in tandem with other well-established cognitive reserve proxies as a contributor to differential clinical outcomes in older populations at risk of age-related and neuropathological cognitive decline.

Keywords

dementia, Alzheimer disease, cognitive reserve, neurodegenerative diseases, music, healthy aging, cognitive aging

Significance Statement

This narrative review advances dementia research by exploring the potential of music engagement as a contributor to cognitive reserve. The findings of this paper suggest that:

(1) Music engagement across the lifespan may preserve a range of neurocognitive functions into later life.
(2) Music engagement across the lifespan preserves cognitive function in a manner consistent with the cognitive reserve hypothesis.
(3) Music engagement interacts with mechanisms associated with age-related and neuropathological decline, moderating symptom expression and incidence.

Introduction

Age-related neurocognitive decline represents a key health challenge for older adults with the typical trajectory of aging predicting a gradual deterioration of cognitive function. Neurodegenerative conditions like Alzheimer's Disease (AD) often present with a rapid downturn in mental abilities, compromising memory, language and overall cognitive function.[1] Globally, it is estimated that over 416 million individuals fall along the AD continuum, with up to 32 million possessing late-stage AD dementia.[2] AD is resistant to conventional pharmacological interventions,[3] which can result in a substantial burden of care dependency on families and worldwide healthcare systems.[2] Accordingly, emphasis has been placed on understanding how modifiable lifestyle factors might contribute to the theorized mechanism of 'reserve', a construct that carries promise of robust cognitive health in later life.[4,5] Several enriching activities such as physical exercise,[6] second language learning[7] and social interaction are believed to benefit cognitive reserve.

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Music is another enriching activity with potential to benefit cognitive reserve. Musical activities are engaging, enjoyable, and emotional, and they often take place in social settings. They can be personally meaningful and may induce coordinated physical activities such as clapping, tapping, or dancing. The various functions elicited by music can be construed as 'active ingredients' that coalesce in a way that interacts with several neurological and neurochemical systems. Indeed, music-based interventions have proven to be an effective therapeutic tool in AD symptom management.[8,9] Thus, the possibility that lifelong music engagement may contribute to the mitigation of age-related and neuropathological decline warrants consideration.

Defining Reserve: Brain Reserve, Brain Maintenance and Cognitive Reserve

The idea of 'reserve' was conceived to explain interindividual differences in cognitive function relative to age-related or pathological neural degeneration.[10] Reserve explains why an equivalent pathological burden of AD may predict intact cognitive performance for some and precipitous cognitive deterioration for others.[10,11] Reserve is proposed to be influenced by three partially interactive sub-processes: brain reserve, brain maintenance and cognitive reserve. Brain reserve reflects individual variability in the brain's anatomical composition, with the model emphasizing a passive resistance to cognitive aging or brain disease inherent in individuals with a physiological disposition towards greater cortical volume and density, amongst other factors.[12] Brain reserve operates as a threshold model, wherein once the pathological burden of disease surpasses the brain's available matter delegated to support cognitive processes, rapid functional decline becomes inevitable. Brain maintenance, on the other hand, reflects a more active neural capacity to mitigate the development of age-related or neuropathologic changes.[12,13] While the precise underlying mechanisms remain under investigation, brain maintenance is thought to involve the repair and preservation of neural resources on a genetic, molecular, cellular and cortical level.[13] Cognitive reserve (CR) is also considered an active neural mechanism and is theorized to optimize neural processes through compensatory cognitive strategies.[12,14] Most of the reviewed research on the benefits of music engagement pertains to its role in promoting CR; evidence for its role in brain reserve and brain maintenance is more indirect.

The neural implementation of CR is thought to be facilitated by two mechanisms: neural reserve and neural compensation. Neural reserve typically equates to the efficiency, capacity and flexibility of cognitive networks while neural compensation refers to the recruitment of neural resources in response to cognitive demand.[12] During neural compensation, specialized networks are recruited to better accomplish tasks, compensating for areas that may exhibit suboptimal performance due to age-related or pathological changes.[12] There are four key predictions of CR, each of which will be considered in this review. First, at matched neurological health, individuals with high CR should demonstrate enhanced cognitive performance compared to those with low CR. Second, at equivalent levels of cognitive performance, individuals with high CR can often exhibit substantial neural decline compared to those with low CR, indicating increased resilience to clinical outcomes of brain deterioration in high CR individuals. Third, the point where cognitive decline begins (point of inflection) will be delayed in those with high CR compared to those with low CR. Lastly, once the symptoms of decline emerge, the pace of disease progression will be faster in those with high CR compared to those with low CR, given their increased levels of neural decline.[10,11]

CR is assumed to be a byproduct of a complex gene-environment interaction wherein modifiable socio-behavioral factors such as level of education, occupational complexity, physical activity, socioeconomic status, and leisure activities contribute to individual differences in CR capacity.[13] In estimations of CR, these factors, known as CR proxies, must be considered as covariates and incorporated into the clinical understanding of measurable neurocognitive differences. The extent of engagement, level of effort required, and time of uptake for these socio-behavioral proxies are thought to influence their unique contribution to CR capacity.

It has been proposed that any continuous and sufficiently stimulating activity may be a source of CR,[13] and hence music engagement is also a potential CR proxy. Music engagement is an enjoyable experience that recruits a wide range of cognitive functions and across long periods of engagement, may help to mitigate cognitive decline. However, three challenges limit the conclusions that may be drawn. First, unlike other contributors to CR, music engagement encompasses several forms of activity, including singing, instrument playing, dance, and passive music listening. As a result, summarizing and interpreting evidence is a challenge, as there is heterogeneity not only between study designs but in the forms of engagement considered. Second, the unique contributions of various music elements to CR are difficult to elucidate, given passive forms of music engagement do not require specialized learning, whereas active forms require training of specialized cognitive functions during mastery (e.g., instrumental learning, dancing). Third, there is little extant research specifically designed to evaluate music engagement in the context of CR, so not all predictions of the hypothesis have been directly tested. In short, despite converging evidence, a full assessment of the role of music in CR remains to be completed. Nevertheless, this review evaluates evidence for the role of music engagement in building reserve across the lifespan, drawing on studies that directly or indirectly support predictions of CR, and on theories that may shed light on underlying mechanisms.

Methodological Approach

This narrative review drew upon protocols for search strategies outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P).[15] Pubmed, PsycINFO, Medline, Web of Science, Cochrane

Library, Embase, Scopus and Science Direct databases were used to identify literature investigating the associations between music engagement, training or expertise and cognitive reserve. To fully explore the extent of music's relationship to reserve, terms related to cognitive health were also included in the search, such as neuroplasticity, neuroprotection, and brain reserve, as well as those implicated with cognitive deterioration such as Dementia, Alzheimer's Disease and Mild Cognitive impairment. For example, one search strategy in Pubmed that was limited to peer-reviewed articles was as follows: TITLE-ABS-KEY ("cognit*" OR "neuro*" OR "cognitive health" OR "cognitive reserve" OR "brain reserve" OR "neuroprotection") AND ("Aging" OR "Older Adults") AND ("Cognitive decline" OR "Neurodegeneration" OR "Dementia" OR "Alzheimer*" OR "MCI" OR "Mild Cognitive impairment") AND (Prevent*) AND (music*). The publication year was not restricted and included articles available up until 25th August 2023.

A total of 661 articles were identified from the eight databases (PubMed: N = 72; APA PsycINFO & Medline via Ovid: N = 72; Web of Science: N = 79; Cochrane Library: N = 43; Embase: N = 100; Scopus: N = 58; Science Direct: N = 237). After removing duplicates, we assessed titles and abstracts to gauge suitability to the overarching research synthesis aim and excluded articles that did not meet the criteria. The criteria included: healthy older adults, older adults with dementia or mild cognitive impairment; inclusion of music engagement as a factor; and inclusion of cognitive reserve as an outcome of interest. Additionally, we included relevant articles from reference lists of published work and authors' personal reference databases. Ninety-one eligible articles were finally included in this narrative review.

Cognitive Benefits of Music Engagement Across the Lifespan

Music is a unique multisensory experience that engages an array of neurocognitive resources to facilitate the interplay between music perception and production.[16] Music engagement is characterized by incremental task difficulty, oscillations in arousal states, and performance related reward-motivation feedback loops.[17-19] The dopaminergic reward system is also implicated in active music participation[20] as well as other neurochemical mechanisms speculated to promote neurogenesis[21] and neuroplasticity,[22] which may preserve neurocognitive function into later life. Involvement in music is thought to help maintain cognitive, emotional and neurological function in older adults, with the impact of these benefits dependent on the age of onset, type of training, intensity of musical activity and maintenance of skills into older age.[23]

Music-based therapies are increasingly used as a non-pharmaceutical treatment for individuals living with AD,[9,24,25] and regions responsible for music perception and skill remain relatively preserved throughout disease progression.[26] Music is used to improve mood,[17] trigger autobiographical memories,[27] and support a sense of self[28] even into the later states of disease progression.[29] According to the Therapeutic Music Capacities Model (TMCM), these benefits in AD populations may arise from the multifaceted nature of music experience, with its capacity to engage attention, evoke emotions, support personal memories, strengthen social bonds, trigger physical movement and coordinated (rhythmic) action, and interact with attitudes and beliefs.[17]

Although functional and structural neural degradation during aging often leads to impaired recruitment of task-relevant brain regions and global cognitive processes,[4] participation in musical activities, whether passive listening, music coordinated movement (physical activity or dance), singing or playing an instrument, is associated with a range of robust cognitive functions. Such functions may include those related to auditory processing, motor skills, memory, timing, and executive functions.[30,31] Although certain benefits may reflect 'near' transfer, many benefits may reflect overall brain health arising from long-term participation in enriched contexts associated with music, as described by the TMCM. While existing research is often correlational, evidence has been reported that music engagement may confer cognitive benefits in children, as well as healthy younger and middle-aged adults, suggesting that music engagement enhances the ability of people to meet the cognitive demands of certain non-musical tasks.[30,32] For example, music-related auditory processing abilities, involved in detecting acoustic cues (rhythm, pitch and timbre), processing syntactic or semantic information, and integrating relevant semiotic meaning (implicit in prosodic patterns) may provide utility to language perception.[32,33] Patel's OPERA hypothesis suggests this type of transfer can occur because of neural overlap in related substrata, high precision of acoustic processing, recruitment of emotional and attentional resources, and repetitive activation of the neurocognitive network through music practice.[33] Evidence suggests that a range of music-related cognitive functions are enhanced in musicians,[32] and there is also evidence that several cognitive functions in musicians are maintained in older age, with aging musicians exhibiting relatively preserved speech perception[34] and auditory processing ability.[35,36]

Similarly, Hanna-Pladdy and Gajewski[37] reported that older musicians exhibit enhanced phonemic fluency, verbal working memory, verbal immediate recall, as well as superiority in visuospatial and motor domains when compared with matched non-musicians.[37] This cognitive advantage in older musicians may be related to their lifelong engagement with music, which involves repetitive visuospatial, motor, and vocal activities such as reading sheet music, playing instruments, and singing. Further, music performance involves memory and attentional demands (general attention, vigilance, selective and sustained attention)[38] as well as executive functions required to inhibit irrelevant information, monitor song progression and adapt skills during a performance.[39,40] However, evidence for 'far' transfer abilities in older adults is sparse, with only a few correlational studies demonstrating musician advantage in executive function,[41] processing speed and working memory.[42] Causal inferences cannot be

concluded from these findings: music engagement might promote positive neurocognitive outcomes, but it is also plausible that people who engage with music activities are predisposed to enhanced neurocognitive functions that are less susceptible to decline.

Longitudinal designs, in contrast to cross-sectional studies, may better control for this ambiguity, although there are unavoidable biological, environmental, and socio-behavioral (SES, IQ and education) factors that may contribute to positive associations between musicianship and enhanced cognitive functions. One analysis of a longitudinal dataset, which accounted for many of the abovementioned factors, revealed a small but statistically reliable association between playing a music instrument and general cognitive ability across the lifetime (between ages 11 and 70, minimally adjusted $\beta = .200$, fully adjusted $\beta = .129$).[43] Thus, it appears music engagement may yield benefits for both domain-specific and broad-spectrum cognitive functions, which, in turn, may foster resilience against age-specific cognitive deterioration while optimizing cognitive domains which remain intact in later life.[23] Considering these wide ranging associations, it is reasonable to assume that music engagement may serve as a complementary lifestyle activity to enrich cognitive health of an aging population.[16] Table 1 summarizes the key findings regarding cognitive benefits in older adult musicians.

Music Engagement as a Source of Cognitive Reserve

Behavioral, epidemiological and neuroscientific evidence broadly supports the predictions of the CR hypothesis for music engagement, though additional research is needed to thoroughly evaluate the specific outcomes associated with CR. For instance, the first prediction of the CR hypothesis is that individuals with high CR will possess advanced cognitive skills when compared to low CR individuals with a similar level of brain health.[10] In support of this prediction, a study by Böttcher et al.[44] examined differences between neurocognitive health in older instrumental musicians and well-matched older non-musicians, using cortical gray matter volume as a global measure of brain integrity. An analysis of structural features revealed no significant differences between musicians and controls in atrophy susceptible pre-selected regions of interest, including higher-order frontal, temporal and hippocampal areas, indicating a similarity in brain health. Despite this, musicians demonstrated an advantage in global cognitive function as well as preserved working memory, executive function and visuospatial ability. Although musicians possessed greater overall gray matter volume (which was attributable to a small volumetric discrepancy in the somatosensory cortex), the regions generally associated with implementing the abovementioned cognitive functions were similar between groups, indicating that musical experience may increase the efficiency of these neurocognitive networks, preserving functionality into older adulthood. Importantly, groups were one-to-one matched in diagnostic status, gender, education, intelligence, socioeconomic status, and physical activity, suggesting that music engagement across the lifespan may contribute to CR above and beyond well-established proxies of CR.[49]

The second prediction of the CR hypothesis is that individuals high in CR develop greater resilience to neural decline, such that at matched levels of cognitive health, they will demonstrate a higher degree of brain deterioration when compared to those with low CR.[10] Notably, this prediction pertains to populations experiencing neural decline, and does not imply any greater risk of neurodegeneration in people with high CR. Rather, it indicates that people with high CR should have better cognitive function in spite of age-related or pathological decline in neural integrity. The most compelling evidence for this prediction was reported by Porat et al.[45] who examined differences in gray matter atrophy between aging dancers and non-dancers (with both dancing and non-dancing groups consisting of cognitively healthy and cognitively impaired individuals). The elderly dancers, who were well-matched in cognitive status, age, level of education and gender, had thinner bilateral gray matter volume when compared to non-dancers.[45] Furthermore, elderly dancers performed better on learning and memory tasks, indicating a resistance to the effects of brain pathology, as well as a more efficient use of available neural resources.[45]

The third prediction of CR suggests that individuals with high CR clinically express symptoms of decline at a later point (inflection) than those with low CR.[10] Ferrari et al.[46] examined the preventative benefits of education, vascular risk and leisure activities (including passive music listening and singing, among other lifestyle activities) on AD-related prognostic outcomes. Each of these factors was found to contribute to a delayed age of dementia onset in carriers of apoliprotein E (EPOE) ε4, a prominent genetic risk factor for AD and dementia.[46] Individuals with high education, high leisure activity, and no vascular risk exhibited a 1.2-2.2-year delay in the age of dementia onset, which was comparable to outcomes in those without the APOE ε4 gene variant when matched for these factors. In contrast, a more recent study which attempted to estimate the age of MCI onset relative to early life music and language instruction found that only language training was associated with a delay in cognitive impairment.[47] However, this study did not account for continuous engagement with these practices, focusing only on the influence of childhood and adolescent (<18) instruction (with at least 5 years of music or language education). It should be of note that both of the abovementioned studies indicated that these leisure activities decreased the incidence of AD and MCI respectively.[46,47]

Several prospective studies examining the risk of developing AD have indicated differences in disease incidence between musicians and non-musicians. Firstly, a large gerontological study consisting of 52,601 older adults, indicated that karaoke and instrumental activity were associated with

Table 1. Key Evidence for Cognitive Advantages in Older Adult Musicians.

Study	Study Design	Cognitive status	Age	N	Independent variable	Confounders	Results
Grassi et al, 2017	Cross-sectional	No cognitive impairment	Musicians 72.25 (6.71), non-musicians 72.7 (6.71)	40 (20 professional musicians, 20 non-musicians)	Musicians (had 46-80 years of music training and practice) vs non-musicians	Education and vocabulary score	Auditory processing ability, working memory and visuospatial abilities: musicians > nonmusicians
Hanna-Pladdy & Gajewski, 2012	Cross-sectional	No cognitive impairment	Musicians 68.81 (5.15), musicians 68.45 (4.45)	70 (33 musicians, 37 non-musicians)	Musicians (more than 10 years of instrumental musical participation) vs non-musicians (less than 1 year of musical participation)	Matched on age and education	Phonemic fluency, verbal working memory, verbal immediate recall, visuospatial judgment, and motor dexterity: musicians > non-musicians; Early age of musical acquisition (before age 9) predicted enhanced verbal working memory
Hanna-Pladdy & MacKay, 2011	Cross-sectional	No cognitive impairment	Non-musicians 69.7 (7.9), low activity musicians 69.5 (6.6), high activity musicians 70.8 (6.3)	70 (21 non-musicians, 27 low activity, 22 high activity)	Non-musicians (never played an instrument), low activity musicians (1-9 years musical instrument playing experience), high activity musicians (at least 10 years musical instrument playing experience)	Matched on age and education	Delayed non-verbal memory, visuospatial sequencing, naming, and executive processes: High activity musicians > nonmusicians
Okely et al, 2022	Longitudinal (1947, and five waves between 2004-2019)	Non-demented	69.5 (0.83) in 2004	366 (117 played a musical instrument)	Experience of playing a musical instrument	Age, gender, education, adult occupational class, childhood environment, chronic disease history	Experience of playing a musical instrument associated with lifetime change in global cognitive ability (β = 0.129, p = .002)

trend level decreased risk of dementia in men and a significantly decreased risk of dementia in women.[48] Although the discrepancy between genders initially raised questions, more women (72%) than men (28%) engaged in multiple forms of musical activity, suggesting that richer levels of music engagement may have contributed to these differential outcomes. Given the scale of the study and the adjustment for relevant covariates, the data provide strong support that music engagement may assist in the prevention of dementia.[48]

In the same year, a meta-analysis investigating musical instrument playing across the lifespan, reported a 59% reduction in the likelihood of being diagnosed with dementia in musically engaged individuals, however, the size of the evidence base utilized (n = 2) and risk of reverse causality may limit interpretation of these results.[49] In the following year, Arafa and Colleagues[50] synthesized findings from studies included in the assessment by Walsh et al.[49] (including studies by Hughes et al.[51] and Verghese et al.[52]) alongside their own largescale prospective study. The collective outcomes suggested that musicians had a 36% lower likelihood of developing dementia compared to those who did not play a musical instrument.

Other evidence that music engagement impacts upon the incidence of dementia comes from a population-based cotwin design study, in which musically engaged twins were compared with their non-musical cotwin.[53] Although only 24.8% of the sample was monozygotic (sharing 100% of their genetic makeup), genetic factors in this study remained significantly more controlled than standard case-control studies. Furthermore, the study also accounted for selected protective factors such as level of education and physical activity. The results indicated that musically engaged twins had a 64% lower likelihood of developing MCI and dementia, supporting claims that differences between musicians and non-musicians in dementia incidence are largely attributable to music training rather than preexisting biological differences.[53] Table 2 summarizes the most significant studies regarding the risk of dementia in musicians compared to non-musicians.

The final prediction from the CR hypothesis is that once symptoms of dementia appear, they progress more rapidly in high CR compared to low CR individuals.[10] Based on a 60-year longitudinal study, Romeiser et al.[54] found that high-school engagement in instrumental training was associated with a higher baseline but more rapid decline in episodic memory (measured with immediate and delayed recall tasks) across a 7-year period (~65 to ~72), compared to those with no high-school music engagement. The finding suggests that early music experience may delay age-related episodic memory decline until late in neurodegenerative progression.[54] That is, high CR masks the clinical symptoms of neural decline until age-related or pathological burden overwhelms the compensatory strategies that preserve cognitive function, resulting in a more rapid decline. Nevertheless, high CR is associated with higher functionality during the early stages of neural decline, allowing for a better quality of life throughout the course of disease.[10]

Romeiser and Colleagues[54] also observed that individuals high in continuous music engagement, who maintained consistent musical practice across follow-up time points throughout adulthood, maintained higher episodic memory outcomes across a 7-year period (from ~65 to ~72) than those with intermittent or no continuous music engagement. Thus, continued music engagement across the lifespan may help to maintain an advanced level of cognitive function until later in life. This finding is consistent with the preserved differentiation view from the 'use it or lose it' hypothesis: those with a higher cognitive ability, built from long-term music engagement, may maintain a trend of higher cognitive ability over their lifetime.[55] Table 3 summarizes the key evidence regarding music engagement as a proxy for CR.

Mechanisms Related to Music Engagement in Dementia Prevention

Thus far, evidence suggests that music engagement shares several characteristics with well-established CR proxies, wherein lifetime music training may work as a protective mechanism against aging. However, similar to other CR proxies, music engagement may not directly prevent the accumulation of neuropathology. Instead, music may offset the impact of neurodegeneration by delaying symptomatic cognitive impairment. Therefore, cognitive enrichment from music engagement may only provide transient benefits in preventing symptoms of AD in the presence of accumulated amyloid-β (Aβ) peptide plaques, intracellular tau neurofibrillary bundles, and pre-existing genetic factors such as the presence of the apolipoprotein E (APOE) ε4 allele.[56] Such biological factors are at the core of AD pathology and are thought to disrupt mitochondrial function, reduce metabolic activity, and increase oxidative stress and neuroinflammation.[57]

Leisure activities, such as music engagement, may reduce stress and modulate neuroendocrine responses, reducing inflammatory immune activity.[9,58] Stress damages the nervous system through the hypersecretion of corticosteroids, resulting in neuroinflammatory responses that can damage regions such as the hippocampus, amygdaloid complex and frontal lobe.[21,59] Given that music-induced positive emotions may be associated with decreased physiological stress,[60] engagement with this activity across the lifespan may mitigate stress-related neurodegeneration, providing protective effects against AD pathology.[9] Such reductions in stress are more evident when personally-preferred music is administered to older adults with AD.[61] Personally-meaningful music and associated memories are known to be remarkably preserved in some forms of dementia.[62] Similarly, musically oriented spiritual practices such as chanting also contribute to reductions in the stress hormone, cortisol.[63]

Thus, one source of the benefit of music engagement for CR is that it can help to reduce physiological stress, like other leisure

Table 2. Summary of Key Studies Regarding the Risk of Dementia in Musically Engaged Individuals.

Study	Study design	Cognitive status	Age	N	Independent variable	Confounders	Results
Arafa et al, 2021	Longitudinal (four waves in 2010-2019)	Not mentioned	74.1 (6.1)	52601 (44562 no musical activity, 7303 engaged in one, 736 engaged in more than one)	Engagement in no, one, or more than one musical activity	Age, sex, area, marital status, income, education, walking, friends, leisure cognitive activities, mutual assistance, daily activities, smoking, alcohol, body mass index, disease	Involving in one and more than one musical activity was associated with a decreased risk of dementia; Playing a musical instrument only and practicing karaoke only were associated with a reduced risk of dementia; but this effect was not found in men
Balbag et al, 2014	Cross-sectional twin study (Screening from 1998 to 2001)	157 cognitive impairment; 157 healthy	Cognitive impairment 78 (6.1), healthy 77.9 (6.1)	314 (157 twin pairs)	Musicians (played music frequently and/or occasionally) vs non-musicians	Age, sex, education, physical activity	Playing a musical instrument was significantly associated with less likelihood of dementia and cognitive impairment
Hughes et al, 2010	Longitudinal (1987-2002 at 2-year intervals)	831 non-demented, 111 dementia at baseline	Non-demented 75.42 (4.87), dementia 78.92 (5.4)	942 (4.99% played musical instruments)	Hobby activities (whether they engaged in leisure activities)	Age, gender, education, depression, physical exercise, functional impairment, self-reported health, medication use, recruitment status	Playing musical instrument was not a statistically significant predictor of the risk of developing dementia
Wilson et al, 2015	Longitudinal (began in 1997, with a mean follow-up duration of 5.8 years)	No cognitive impairment at baseline	78.7 (7.4) at baseline	964 (346 without music instruction, 360 with 1-4 years, 258 with >4 years)	Before 18, without music instruction, lower level of music instruction (with 1-4 years), higher level of music instruction (>4 years)	Age, sex, education	Higher level of music instruction was associated with lower risk of MCI relative to those with no music instruction; Music instruction was not associated with later age of onset nor the rate of global cognitive decline
Verghese et al, 2003	Longitudinal (1980-2001)	No cognitive impairment at baseline	Non-dementia 78.9 (3.1), dementia 79.7 (3.1)	469 (345 non-dementia, 124 dementia)	Activity (participated in an activity several days or more per week) vs control (participated weekly or less frequency)	Age, sex, education, chronic medial illness, baseline cognition, other leisure activities	Playing musical instruments and dancing were associated with a reduced risk of dementia

Table 3. Summary of Key Evidence Supporting Music Engagement as a Proxy for Cognitive Reserve.

Cognitive reserve prediction	Study	Study design	Cognitive status	Age	N	Independent variable	Confounders	Results
Prediction 1	Böttcher et al, 2022	Cross-sectional	43 healthy, 13 with a family history of AD, and 84 with SCD	Musical activity group 68.23 (6.62), control group 69.01 (5.44)	140 (70 in each group)	Musical activity group (have played a musical instrument) vs control group (never have played a musical instrument)	Age, sex, education, diagnostic category, crystallized intelligence, socioeconomic status, physical activity	Global cognition, working memory, executive functions, language, and visuospatial abilities: musical activity group > control; Frontal, temporal, or hippocampal grey matter volume: No group difference
Prediction 2	Porat et al, 2016	Cross-sectional	39 healthy and 48 MCI	Dancers 69.55 (9.18), non-dancers 70.47 (8.16)	87 (39 healthy and 48 MCI)	Dancers (with previous dance experience) vs non-dancers (without dance experience)	MCI diagnosis	Grey matter thickness in the primary motor, somatosensory and prefrontal cortical regions: Dancers thinner than non-dancers
Prediction 3	Ferrari et al, 2013	Longitudinal (began in 1987, with 9-year three-waves follow-up)	No cognitive impairment in baseline	Non-ε4 carriers 80.5 (4.7), ε4 carriers 80.1 (4.2)	932 (667 non-ε4 carriers, 265 ε4 carriers)	Leisure activity score: low, moderate, and high (high score in all three components - mental, social, and physical component)	Age, sex, global cognition, body mass index	High activity scores were related to a decreased risk of dementia and AD, even among the APOE ε4 carriers; The ε4 carriers with high leisure activities experienced a delay in dementia onset
Prediction 4	Romeiser et al, 2021	Longitudinal (six waves in 1957-2011)	Not measured	About 65 in 2004	5718	High school musical engagement (HSME): No (0 musical performance groups), moderate (1-2), high (3+); Musical engagement in adulthood (MEA): Continuous (all follow-up time points), intermediate (at one point or another time), never	High school IQ, educational attainment, sex, previous stroke, childhood socioeconomic status	High HSME and continuous MEA were associated with higher memory scores at age 65; High HSME showed a significantly steeper cognitive decline; The rate of cognitive decline did not differ between continued MEA groups

Abbreviations: AD = Alzheimer's Disease; MCI = mild cognitive impairment; SCD = subjective cognitive decline.

activities. Ferrari et al.[46] reported that greater engagement in leisure activities, including singing or listening to the radio, resulted in a delay of disease onset as well as a decrease in incidence of AD irrespective of the presence of the APOE ε4 allele, which is known to significantly increase the risk of Aβ deposition and the incidence of dementia.[64] Results showed that carriers of the APOE ε4 allele who engaged regularly in leisure activities followed a similar pattern of disease progression to non-ε4 carriers who were comparably engaged in leisure activities.[46] Similarly, a study by Zhang et al.[58] found that productive activities (housework, reading newspapers/books, and watching tv/listening to the radio) and social leisure activities (playing cards/mahjongg, engagement in social work, and traveling) had a robust association with a reduction in the risk of APOE ε4-related cognitive decline.[58] Interestingly, productive leisure activities were more protective of cognitive functions among APOE ε4 carriers than passive social activities. These results suggest that individuals carrying the APOE ε4 allele may be more dependent on active lifestyle-related factors to protect cognitive functions from neural decline.[58] Although, Zhang et al.[58] only revealed trend level improvements in to APOE ε4 related cognitive decline from social leisure activities, previous studies have demonstrated a more robust association between social activities and protection against dementia.[65] A recent umbrella review highlighted that participation in music-related performing arts activities across the lifespan, including many group activities, conferred benefits across seventeen health domains including stress and cognitive ability.[66] Collectively, these findings suggest the social aspect of leisure activities may be one important factor in preventing neurocognitive decline.

Emerging epigenetic evidence also points towards the regulatory role of music engagement on gene-expression and microRNAs related to neurocognitive function.[67,68] For instance, Kanduri et al.[69] observed a differential expression in genes related to cognitive function, learning and memory in forty-eight healthy adults of varying musical ability after listening to classical music (relative to a non-music listening control group).[69] Similarly, Nair et al.[70] found that following a music listening task, professional musicians exhibited an upregulation in peripheral blood microRNAs, which have been found to repress inflammatory and neurodegenerative processes.[70] In a following study, Nair et al.[67] reported that music-listening in non-experts interacted with the upregulation of several microRNAs related to neuronal activity, dopamine metabolism and cognitive function.[67] These findings are consistent with reports of music-induced dopamine modulation, which is thought to be primarily enacted by rhythmic perception, entrainment and synchronicity, promoting motor control, reward, learning, memory, and motivation.[20] A recent review by Navarro et al.[68] also highlighted an important dopamine and music-related gene, SCNA, known to encode the protein Synuclein Alpha (α-syn), a primary component of Lewy Bodies (pathological features of Parkinson's Disease and Lewy Body dementia).[68] Although the precise relationship between music, SCNA and α-syn remains unclear, this gene may be of interest to future research in AD, given recent evidence that α-syn directly interacts with Aβ and tau deposition, exacerbating cognitive decline.[71] Taken together, these findings suggest that music-listening may have an influence on the human transcriptome, supporting healthy neuronal processes, while mitigating mechanisms related to neurodegeneration.

Music engagement also appears to modulate the expression of miR-132, a mirco-RNA that may play a regulatory role in tau protein expression.[68] The pathological accumulation of tau has recently been argued to have a stronger relationship with patterns of neurodegeneration and clinical manifestations of AD than amyloid-β (Aβ).[72] In light of recent research linking higher levels of well-established CR proxies like education and physical activity with decreased tau pathology, one might assume that CR and tau accumulation have an inverse relationship.[6,73] Consequently, the regulatory role of music on miR-132 and the effect of this gene on tau expression may be of significance to music engagement in relation to CR. Supporting this idea is evidence suggesting that the expression levels of miR-132 within hippocampal and cortical regions are lower in those with AD and MCI,[74] providing further reason to believe that music-induced upregulation of this microRNA may interact with tau accumulation and provide some neuroprotective benefits across the lifespan.[67] miR-132 is also activated by proteins associated with plasticity and neurogenesis (i.e. CREB and BDNF respectively).[68] BDNF modulated neuroplasticity is strongly associated with music exposure in animal models and has shown associations with dopaminergic function, learning behaviors, mood and immune responses.[75]

Nair et al.[67] noted that music-listening also promoted an upregulation in gene-expression related to neuroprotection, neurogenesis and synaptic neurotransmission, while finding downregulation in genes responsible for neurodegeneration.[67,68] While the trajectory of typical brain aging involves the reduction of brain volume and integrity, music training appears to be associated with both short- and long-term neural integrity,[22,23] whereby repeated cognitive demands implemented by music-related substrata trigger functional and structural adaptations that may counteract age-related atrophy.[18,76] Rus-Oswald and colleagues[77] found that older instrumental musicians maintained stable structural integrity relative to age, in specific brain regions such as the ventrolateral prefrontal cortex and premotor cortex compared to older non-musicians. Older musicians also retained features of a 'younger' brain, with the shape and gyrification of the auditory cortex (in particular Herschl's gyrus) being comparable to that found in younger musicians.[77] These observations align with evidence reported by Rogenmoser et al.[78] wherein the brain anatomies of amateur musicians resembled those of people considerably younger, indicating that music engagement may promote 'age-decelerating' effects. Structural brain changes also appear within white matter tracts, with young and middle-aged adult musicians typically possessing enlargement in the corpus callosum[79,80] and widespread differences in white matter organization across frontal, occipital and temporal regions as well as the corticospinal tract and cerebellum[81-85] Preliminary evidence suggests that some of these changes may persist into older age among musicians.[86]

Increased functional activity has also been identified in older musicians, whereby enhanced functional activation has been observed in frontotemporal, sensorimotor and parietal networks.[77] Stronger functional connectivity has also been found between hippocampal and cerebellar regions in aging instrumental musicians when compared to cognitively and socio-behaviorally matched non-musicians.[87] Zhang et al.[88] also noted the preservation of functional connectivity in sensorimotor regions among older musicians, proposing that these effects were regulated through compensatory frontoparietal recruitment and deactivation of the default mode network.[88] Such findings suggest that musicianship may be associated with structural and functional preservation of 'at risk' brain regions during aging. Thus, music engagement could improve brain health through both neuroplastic adaptations and by building cognitive reserves across the lifespan.[23] However, it should be noted that a scoping review by Schneider and colleagues suggested a lack of consistency between (the largely) correlational studies investigating music-induced neuroplasticity, warranting the need for more robust research on the association between music engagement and this neural mechanism[89] Table 4 summarizes the key evidence for functional and structural plasticity in older adult musicians.

Table 4. Key Evidence for Structural and Functional Plasticity in Older Adult Musicians.

Study	Study design	Cognitive status	Age	N	Independent variables	Confounders	Results
Rus-Oswald et al, 2022	Cross-sectional	No cognitive impairment	Musicians 76.6 (5), non-musicians 74.9 (3.4)	31 (16 musicians, 15 non-musicians)	Musicians (previously worked in the professional musical sector) vs non-musicians (not active in musical activity)	Matched on age, gender, and education	MOCA, TMT, VST, Raven, verbal span, forward/backward, and visual span: no group difference Parts of the contralateral prefrontal cortex and premotor cortex showed stable or even increasing thickness values in the musicians with increasing age
Yamashita et al, 2021	Cross-sectional	No cognitive impairment	Musicians 70.8 (4), non-musicians 71.4 (4.6)	60 (30 musicians, 30 age-matched non-musicians)	Musicians (received musical instrument training for at least 20 years) vs non-musicians (with no or less than 3 years of musical experience)	Sex, age, educational level, levels of cognitive activity, exercise, work, family care, volunteering	Verbal functioning and executive function: musicians > non-musicians Grey matter volumes in both sides of the cerebellum: musicians > non-musicians Cerebellar-hippocampal functional connectivity: musicians > non-musicians
Zhang et al, 2023	Cross-sectional	No cognitive impairment	Musicians 65.12 (4.06), non-musicians 66.64 (3.4)	50 (25 musicians, 25 non-musicians)	Musicians (had at least 32 years of musical training) vs non-musicians (had less than two years of musical training)	/	Neural alignment in bilateral sensorimotor areas: musicians > non-musicians Musicians showed stronger activation in left frontal-parietal regions Stronger deactivation in the left angular gyrus (a core default mode network): musicians > non-musicians

Abbreviations: MOCA = Montreal Cognitive Assessment Scale; TMT = Trail Making Test; VST – Stroop Colour-Word Test.

Although music appears to have a fundamental relationship to several mechanisms related to protection against age-related and neuropathological decline, the relationship of music engagement with amyloid-β pathology remains relatively unexplored in the context of CR. Aβ has historically been considered a key pathology of AD, with amyloid burden typically exhibiting an inverse relationship with AD symptomology[90] However, the association between Aβ and CR in general appears to be more nuanced, with studies examining cognitively enriching CR proxies like education[73,91] and bilingualism[92] reporting conflicting results. Although an interventional study examining the effect of a 12-week musical listening program (alongside a mind-body program) on cognition and blood biomarkers indicated some acute changes in plasma Aβ, telomere length, telomerase activity, as well as improvements in cognition relative to music engagement,[93] very little is currently known about how music engagement across a lifespan may impact Aβ accumulation.

Despite this, music may be able to contribute towards a well-recognized moderator of AD pathology, physical exercise. In an assessment of post-mortem brain pathology, Buchman et al.[6] demonstrated that individuals who reported greater total daily physical activity and motor ability were associated with better cognition (assessed proximal to death) independent of amyloid burden and tau pathology.[6] Similar results were demonstrated in a more recent study by Grasset et al.[94] where findings indicated that high physical activity attenuated the impact of plasma Aβ42/40 on cognitive function and dementia risk.[94] Given that weekly dance practice has been shown to lead to structural brain improvements and cognitive health beyond the effects of exercise alone,[95] it is plausible to think that music and exercise in conjunction (such as dance) could represent a more robust approach to building cognitive reserve.[94,96] Further, Mitterová et al.[97] suggested that there was a robust link between CR and dance-related brain plasticity. The authors longitudinally examined dance-induced neuroplastic changes in older adults, suggesting that brain plasticity was moderated by CR capacity (proxied by education). This finding suggests that high CR individuals may have a higher capacity for plasticity at an older age, which may lead to better interventional outcomes.[97]

Concluding Remarks

The reviewed literature points to evidence suggesting that music engagement throughout the lifetime is a moderating factor in neurocognitive function, consistent with well-established proxies of CR. However, a key challenge in understanding music as a contributor to CR is the sheer diversity in forms of music engagement. This heterogeneity in research poses a challenge for interpretation, given that benefits to CR may differ from one form of music engagement to another. Furthermore, much of the existing evidence is relatively indirect and incidentally uncovered as a byproduct of research on a different scientific question. As a result, evidence supporting music engagement as a contributor to CR remains somewhat inconclusive. Future research could approach the CR hypothesis with a more focused examination of the core predictions of CR. Such research could also help to identify forms of music engagement that are most promising in building CR across a lifespan.

Despite the need for dedicated research in this field, the existing evidence is convergent with findings regarding well-established CR proxies, suggesting that individuals with high music engagement can expect better clinical outcomes when matched to non-musicians in neurological health, and can maintain their cognitive function even in the face of neurodegenerative burden. Music engagement across the lifespan also appears to interact with the age of onset for cognitive decline and dementia, providing resilience to the effects of neural degeneration on cognition throughout the aging process, promoting a better quality of life for longer. In short, music engagement, as a lifestyle-enriching experience, should be considered in tandem with other established CR proxies as a tool for promoting neurocognitive health across the lifespan.

Appendix

Abbreviations

AD	Alzheimer's Disease
CR	Cognitive reserve
Aβ	Amyloid Beta
APOE	Apolipoprotein E
SCNA	Alpha-synuclein gene
CREB	cAMP response element-binding protein
BDNF	Brain-Derived Neurotrophic Factor
TMCM	Therapeutic Music Capacities model
α-syn	Alpha-synuclein

Acknowledgments

We thank Bond University and Macquarie University Music, Sound, and Performance Research Group for feedback and support.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This research was supported by a Discovery Project grant awarded to W.F.T. by the Australian Research Council (DP210101247).

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