MEASURING PHYSIOLOGICAL RESPONSES TO THE ARTS IN PEOPLE WITH DEMENTIA

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ABSTRACT

The dementias are a group of progressive symptoms that have multiple causes, usually caused by disease or injury of the brain, affecting higher brain functions such as language, perception, memory, reasoning and mood; they can also be associated with changes in personality. Arts interventions and interaction with the arts can create meaningful, positive experiences for people with a dementia, as well as improve quality of life. Qualitative research in particular, has been able to describe the emotional responses the arts can produce, but quantifiable changes have not been well documented. Physiological measurements such as stress hormone levels and galvanic skin response show promise in being able to quantify such responses. When taken together, these can give a picture of the kinds of physiological outcomes that are associated with positive affect and improvements in mental wellbeing in the context of arts interventions. This review provides a critical overview of the studies which measure some form of physiological outcome in response to the arts or an arts intervention in people with dementia, and indicates how future research in this area can help to broaden our understanding of the effects of the arts in dementia research and care.

1. Introduction

1.1. The arts and dementia

Although the review will focus on the physiological aspects within this field, it is important to realise the wider context in which the review sits. Much has been written about the arts in relation to dementia and about their therapeutic role in dementia care[1]. There have been several cases of individuals developing novel artistic abilities after developing different dementias including FTD[2] and AD[3] among others[4]. Additionally, studies have documented changes in artistic style of those already producing art during the progression of the condition[5,6,7]. It has also been suggested that different dementias may confer distinct features in the work which is produced[8] due to the different patterns of degeneration exhibited. In AD, for example, it is possible that degeneration of cortico-cortical connections between columns in occipital cortex with similar orientation preference can lead to problems with contour detection[9]. However, semantic or conceptual changes in artistic content are likely due to degeneration affecting higher, more complex networks[8].

Furthermore, evidence from psychological and affective reports suggests that arts interventions can be beneficial to the mental wellbeing of people with dementia, as well as create positive personal experiences[10,11,12,13]. Relatedly, it has been suggested that music may evoke complex emotional states via the entrainment of areas of the brain outside emotional systems, and that activation and enhancement of attention and memory related networks by music may contribute to a reduction in confusion[14].

The vast majority of research within the dementias has attempted to understand the mechanism of neurodegeneration with the hope of finding cures. There is no certainty about how long this will take. As such, it is important to consider quality of life and mental wellbeing 'in the moment', and arts interventions are good examples of how this can be done. 'In the moment' refers to brief experiences during interventions which may be highly meaningful to those involved, even if no lasting effect is observed[15].

1.2. Aims and objectives

The review brought together research from dementia, the arts, and physiological responses, and sought to look at the relationships between these fields (Figure 1).

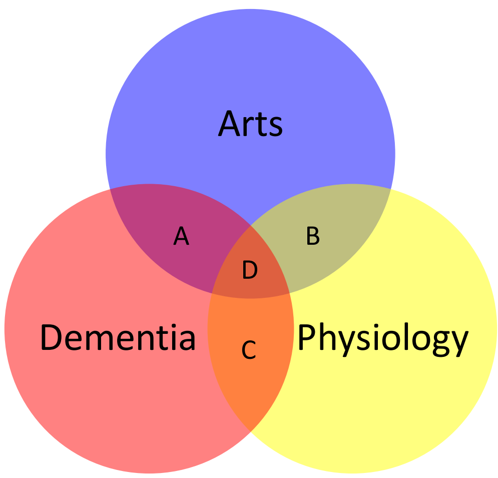

Figure 1. *Fields of research relevant to the review*: The arts and dementia (A); physiology and the arts (B); physiology and dementia (C); physiology, the arts and dementia (D)

Of these fields, the greatest body of research lies in the relationship between the arts and dementia (area A). This review did not focus primarily on this relationship, but rather, focused on those areas of research which took into account the physiological responses of the participants with dementia who engaged in art activities (areas B, C and D). In looking only at studies which measured physiological responses, few focused on both the arts *and* dementia (area D), with more addressing, either the arts (area B) or dementia (area C). Some papers also documented the physiological responses of people with dementia (PWD) to broadly relevant stimuli such as emotionally salient sounds or images.

The objective of this review was to understand what is currently known about physiological responses to the arts in people with dementia, as well as infer what other responses might be expected based on information from healthy controls. Additionally, the significance of such responses will be discussed.

Physiological responses are important as they can be indicators of the effects of an intervention when a subject is less able to communicate those through speech. This could be due to the progression of a dementia, or due to a specific type of dementia, such as SD or PNFA (see Table 2 for a definition of terms), which makes verbal communication more difficult[16]. However, when a method of self-report is possible or affective data are also available, correlations between those and the physiological outcomes can be drawn, and inferences about the significance of the outcomes made.

1.3. Methodology

The search was conducted using PubMed and Web of Knowledge with the search terms ((Alzheimer's OR dementia) AND (music therapy OR arts therapy)), followed by ((Alzheimer's OR dementia) AND (music therapy OR arts therapy) AND (physiolog* OR physiology)). A second search was then conducted on the same databases using the terms ((Alzheimer's OR dementia) AND (music OR arts OR art) AND (physiolog* OR physiology)), this turned up 432 new records not contained in our initial search. Finally, a search using the terms ((Alzheimer's OR dementia) AND (music OR arts OR art) AND (neurosonolog* OR neurosonology)), as well as ((Alzheimer's OR dementia) AND (music OR arts OR art) AND (transcranial Doppler)) was conducted. This final search turned up 1 new record. The inclusion criteria were: any data-analytic study published in a peer-reviewed journal involving PWD as subjects that had a quantitative or mixed-methods design with a physiological outcome measure. The first and third authors independently assessed the methodological quality of each study using the PEDro scale, which provides a score from a low of zero to a high of ten [89]; there were just 4, one point discrepancies. These were subsequently discussed and resolved with the second author, resulting in 100 percent interrater reliability. A summary of the search process can

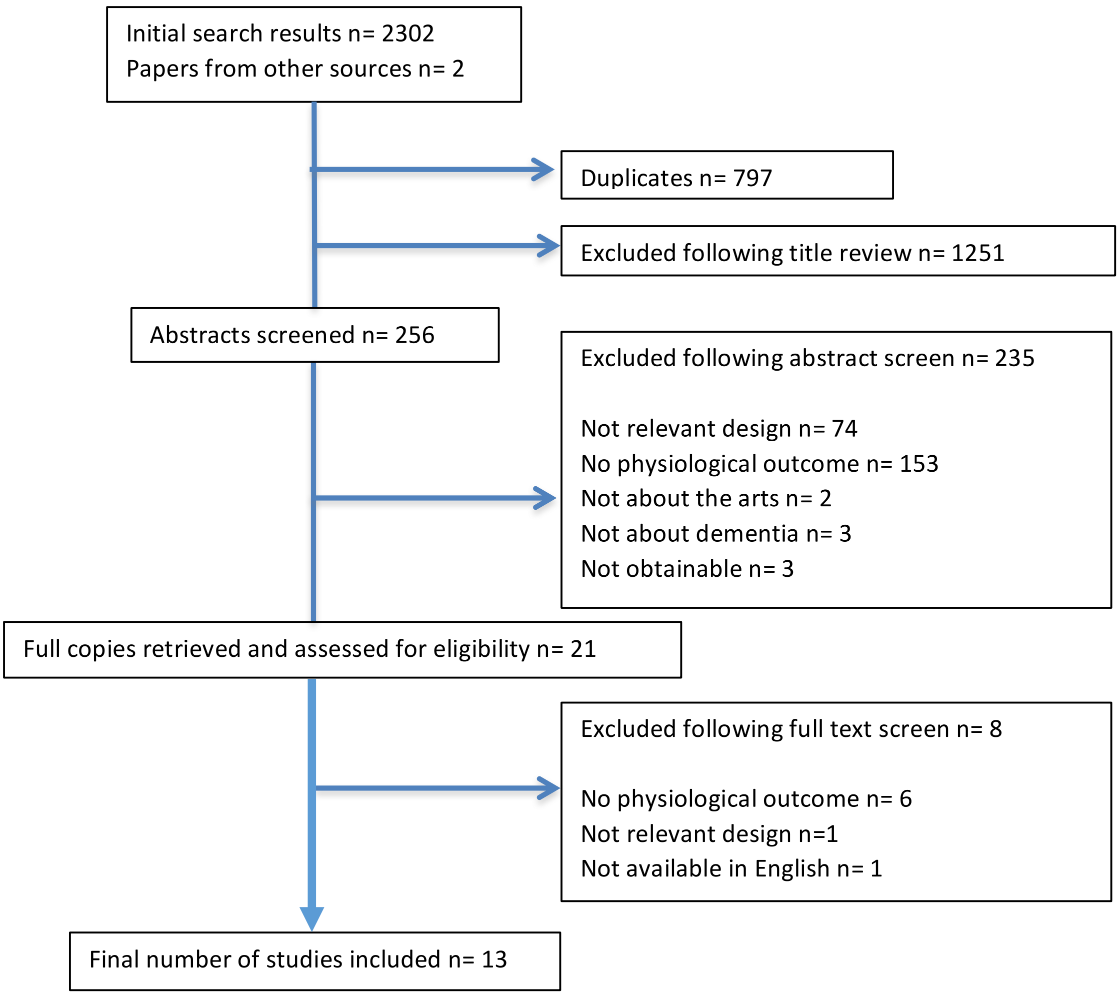

Figure 2. *Flow chart depicting the search process*

be found in Figure 2, whereas a summary of the eligible papers can be found in Table 1, and detailed in section 5.

Table 1: Summary of reviewed papers.

Study and dementia type	Nexp(Ncon)	Type of intervention	Outcomes measured	Main findings	Setting	PEDro score
Norberg et al.[72] Sweden (AD)	2(0)	12 day intervention involving music	HR Respiration rate	↑ HR after specific songs ↓ respiration rate after specific songs	Residential care	1
Kumar et al.[63] USA (AD)	20(0)	MT 4 weeks (20 sessions)	Plasma melatonin, adrenaline & noradrenaline	↑ melatonin at 4 weeks & 6 week follow up ↑ adrenaline, noradrenaline at 4 weeks	Residential care	3
Suzuki et al.[64] Japan (AD, VD)	10(13)	MT 8 weeks (16 sessions)	Salivary CgA	↓ CgA at 8 weeks	Hospital	5
Kurita et al.[73] Japan (CVD)	12(0)	1 MT session of 30 minutes	HRV	↑ pNN50, HF, RMSSD during MT ↓ HF/LF during MT	Hospital	4
Takahashi et al.[68] Japan (AD, CVD, DLB)	24(19)	MT 2 years (once weekly)	Systolic blood pressure Salivary cortisol	↓ systolic blood pressure in MT group at 2 years ↓ salivary cortisol in MT group at 2 years*	Residential care	5
Suzuki et al.[65] Japan (AD, VD)	8(8)	MT 3 months (twice weekly)	Salivary CgA & IgA (from 6 participants in each group)	↓ CgA at 3 months & 1 month follow up	Hospital	6
Okada et al.[67] Japan (CVD)	50(32)	MT 10 weeks (10 sessions)	Plasma IL-6, TNFα, adrenaline, Noradrenaline HRV	↓ IL-6, adrenaline, noradrenaline immediately after each MT session ↑ pNN50, HF, RMSSD during MT	Hospital	5
Raglio et al.[74] Italy (AD, MD, CVD)	10(10)	MT 15 weeks (30 sessions)	HRV	↑ pNN50 in 50% of exp. group at 15 weeks*	Residential care	7

Fukui et al.[70] Japan (AD)	6(0)**	MT, music-only and therapy-only conditions over 1 month	Salivary 17β-estradiol, testosterone	↑ 17β-estradiol after the music-only and MT sessions ↑ testosterone after MT sessions	Residential care	5
Sakamoto et al.[75] Japan (AD)	26***(13)	MT or passive music intervention 10 weeks (10 sessions)	HR HRV	↓ HR immediately after MT in both interactive and passive groups**** ↑ HF immediately after MT in both interactive and passive groups****	Residential care	9
Chu et al.[69] Taiwan (Not specified)	52(52)	MT 6 weeks (12 sessions)	Salivary cortisol	No significant change	Residential care	7
Hsu et al.[76] UK (AD, DLB, FTD, MD, VD)	9(8)	MT 5 months (once weekly)	HR SCR	not yet published	Residential care	6
Valdiglesias et al.[66] Spain (Not specified)	18***** (0)	Music or MSSE intervention 16 weeks (32 sessions)	Salivary CgA	No significant change	Residential care	8

Nexp is the number of participants in the experimental group
Ncon is the number of participants in the control group
CVD indicates patients with cerebrovascular disease and dementia
**indicates a result which was not statistically significant*
***all six patient received a music only, therapy only, and MT session*
**** of these 26, 13 were in a 'passive' music listening group and 13 in an 'active' MT group*
***** this effect was found to be greater in the interactive than in the passive MT group*
******this study involved two groups of nine, one receiving a music intervention and the other Multisensory Stimulation Environment (MSSE) intervention.*

2. The use of physiological measurements

2.1. Correlation of different physiological parameters with emotional state

One advantage of using physiological measures during an arts intervention is the ability to collect information not dependant on memory recall or verbal abilities. If the aim of an arts intervention is to improve the wellbeing or emotional state of the recipient, it is feasible that physiological outcomes can help to indicate this kind of improvement. The relationship between internal emotional state and externally measured physiological parameters is undeniably complicated and beyond the scope of this review (see Sequeira et al.[17] on the role of autonomic data in understanding emotional processing). However, there is evidence that changes in specific physiological measures are indicative of changes in one's emotional state.

Affect and mental wellbeing are associated with differing levels of certain biomarkers. A meta-analysis found that clinical depression is associated with higher levels of pro-inflammatory cytokines, and in particular that levels of IL-6 and TNFα tend to be significantly higher in depressed patients relative to controls[18]. Clinical anxiety is also associated with higher levels of IL-6, among other pro-inflammatory cytokines[19], and people with a greater self-reported trait negative affect tend to show higher levels of TNFα[20]. It has also been reported that a large number of pro-inflammatory cytokines which are significantly increased during depression relative to controls, including IL-6, are reduced to normal levels after successful therapy[21].

As well as associations with negative affect, it appears that positive affect negatively predicts for levels of pro-inflammatory cytokines. It was found that, in a healthy population, positive affect negatively predicted for IL-6 levels and additionally that some individual positive emotions such as awe (as assessed by the dispositional positive emotions scale, DPES[22]) were more strongly predictive than others[23]. This has significance in that emotions such as awe are often associated with the way in which visual art and music are experienced[24,25,26], and so similar outcomes might be expected within the context of arts interventions.

Decreased HRV may also be associated with depression and negative affect. A study of patients with coronary heart disease found that over a 24 hour period, HR was significantly increased and the vast majority of HRV parameters were reduced in a depressed group as compared to a non-depressed group[27]. The same is also true when considering depression in a broader population, and more severe depression may confer a larger decrease in HRV[28].

2.2. Problems of measurement

It is important to consider how an arts intervention will affect physiological variables not only through the artistic content, but also through how variables are measured. Some methods of measurement may induce stress (e.g. blood samples), thereby distorting the pattern of outcomes produced by the intervention[29]. For example, wearing a blood pressure cuff can have a negative impact on the experience of people about to hear live music[30]. Additionally, when measuring physiological responses to emotional situations, it was found that participants, when asked to report their feelings, show markedly different cardiovascular responses to those who are not asked to do so[31]. However, this was only the case for states of anger, and it is unclear whether the same pattern would be observed for other emotional states or for other kinds of physiological response.

Methods of measuring physiological outcomes which are less intrusive, and do not affect the setting of the intervention, are preferable in most cases. For example, if the context of being in an art museum is important for the intervention, then a technique which does not limit movement may be important. Considering this, novel methods of measuring electrodermal activity (among other parameters) are available; such methods are non-obtrusive and allow real-time data collection in a flexible, non-clinical setting[32].

When considering endocrinological measurements, it has been shown that the popular method of immunoassaying may give an overestimate of the levels of some steroid hormones to quite a large degree[33]. A method using a chromatography-based assay has been developed which gives an accurate measurement of seven steroid hormones (including cortisone, cortisol and DHEA) from saliva[34]. Such methods may have potential use in arts interventions, as being able to obtain such high accuracy from saliva is highly preferable to using a more intrusive method such as blood sampling.

3. Physiological responses to the arts

This section focuses on physiological responses in people who do not have a dementia. The majority of papers chosen look at such responses in healthy controls, with the aim of identifying what kinds of responses may be typical when participating in artistic or creative activities. To this end, studies which look at such responses in other complex health conditions (e.g. stroke, Parkinson's disease) have, for the most part, been avoided. Furthermore, the majority of the research in this area considers the effects music as opposed to other art forms, and the physiological effects of music in a broad population have been well documented[35].

3.1. Skin conductance response

Stress is often associated with an increase in SCL. It has been reported that while carrying out a stressful task, SCL increased significantly less in subjects listening to low-tempo music than those listening to high-tempo music[36]. Sandstrom and Russo[37] found that, following an acute stressor, peaceful music reduced SCL significantly more than a white noise control, whereas happy, agitated and sad music did not.

When viewing artworks in a museum, certain aesthetic-emotional assessments of the viewers were found to be significantly associated with SCV, but not with SCL[38,39]. However, it has previously been reported that SCL associated with arousal is higher when viewing more structurally complex artwork[40]. This discrepancy may be due to the fact that only one of the studies[40] considered the structural complexity of the work, whereas the other[38] did not. It is also relevant, however, that one was carried out in a museum environment and the other in a laboratory setting.

3.2. Cardiovascular

Accomplished musical performance is known to induce a state of 'flow'[41] in those performing[42]. This rewarding psychological state comes about as a result of high attention and positive affect, and has a number of physiological correlates. It has been shown that flow during piano playing was associated with increased total HRV, low frequency to high frequency band ratio (LF/HF) and respiratory depth, as well as decreased heart period and zygomaticus major muscle activity[43]. Increased LF/HF ratio is often taken to indicate increased sympathetic tone[44]. Musical performance can also increase stress levels, and it has been suggested that this increase may manifest itself as a reduction in the complexity of cardiovascular responses during high-stress performance[45]. Additionally, it was found that HR as well as the LF/HF ratio were higher in musicians when they were performing music than when they were listening to music, indicating increased sympathetic activity[46].

A study on the effect of listening to music of different tempi found that blood pressure, heart rate, and the LF/HF ratio increased proportionally to the tempo of the music[47]. Another study found that during a stressful task, HR was decreased significantly more by low tempo than by high tempo music[36], and in a study comparing music of varying tempi and moods it was found that HR was significantly decreased only by peaceful, low-tempo music[37].

Tschacher et al.[38] found that for subjects viewing artworks in a museum, raised HRV was significantly associated with viewing 'beautiful', 'surprising' and 'humorous' pieces, and that HR was also associated with certain aesthetic aspects of the works.

3.3. Endocrinological

The effect of musical performance on endocrinological outcomes is heavily dependent on the context of the performance. It was found that singing in a high stress condition (with an audience) led to an increase in cortisol and cortisone, whereas singing in a low stress condition led to a decrease in both, although both conditions were associated with a decrease in the cortisol/cortisone ratio[48]. In terms of mental wellbeing, a study involving people receiving mental health services found that a 10 week group-drumming intervention led to a significant decrease in depressive symptoms, which was associated with a shift from a pro-inflammatory to an anti-inflammatory immune profile[49]. Listening to relaxing music has been found to cause a decrease in cortisol[36], as well as IL-6 and adrenaline[50]. Also, attending live concerts can reduce glucocorticoid secretion and decrease the cortisol/cortisone ratio[51]. In a study involving watching film clips of different moods, it was found that humorous film clips led to a decrease in TNFα, and an increase in IL-2 and IL-3, with the reverse effect seen after viewing horror film clips[52].

4. Physiological responses to emotionally salient stimuli in people with dementia

The physiological data from people with dementia tend to differ from those of the general population when considering responses to emotionally salient stimuli. Additionally, there seems to be some dissociation in this response between patients with different forms of dementia, and emotionally salient images or sounds are examples of stimuli which can produce this kind of response[53,54,55,56,57].

4.1. Pupillometry

In healthy controls, tones which rise in intensity (looming tones) are rated as more unpleasant than those which fall in intensity (withdrawing tones), and looming tones produce greater changes in HR and SCR[58]. Fletcher et al.[53] found that looming tones also produced a significantly greater pupil dilation response than withdrawing tones in healthy controls, and were rated as more alerting on average. They found that for dementia patients, this difference remained for patients with SD, but was lost for patients with AD and PNFA. Further differentiation in these kinds of responses was seen between dementia patients in response to identifiable emotional sounds, in that PNFA and SD patients displayed a correlation between valence ratings for highly valent emotional sounds and pupil response. This correlation was not seen for patients with bvFTD or AD[54]. In another study it was found that, relative to healthy controls, bvFTD, SD and AD patients, but not PNFA patients, also showed an inability to determine whether or not randomly paired sounds came from the same source. Performance on this task was inversely correlated with the increase in pupil dilation seen when hearing real versus synthetically produced sounds[55]. These kinds of physiological responses may be a novel manifestation of the relative inability of some dementia patients to process auditory semantic ambiguity for emotionally significant stimuli[55].

4.2. Skin conductance response

These kinds of differential physiological responses are likely to be, at least in part, the result of varying levels of emotional processing in different forms of dementia. Patients with FTD are known to display an increased level of 'emotional blunting', relative to patients with other forms of dementia, such as AD[59]. This is seen, for example, in their deficit in understanding emotional expression in faces[60]. Importantly, this disrupted emotional processing seems to confer a differential physiological response as well. Patients with bvFTD showed a lower SCR both before and after a startle stimulus than did patients with AD and healthy controls, which is indicative of a lower baseline sympathetic tone[56]. Balconi et al.[57] found that patients with frontotemporal forms of dementia showed altered physiological responses to affective images of varying arousal and valence. Regardless of stimulus category (e.g. pleasant low arousal, unpleasant high arousal), both bvFTD and avPPA groups showed lower SCR values, relative to healthy controls and patients with AD. Additionally, healthy controls and AD patients showed a significant correlation between SCR and the valance/arousal ratings they gave for each image, whereas bvFTD and avPPA patients showed no such correlation.

4.3. Cardiovascular

Balconi et al.[57] also reported that, when viewing affective images, bvFTD patients showed a significant increase in HR, relative to healthy controls and AD patients. Healthy controls and

AD patients also showed a correlation between HR and their valence/arousal ratings for each image, whereas bvFTD and avPPA patients did not. In essence, those with FTD show a mismatch between implicit and explicit emotional salience processing[57].

The kinds of results described above give examples of physiological indicators of altered emotionality in people with dementia, both relative to healthy controls, and relative to groups with different forms of dementia. It is suggestive of the physiological responses one might expect to see when people engage with art, and process the emotionally salient features of art.

5. Results: physiological responses to the arts in people with dementia

When considering only people with dementia, the research into physiological responses to the arts appears to only take into account responses to music or MT, with no substantial research focusing on empirical measurement of physiological parameters in response to other art forms. Relatedly, while much has been written on the advantages of music interventions for people with dementia, only some of this work has taken into account the physiological changes seen during these interventions as opposed to behavioural or affective changes[61]. In a 2013 meta-analysis of MT and dementia, only 4 of the 21 papers included measured a physiological parameter of some sort, although MT was shown to have a significant effect on physiological outcomes in dementia patients[62]. These studies, among others, are detailed below and in Table 1.

5.1. Endocrinological

MT has been shown to have an effect on a number of endocrinological measures in people with dementia. It was found that after a 4 week MT course for AD patients, levels of melatonin in the blood were significantly increased both immediately after the 4 weeks and increased further at a 6 week follow up, while adrenaline and noradrenaline levels had increased significantly after 4 weeks but returned to baseline levels at a 6 week follow up[63]. It has also been reported that MT for patients with AD and VD led to significantly decreased levels of salivary CgA by the end of an 8 week course relative to controls, although no short-term changes were seen immediately before and after each session[64]. This reduction in salivary

CgA was reported indicate a reduction in stress levels. A later study measured both salivary CgA and IgA levels in AD and VD patients over the course of a 3 month MT intervention[65]. It was found that mean salivary CgA levels had significantly decreased by the end of the 3 months in and that this level remained low at a 1-month follow up measurement, however no significant change was observed in salivary IgA levels[65]. Contrary to this, some research found that salivary CgA did not change as a result of a 16 week MT course[66]. Salivary CgA measurements were taken before and after each session of MT and no significant difference was found at any point during the course.

A study comprising 83 participants with CVD and dementia found that 10 sessions of MT significantly decreased plasma levels of IL-6 in those receiving the therapy relative to controls not receiving MT, but had no effect on plasma TNF levels. In addition, plasma adrenaline and noradrenaline levels also significantly decreased for patients receiving MT relative to controls[67]. A longer-term study over the course of two years for people with moderate and severe dementia (AD, CVD and Parkinson-type dementia) found that mean saliva cortisol levels decreased for participants receiving MT and increased for participants not receiving MT. However, these changes were not statistically significant[68]. This lack of significance may have been due to the variation in severity of the dementias, as in both groups those with more severe cases of dementia had higher cortisol levels[68]. Additionally, over a period of two years it would have been difficult to control for other external factors which may have altered the levels of these biomarkers in individual patients (e.g. emotionally significant events or other health issues). More recently, a larger study of 102 people with dementia found that a 6 week MT course had no significant effect on salivary cortisol levels[69]. There was no difference in cortisol levels between the control group receiving normal care and the MT group, and no significant difference between the baseline level before MT and the level at the end of the therapy[69]. Given the fact that both interventions[68,69] had a positive effect on the participants, it seems as though salivary cortisol may not be a reliable biomarker for quantifying the effects of MT in people with dementia.

Fukui et al.[70] conducted a mixed music and normal therapy intervention over the course of 1 month, measuring salivary 17β-estradiol and testosterone as the physiological outcomes. The six subjects with AD received all of therapy-only, music-only and MT sessions, and the samples were taken before and after each session[70]. It was found that salivary 17β-estradiol increased significantly as a result of the music-only and MT sessions, although did not change as a result of the therapy-only sessions. Salivary testosterone was found to increase significantly as a result of the MT, but did not change significantly as a result of the music-only or therapy-only sessions. From this, it is suggested that MT may have potential as an alternative[70] to the hormone replacement therapy often used to try and slow the progression of AD[71].

5.2. Cardiovascular

Norberg et al.[72] conducted a study involving two AD patients receiving a 12-day intervention over 16 sessions of listening to selected songs and touching physical objects. It was found that, for both subjects, significant increases in HR were seen after specific songs. As the sample size and amount of data collected in this study was so small, it is hard to draw any real conclusions from these results.

A study of 12 hospitalised patients with CVD and dementia found that a 30 minute MT session had a significant effect on HRV parameters recorded via ECG, namely an increase in HF, RMSSD and pNN50, and a decrease in LF/HF[73]. However, this study did not include a control and measurements were only taken over one session. Similar results were later reported in a larger controlled study over a number of sessions, with HF, RMSSD and pNN50 increasing during MT relative to controls not receiving MT, but with the LF/HF ratio not changing significantly[67]. HF, RMSSD and pNN50 are indicative of parasympathetic activity whereas LF/HF is indicative of sympathetic activity[44], suggesting that MT increased parasympathetic activity in both of these studies.

Raglio et al.[74] measured the effect of a 15-week MT course on HRV in 10 dementia patients. Rather than measure HRV during the sessions, the recordings were made for 24 hours before the start of the course and for 24 hours at the end of the course. There was found to be no significant difference in HRV by the end of the course. However, pNN50 did increase in 50% of the MT group patients, the majority of whom also showed a decrease in depression according to a neuropsychological assessment, suggesting that MT may have increased HRV and decreased symptoms of depression[74]. There has also been research into the relative effects of 'interactive' MT sessions and 'passive' music interventions in patients with severe AD[75]. Over the course of 10 weeks, the 'passive' group simply listened to music whereas as the 'interactive group' participated in other activities such as singing and clapping. HR and HF measurements were made for five minutes before and after each session and it was found that relative to controls, both groups showed a decrease in HR and an increase in HF after the sessions, indicating greater parasympathetic activity. This effect was larger in the interactive MT group[75].

It has been reported that MT can prevent long term increases in systolic blood pressure in older people with dementia. In an investigation on elderly patients with dementia, it was found that the group not receiving MT showed a significant increase in systolic blood pressure after two years, whereas a group who were receiving MT over the two years did not[68].

5.3. Rate of respiration

Norberg et al. reported that for one of the two participants in their study, rate of respiration was significantly decreased after specific songs, and also that an overall decrease was seen for this individual during the course of the intervention[72].

5.4. Skin conductance response

There is currently no published SCR data from people with dementia in response to the arts. However, one group recorded SCR data during an MT intervention in a care home setting, and will analyse this data in a later publication[76].

6. Discussion

The body of research examining physiological responses to arts activities or arts interventions within dementia is currently very limited, such that there were only 13 papers that met inclusion criteria. Of these, five studies had no non-arts intervention control group[62,63,66,70,72], and another did not publish the physiological data which was collected during the intervention[76]. The methodological quality of the studies, as assessed by the PEDro scale, also varied. This may be related in part, to the emerging and novel nature of this research area. Yet the studies reviewed all have been able to make contributions to an initial understanding and appreciation of physiological responses to arts activities and arts interventions within the dementias.

In terms of the outcomes measured, seven of the 13 papers measured a cardiovascular outcome[67,68,72,73,74,75,76], eight of the papers measured an endocrinological outcome[63,64,65,66,67,68,69,70], one measured galvanic skin responses but did not publish the data[76], and one measured rate of respiration[72]. Also, four studies measured more than one kind of outcome[67,68,72,76]. Data about galvanic skin responses[56,57] and pupil dilation[53,54,55] in people with dementia have been published, although these were measured in response to emotionally salient stimuli rather than to an arts intervention.

The papers detailed in this review differed in terms of the time course over which they measure these outcomes, with six documenting changes over the course of the individual sessions of an arts intervention[66,67,70,72,73,75] and six documenting longer-term changes over the entire course of an arts intervention[63,64,65,68,69,74]. HR and HRV were used most often as short term indicators of the effect of an intervention and statistically significant changes in HR and HRV were observed in all such studies[67,72,73,75]. One study measured HRV before and after the entire course of an intervention but reported no statistically significant changes[74]. Endocrinological measurements were used most commonly as an indicator of the long term effects of an intervention[63,64,65,68,69], although two studies did not report statistically significant changes in this context[68,69].Two studies used endocrinological measurements to assess the short-term effects of the sessions of an intervention[66,70], with one reporting a significant change[70]. The time course over which the outcome is measured can have an effect on the result observed, as adrenaline and noradrenaline were found to decrease immediately after MT sessions[67], but to increase by the end of a 4-week MT course[63].

Four of the studies involved the participants or a group of participants receiving a music intervention that did not have a therapy element to it[66,70,72,75], whereas in the rest of the studies all participants in a non-control group received MT. Of these four studies, two[70,75] provided a comparison between the relative effects of MT sessions versus more passive music interventions, with both finding that MT more reliably produced significant changes in the outcomes they were measuring.

Two studies measuring CgA reported a decrease[64,65], although one study reported no significant change[66] suggesting that it may not be good biomarker for stress during a music intervention. However, it may be significant that this study involved music interventions with no therapy element, whereas those that did report a change involved MT. Apart from these discrepancies, outcomes measured in more than one study (excluding those results not yet published[76]) tended to change in the same way. Both studies measuring salivary cortisol reported no statistically significant changes[68,69], and all studies measuring HRV reported changes indicative of increased parasympathetic activity[67,73,74,75].

6.1. Limitations

There is a limited amount of research on physiological responses to the arts in people with dementia, and a number of the studies reviewed in this section suffer from small sample size or lack of a control group. The studies presented also have key differences in terms of the setting of the intervention, the outcomes measured and the types of dementia examined. This makes comparison between such pieces of research, as well as similar research done in healthy controls, difficult, as results could be attributed to a number of different variables.

As of yet, there is no research which measures physiological responses to the arts outside music, and such research will be required in order to build up a more complete picture of the interaction between the arts and physiology for people with dementia. Music interventions should also not be considered a single entity. In this context, the presence or absence of a therapy element in an intervention can be important. Additionally, different physiological outcomes will be observed dependent on the context and setting of the intervention, as well as the type of music used. In healthy controls, it was found that low-tempo music, but not high-tempo music, was associated with lower SCL as well as a parasympathetic shift in terms of HRV[36,37,47]. For musical performance, it has been shown that performing in a high-stress setting increases levels of cortisol and cortisone, whereas they decrease in a low-stress setting[48].

In people with dementia, certain types of music have even been found to produce a negative effect and increase the frequency of behavioural disturbances during the course of the therapy[77]. Additionally, 'interactive' MT sessions, during which the recipients are encouraged to sing and clap, have a greater effect on HR and HRV than 'passive' music interventions, in which recipients simply listen[75]. Considering that nine of the 13 studies were conducted in residential care [63,66,68,69,70,72,74,75,76] and four of them in a hospital[64,65,67,73], the setting may well have had an effect on outcomes. Moreover, factors such as the musical background of participants[78], or the severity of their dementia[79] have been shown to have an effect on the way in which they experience MT. Oftentimes these factors are either not considered, or the selection process makes them hard to control.

6.2. Future research

Despite a limited amount of research and various inconsistencies between different studies, it is still possible to suggest directions for future research based on the results of the current review. The following should be considered as critically important when measuring a physiological outcome in response to an arts intervention:

- Type and severity of dementia
- Type of intervention (e.g. interactive/passive, therapy element/no therapy element)
- Social and physical setting of the intervention (e.g. residential care /hospital, individual/group session)
- Qualities of the stimulus (e.g. high-/low-tempo music)
- How outcomes are measured (e.g. saliva sampling/HR/SCL)
- Time course of measurement (short-/long-term effect)

It has been suggested that art production or engagement in creative activities can induce a state of 'flow'[41] in dementia[80], for example the completion of jigsaw puzzles by SD patients[81]. As the induction of this state during arts activities in healthy controls has a number of associated physiological changes[43], similar responses might be expected in people with a dementia and future research could focus on observing these. Additionally, physiological responses to emotionally salient stimuli differ between people with dementia and healthy controls, as well as between people with different forms of dementia[53,54,55,56,57]. Music played during MT can be considered as emotionally salient, and the fact that at least five of the studies included people with different forms of dementia[64,65,68,74,76] may well have impacted the pattern of physiological outcomes that were observed. The experimental design of future studies must also take into account the baseline physiological characteristics of individuals with different forms of dementia. For example, people with bvFTD have been shown to have increased frequency and severity of autonomic symptoms (e.g. blood pressure, gastrointestinal, thermoregulatory, urinary and sleep problems[82]) and resting heart rate[83] relative to both healthy controls and individuals with AD. Ideally, future research should look at the outcomes seen in different forms of dementia separately.

There are advantages in measuring multiple outcomes at once (e.g. HRV and SCR) as this not only increases the likelihood of detecting a response, but also enhances the kinds of interpretations that can be made. Physiological measurements should not be considered an alternative to qualitative methods such as interviews and observations, however. They act to complement such methods, but do not convey the same level of personal detail. For example, small but significant 'in the moment' responses may be hidden by data which has been averaged over time. As well as this, the same physiological response may result from a variety of emotional responses. An increase in HR could be indicative of a positive feeling of excitement or a negative feeling of stress, likewise increases in stress hormone levels may indicate positive stimulation rather than distress. In conditions such as FTD where there is a level of disrupted emotional processing[59,60], one might expect discrepancies between qualitative reports of emotional stimuli and observed physiological outcomes. Given this, it is important to consider physiological outcomes alongside either qualitative reports of emotion or data from standardised questionnaires where possible (for example in early- or middle-stage dementia).

Nonetheless, the kinds of physiological responses observed have been linked with positive changes in mental wellbeing and quality of life. For example, decreases in IL-6 have been reported in response to MT for dementia patients[67]. Such decreases have been found to correlate with the reduction of depressive symptoms after therapy[21], and lower levels of IL-6 are associated with greater positive affect in healthy controls[23]. Additionally, people with dementia who showed increased parasympathetic activity at the time of MT have gone on to show long term reductions in BPSD[65]. In studies where significant changes in more than one kind of physiological outcome were reported[67,68], these changes were congruent in indicating these kinds of favourable shifts. Results like this demonstrate that arts interventions are genuinely beneficial for the recipients, and this benefit is seen to some degree in the physiological outcomes measured. Such outcomes do, however, need to be investigated across different types of dementia, and the scope of the research in terms physiological outcomes measured and forms of arts intervention used must be greatly expanded. In particular, non-invasive physiological measures[32] may be helpful in providing information about those with more severe impairment, who are unable to provide subjective accounts of affective responses or where it may be difficult for care staff to ascertain levels of wellbeing. Such methods also allow for a more naturalistic experience as they do less to interfere with the social and physical setting of the intervention, and should be considered as the most appropriate for future research in this area.

Another avenue for future research includes the genetic analysis of dementias, where a number of associations between genes and specific traits have been identified[84,85,86,87]. Given these types of variations in phenotype and symptomatic presentation of a dementia, differences between individuals in this regard could well have an effect on their emotional or physiological response during an arts intervention. Indeed, associations between MAPT and C9orf72 mutations in FTD patients and their responses to auditory stimuli have previously been identified[88], which has implications for interventions with a musical element.

Table 2: List of abbreviations

AD	Alzheimer's disease
(av)PPA	(aggramatic variant) Primary progressive aphasia
BPSD	Behavioural and psychological symptoms of dementia
(bv)FTD	(behavioural variant) Frontotemporal dementia
CgA	Chromogranin A
CVD	Cerebrovascular disease
DHEA	Dehydroepiandrosterone
DLB	Dementia with lewy bodies
ECG	Electrocardiogram
HF	High frequency band (ECG)
HR	Heart rate
HRV	Heart rate variability
IgA	Immunoglobin A
IL-2	Interleukin-2
IL-3	Interleukin-3
IL-6	Interleukin-6
LF	Low frequency band (ECG)
LF/HF	Low frequency to high frequency band ratio (ECG)
MD	Mixed dementia
MT	Music therapy
PNFA	Progressive nonfluent aphasia
pNN50	Percentage of successive RR-intervals greater than or equal to 50ms (ECG)
RMSSD	Square root of the mean of the squared differences between adjacent intervals (ECG)
SCL	Skin conductance level
SCR	Skin conductance response
SCV	Skin conductance variability
SD	Semantic dementia
TNFα	Tumor necrosis factor alpha
VD	Vascular dementia

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