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CONCISE REPORT

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The effect of the severity of neurocognitive disorders on emotional and motor responses to music

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Abstract

The successful design of musical interventions for dementia patients requires knowledge of how rhythmic abilities change with disease severity. In this study, we tested the impact of the severity of the neurocognitive disorders (NCD) on the socioemotional and motor responses to music in three groups of patients with Major NCD, Mild NCD, or No NCD. Patients were asked to tap to a metronomic or musical rhythm while facing a live musician or through a video. We recorded their emotional facial reactions and their sensorimotor synchronization (SMS) abilities. Patients with No NCD or Mild NCD expressed positive socioemotional reactions to music, but patients with Major NCD did not, indicating a decrease in the positive emotional impact of music at this stage of the disease. SMS to a metronome was less regular and less precise in patients with a Major NCD than in patients with No NCD or Mild NCD, which was not the case when tapping with music, particularly in the presence of a live musician, suggesting the relevance of live performance for patients with Major NCD. These findings suggest that the socioemotional and motor reactions to music are negatively affected by the progression of the NCD.

KEYWORDS
aging, Alzheimer's disease, dementia, music intervention, sensorimotor synchronization, social interaction

INTRODUCTION

The intriguing sensitivity to music of patients with dementia has been widely described. This observation led to the development of music-based interventions to improve emotional, social, and cognitive functioning in patients with neurocognitive disorders (NCD), such as Alzheimer's disease, vascular dementia, or mixed dementia.[1,2] Those interventions can take diverse forms from passive music listening in isolation to active music making in groups. Some studies demonstrated that active interventions, during which patients are encouraged to sing or move with the musical beats, provide larger benefits than passive ones whereby patients only listen to music without motor incentive.[3,4] This finding suggests that the ability to synchronize movements with a musical rhythm, which is relatively spared in patients with NCD, may contribute to the positive impact of these interventions on patients' behavior and well-being.[5,6] Consequently, designing efficient musical interventions requires a better understanding of the change in rhythmic abilities and emotional responsiveness to music with the severity

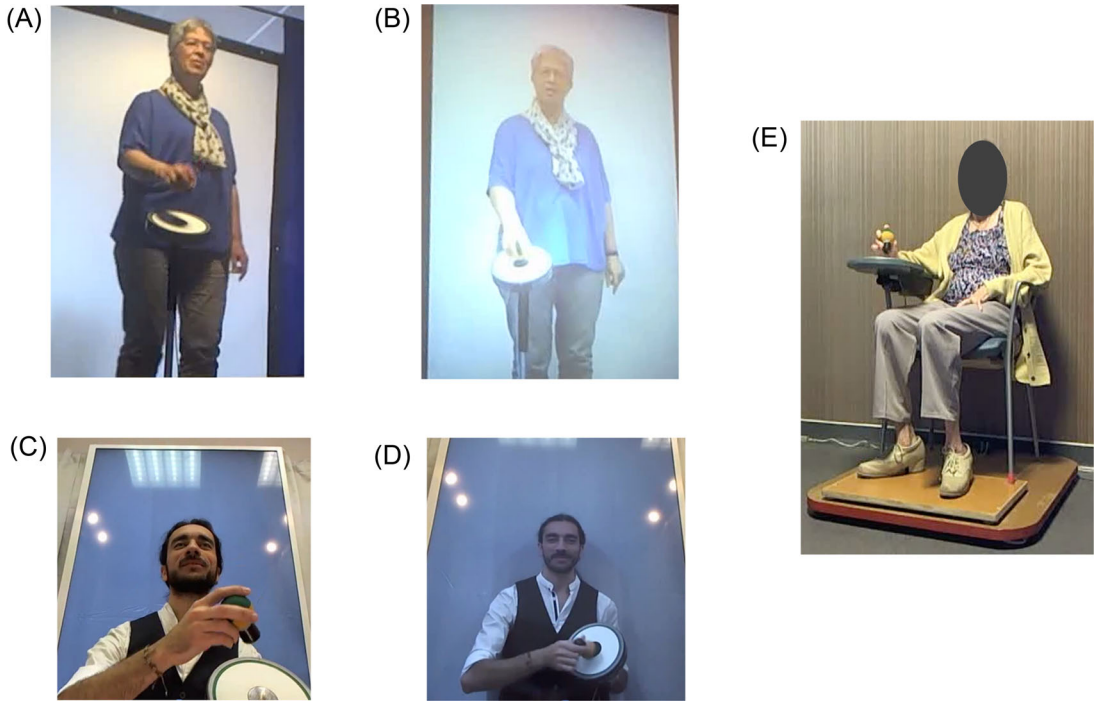

FIGURE 1 Experimental setup. The musician facing the patients was present live (A and C) or through a life-sized video (B and D). Panels A and B correspond to the day hospital study (No NCD and Mild NCD groups), whereas panels C and D correspond to the nursing home study (Major NCD group). The patients performed the SMS task by tapping on a tablet fixed to the chair's right armrest (E). Abbreviations: NCD, neurocognitive disorder; SMS, sensorimotor synchronization.

of the disease. The present study aims at assessing the effect of the social context on the ability to move with the beat and the emotional sensitivity to music in patients with Major and Mild NCD (determined according to the DSM-5 criteria) as compared to patients with No NCD.

In two previous studies, we tested the socioemotional and motor responses to music in patients with NCD from different etiologies (Alzheimer's disease, vascular dementia, or mixed dementia). We developed an experimental setup adapted to elderly people to evaluate their responses to music (Figure 1), already described in previous studies.[7–9] To assess the ability to move with the rhythm, we asked elderly people to tap with their hands and measured their sensorimotor synchronization (SMS), that is, the regularity and precision of their taps compared to the beats. The socioemotional engagement during the task was simultaneously measured by recording the patients' production of emotional facial expressions (EFEs). The tapping task was done in front of a musician singing along with the music and tapping with the rhythm to encourage and motivate participants to engage in the task. The presence of the musician could be either live or virtual via a prerecorded video projected onto a life-sized screen. In three studies,[7–9] we used this setup to compare patients' socioemotional engagement, as well as their SMS ability, when listening to music compared to a metronome, and facing a live musician compared to a virtual one. Our first study focused on a group of patients with Major NCD,[9] whereas the two other ones compared the behavior of patients with Mild NCD to matched elderly individuals with No NCD.[7,8] These studies demonstrated that the EFE production was reduced in patients with Mild NCD as compared to patients with No NCD, although they both expressed more positive EFE when listening to music than to a metronome.[8] We also found no positive reaction to music in patients with Major NCD.[9] All these results suggest a reduction of the positive emotional response to music with the progression of the severity of the neurodegenerative disease, which is in line with the study by Garrido et al., which illustrated that the emotional reaction to music may decrease with disease progression.[10] Yet, it remains difficult to provide firm conclusions considering that patients with Major NCD were older than patients with Mild NCD or No NCD. Moreover, these studies revealed that patients with NCD were able to perform the SMS task with higher precision with a metronome than with music, in agreement with a classical observation in tapping tasks.[11] Indeed, SMS with a musical sequence requires extracting and anticipating the strong beats within a melody. Such synchronization is, therefore, more difficult to achieve than synchronization with a regular metronomic sequence composed exclusively of strong beats. They also tapped more consistently facing a video of the musician than a live performance, which might be due to social pressure induced by the live presence of the musician as an observer.[12] Since the SMS performance of patients with Mild NCD or with No NCD was not directly compared to the SMS performance of patients with Major NCD, we were not able to clarify whether or not patients with more severe NCD are impaired in this tapping task.[7,13]

According to the literature, SMS is underpinned by two cerebral networks differently involved depending on the specificities of task.[14] Simple SMS tasks with subsecond intervals are based on activity in the cerebellum, the premotor and primary motor cortices, the supplementary motor area, and the basal ganglia, whereas more cognitively

demanding tasks involved the parietal and frontal cortices.[15] Considering that the beginning of NCDs (i.e., Alzheimer's disease, vascular dementia, or mixed dementia) affects the parietal and prefrontal cortices, we expected that simple SMS tasks with subsecond intervals would be relatively spared in patients with Mild NCD. At a later stage of the disease, additional brain structures might be affected, including motor areas, and, therefore, lead to SMS deficiencies whatever the specific task. We used an 800 ms paced metronome to match the comfortable paced tempo of an aged population.[16] At this pace, we hypothesized that SMS is affected in patients with Major NCD, but may be relatively preserved in patients with Mild NCD, as compared to patients with No NCD.

In this study, we tested the impact of NCD severity on socioemotional and motor responses to music. We selected three groups of participants from our previous studies[7–9] matched in terms of age and gender but with different NCD severity. We, therefore, compared the results of two patient groups presenting NCD at different stages of the disease (Mild NCD and Major NCD) to a group of elderly participants without cognitive impairment (No NCD). All these participants were instructed to tap with a metronomic or a musical rhythm while facing a musician. The musician was also doing the tapping while being present live or in a video. We analyzed participants' socioemotional reactions via the production of positive EFEs. SMS ability was operationalized as the consistency and accuracy of participants' tapping. We predicted a progressive decline of positive socioemotional reactions to music as a function of disease progression. Moreover, we expected that SMS abilities will be diminished at the most severe stage of neurodegenerative disease. The study design calls for testing the relationship between the SMS and the emotional responses to music as a function of the severity of the NCDs, we, therefore, looked at correlations between patients SMS performances, EFE production, and cognitive impairment.

MATERIALS AND METHODS

Participants

Seventy-five right-handed patients were included in this study. Patients aged from 77 to 94, already involved in our previous studies,[7–9] were selected according to the severity of NCDs, as defined by the Diagnostic and Statistical Manual of Mental Disorders—Fifth Edition criteria[17] in order to obtain three groups of patients matched in terms of age and sex, but who only differed in terms of Mini-Mental State Examination (MMSE). The MMSE was used to provide a continuous measure that is linked to neurocognitive impairment. Two groups of patients were recruited at the Bateliers Day Hospital (Lille University Medical Center, Lille, France) during a scheduled consultation for memory problems or falls. After the patients had participated in the study and at the end of a consultation day, a geriatrician made the diagnosis of No NCD or mild NCD. One group consisted of patients with no signs of an NCD at the time of testing (No NCD; $n = 22$), and another group was composed of patients with a mild NCD (Mild NCD; $n = 25$). They were native French speakers and were all living at their homes (except for two patients living in a nursing home). They received no drug treatment for memory problems. The third group of patients was recruited at the Nursing Home Sint-Franciscus (a care institution for the elderly, Kluisbergen, Belgium). This group consisted of patients with a major NCD (Major NCD; $n = 18$), diagnosed by a geriatrician. They were native Dutch speakers and were all living in nursing home. Five patients out of 18 received drug treatment for memory problems. The etiology of the mild and major NCD was Alzheimer's disease, vascular dementia, or mixed dementia. Both studies received the approval of an ethics committee. Written informed consent was obtained from each participant, a family member, or a legal representative.

Design and procedure

Each participant was tested individually and was asked to tap on a tablet in time with the beat of the sound sequence. The tapping task was performed in front of a musician who synchronized the tapping with the sound sequence. The sound sequence was either a metronomic sequence or a musical sequence without lyrics, but in this latter condition, the musician sang the song's lyrics.

Two social contexts were tested. In the video condition, the musician appeared in front of the participant on a life-size screen. In the live condition, the musician faced the participant in person. In the live condition, the musician was instructed to act as similar as possible to the prerecorded condition. A 60-s metronomic and musical sequence was analyzed. Both sequences were presented at the same tempo (interonset interval [IOI] of 800 ms, corresponding to 75 beats per minutes [bpm]). The musical sequence used in each country was a karaoke version of a very familiar song and had a ternary metric. Only data obtained from one of the four songs (tempo at 75 bpm) used in the nursing home study[9] were analyzed in the present study. The experimental methodology used in the day hospital and the nursing home studies is summarized in Table 1.

Data analysis

SMS measures were analyzed on 64 beats for each condition using circular statistics[18] with the CircStat Matlab Toolbox,[19] which is a robust tool to quantify SMS when there is not a perfect match between the number of taps and the number of the pacing stimuli.[20,21] Thus, it is appropriate when participants tend to miss taps or tap more than once in response to one beat. The analysis provides a measure of participants' consistency and accuracy in each condition. Consistency ranges from 0 to 1, with 1 corresponding to perfect consistency (all taps occurred at the same delay to the beat) and 0 corresponding to an absence of synchronization (the taps were randomly distributed between the beats). We applied an arcsine transformation to the consistency ($\sin^{-1}\sqrt{X}$) before the analysis to normalize the distribution. Figure 2 depicts consistency without the transformation to improve reading clarity (to keep a data range from 0 to 1). Accuracy corresponds

TABLE 1 Experimental method used in the day hospital study in Lille, France, (No NCD and Mild NCD groups) and the nursing home study in Kluisbergen, Belgium (Major NCD group)

	Day hospital study[7,8] No NCD/Mild NCD	Nursing home study[9] Major NCD
Distance to the musician	250 cm	200 cm
Distance to the screen	215 cm	270 cm
Size of the screen	125 × 165 cm	158 × 92 cm
Song		
Title	La Java Bleue	Zie ik de lichtjes van de schelde
Duration	60 s	60 s
IOI	800 ms	800 ms
Musician		
Gender	Male	Female
Position	Seated	Standing
Musician verbal behavior during the task		
Metronome	Say "Ta" on each beat	Stay silent
Music	Sing the song	Sing the song

Abbreviation: NCD, neurocognitive disorder.

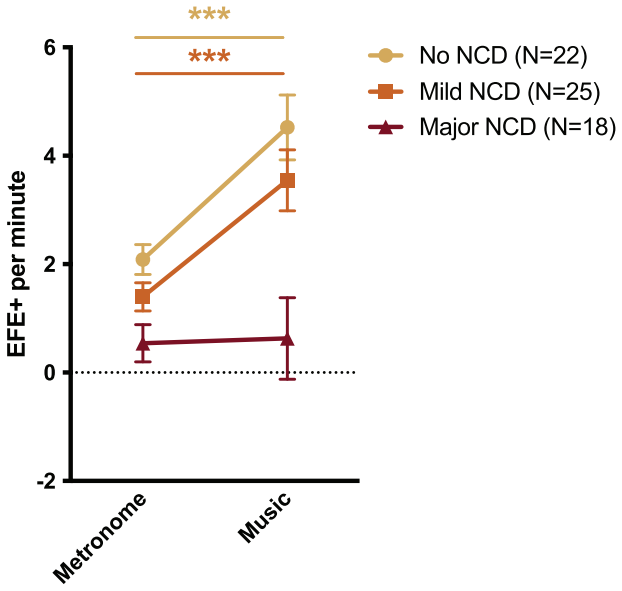

FIGURE 2 Analysis of EFE+. This figure reports the mean frequency of positive emotional facial expressions (±SEM) depending on the auditory sequence (metronome or music) in the three experimental groups (No Neurocognitive Disorder/Mild Neurocognitive Disorder/Major Neurocognitive Disorder). Patients with Major NCD did not express more positive emotions listening to music compared to a metronome, contrary to patients with No NCD or Mild NCD. Asterisks indicate significant differences (***$p < 0.001$). Abbreviations: EFE, emotional facial expressions; NCD, neurocognitive disorder.

to the mean delay to the beats of participants tapping. Accuracy was calculated only if a participant's taps were not randomly distributed. Random distribution of taps was tested using the Rayleigh test for circular uniformity.[18,22]

We analyzed participants' socioemotional reactions by measuring the frequency (number of behaviors per minute) of positive emotional facial expressions (EFEs+) according to the Facial Action Coding System.[23] The coding was computer-assisted and performed using Behavioral Observation Research Interactive software.[24] Two independent observers, who were blind to the condition, analyzed the videos (without the audio recording) and recorded the frequency of EFE+ per minute through the use of a keyboard. Interobserver ($r = 0.95$ in the day hospital study, $r = 0.72$ in the nursing home study) agreement was checked against literature criteria.[25]

Overall, the experimental design included one between-subjects factor (GROUP, with three levels: No NCD/Mild NCD/Major NCD), and two within-subjects factors (AUDIO, with two levels: metronomic/musical; and SOCIAL CONTEXT, with two levels: video/live). The experimental conditions' order of presentation was counterbalanced. The statistical analyses were conducted at a 95% confidence level. A p value less than 0.05 was considered as statistically significant. The EFE+ frequency and the SMS consistency and accuracy for each group in all conditions are available in the Supplementary Materials (Table S1).

RESULTS

Preliminary analyses

The demographic data of the groups are summarized in Table 2. One-way ANOVA revealed no effect of GROUP on age, but a significant effect of GROUP on MMSE scores ($F(2,61) = 105$, $p < 0.001$, $\eta^2 = 0.78$). The mean MMSE score was lower in the Major NCD group than in the Mild NCD group (Fisher's post-hoc test: $p < 0.001$), which was lower than the No NCD group (Fisher's post-hoc test: $p < 0.001$). A Pearson's

TABLE 2 Demographic information of the three groups of participants

	No NCD $N = 22$	Mild NCD $N = 25$	Major NCD $N = 18$
Age	85.6 ± 4	85.9 ± 3	87.6 ± 5
Gender (Female/Male)	17/5	21/4	14/4
MMSE (out of 30)	28.0 ± 2	21.3 ± 4	15.5 ± 3[a]
Years of education	16.9 ± 4	15.7 ± 3	N/A

Note: Data are shown as the mean ± standard deviation.
Abbreviations: MMSE, Mini-Mental State Examination scores; NCD, neurocognitive disorder; N/A, not available.
[a]Data missing for one participant.

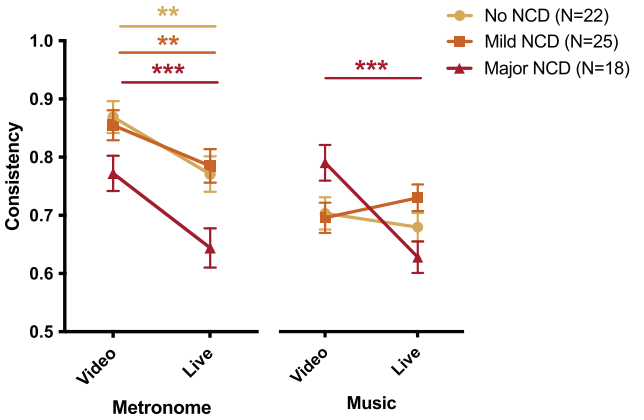

FIGURE 3 Analysis of SMS consistency. This figure reports mean synchronization consistency (±SEM) depending on the type of auditory sequence (metronome or music) and the social context (video or live) in the three experimental groups (No Neurocognitive Disorder/Mild Neurocognitive Disorder/Major Neurocognitive Disorder). In the metronome condition, all groups exhibited more consistency in front of a video than in a live performance of the musician. In the music condition, only patients with a Major NCD showed a sensitivity to the social context, with a lower consistency facing a live performance than a video. Asterisks indicate significant differences (**$p < 0.01$; ***$p < 0.001$). Abbreviation: NCD, neurocognitive disorder.

χ^2 test revealed no group difference in terms of sex distribution. A Student's *t*-test revealed no group difference between the No NCD and the mild NCD groups in terms of the level of education (those data were not available for the major NCD group).

EFE+

A three-way ANOVA was conducted on EFE+ frequency with the factors AUDIO (metronome/music), SOCIAL CONTEXT (video/live), and GROUP (No NCD/Mild NCD/Major NCD). The analysis revealed main effects of the factors AUDIO ($F(1,62) = 34.6$, $p < 0.001$, $\eta^2 = 0.36$) and GROUP ($F(2,62) = 12.0$, $p < 0.001$, $\eta^2 = 0.28$), as well as a two-way interaction between AUDIO and GROUP ($F(2,62) = 6.21$, $p < 0.01$, $\eta^2 = 0.17$) (Figure 2). While participants with No NCD or Mild NCD expressed more EFE+ in response to music than in response to a metronome (for both groups: Fisher's post-hoc test: $p < 0.001$), this was not the case for patients with Major NCD. Moreover, the latter participants expressed fewer EFE+ than participants with No NCD and with Mild NCD in the music condition (for both groups: Fisher's post-hoc test: $p < 0.001$) and fewer EFE+ than the No NCD group in the metronome condition (Fisher's post-hoc test: $p < 0.05$).

We tested the relationship between patients' MMSE and age as well as EFE+ in each of the four experimental conditions (Metronome Video, Metronome Live, Music Video, and Music Live) with Pearson's correlation. For each experimental condition, the EFE+ were correlated with the MMSE (*metronome video*: $r(64) = 0.397$, $p = 0.001$, *metronome live:* $r(64) = 0.406$, $p < 0.001$, *music video:* $r(64) = 0.477$, $p < 0.001$, *music live:* $r(64) = 0.466$, $p < 0.001$).

SMS consistency

A three-way ANOVA was conducted on SMS consistency with the factors AUDIO (metronome/music), SOCIAL CONTEXT (video/live), and Group (No NCD/Mild NCD/Major NCD). Analysis revealed main effects of SOCIAL CONTEXT ($F(1,62) = 36.8$, $p < 0.001$, $\eta^2 = 0.372$) and AUDIO ($F(1,62) = 16.4$, $p < 0.001$, $\eta^2 = 0.21$), two-way interactions between SOCIAL CONTEXT and GROUP ($F(2,62) = 7.07$, $p < 0.01$, $\eta^2 = 0.19$), between AUDIO and GROUP ($F(2,62) = 6.63$, $p < 0.01$, $\eta^2 = 0.18$), and between AUDIO and SOCIAL CONTEXT ($F(1,62) = 4.13$, $p < 0.05$, $\eta^2 = 0.062$). Analysis also revealed a significant three-way interaction between the factors AUDIO, SOCIAL CONTEXT, and GROUP ($F(2,62) = 8.25$, $p < 0.001$, $\eta^2 = 0.21$) (Figure 3).

In the metronome condition, all groups' consistency was higher in the video compared to the live condition (Fisher's post-hoc test: $p < 0.01$ for the No NCD and Mild NCD groups, $p < 0.001$ for the Major NCD group). Moreover, patients with Major NCD had lower SMS consistency than patients with No NCD and Mild NCD in the video condition (Fisher's post-hoc test: $p < 0.05$ for both comparisons) and had a lower consistency than patients with No NCD (Fisher's post-hoc test: $p < 0.01$) as well as with Mild NCD (Fisher's post-hoc test: $p < 0.05$) in the live condition.

In the music condition, the Major NCD group had higher consistency in the video condition than in the live condition (Fisher's post-hoc test: $p < 0.001$), whereas there was no effect of social context in the two other groups. Moreover, patients with Major NCD had higher consistency than patients with No NCD or with Mild NCD (Fisher's post-hoc test: $p < 0.01$ for both comparisons) in the video condition, but they had a lower consistency than those with Mild NCD in the live condition (Fisher's post-hoc test: $p < 0.01$).

We tested the relationship between patients' MMSE and age as well as SMS consistency in each of the four experimental conditions (Metronome Video, Metronome Live, Music Video, and Music Live) with Pearson correlation. In both video and live metronome conditions, SMS consistency was correlated with the MMSE (*metronome video*:

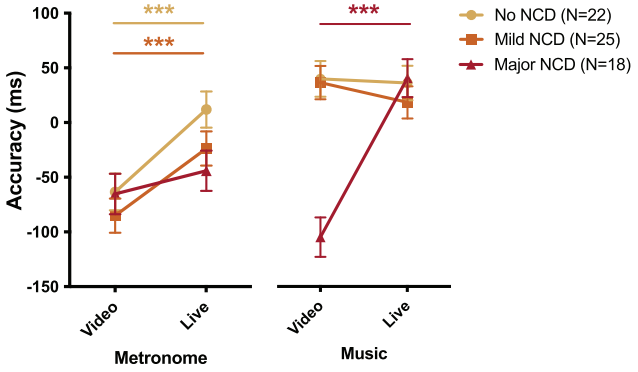

FIGURE 4 Analysis of SMS accuracy (in ms). This figure reports mean synchronization accuracy (±SEM) depending on the auditory sequence (metronome or music) and the social context (video or live) in the three experimental groups (No Neurocognitive Disorder/Mild Neurocognitive Disorder/Major Neurocognitive Disorder). In the metronome condition, all groups anticipated more taps in front of a video than during a live performance of the musician. In the music condition, only patients with a Major NCD showed a sensitivity to the social context, with lower anticipation while facing a live performance than a video recording. Asterisks indicate significant differences (***$p < 0.001$). Abbreviations: NCD, neurocognitive disorder; SMS, sensorimotor synchronization.

($r(64) = 0.327$, $p < 0.01$), *metronome live*: $r(64) = 0.280$, $p < 0.05$) but not with age. In the video music condition, SMS consistency was not correlated with patients' MMSE or age. Conversely, in the live music condition, SMS consistency was correlated with the MMSE ($r(64) = 0.254$, $p < 0.05$) and with age ($r(64) = -0.331$, $p < 0.01$). As age and MMSE were correlated with each other ($r(64) = -0.383$, $p < 0.01$), we did a linear regression to determine if both variables independently explain the SMS consistency in the music live condition. We found that the SMS consistency is explained by patients age ($R^2 = 0.110$, $F(1,63) = 7.78$, $p < 0.01$) and adding the MMSE did not significantly improve the model.

SMS accuracy

A three-way ANOVA carried out on SMS accuracy revealed main effects of AUDIO ($F(1,62) = 79.4$, $p < 0.001$, $\eta^2 = 0.56$), SOCIAL CONTEXT ($F(1,62) = 33.2$, $p < 0.001$, $\eta^2 = 0.35$), and GROUP ($F(2,62) = 3.68$, $p < 0.05$, $\eta^2 = 0.11$). We also found two-way interactions between AUDIO and GROUP ($F(2,62) = 6.36$, $p < 0.01$, $\eta^2 = 0.17$) and between SOCIAL CONTEXT and GROUP ($F(2,62) = 5.38$, $p < 0.01$s, $\eta^2 = 0.18$). Finally, there was also a three-way interaction between AUDIO, SOCIAL CONTEXT, and GROUP ($F(2,62) = 26.0$, $p < 0.001$, $\eta^2 = 0.46$) (Figure 4).

In the metronome condition, patients with No NCD and Mild NCD tapped earlier in the video than the live condition (Fisher's post-hoc test: $p < 0.001$ for both groups), but patients with Major NCD did not. There was no group difference in the metronome condition.

In the music condition, patients with Major NCD tapped earlier in the video than in the live condition (Fisher's post-hoc test: $p < 0.001$), which was not the case for patients with No NCD and Mild NCD. Moreover, in the video condition, patients with Major NCD tapped earlier than patients with No NCD and Mild NC (Fisher's post-hoc test: $p < 0.001$).

We tested the relation between patients MMSE and age as well as SMS consistency in each of the four experimental conditions (Metronome Video, Metronome Live, Music Video, and Music Live) with Pearson correlation. In both video and metronome conditions, SMS accuracy was not correlated with MMSE or age. In the video music condition, SMS accuracy was correlated with the MMSE ($r(64) = 0.457$, $p < 0.001$). In the live music condition, SMS accuracy was not correlated to MMSE or age.

Correlations between the EFE+ and SMS performances

We tested the relationship between EFE+ and SMS (consistency and accuracy) in each of the four experimental conditions (Metronome Video, Metronome Live, Music Video, and Music Live). In both video and live metronome conditions, there was no significant correlation between EFE+ and SMS performances. In the music video condition, we found a significant correlation between the EFE+ and SMS accuracy ($r(64) = 0.383$, $p < 0.01$) and no correlation between EFE+ and SMS consistency. As EFE+ and SMS accuracy were also correlated with MMSE in these experimental conditions, we did a linear regression to determine if both the MMSE and the EFE+ explained SMS accuracy independently. We found that the MMSE predicts SMS accuracy ($R^2 = 0.209$, $F(1,62) = 16.4$, $p < 0.001$), but adding the EFE+ in the regression did not significantly improve the model. In the live music condition, there was no significant correlation between EFE+ and SMS performances.

DISCUSSION

The aim of this study was to examine the effect of the severity of NCDs (Alzheimer's disease, vascular dementia, or mixed dementia) on the socioemotional and motor responses to music rhythm. We examined the production of EFE+ and SMS abilities in elderly patients with either No NCD, Mild NCD, or Major NCD in different musical and social contexts. Patients with No NCD or Mild NCD expressed more positive emotions when listening to music than to metronome, suggesting that they positively react to music. However, this effect was not observed in patients with Major NCD, indicating that the positive emotional impact of music seems to diminish in the severe stage of NCDs. Moreover, we found that emotional reactivity diminished with MMSE scores. In line with our previous studies, SMS consistency was globally better with a metronome than with music, and it was better when the patient was facing a video than during a live performance. When synchronizing with a metronome, patients with Major NCD showed less consistency than those with No NCD or Mild NCD. Moreover, SMS consistency with a metronome diminished with MMSE scores. This result demonstrated that SMS to a simple beat is linked to the NCD severity and is significantly affected at advanced-stage NCDs. The SMS results in the music

condition were less straightforward. Whereas SMS scores of patients with No NCD or Mild NCD were not affected by the social context when tapping with music, patients with Major NCD were less constant and tapped later in the live condition than in the video condition. Moreover, their taps were more constant than the ones of the two other groups in the video condition, but not in the live condition. This surprising finding suggests that patients with Major NCD do not respond in the same way to changes in social contexts when listening to music compared to patients with No NCD or Mild NCD. Finally, we found no relationship between the production of EFE+ and SMS performances.

As previously established, music elicited more EFE+ than a metronome in patients with No NCD or Mild NCD.[8] According to our previous study, patients with Mild NCD also produced fewer positive facial expressions than patients with No NCD. The lack of difference in the present study between Mild NCD and No NCD might be due to low statistical power for this comparison (i.e., smaller sample size). Even if several lines of evidence suggest a relatively spared emotional response to music in patients with dementia even at a severe stage of the disease,[26,27] the lack of positive emotional responses to music in patients with Major NCD is in agreement with the findings reported by Garrido et al., which suggested that musical pleasure declines for people with dementia with severe cognitive impairment.[10] We also found that EFE+ production declined with patients MMSE. At the present time, it is difficult to explain the reason for this decline. It could be due to a deficit in the processing of musical information, leading to difficulties extracting musical features, such as rhythm or pitch, or to lower emotional sensitivity to music. However, EFE+ decreased with MMSE in musical situations as well as when tapping to a metronome, indicating that the EFE+ deficit is not specific to music. Thus, it could be related to the development of mood disorders, such as depression and apathy, frequently associated with dementia.[10] In any case, the socioemotional engagement in elderly patients with Major NCD should be examined in detail, since it might constitute a diagnostic marker of neurodegenerative disease progression and a prognostic marker of the effectiveness of music therapy.

In the present study, we found that patients with Major NCD obtained lower SMS consistency with a metronome compared to patients with Mild NCD and No NCD. This result expands upon our previous finding[7] and suggests that a more severe NCD can affect patients' ability to synchronize with a simple beat such as one produced by a metronome. Few studies have examined rhythmic abilities in patients with dementia,[28–30] but the tasks used were more complex than the present one (for a review, see Ref. 13). To the best of our knowledge, none of them compared patients with Major NCD to less impaired patients (Mild NCD). One of the reasons for this absence of studies might be due to the difficulty in creating a task adapted to this clinical population. We also found that SMS consistency was correlated to patients' MMSE when tapping with a metronome. Our study is the first to demonstrate a deficit in SMS in a very simple synchronization task using a comfortable pace in patients with Major NCD as well as degradation of SMS consistency with disease severity.

An unexpected finding in this study concerns SMS to music. When tapping to music with the live musician, the consistency and accuracy of patients with Major NCD were not different from those of patients with No NCD. Moreover, SMS consistency in this condition was correlated with age but MMSE, which was observed in the metronome conditions. It appears that in live music situations, NCD severity does not impact SMS consistency. This finding contrasts with the results obtained when watching a video recording. SMS accuracy in this context was correlated with patients' MMSE, whereby earlier taps were associated with lower MMSE. Additionally, patients with Major NCD were more constant and tapped earlier (i.e., before the beats) than patients with No NCD or Mild NCD. This large behavioral difference between the groups in the music video condition is highly surprising, especially because the performance of patients with Major NCD condition appeared to be better than that of people with mild NCD and No NCD. Those results are difficult to interpret for the moment and require further investigation. What is important to note here is that although patients with Major NCD have performed very differently than people with No NCD when facing a video of the musician, their performance became comparable when tapping to music in the presence of a live performance. This emphasizes the effectiveness of a live musical performance to stimulate patients with Major NCD, as it is the only condition in which their SMS performance (i.e., their consistency and accuracy) was not different from those of patients with No NCD. Live music is also the only condition in which SMS performances were not related to patients' MMSE but to their age, suggesting that in this situation, patients' behaviors were comparable irrespective of disease severity.

To conclude, we demonstrated in this study that even if rhythmic abilities and emotional responsiveness to music are usually described as relatively spared in dementia, the severity of the neurodegenerative disease seems to affect these abilities. These novel results need to be replicated and further investigated with larger groups of patients tested with the exact same protocol. The number of positive emotional reactions decreases with the progression of the neurodegenerative disease and suggests that musical interventions need to be adapted depending on the stage of the disease. Patients were still able to perform an SMS task even with a Major NCD, but their profile of responses differed from the ones obtained by patients with No NCD or with a Mild NCD. Interestingly, in the musical conditions, we found no differences in SMS performance between participants with Major NCD and those with No NCD in the presence of the musician, and no association between those performances and patients NCD severity. It appears that the use of a live musician may be particularly relevant in musical interventions for patients at an advanced stage of dementia.

AUTHOR CONTRIBUTIONS

M.G., L.S., M.L., and S.S. designed the study. M.G. carried out the experiments. M.G. and L.H. analyzed the data. M.G., L.H., L.S., M.L., and S.S. discussed the results. L.H. and S.S drafted the manuscript. L.H., L.S., M.L., D.H.G., and F.P. revised the manuscript.

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COMPETING INTERESTS

The authors declare no competing interests.

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SUPPORTING INFORMATION

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