

SHORT COMMUNICATION

Abnormal musical pacemaker in a patient with musical hallucinations

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Music creation requires a highly orchestrated temporal pattern. The study of a patient with repetitive musical hallucinations enabled us to examine temporal pacemakers in music production. Here, we show that the pattern of faster silent production of a chosen tune compared with its production aloud was reversed when the patient produced the hallucinatory tune. This observation might suggest the utilization of a pacemaker(s), which functions differentially during the disease.

Introduction

The creation and the estimation of time durations are an intriguing and complex cognitive phenomenon. Do we possess an internal clock or a pacer? Is it affected during the disease and how? As music requires a highly orchestrated temporal pattern of hundreds of milliseconds, one may postulate that an internal time keeper is an essential component of its generation. Accordingly, the creation of music might serve as a research vehicle to examine the subjective estimation of time durations and the possible role of internal pacemakers.

Musical hallucinations have a prevalence of 0.16–2.5% [1], usually occur spontaneously and sometimes are associated with structural brain disease, hearing impairment, psychiatric disorders, epilepsy and intoxication [1–4]. Patients report of tunes repeatedly playing within their head in the absence of corresponding external auditory stimulus.

A patient with repetitive musical hallucinations enabled us to study the internal estimation of time durations related to a single event under normal conditions and during disease.

Case report

A 74-year-old right-handed female without musical training presented with 2 months duration of musical hallucinations. She denied other auditory complaints aside from hearing loss secondary to Menier's disease. Segments of European classical music heard by her recently would repeatedly play in her head till it would stop or be replaced by another tune. The length of the repeating musical fragments varied, but usually lasted < 30 s. Her past medical history was notable for two episodes of transient global amnesia (TGA) 23 and

12 years prior to the appearance of the musical hallucinations. A brain magnetic resonance imaging (MRI) taken during the second episode demonstrated a right temporal cyst (Fig. 1). Although she was an avid listener to classic European music, she could not read music nor play any musical instrument.

Her general and neurological examinations were normal and no cognitive abnormality was present. She scored 30/30 on the Mini Mental Status Examination and 96/100 on the Addenbrooke's mental evaluation [5]. Electroencephalogram was normal. Brain computed tomography (CT) scan did not demonstrate any change from several previous neuroimaging studies (MRI and CT). Audiometry showed severe bilateral sensory-neural deficit. A therapeutic trial with phenobarbital did not affect her auditory hallucinations.

Experimental Study

The patient and 11 healthy controls without any history of neurological or hearing impairment and mean age of 44 ± 7 were examined.

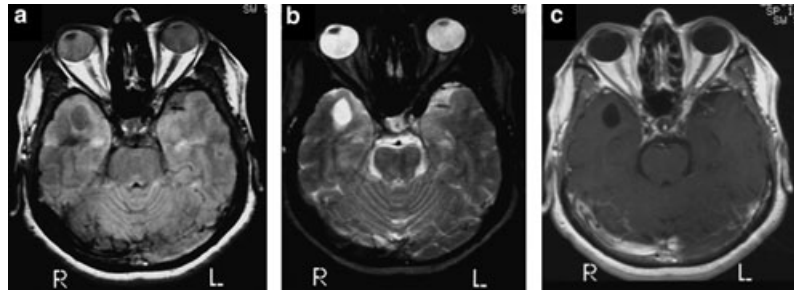
Subjects were asked to produce tunes by singing or humming, and we recorded the production time. The tunes, which were either tunes of choice ('chosen tune') or hallucinatory tunes, were produced in the following three tasks.

Intentional Production of a Chosen Tune

We recorded the time required for both the patient and the control subjects to produce a tune chosen by each of them under two conditions: (i) tune produced intentionally silent (imagery production of the tune [6]) and (ii) tune produced intentionally aloud. The subjects had to choose a tune of 4–10 s, and the duration was verified prior to the start of the experiment. There were no restrictions as to the nature or source of the tune. The silent and aloud conditions were assigned to six randomly presented blocks with 10 repetitions each, and a total of 30 recordings for each condition.

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Figure 1 Magnetic resonance imaging study of the patient following the last TGA episode, 13 years prior to presentation, demonstrating a right temporal cyst. (A, Axial FLAIR; B, Axial T2; C, Axial T1 with contrast).



Intentional Production of a Hallucinatory Tune

We recorded the time required for the patient to experience or produce her current hallucinatory tune. In this task, only the patient participated as only she experienced hallucinatory tunes. Similar to the previous task, there were two conditions in this task: (i) the hallucinatory tune produced intentionally silent and (ii) the hallucinatory tune produced intentionally aloud. The conditions were blocked similar to the recording in previous task.

Intentional and Spontaneous Production of a Hallucinatory Tune

We recorded the time required for the patient to experience spontaneously or produce intentionally her current hallucinatory tune. Accordingly, there were three conditions in this task: (i) the hallucinatory tune produced intentionally silent, (ii) the hallucinatory tune produced intentionally aloud and (iii) the hallucinatory tune produced spontaneously (the time required for the patient to experience the hallucinatory tune). The three conditions were assigned to 18 counterbalanced blocks with five recordings in each block and a total of 30 recordings for each condition.

Time durations required to complete a tune were recorded using a G4 Mac computer and the PSYSCOPE software by hitting the 'M' key at the start and the 'N' key at the completion of each tune [7].

Results

Intentional production of a chosen tune (Table 1).

In controls and the patient, intentional silent production of a chosen tune was statistically significant shorter than the singing aloud of the same tune. Control subjects needed 6382 ± 1724 ms to complete a tune silently and 7318 ± 1972 ms to produce it aloud ($P < 0.0001$); the patient required 7741 ± 388 ms, and 8384 ± 212 ms, respectively ($P < 0.0001$).

In order to account for the differences in reaction times amongst the subjects, we calculated for each the ratio between producing the tune aloud to producing it

Table 1 Mean time required to complete a tune of choice aloud and silent by the patient and the control subjects

	Chosen tune (mean time in ms \pm SD)		<i>P</i>	Aloud/silent
	Silent	Aloud		
Controls	6382 ± 1724	7318 ± 1972	$P < 0.0001$	1.16 (95% CI: 1.02–1.23)
Patient	7741 ± 388	8384 ± 212	$P < 0.0001$	1.08

silently. The ratio for controls was 1.16 (95% CI –1.02–1.23) and for the patient 1.08, within the CI of the controls. Therefore, there was no difference between the performance of the patient and the controls in this task.

These findings suggested that: (i) production of a musical tune silently takes less time than its production aloud; (ii) there is a fairly constant adherence to time in repeated production of an identical tune.

Intentional production of a hallucinatory tune

Intentional production of a hallucinatory tune by the patient was statistically significant slower with the production of the hallucinatory tune silent compared with its production aloud (8094 ± 1189 ms, 6850 ± 213 ms, $t = 5.63$, $P < 0.0001$). The ratio between producing the tune aloud to its production silently was 0.85 and is outside the 95% CI for controls in the first part of the experiment. Hence, the pattern of faster silent production of a tune was inverted.

Intentional and spontaneous production of a hallucinatory tune (Fig. 2)

The time required for the patient to experience a hallucinatory tune spontaneously was $10,707 \pm 566$ ms compared with $10,369 \pm 1263$ ms when it was produced intentionally silent and 9885 ± 395 ms when it was produced intentionally aloud. ANOVA revealed a condition effect ($F = 6.38$, $P = 0.0027$). *Post hoc* analysis demonstrated that the spontaneous production of the hallucinatory tune was significantly slower than the production of the same tune voluntarily and intentionally aloud ($P < 0.0001$).

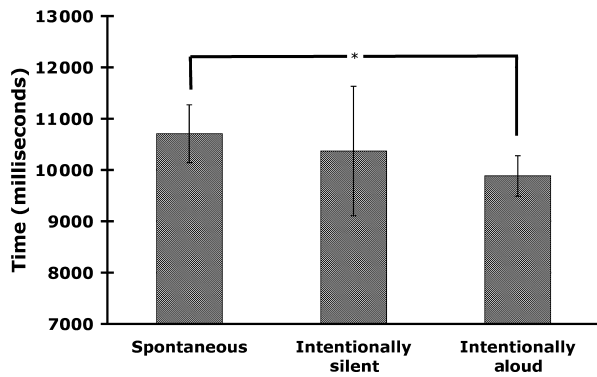


Figure 2 Mean reaction time in milliseconds to complete a hallucinatory tune in the three conditions of part 3. (* $P < 0.0001$).

Discussion

Biological pacemakers are part of an internal clock system, similar to those designed by man, and are expected to control event durations or temporal intervals in a precise and predicted pattern. The performance of the controls and the patient in the first part of the experiments confirmed the existence of such a time keeper. As expected, both patient and controls were slower with the actual production of a tune compared with its mental imagery and the ratio between the two conditions was in a narrow range (95% CI -1.02 to 1.23). The existence of such a pacemaker was fostered by the finding that even when this constant pattern was entirely reversed as the patient was asked to perform the unsolicited hallucinatory tune, the complete adherence to time durations during the repetitions remained unchanged.

This reversal of pattern can imply that the hallucinatory tune is activated by an independent and aberrant neural mechanisms with a different time keeper, which follows other rules (longer durations for musical imagery compared with actual production of a tune), or that the hallucinatory tune itself differs from the original tune and thus cannot be compared. Alternatively, this result could represent the action of a single pacemaker within a frame of an internal clock: as time processing is influenced by attention and working memory, it could be argued that the timing of a hallucinatory tune requires different memory and attentional resources, especially so, when the tune is attended to and not produced, as in the third part of the experiment. Differential allocation of neural resources for the hallucinatory tune may therefore bring about this differential pattern [8], and is in accordance with the observation that irregular and unpredicted appearance of a stimuli influence the reaction times [9]. It could also be argued that non-central nervous system factors, such as heart rate, could have caused the effect observed.

However, as the different conditions were presented in random blocks, we believe that this is not the case.

The functional locus of the impairment in our patient is not clear. It could be argued that the abnormal pattern observed arises at the level of execution and that the abnormal pacemaker is involved only in motor execution. However, as the patient showed a reversal of the timing ratios of the actual and imagery production of the hallucinatory tune, the pacemaker is probably involved in more than just tasks of motor production.

The anatomical source of the hallucinations in our patient is unknown. It is intriguing that the patient had a structural damage in the region responsible for auditory sensation and interpretation. Our findings could theoretically also represent secondary functional changes in auditory processing in response to peripheral hearing loss.

Regardless of the primary abnormality, our findings suggest that the music production under normal conditions and during disease is dependent upon the differential action of an internal pacemaker. Further studies, looking at other variables such as rhythm and musical motifs in the timing of the production of musical extracts can shed more light on this issue.

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