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Transient deficit in acute stroke: a case of musical hallucinations

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ABSTRACT

We reported a case of a 62-year-old female patient affected by musical hallucinations (MHs) as a transient symptom after an ischemic stroke in the right middle cerebral artery. CT scan showed widespread cortical and subcortical hypodensity associated with moderate hemorrhage involving the lentiform nucleus, insular cortex, and caudate nucleus. The patient had no history of psychiatric disorders, hearing defects, or epilepsy. MHs appeared one week after the stroke and spontaneously vanished 10 days after their onset. From our perspective, the early activation of MHs after unilateral brain injury, and their timing of resolution, can be explained according to the "interhemispheric imbalance theory". According to this theory, in the minutes or weeks following the onset of a focal cerebrovascular event, a series of changes in global brain connectivity occur leading to a temporary imbalance in interhemispheric excitation.

Keywords: stroke; musical hallucination; brain injury

1. Introduction

A stroke is the sudden onset of signs and/or symptoms that can be related to focal and/or global abnormalities of brain function, lasting longer than 24 hours, and not being related to any other obvious cause but cerebral vasculopathy (Bolognini & Tesio, 2015). After a stroke, the affected hemisphere may be doubly impaired, both due to the cerebrovascular event itself and the unbalanced inhibition from the unaffected hemisphere (Khedr et al., 2009). In fact, a secondary effect of the unilateral lesion is the alteration of modulatory activity that the two hemispheres exert on each other: the activity of the contralesional hemisphere, unaffected by the stroke, is no longer adequately modulated by the injured one. The non-injured hemisphere then becomes uninhibited, or hyperactivated. Contralesional hyperactivation results in increased inhibitory influences on the hemisphere in which the injury/lesion occurred. This phenomenon has its maximum expression in the subacute phase. Thereafter, there is a progressive reduction of contralesional hyperactivation with a tendency to return toward a balance of interhemispheric interactions similar to that observed under normal conditions (Ward, 2004).

In the motor domain these effects underlie the use of well-validated neuromodulation techniques in the acute and post-acute phase after an acute event, which either consists in inhibiting the uninjured hemisphere or exciting the injured one to facilitate the return of interhemispheric balance (Lefaucheur et al., 2020). The motor consequences of this initial hemispheric imbalance have been studied extensively for three main reasons: their prevalence in post-stroke outcomes, their importance in the patient's functional recovery, and the difficulty of investigating other domains, such as sensory or cognitive, in patients who are often very attentively impaired and impossible to test in the early post-stroke days. This does not exclude the possibility that transient deficits may affect other domains because of interhemispheric imbalance.

In the case we'll present, we speculate that an imbalance between the hemispheres is what's causing a sensory impairment, particularly musical hallucinations.

Hallucinations are defined by Esquirol (1838) as "perception without object", which means perception of a sensory stimulus in absence of an actual external source (Brasic, 1998; Calabrò et al., 2012; Lampl et al., 2005; Woo et al., 2014). Hallucinations can manifest in different sensory modalities such as sight, hearing, or smell; here, musical hallucinations (MHs) are considered a type of complex auditory hallucinations. MHs are disorders of complex sound processing (Calabrò et al., 2012; Evers & Ellger, 2004; Griffiths, 2000), in which patients report sounds, songs, or melodies despite the absence of acoustic stimuli (Berrios, 1990; Evers, 2006). Thus, MHs are not only about sound

perception, but also about semantic and musical memories (Woo et al., 2014). Indeed, they include well-known religious, folk or popular songs, usually heard during childhood and adolescence (Calabrò et al., 2012). MHs have been reported as arising from lesions of early stages of sound processing (brainstem, pons, thalamus and auditory radiation), and of higher-level auditory association cortices, such as the temporal lobe (Cope & Baguley, 2009) and insula (Isolan et al., 2010).

There are two main theories in literature about the etiology of auditory hallucinations in acute stroke: the "stimulation theory" and the "inhibition theory". The stimulation theory explains the origin of auditory hallucination as caused by seizures or electrical and neurochemical stimulators. The inhibition theory is based on the disruption of normally inhibitory function, resulting in a disinhibition phenomenon that involves a reduced corticocortical connectivity neural network (Lampl et al., 2005).

Hereafter we describe the case of A.P., a 62 years-old woman that developed MHs following an ischemic stroke to the right middle cerebral artery.

2. Case

Patient A.P. (62 years old, right-handed, non-musician female with 8 years of education) was admitted to our rehabilitation center following a localized ischemic stroke located in the right middle cerebral artery. A CT scan showed cortical and subcortical hypodensity in the frontal and opercular regions, in the insula, in the right temporal pole and lateral temporal, and right striatum, associated with moderate hemorrhage involving the lentiform nucleus, the insular cortex and the caudate nucleus head (Figure 1). The patient had no history of psychiatric disorders or hearing defects, neither did she suffer from epilepsy (EEG showed no abnormalities).

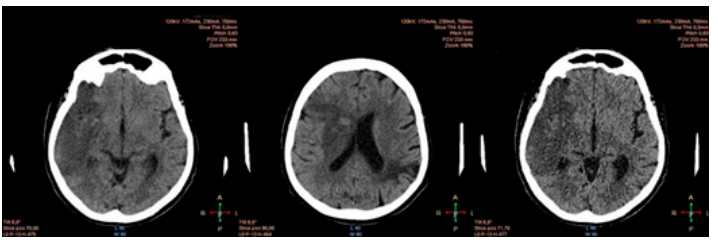

Figure 1. CT brain scan showing an ischemic stroke in the patient's right middle cerebral artery

Her musical hallucinations arose one week after the stroke. They consisted of frames of popular Italian songs and religious Christmas melodies (i.e., "Vecchio Scarpone", "Tu scendi dalle stelle" or "Astro del ciel") which represented A.P.'s musical background. A.P. was aware that what she perceived was independent of any external sound source; for this reason, we should speak of hallucinosis rather than hallucinations, but, for simplicity, we'll continue to refer to this phenomenon as MHs (Cavaliere et al., 2018; Vanneste et al., 2013). Furthermore, when A.P. was engaged in a task or conversation, her hallucinations would decrease in volume and then increased again as soon as she was left alone. She described her experience as the incessant sound of a radio.

A.P. was globally oriented towards the person, place, time, and situation and adequate in the patient-examiner relationship. Clinical observations and the neuropsychological assessment (Tables 1 and 2) revealed preserved intensive components of attention and altered selective components of attention consistent with a framework of unilateral spatial neglect. In particular the evaluation showed the presence of left unilateral spatial neglect in peripersonal and extrapersonal space. Executive functions such as visuoconstructive planning, cognitive flexibility, estimation ability, problem solving and inhibition of automatic responses were also found to be impaired. In contrast, mnestic function was preserved. Injury also led to hemiparesis in her left upper and lower limbs.

A.P.'s MHs were not treated pharmacologically and resolved spontaneously, finally disappearing 10 days after their onset.

Table 1. Results of A.P.'s neuropsychological assessment: screening test. Raw scores and cut-off scores are reported. References to the normative studies are reported for detailed information about the tests and their Italian standardization (Mancuso et al., 2016). Performances below the cut-offs are in bold

Oxford Cognitive Screen (OCS)			
	Raw Score	Cut-Off	Comment
Naming of figures	**3**	**3.1**	**Impaired**
Semantics/indication of figures	3	3	Spared
Orientation	4	3.9	Spared
Field of view	**3**	**4**	**Impaired**
Sentence reading	**13**	**14.6**	**Impaired**
Writing numbers	3	2.8	Spared
Calculation	**3**	**3.4**	**Impaired**
Incomplete hearts (correct total)	**33**	**44.3**	**Impaired**
Incomplete hearts (space asymmetry)	1	<-3 or >3	Spared
Incomplete hearts (objects asymmetry)	**9**	**<-2 or >2**	**Impaired**
Gesture imitation	**3**	**9**	**Impaired**
Deferred memory and recognition			
Verbal memory: recall	4	2.7	Spared
Episodic memory: recognition	4	3.6	Spared
Executive functions: task switching			
Baseline score	**8**	**10.6**	**Impaired**
Executive functions score	**7**	**3**	**Impaired**

Table 2. Results of A.P.'s neuropsychological assessment: test evaluating attention, executive functions and memory. Raw, regression-adjusted scores (i.e., raw scores adjusted for age and education with multiple regression analysis) and cut-off scores (to be compared with the patient's adjusted score) are reported. References to the normative studies are reported for detailed information about the tests and their Italian standardization. Performances below the cut-offs are in bold

	Raw Score	Correct Score	Cut-Off	Comment
ATTENTION FUNCTIONS				
Attentional Matrices (Spinnler & Tognoni, 1987)	38	37.25	≥31	Spared
Digit Span forward (Monaco et al., 2013)	5	5.13	≥4.26	Spared
Digit Span backward (Monaco et al., 2013)	3	3.19	≥2.65	Spared
Line deletion test (Albert, 1973)				
Total omission errors	**3/40**			
Omission errors to the left	**3**	**-**	**≤2**	**Impaired**
Omission errors to the right	**0**			
Difference left-right errors of omission	**3**			
EXECUTIVE FUNCTIONS AND VISUO CONSTRUCTIVE ABILITIES				
Rey–Osterrieth Complex Figure Immediate Copy (Caffarra et al., 2002)	**13.5**	**14.5**	**≥28.88**	**Impaired**
Clock drawing test (Caffarra et al., 2011)	**4**	**4.25**	**≥6.55**	**Impaired**
EXECUTIVE FUNCTIONS				
Verbal Fluency – Letters (Carlesimo et al., 1996)	27	30	≥17.35	Spared
Verbal Fluency – Categories (Zarino et al., 2014)	35	37	≥23.59	Spared
Stroop Test (Caffarra et al., 2002)				
Interference effect Errors	**30**	**29.25**	**≤4.23**	**Impaired**
Interference effect Time	3	-2.25	≤36.91	Spared
Wisconsin Card Sorting Test (Laiacona et al., 2000)				

Global score	**128**	**114.1**	**≤90.5**	**Impaired**
Perseverative Responses	**93**	**83.6**	**≤42.6**	**Impaired**
Non-perseverative errors	25	22	≤30	Spared
Weigl Sorting Test (Spinnler & Tognoni, 1987)	10	9.5	≥4.25	Spared
Verbal Reasoning Test (VRT) (Basagni et al., 2017)	**39**	**44.14**	**≥65.17**	**Impaired**
Cognitive Estimation Task (Della Sala et al., 2003)	**19**	**-**	**<18**	**Impaired**
MEMORY FUNCTIONS				
Short Story (Carlesimo et al., 2002)				
Immediate recall	6.8	6.8	≥3.1	Spared
Delayed recall	4.8	5	≥2.39	Spared
Rey Auditory Verbal Learning test (RAVLT) (Carlesimo et al., 1996)				
Immediate recall	44	46.3	≥28.53	Spared
Delayed recall	9	9.7	≥4.69	Spared
Rey–Osterrieth Complex Figure Delayed Copy (Caffarra et al., 2002)	**5**	**8.5**	**≥9.47**	**Impaired**

3. Discussion

Musical hallucinations consist of the perception of music in absence of an actual external musical source. The theory of interhemispheric inhibition following an acute event can be used to explain how MHs might manifest after a brain event and then vanish on their own, as in A.P.'s case. Moreover, the temporal evolution of this mechanism is perfectly superimposable to the case of A.P.: interehemispheric inhibition has its maximum expression in the subacute phase followed by a progressive reduction until the return to full equilibrium (Ward, 2004).

Her hallucinations indeed followed this pattern, arising a week after the stroke, and disappearing after 10 days. Indeed, in the acute phase after a cerebrovascular event, various mechanisms are activated before the brain returns to its normal balance and one of these mechanisms is precisely that of interhemispheric imbalance. As mentioned above, there are two theories that

have tried to explain auditory hallucinations in acute stroke: the "activation theory" and the "inhibition theory". As already stated by Braun et al. (2003) in the specific case of musical hallucinations, the theory of inhibition seems to be the most suitable to explain the phenomenon. According to them, the most likely mechanism to explain post-lesion MHs is the release of inhibition from the auditory cortex by other cortical auditory neural assemblies, including those in the contralateral hemisphere (Braun, 2003). In case of MHs the lesioned area could contain mainly inhibitory connections for the specific sensory modality. These inhibitory neurons would normally regulate brain circuits containing complex sensory representations; when damaged, they could result in compensatory overactivation of the adjacent tissue, causing MHs (Calabrò et al., 2012). In our case, we hypothesize that the hallucinations were not due to a definitive lesion of the inhibitory circuits as mentioned above, but rather to interhemispheric imbalance: the uninjured hyperactivated hemisphere acted just like an injury by inhibiting this inhibitory circuit (thus activating it) and that therefore the MHs emerged and then disappeared with the return to the normal balance.

Another interesting issue concerns the modulation of the phenomenon as reported by the patient: MHs increased in intensity when the patient was alone and in a quiet place e.g. in her room. This is consistent with literature that reports how silence facilitates hallucinatory perception due to an altered signal-noise ratio (Knobel & Sanchez, 2009). In this case, MHs seemed to be sensitive to external auditory stimuli or to the engagement in cognitive tasks involving the verbal system, suggesting a role of competing auditory input in MHs perception. Literature on auditory hallucinations largely comes from studies of psychiatric or hypoacusis patients that report how administering external stimuli (e.g. music, audiotape, talking to someone) or improving auditory function could reduce the severity of hallucinations (Coebergh et al., 2015; Gallagher, Dinan, & Baker,1994; Na & Yang, 2009; Shergill et al., 1998). Unfortunately, A.P.'s MHs vanished during the first day of hospitalization in our center hindering further investigation of the role of competitive auditory input in the modulation of the phenomenon (e.g. by administering music-related tasks).

4. Conclusion

A case of musical hallucinations following an ischemic stroke of the right middle cerebral artery is reported in this paper. Although motor deficits are the best known of the typical transient deficits in the acute post-stroke phase because they are the most observable at a stage when patients are difficult to

test, this kind of deficits can also affect other domains. In our case, the transient deficit occurred at the sensory level, specifically in the form of MHs. We tried to interpret the occurrence of this transient phenomenon according to the "interhemispheric imbalance" theory. The increase of MHs could be, in fact, the result of hyperactivity of areas close to the brain lesion during the acute phase, while their disappearance could be related to a functional recovery of the interhemispheric balance prior to the injury. However, it is important to consider the speculative nature of our interpretation, which is one of the major limitations of the current study. It is not possible to carry neurofunctional data to support this thesis but based on relevant literature it is highly probable that what we observed was the consequence of interhemispheric imbalance as a common reversible process in unilateral damage.

An interesting future perspective would be to turn more attention to the transient phenomena that occur following an ischemic event, to investigate their mode of presentation, their course, and the timing of their disappearance. Further studies on this topic would not only allow to confirm the hypothesis of interhemispheric imbalance underlying the occurrence of auditory hallucinations in the case we presented but would also allow to provide useful guidelines for the treatment of symptomatology following a brain event. Such phenomena tend to resolve spontaneously following the specific timing of post-stroke recovery and therefore do not require the setting of specific drug therapy.

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