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Acute loss of psychic self-activation after cardiac arrest and delayed bilateral pallidal lesions on brain MRI

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ABSTRACT

The delay between cardiac arrest and brain MRI is usually extremely different in the few cerebral imaging studies assessing the affected brain areas. We report an unusual case of loss of psychic self-activation appeared immediately after a cardiac arrest in a middle age patient. The first brain MRI, one month after the vascular event, did not show the classical lesions typically reported, such as lesion of the caudate nucleus or the globus pallidus. Two years later, although the cognitive performances of our patient were improved, a second brain MRI demonstrated bilateral pallidal lesions, suggesting a possible mechanism with delayed hypoxic lesions.

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Introduction

Despite many prior neuroimaging studies after cardiac arrest, a clear link has not been established between imaging findings and cognitive outcomes. Part of the problem lies in the variable delays of imaging after cardiac arrest, ranging from 1 day to 10 months in various studies. Another problem is the paucity of studies; only four cases of serial MRIs after cardiac arrest have been described. (Falini et al., 1998; Kano et al., 2006; Konaka, Miyashita, & Naritomi, 2007). One patient performed four brain MRI between 2 days and 7 weeks after cardiac arrest (Falini et al., 1998) and the three other patients performed two brain MRI between 1 and 17 days (Kano et al., 2006; Konaka et al., 2007). Three out of these four cases demonstrated delayed development of post-ischemic changes, but the last brain MRI of the fourth patient without lesion was performed only 8 days after the cardiac event. Moreover, only three studies have evaluated the brain lesions underlying the neuropsychological deficits, with MRI scans performed after cardiac arrest, from 1 to 47 days (Roine, Raininko, Erkinjuntti, Ylikoski, & Kaste, 1993), from 6 to 22 months (Grubb et al., 2000), and from 4 to 62 months (Horstmann et al., 2010), respectively. No correlation between focal damages on MRI and cognitive performances was found in these three studies. The most common explanation of this discrepancy lies on an extensive brain damage, leading to the combination of several cognitive deficits, including impairment of the memory and the executive functions (Horstmann et al., 2010; Lim, Alexander, LaFleche, Schnyer, & Verfaellie, 2004). Actually, correlations between global cerebral atrophy and memory impairment were found in accordance with this hypothesis (Grubb et al., 2000; Horstmann et al., 2010). However, it remains unclear why focal lesions observed after cardiac arrest do not lead to selective

cognitive deficits linked to the topography of these lesions. Here, we report the case of a man who suffers from loss of psychic self-activation, a cognitive state similar to abulia with mental emptiness. These symptoms appeared immediately after a cardiac arrest, without focal lesion explaining the cognitive deficit one month after the vascular event, but with delayed bilateral pallidal lesions two years later.

Clinical report

A 49-year-old man, with no medical history, suffered an out-of-hospital cardiac arrest. His neighbor initiated cardiopulmonary resuscitation after less than 5 min. The medical team found ventricular fibrillation, persistent after administration of three external countershocks and 7 mg of adrenalin. Restoration of spontaneous circulation was obtained after a venoarterial extracorporeal membrane oxygenation (ECMO) support, one another external countershock and 1 mg of adrenalin. The low-flow was estimated to 90 min. Biological analysis, including hemoglobin and toxic panel, was normal. Angiography revealed a 50% stenosis in the marginal artery. He was supported with ECMO for 7 days and was treated for septic shock due to aspiration pneumonia during 10 days. The first neurologic examination 3 days later showed delirium – with temporo-spatial disorientation and fluctuating level of arousal – and a transient mild right hemiparesis, without aphasic symptoms or any other deficit. Arousal improved during the next few days, but severe apraxia and memory impairment were immediately noticed as soon as the patient was conversational. Brain CT-scan performed at this time was normal. Four months after the cardiac arrest, while he recovered enough to clearly understand our explanations, he

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gave his written consent to participate in this study (ClinicalTrials.gov ID: NCT01304576), which was approved by an independent ethics committee.

During the follow-up, the spontaneous speech was coherent but less fluent. He said he had no thoughts about anything and showed affective indifference towards his family. He never expressed any anxiety or significant depressive affect. The only compulsive activity involved food ingestion, but without any interest in this activity. Although he was very active in his professional and familial life before the cardiac arrest, he could spend hours seating without speaking or taking any initiative. His wife described a major inertia, needing her to start actions for him, such as washing and dressing.

Methods

Our patient underwent a series of standardized cognitive tests, administered by the same neuropsychologist (DP), over three sessions, 40 days after cardiac arrest, 5 months and 2 years later (see [Table 1](#) for details).

A clinical brain 1.5T MRI (Avanto, VB17 software version, Siemens healthineer, Erlangen, Germany) was performed 30 days after cardiac arrest, using a standardized procedure, including 3D T2 Flair weighted imaging (slice thickness 1 mm, TR 5000 ms, TE 355 ms), axial gradient echo sequences imaging (4 mm, TR 945 ms, TE 19.1 ms), axial tensor imaging (4 mm, TR 7900 ms, TE 108 ms), and axial T1 weighted imaging (4 mm, TR 539 ms, TE 12 ms). A second brain MRI with the same machine was performed 2 years later according to the same acquisition parameters, at the exception of the gradient echo sequences replaced by T2 star weighted angiography (SWAN).

Results

Neuropsychological results are summarized in [Table 1](#). Scores were pathological below the 5th percentile. Cognitive tests demonstrated verbal episodic memory deficit with a significant improvement during the two years follow-up period: Cued recalls were better, demonstrating a real enhancement of the cue efficiency. Cognitive executive deficit was obvious over the three sessions, affecting reasoning, flexibility, inhibition and generation capacities, as revealed by the WCST, the TMT, the Stroop test and verbal fluencies, respectively. A slight improvement was noticed, especially for the WCST and the TMT. According to the Apathy Inventory filled by himself and by his wife, he was more aware of his difficulties at the last session of tests.

First brain MRI showed a circumscribed flair high-signal intensity localized in the anterior part of the left putamen ([Figure 1\(a\)](#)) but no other lesion to explain the major inertia. Diffusion tensor imaging did not find any acute abnormalities. Although axial gradient echo sequences showed a symmetrical bilateral pallidal low-signal intensity ([Figure 1\(c\)](#)), CT-scan demonstrated no argument for recent, especially hemorrhagic, lesions. Two years later, a symmetrical bilateral pallidal flair high-signal intensity was clearly apparent ([Figure 1\(b\)](#)), while the SWAN low-signal intensity appeared to be more extensive, involving the whole lenticular nuclei ([Figure 1\(d\)](#)). The hypothesis of neurodegeneration with brain iron accumulation (NBIA) led to a complete blood metabolic assessment without any argument for

neuroferritinopathy or aceruloplasminemia: plasma iron concentration, plasma ferritin level and serum ceruloplasmin were normal.

Discussion

We report the brain MRI results in a 49-year-old man 30 days and 2 years after cardiac arrest and the detailed analysis of his cognitive abilities over two years. To summarize, our patient suffered from a typical loss of psychic self-activation (Laplaine, 1990), with an improved but persistent deficit over the time. Surprisingly, neuroimaging did not support any explanation for this syndrome in the first place, but only later during the follow-up, with the late appearance of the bilateral pallidal lesions. According to this result, two questions need to be resolved. First, what are the classical lesions observed in case of loss of psychic self-activation, or similar syndromes? Second, is it possible that a mechanism of delayed hypoxic lesions could explain this discrepancy?

Loss of psychic self-activation is sometimes compared to pure psychic akinesia, abulia or athymormia (Habib, 2004). This behavioral impairment shares common features with apathy, such as a lack of motivation, but is mainly characterized by feelings of mental emptiness (Laplaine, 1990). Bilateral pallidal lesions are demonstrated in most cases (Kaphan et al., 2014), although bithalamic infarction (Engelborghs, Marien, Pickut, Verstraeten, & De Deyn, 2000) and bilateral infarct in the caudate nuclei (Rodier, Tranchant, Mohr, & Warter, 1994) have been reported. Interestingly, isolated lesions of the putamen had never been associated with this syndrome. In a metaanalysis of 240 cases with basal ganglia lesions, 20 patients with isolated putaminal lesions did not suffer from any behavioural disorder, although 11 out of 43 patients with isolated lesions of the caudate nucleus and 4 out of 17 patients with isolated lesions of the globus pallidus demonstrated abulia (Bahtia & Marsden, 1994). In a recent review of neuroimaging studies regarding anatomical correlates of apathy, basal ganglia lesions involved caudate nucleus, nucleus accumbens, ventral pallidum, and medial thalamic nuclei, but not the putamen (Le Heron, Apps, & Husain, 2017). In our patient, it seems unlikely that initial putaminal lesion could explain symptoms, while a correlation with the bilateral pallidal lesions 2 years later seems more accurate. Then, our case raises the question about delayed hypoxic lesions depending on the cardiac arrest.

Cognitive deficits after cardiac arrest result from damage to grey matter regions vulnerable to hypoxia, such as the hippocampus (Horstmann et al., 2010), but also basal ganglia (Choi et al., 2010) and white-matter regions (Van der Eerden et al., 2014). Cortical, subcortical and white-matter changes in MRI studies at the acute stage of anoxic-ischemic encephalopathy may appear within 7 days of brain insult (Chalela, Wolf, Maldjian, & Kasner, 2001). Interestingly for our purpose, experimental studies demonstrated delayed excitotoxicity in selectively vulnerable neurons leading to the delayed development of pathological changes (Lin, 2013). Delayed post-hypoxic leukoencephalopathy is a rare condition, characterized by delayed cognitive deterioration after an average symptom-free period of 2 weeks following hypoxemia, and delayed extensive bilateral MRI white-matter abnormalities (Lin, 2013). A possible mechanism may relate to the arrest of the replacement of myelin-related proteins, which half-life range

Table 1. Results of the standardized neuropsychological assessment.

Cognitive function	Test	Max	Score (40 days)	Score (5 months)	Score (2 years)
Global efficiency	MMSE	30	19*	24	28
Praxis	Praxis evaluation battery	8	7	7	8
	Rey copy	36	ND	28	32
Verbal memory	Immediate recall	16	0	14	14
	FCSRT Sum of 3 free recall	48	ND	2*	8*
	FCSRT Sum of 3 total recall	48	ND	19*	30*
	FCSRT Differed free recall	16	ND	0*	6*
	FCSRT Differed total recall	16	ND	4*	13*
Working memory	Digit span (forward/backward)	NA	4/4	8/8	7/3*
	Spatial span (forward/backward)	NA	4/4	5/4	5/4
Cognitive Executive functions	WCST Number of categories produced	6	ND	3*	5
	WCST Number of errors and perseverative errors	NA	ND	41*	25*
	TMT Part A (sec.)	NA	52	28	24
	TMT Part B (sec.)	NA	failed	87	77
	TMT Total number of errors	NA	NA	0	0
	Stroop Naming time (sec.)	NA	138*	87*	86*
	Stroop Reading time (sec.)	NA	68*	53*	48
	Stroop Interference time (sec.)	NA	>240*	180*	152*
	Stroop Total number of errors	NA	NA	0	0
	Literal verbal fluency	NA	1*	5*	8*
	Categorical verbal fluency	NA	3*	12*	8*
Behavioral executive deficit – DBI (intensity)	Reduction of activities	12	ND	8*	ND
	Irritability	12	ND	6*	ND
	Hyperactivity	12	ND	2	ND
	Lack of anticipation	12	ND	8*	ND
	Perseverations	12	ND	4*	ND
	Lack of interest	12	ND	8*	ND
	Euphoria	12	ND	4*	ND
	Disorders of sexual conduct	12	ND	0	ND
	Anosognosia	12	ND	8*	ND
	Confabulations	12	ND	0	ND
	Disorders of social conduct	12	ND	6*	ND
	Environmental dependency	12	ND	6*	ND
Apathy	Apathy inventory (patient/wife)	36	0/ND	6/15	32/32
Mood disorder	HARS	56	0	0	0
	MADRS	36	4	1	11

MMSE = Mini Mental State Examination; FCSRT = French adaptation of the Free and Cued Selective Recall Reminding Test; WAIS-III = Wechsler Adult Intelligence Scale – 3rd edition; WCST = Wisconsin Card Sorting Test; TMT = Trail Making Test; sec. = seconds; DBI = Dysexecutive Behavior Inventory (intensity score), HARS = Hamilton Anxiety Rating Scale; MADRS = Montgomery and Asberg Depression Rating Scale; * = pathologic (<5th percentile); NA = not applicable; ND = not done.

between 19 and 22 days (Meyer, 2013). However, there is occasional bilateral globus pallidus necrosis attributed to prolonged hypoxemia, especially after anemia or intoxication, for example, carbon monoxide intoxication (Prockop & Chichkova, 2007). In this condition, the asymptomatic period was observed up to 240 days (Prockop & Chichkova, 2007). The main explanation lies in the vulnerability of poor vascularization and watershed areas between two sources of blood supply, which is the case of the globus pallidus (Prockop & Chichkova, 2007). Moreover, delayed damage appearing after cardiac arrest may be related to a secondary ischemic injury (Lin, 2013). In our patient, an asymptomatic cognitive period could be masked by resuscitation procedures. The long period of low-flow and hypotension may explain the consecutive bilateral pallidal lesions. Considering the SWAN signal abnormalities demonstrated by the second brain MRI, we cannot exclude a predisposing factor, potentially responsible for the unusual evolution of cognitive symptoms and their neural correlates. It remains unclear why these lesions were not apparent on the brain MRI one month later, although the cognitive deficit was apparent earlier. One possible explanation could be that the initial small abnormalities on gradient echo sequences match with hemorrhagic conversion, despite a normal first brain CT scan, and that a secondary

process involving glial reaction or fibrosis led to the Flair signal abnormalities on the second brain MRI.

Several limitations have to be mentioned. The first one is the lack of neuroimaging between one month and two years (as well as prior to one month). So, it is not possible to determine the exact time of appearance of the pallidal lesions, during this time period. Second, gradient echo and SWAN sequences are not comparable enough to analyze the evolution of hemorrhagic lesions. Finally, our study is a single subject case report and suffered from limitations inherent to this kind of study.

Our case provides evidence for delayed basal ganglia lesions despite acute cognitive impairment, even one month after cardiac arrest. Serial MRI data in patients suffering from cardiac arrest, but also other various neurologic injuries such as concussion or anoxic brain injuries, may be useful to clarify the pathophysiology of anoxic mechanisms and the neuropsychological correlates.

Disclosure statement

No potential conflict of interest was reported by the authors.

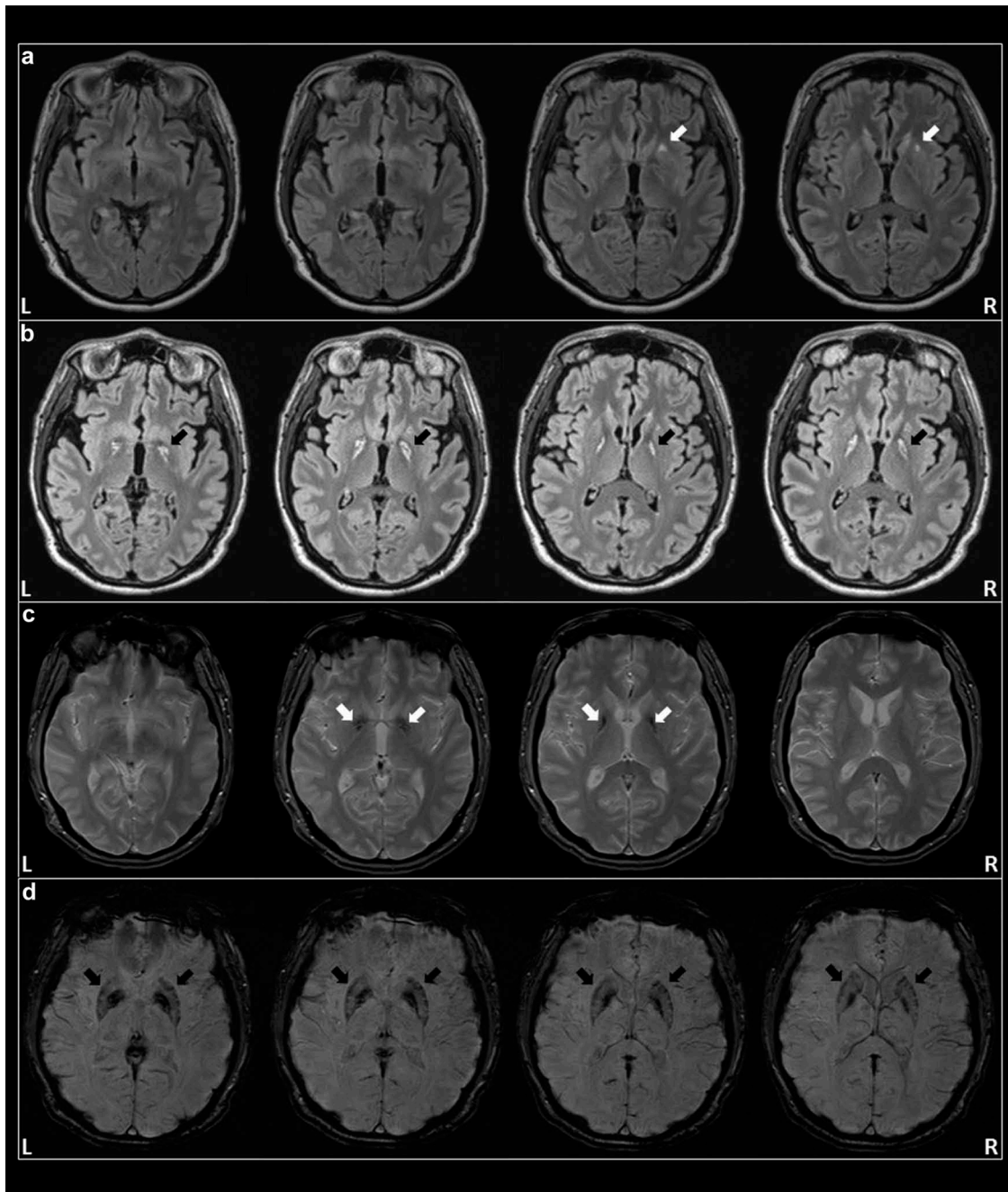


Figure 1. Axial cerebral MRI: [To view this figure in color, please see the online version of this journal].

(a) performed at 30 days and showing a circumscribed high-signal intensity localized in the anterior part of the left putamen (white arrows); (b) performed 2 years later and showing a symmetrical bilateral pallidal high-signal intensity (black arrows), in addition to the lesion in the left putamen; (c) gradient echo sequences performed at 30 days and showing small symmetrical bilateral pallidal low-signal intensity (white arrows); (d) susceptibility weighted imaging performed 2 years later and showing increasing symmetrical bilateral low-signal intensity involving the all lenticular nucleus on both sides (black arrows). L = left; R = right

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