Evidence for Brain Activation in Patients With Takotsubo Cardiomyopathy

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Background: It remains to be elucidated whether brain activity is altered in takotsubo cardiomyopathy.

Methods and Results: We measured cerebral blood flow (CBF) in 3 consecutive patients with takotsubo cardiomyopathy using 99mTc ethyl cysteinate dimmer single photon-emission computed tomography (SPECT) in the acute and chronic phases. In all patients, CBF was significantly increased in the hippocampus, brainstem and basal ganglia and significantly decreased in the prefrontal cortex in the acute phase, which changes subsided in the chronic phase with full recovery of cardiac wall motion.

Conclusions: These results provide the first direct evidence for brain activation in takotsubo cardiomyopathy. (Circ J 2014; 78: 256–258)

Key Words: Brain, SPECT, Stress, Takotsubo cardiomyopathy

Takotsubo cardiomyopathy is a reversible cardiac wall motion abnormality without significant coronary artery diseases and is typically preceded by emotional or physical stress. However, it remains unknown whether brain activity is altered in takotsubo cardiomyopathy. In the present study, we thus examined cerebral blood flow (CBF), a well-established index of brain activity, in 3 patients with takotsubo cardiomyopathy using single photon-emission computed tomography (SPECT).

Methods
(See Supplementary File 1)

Results
A preceding stressor was present in all 3 patients (Table S1). Only patient 3 suffered from severe pain in the left intercostal space at onset; patients 1 and 2 did not have overt chest pain. In all 3 patients, we were able to confirm normalization of cardiac wall motion in the chronic phase within 1 month of onset, using left ventriculography in patient 1 (Figures 1A,B) and echocardiography in patients 2 and 3 (data not shown). Notably, the SPECT images demonstrated significant CBF increase in the hippocampus, brainstem and basal ganglia and significant CBF decrease in the prefrontal cortex in the acute phase in all 3 patients (Figures 1C,E,G), which changes gradually subsided but were still present in the chronic phase (Figures 1D,F,H). Indeed, the number of voxels with significant CBF decrease was comparable between the 2 phases (Figure 2A), whereas that with significant CBF increase was significantly decreased in the chronic phase (Figure 2B).

Discussion
The novel findings of the present study are: (1) brain activation is associated with takotsubo cardiomyopathy and (2) recovery of the cardiac wall motion abnormality precedes that of brain activation. To the best of our knowledge, this is the first study providing direct evidence for brain activation in takotsubo cardiomyopathy.

Although brain activation has been implicated in takotsubo cardiomyopathy, direct evidence for the notion remains to be examined. Cardiac images, such as magnetic resonance imaging or myocardial SPECT, have been reported in the diagnosis of takotsubo cardiomyopathy. In the present study, using brain SPECT, we were able to demonstrate for the first time brain activation in patients with takotsubo cardiomyopathy. Indeed, brain activity patterns such as CBF increase in the hippocampus, brainstem and basal ganglia and CBF decrease...
in the prefrontal cortex were consistently observed in all the patients. Acute stress suppresses the prefrontal cortex but activates the subcortical regions (e.g., the hippocampus, brainstem and basal ganglia), which was noted in our patients with takotsubo cardiomyopathy, indicating the involvement of acute brain stress in the pathogenesis of the disorder.

Although acute chest pain associated with takotsubo cardiomyopathy, which is a significant physical stress, could affect brain activity, only patient 3 suffered from overt chest pain. Thus, preceding emotional or physical stress, which had occurred for all 3 patients, may be the major inducer of brain activation in takotsubo cardiomyopathy.

However, acute stress is not always associated with takotsubo cardiomyopathy. One of the hypotheses for the pathophysiology of takotsubo cardiomyopathy is abnormal sympathetic arousal with or without a stressor. Stress activates the sympathetic nervous system and brain regions associated with sympathetic arousal.
brainstem and basal ganglia has been reported to be associated with sympathetic arousal.\(^7\) Moreover, sympathetic arousal is induced not only by stress but also by other causes such as exercise and pheochromocytoma, which have also complicated takotsubo cardiomyopathy.\(^8,9\) Thus, the possible involvement of sympathetic arousal in the pathophysiology of takotsubo cardiomyopathy may explain that acute stress is not always associated with the condition.

Furthermore, brain activation remained to some extent even after full recovery of cardiac wall motion, suggesting a long-lasting psychological stress in takotsubo cardiomyopathy.\(^10,11\) In this sense, stress management such as cognitive behavioral therapy may be important for the management of patients with takotsubo cardiomyopathy.\(^12,13\)

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Disclosures

None.

References


Supplementary Files

Supplementary File 1

Methods.

Table S1. Characteristics of 3 patients with takotsubo cardiomyopathy