We thank Dr Madias for his interest and valuable comments on our work. In our study with single-photon emission computed tomography (SPECT), we were able to demonstrate for the first time an increase in cerebral blood flow (CBF) in the hippocampus, brainstem and basal ganglia and decreased CBF in the prefrontal cortex at 1–4 days after onset, which diminished but still partially remained at 28–39 days after onset, in the 3 consecutive patients with takotsubo cardiomyopathy. Thus, we agree with Dr Madias that a third assessment of CBF in the more chronic phase may provide further insights into the potential brain activation at baseline in patients who are fated to develop takotsubo cardiomyopathy in response to acute stress. We also would like to respond to Dr Madias’s valuable 5 additional comments as follows.

First, activation of the subcortical regions and deactivation of the prefrontal cortex under acute stress have been recently noted. Thus, the CBF pattern noted in our study may not be specific for takotsubo cardiomyopathy. Interestingly, in our study, the CBF alterations in takotsubo cardiomyopathy persisted for 1 month after onset, suggesting that the disorder may not be solely associated with acute stress. It remains to be examined in future studies whether brain activation in patients with takotsubo cardiomyopathy is similar to that in those with other acute stresses (eg, acute coronary syndrome).

Second, brain SPECT may be useful for the follow-up of patients with takotsubo cardiomyopathy to detect those at risk of its recurrence. In our study, brain activation/deactivation remained to some extent even after full recovery of cardiac wall motion, suggesting an involvement of long-lasting psychological stress in the disorder. Recurrence of takotsubo cardiomyopathy has been reported in patients under repeated stress. Thus, brain SPECT may be a useful tool for detecting patients at potential risk for recurrence of the disorder.

Third, because cognitive behavioral therapy can exert beneficial effects on the brain and the heart, such therapy could ameliorate the CBF alterations in takotsubo cardiomyopathy and reduce the likelihood of recurrence of the disorder. Again, brain SPECT could also be useful for monitoring the efficacy of cognitive behavioral therapy in takotsubo cardiomyopathy.

Fourth, echocardiography is a non-invasive method of detecting takotsubo cardiomyopathy, although invasive cardiac catheterization is commonly needed to differentiate between acute coronary syndrome and takotsubo cardiomyopathy. In this respect, a combination of echocardiography and brain SPECT could be a novel non-invasive way of more accurately diagnosing takotsubo cardiomyopathy, although this notion needs to be tested in future studies.

Fifth, of interest, animal models of takotsubo cardiomyopathy have already provided evidence for the involvement of stress or epinephrine in the pathogenesis of the disorder. However, the major limitation of the animal models with takotsubo cardiomyopathy is that there are fundamental differences in the structure of the brains of animals and humans. Thus, the findings obtained in the animal models of takotsubo cardiomyopathy should be carefully interpreted and translated into the clinical setting.

Disclosures
Conflict of interest: None.

References
11. Craig AD. A rat is not a monkey is not a human: Comment on Mogil. Nat Rev Neurosci 2009; 10; 466.

Hideaki Suzuki, MD, PhD
Yasuharu Matsumoto, MD, PhD
Hiroaki Shimokawa, MD, PhD
Department of Cardiovascular Medicine, Tohoku University Graduate School of Medicine, Sendai, Japan

(Related online January 16, 2014)