Proceedings of the 9th World Congress on Electrical Engineering and Computer Systems and Sciences (EECSS'23)
Brunel University, London, United Kingdom – August 03-05, 2023
Paper No. ICBES 131
DOI: 10.11159/icbes223.131

Remodelling of Cerebral FDG Uptake Kinetics in An Acute Stress-Induced Takotsubo-Type Rat Model

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Extended Abstract

Takotsubo cardiomyopathy (TTC), also known as stress cardiomyopathy, was first described in the 1990s in Japan. 85% of the reported cases are post-menopausal women, with sudden and unexpected emotional or physical stress causing an excessive release of catecholamines inducing symptoms similar to a myocardial infarction but without obstruction of the coronary arteries [1]. Until recently TTC was considered transient but recent studies have demonstrated incomplete reversibility of the stress-induced cardiomyopathy and that TTC is a life-threatening cardiomyopathy [2] with high risk of mortality during the acute phase of the disease, increased long-term vascular mortality and high risk of reoccurrence.

Several studies have reported changes in functional brain connectivity using MRI in TTC. Specifically, a reorganization of cortical and subcortical networks has been shown, including areas associated with emotional response and autonomic regulation [3]. Here, using Positron Emission Tomography with glucose analogue, 2'-deoxy-2'-[18F]fluoro-D-glucose (FDG), we have performed a longitudinal study in n=5 female Wistar rats that were intraperitoneally injected with isoprenaline (ISO, 50 mg/kg), to create a rat model mimicking the catecholamine rush described in TTC patients [4]. This study aimed at identifying disease-induced brain FDG uptake changes and their connection with myocardial FDG remodelling both in the acute (2h) and "recovery" (7d) phases of the disease. Employing registration with brain atlas, bull's eye plots and 2-tissues compartment modelling of FDG using PMOD software allowed us to create a longitudinal database of the major FDG kinetic behaviours (kinetic rate constants K1, k2 and k3 and MRGlu). By using inter-regional and inter-temporal Pearson correlations, we were able to identify that 86%, 17%, 47% and 59% of the brain regions were modified in the acute phase for the parameters K1, k2, k3 and MRGlu respectively in comparison with the pre-stress values. During the recovery phases, 16% and 2% of the brain regions remained modified for K1 and k2 respectively. In the heart, we observed a trend towards increased K1 at 2h post-ISO that then returned to pre-stress values, while the decrease in phosphorylation FDG (k3) during the acute phase and increased during the recovery phase. Several inter-organ correlations were observed between the changes in regional cerebral metabolism and in the apical, middle and basal segments of the left ventricle of the heart: 74% of the brain during the acute phase and 2% during the recovery phase. These results highlight the simultaneous, coordinated and non-reversible FDG uptake remodelling of the heart and brain in TTC and open the hypothesis that a dysregulation of autonomic control at the central level might participate in late cardiac dysfunction of TTC.

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