Iron deficiency without anemia is responsible for decreased left ventricular function and reduced mitochondrial complex I activity in a mouse model

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Mots-clés	Cardiomyocyte [8], Complex I [9], Ferric carboxymaltose [10], Iron deficiency [11], Left ventricular function [12], Mitochondrial metabolism [13]
Résumé en anglais	BACKGROUND: Iron deficiency (ID), with or without anemia, is frequent in heart failure patients, and iron supplementation improves patient condition. However, the link between ID (independently of anemia) and cardiac function is poorly understood, but could be explained by an impaired mitochondrial metabolism. Our aim was to explore this hypothesis in a mouse model. METHODS AND RESULTS: We developed a mouse model of ID without anemia, using a blood withdrawal followed by 3-weeks low iron diet. ID was confirmed by low spleen, liver and heart iron contents and the repression of HAMP gene coding for hepcidin. ID was corrected by a single ferric carboxymaltose (FCM) injection (ID + FCM mice). Hemoglobin levels were similar in ID, ID + FCM and control mice. ID mice had impaired physical performances and left ventricular function (echocardiography). Mitochondrial complex I activity of cardiomyocytes was significantly decreased in ID mice, but not complexes II, III and IV activities. ID + FCM mice had improved physical performance, cardiac function and complex I activity compared to ID mice. Using BN-PAGE, we did not observe complex I disassembly, but a reduced quantity of the whole enzyme complex I in ID mice, that was restored in ID + FCM mice. CONCLUSIONS: ID, independently of anemia, is responsible for a decreased left ventricular function, through a reduction in mitochondrial complex I activity, probably secondary to a decrease in complex I quantity. These abnormalities are reversed after iron treatment, and may explain, at least in part, the benefit of iron supplementation in heart failure patients with ID.

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Liens

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