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Kai Zou

University of Massachusetts Boston

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ROUX-EN-Y GASTRIC BYPASS SURGERY REGULATES MITOCHONDRIAL DYNAMICS PROTEINS IN PRIMARY HUMAN MYOTUBES DERIVED FROM SEVERELY OBESE HUMANS

Kai Zou, PhD¹, J. Matthew Hinkley, PhD², Sanghee Park, PhD², Donghai Zheng, PhD², G. Lynis Dohm, PhD², Joseph A. Houmard, PhD²

¹Department of Exercise and Health Sciences, University of Massachusetts Boston; ²East Carolina Diabetes and Obesity Institute, East Carolina University, Greenville, NC

Mitochondrial dynamics including mitochondrial fission (e.g., Dynamin-related protein 1 (Drp1) and Fission 1 (Fis1)) and fusion (e.g., Mitofusin 2 (MFN 2)) regulates mitochondrial homeostasis. Defects in mitochondrial dynamics are suggested to contribute to skeletal muscle mitochondrial dysfunction and insulin resistance associated with severe obesity. Roux-en-Y gastric bypass (RYGB) surgery markedly improves metabolic health as indicated by enhanced substrate oxidation and insulin action in skeletal muscle. However, the underlying cellular mechanisms responsible for these are unclear and could possibly be due to the improvement of mitochondrial dynamics.

PURPOSE: The purpose of this study was to determine whether RYGB surgery improves mitochondria dynamics proteins in primary human myotubes from severely obese humans.

METHODS: Primary skeletal muscle cells were isolated from muscle biopsies obtained from six lean subjects (BMI = 23.4 ± 0.6 kg/m²) and six RYGB patients prior to, 1-month and 7-months after surgery (BMI = 50.2 ± 2.0 , 43.2 ± 2.8 and 35.7 ± 2.2 kg/m², respectively) and were differentiated to myotubes. On day 7 of differentiation, myotubes were harvested for further assessing the expressions of mitochondria dynamics proteins.

RESULTS: Before surgery, Drp1^{Ser616} phosphorylation and Fis1 expression were significantly higher in myotubes derived from severely obese patients when compared to lean controls (41% and 26%, respectively, $P < 0.05$). While there were no improvements at 1-month post-surgery, Drp1^{Ser616} phosphorylation and Fis1 expression were significantly decreased in myotubes from severely obese humans at 7-months post-surgery (Pre vs. 7-months post: 0.046 ± 0.004 vs. 0.035 ± 0.003 ; 0.023 ± 0.008 vs. 0.014 ± 0.003 AU; respectively, $P < 0.05$), and not statistically different from lean controls. However, MFN2 expression did not change post-surgery in comparison to pre-surgery.

CONCLUSION: These data suggest that RYGB surgery reduces obesity-induced rise in mitochondrial fission, but not fusion in primary human myotubes derived from severely obese humans.

Contact:

Kai Zou
University of Massachusetts Boston
kai.zou@umb.edu