IP3 receptor blockade restores autophagy and mitochondrial function in skeletal muscle fibers of dystrophic mice

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© 2018 Duchenne muscular dystrophy (DMD) is characterized by a severe and progressive destruction of muscle fibers associated with altered Ca2+ homeostasis. We have previously shown that the IP3 receptor (IP3R) plays a role in elevating basal cytoplasmic Ca2+ and that pharmacological blockade of IP3R restores muscle function. Moreover, we have shown that the IP3R pathway negatively regulates autophagy by controlling mitochondrial Ca2+ levels. Nevertheless, it remains unclear whether IP3R is involved in abnormal mitochondrial Ca2+ levels, mitochondrial dynamics, or autophagy and mitophagy observed in adult DMD skeletal muscle. Here, we show that the elevated basal autophagy and autophagic flux levels were normalized when IP3R was downregulated in mdx fibers. Pharmacological blockade of IP3R in mdx fibers restored both increased mitochondrial Ca2+ levels and mitochondrial membrane potential under resting conditions. Interestingly, mdx mitochondria changed from a fission to an elongated s