

**Author: Azizeh Samadzadeh**

**Title of Thesis:**

**Effect of Moderate-intensity Exercise Training Protocol on Ketamine-induced Adverse Impacts on Mitochondrial Fission and Fusion in Mature Male Rats**

Ketamine (KET) is a dissociative hallucinogenic tranquilizer being abused mostly by teenagers and young adults. The current study was set out to enlighten the effect of moderate-intensity exercise training (MIET) protocol on KET-induced adverse impacts on mitochondrial fission and fusion in testicular tissue of mature male rats. Twenty-four adult male Wistar rats were divided into four equal groups including non-treated control group, KET group receiving 50 mg/kg/day KET intra-peritoneally (IP) for 8 weeks, withdrawal group receiving KET (50 mg/kg/day; IP) for 8 weeks followed by a 8-week drug-free period and KET-MIET group receiving KET (50 mg/kg/day; IP) for 8 weeks followed by a 8-week MIET (moderate-intensity running on a treadmill once daily [5 days/week]). Mitofusin (Mfn) 1, Mfn 2, optic atrophy-1 (OPA1), mitochondrial fission 1 protein (FIS1) and dynamin-related protein 1 (Drp1) mRNA and microtubule-associated protein 1A/1B-light chain 3 (LC3)-1 synthesis levels in testicular tissue were analyzed using reverse transcription polymerase chain reaction and immunohistochemistry techniques, respectively. The MIET down-regulated FIS1, Drp1 and LC3-1 and up-regulated Mfn 1, Mfn 2 and OPA1 compared to KET and withdrawal groups. These findings add weight to the evidence that MIET can inhibit KET-induced mitophagy in testicular tissue of mature male rats through expression re-regulation of genes involved in mitochondrial fission and fusion.

**Keywords:** Exercise; Ketamine; Mitochondrial fission-fusion; Rat