

Metformin Potentiates Glutamate-Stimulated Catecholamines Release in Rat Brain

Reniel Suarez Gonzalez,¹ Yousef M. Aljohani,² Kenneth Kellar,³ and Ghazaul Dezfuli²

¹Georgetown University; ²Georgetown Univ; and ³Georgetown Univ School of Medicine

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Metformin, the most-widely prescribed anti-hyperglycemic agent in the treatment of type-2 diabetes, has recently attracted attention for its effects beyond that of glucose normalization. Of particular interest is metformin's effects in the CNS including but not limited to effects on oxidative stress, cellular senescence, and brain bioenergetics. Despite these important effects, few studies have focused on metformin's effects on neurotransmission in the brain. In this study, we employed an *in vitro* assay to investigate metformin's effect on glutamate-stimulated catecholamine release in the brain of 2-3 months Fischer 344 rats. Particularly, we focused on measuring *in vitro* dopamine (DA) release in slices from the olfactory tubercle and striatum, and norepinephrine (NE) release in slices from the cerebral cortex. Our results show that metformin significantly augments both NMDA mediated glutamate-stimulated DA & NE release in the striatum and olfactory tubercle, and cerebral cortex respectively. While further studies are needed to elucidate the precise mechanism underlying metformin's augmentation of catecholamine release, our findings shed light on a novel CNS effect of metformin. This discovery underscores the potential of metformin to modulate neurotransmission, opening avenues for further exploration and clinical implications.