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Targeting peroxisome proliferator-activated receptors (ppar) for the treatment l-dopa-induced dyskinesias

Andrea Giuffrida

University texas Health Science Center, USA

Abstract

Long-term administration of L-DOPA to Parkinson's disease (PD) patients is accompanied by fluctuations in its duration of action and chorea-like motor complications known as L-DOPA-induced dyskinesias (LID). As L-DOPA is the most effective treatment for PD, there is a strong need to identify new pharmacological targets to control LID while maintaining L-DOPA beneficial effects.LID can be modeled in rats with unilateral 6-OHDA lesions via chronic administration of L-DOPA, which induces increasingly severe axial, limb and oro-facial abnormal involuntary movements (AIMs). Previous studies in our laboratory showed that systemic administration of the PPAR gamma agonist rosiglitazone (5 & 10 mg/kg, i.p.) ameliorated axial, oral and limb AIMs without reducing L-DOPA's anti-parkinsonian activity. Rosiglitazone also attenuated the L-DOPA-induced elevation of dyskinesia (Zif-268 and prodynorphin) and inflammation (COX-2) markers within the denervated striatum. Interestingly, chronic L-DOPA significantly increased the PPAR beta/delta isoform in dyskinetic rats and this elevation was reversed by rosiglitazone treatment. These data suggest that targeting PPAR gamma/delta receptors can ameliorate dyskinetic symptoms, possibly by reducing the underlying neuroinflammatory response observed in PD.

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Biography

Dr. Andrea Giuffrida received his Ph.D from the University of Catania, Italy and completed his postdoctoral studies at the Neuroscience Institute in San Diego and at the University of California Irvine. He is a former AAAS Science & Technology Policy Fellow, and he is currently an associate professor in the Department of Pharmacology at the University of Texas Health Science Center San Antonio and Director of Biomedical Research Development in the Office of the VP for Research. He has published more than 50 papers in peer-reviewed journals and serves as field editor for International Journal of Neuropsychopharmacology.

giuffrida@uthscsa.edu