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Review Article

A Novel Insight into Signaling Pathways, Animal Models, and Interventions in Psychological Stress Induced Muscle Atrophy

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Abstract

A sedentary, inactive, and stressful lifestyle aggravates chronic psychological and stressful conditions in human health. Chronic stress may lead to prolonged release of glucocorticoids like stress hormones and proinflammatory mediators, which may affect the skeletal muscle mass and strength in humans as well as in rodents and eventually lead to muscle atrophy. IGF1/Akt/mTOR decreased when exposed to synthetic stress hormones like dexamethasone. While catabolic factors like FoxO1 and FoxO3a/MSTN/REDD1/KLF15/P85 increased in stress-induced muscle atrophy. IL-1/IL-6/TNFα was also activated under stressed conditions and has been reported to induce muscle wasting. Currently, only a few animal models of stress-induced muscle atrophy have been developed. The review focuses on the mechanism of glucocorticoid release via psychological stress leading to activation of various signaling pathways like IGF-1/Akt, Myostatin, FoxO, REDD1, P85, and inflammatory mediators like TNF-α and IL-1. The review also gives an overview of the animal models of stress induce muscle atrophy along with its manifestations in patients. Lastly, a brief discussion on medical interventions of muscle atrophy is described. This whole compilation of the information at one place will help in further understanding of the mechanisms leading to development of better therapeutics in future.

Keywords: *Psychological Stress; Glucocorticoids; Muscle Atrophy; Muscle Mass*

Abbreviations

ActRIIB: Activin Receptor Like Kinase; ACTH: Adrenocorticotropic Hormone; AT1: Atrogin; BCAA: Branched Chain Amino Acid; BCAT2: Branched Chain Aminotransferase 2; CRF-OE: Corticotropin Releasing Factor Overexpressing; Dex: Dexamethasone; DNA: Deoxyribonucleic Acid; EDL: Extensor Digitorium Longus; eIF4E: Eukaryotic Translation Initiation Factor 4E; 4EBPs: eIf4E Binding Protein; FoxO: Forkhead Box Protein O1; GN: Gastrocnemius; GC: Glucocorticoids; GRB: Glucocorticoid Binding Receptor; GRE: Glucocorticoid Receptor Element; GR: Glucocorticoid Receptor; GSK3β: Glycogen Synthase Kinase 3β; HPA: Hypothalamic Pituitary Adrenal; HSD11β: 11-Beta Hydroxysteroid Dehydrogenase; IGF1: Insulin-Like Growth Factor-1; IR: Insulin Receptor; IRS1: Insulin Receptor Substrate1; IL6: Interleukin 6; IL1: Interleukin1; IL6R: Interleukin 6 Receptor; IKK: IκB Kinase; JAK: Janus Kinase; KLF15: Kruppel-Like-Factor; KO: Knockout; mTOR: Mammalian Target of Rapamycin; MAFbx: Muscle Atrophy F: Box; MSTN: Myostatin; MuRF1: Muscle RING Finger 1; NF: κB: Nuclear Factor Kappa; NEMO: NFκB Essential Modulator; PKB: Protein Kinase B; PI3K: Phosphatidylinositol 3-Kinase; PIP2: Phosphatidylinosi-