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FILIPE REIS SOARES

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O IMPACTO DOS METAIS PESADOS NA PATOGÊNESE E PROGRESSÃO DA DOENÇA DE ALZHEIMER

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Trabalho de Conclusão de Curso apresentado à graduação em Medicina da Escola de Ciências Médicas e da Vida da Pontifícia Universidade Católica de Goiás, sob orientação do professor Dr. Hermínio Mauricio da Rocha Sobrinho.

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O IMPACTO DOS METAIS PESADOS NA PATOGÊNESE E PROGRESSÃO DA DOENÇA DE ALZHEIMER

THE IMPACT OF HEAVY METALS IN THE PATHOGENESIS AND PROGRESSION OF ALZHEIMER'S DISEASE

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Resumo

A doença de Alzheimer (DA) é uma doença neurodegenerativa progressiva e irreversível, relacionada à idade, que leva ao comprometimento cognitivo e da memória. Além da idade e da predisposição genética, outros fatores de risco para o desenvolvimento da DA incluem os fatores ambientais como a exposição a metais pesados, exposições a substâncias tóxicas ocupacionais e a poluição ambiental. Esses fatores podem desempenhar um papel fundamental no início e progressão da doença. O objetivo deste estudo foi descrever as principais alterações fisiopatológicas causadas pelos metais pesados no organismo e sua possível contribuição para o desenvolvimento ou progressão desta doença. **Métodos:** Trata-se de uma revisão bibliográfica narrativa. **Resultados:** A exposição crônica a metais pesados tem se tornado mais comum entre a população mundial à medida que o ritmo agressivo das atividades antrópicas libera quantidades excessivas de metais pesados no meio ambiente. Especialmente os metais pesados não essenciais perturbam a homeostase dos metais essenciais nos níveis celular, tecidual e orgânico. O aumento nos níveis corporais de metais pesados afetam a fisiologia e a imunidade do cérebro, bem como podem contribuir para a formação anormal de espécies reativas de oxigênio no sistema nervoso central e ao acúmulo proteicas tóxicas tais como a proteína β-amilóide e proteína tau induzindo o processo de neurodegeneração cerebral. **Conclusão:** Os metais pesados interagem com a proteína β-amiloide, prejudicam a função da proteína *tau* e causam superprodução de mediadores inflamatórios no cérebro, o que resulta em agregação de placas amiloides no tecido, desestabilização celular e morte neuronal. A perturbação do metabolismo celular, da defesa antioxidante e de respostas imunológicas num cenário de quebra da homeostase dos metais essenciais e acúmulo de metais não essenciais no organismo pode levar ao início e progressão desta doença.

Palavras-chave: Doença de Alzheimer; Metais pesados; Fatores ambientais; Fisiopatologia; Neurodegeneração.

Abstract

Alzheimer's disease (AD) is an age-related, progressive and irreversible neurodegenerative disease that leads to cognitive and memory impairment. In addition to age and genetic predisposition, other risk factors for the development of AD include environmental factors such as exposure to heavy metals, exposure to occupational toxic substances and environmental pollution. These factors can play a key role in the onset and progression of the disease. The aim of this study was to describe the main pathophysiological changes caused by heavy metals in the body and their possible contribution to the development or progression of this disease. Methods: This is a narrative bibliographic review. Results: Chronic exposure to heavy metals has become more common among the world population as the aggressive pace of human activities releases excessive amounts of heavy metals into the environment. Especially non-essential heavy metals disturb the homeostasis of essential metals at the cellular, tissue and organic levels. Increased levels of heavy metals in the body affect brain physiology and immunity, as well as contributing to the abnormal formation of reactive oxygen species in the central nervous system and to toxic protein accumulation such as β-amyloid protein and tau-inducing protein the process of brain neurodegeneration. Conclusion: Heavy metals interact with β-amyloid protein, impair tau protein function and cause overproduction of inflammatory mediators in the brain, which results in aggregation of amyloid plaques in tissue, cell destabilization and neuronal death. Disruption of cellular metabolism, antioxidant defense and immune responses in a scenario of breakdown of essential metals homeostasis and accumulation of non-essential metals in the body can lead to the onset and progression of this disease.

Keywords: Alzheimer's disease; Heavy metals; Environmental factors; Pathophysiology; Neurodegeneration.

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CONCLUSÃO

O excesso de metais está diretamente relacionado às alterações patológicas no tecido cerebral de um indivíduo com DA. A sobrecarga de ferro, além de aumentar a produção de Aβ, gera toxicidade neuronal e comprometimento cognitivo. O cobre, zinco, chumbo e cádmio potencializam a agregação de Aβ. Além disso, o cobre gera dano celular pela produção de EROS; o zinco auxilia na formação de NFTs, inflamação e estresse oxidativo; o chumbo gera um aumento de tau total e hiperfosforilada e na inflamação e o cádmio está envolvido na conformação e auto agregação de tau. A exposição crônica ao manganês resulta em alterações neurodegenerativas e placas Aβ difusas pelo estresse celular. O alumínio interfere na produção, agregação e inibição da degradação de Aβ. Portanto, a perturbação do metabolismo celular, da defesa antioxidante e de respostas imunológicas num cenário de quebra da homeostase dos metais essenciais e acúmulo de metais não essenciais no organismo pode levar ao início e progressão da DA. Os metais pesados interagem com a proteína β-amiloide, prejudicam a função da proteína *tau* e causam superprodução de mediadores inflamatórios no cérebro, o que resulta em agregação de placas amiloides no tecido, desestabilização celular e morte neuronal.

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