Damage-Associated Molecular Patterns and Neuronal Damage Biomarkers in Depression: Systematic Review and Meta Analysis

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Abstract

Aim: We aimed to assess the comparison of these three markers between depressed patients and non-depressed controls.

Methods: We conducted literature search on 3 electronical databases including PubMed, EMBESE, and Web of Science using keyword “S100b AND Depression” and “neuron specific enolase AND Depression” and “HMGB1 AND Depression”. We included comparative studies, cross sectional studies, and case control studies. We excluded studies with irrelevant outcomes and subjects, and with no available full text. 20 eligible studies assessed the level of S100b marker, 6 eligible studies assess the level of NSE, and 3 eligible studies assessed the level of HMGB1. We retrieved data of level of biomarkers in mean±standard deviation (SD) between two groups. We utilized Review Manager Version 5.4.1 software to analyze data.

Results: Findings suggested that our analysis of 20 studies revealed a significant increase in S100b levels among depressed patients compared to healthy controls. (Standardized Mean Difference (SMD): 0.55, Confidence Interval: 0.22-0.89, p=0.001). NSE levels showed no statistically significant difference between the groups across 6 studies (SMD: 0.39, CI: -0.32-1.10; p=0.26). Moreover, HMGB1 levels were also statistically significant difference between the groups in all 3 studies examining this marker (SMD: 1.77, CI: -1.31-4.86; p=0.26). It is important to note that the studies exhibited substantial variation ($I^2 \geq 75\%$), suggesting a need for subgroup interpretation.

Conclusion: This study highlights S100b a potential biomarker for MDD progression. Future research could explore its use in monitoring treatment effectiveness.

Introduction

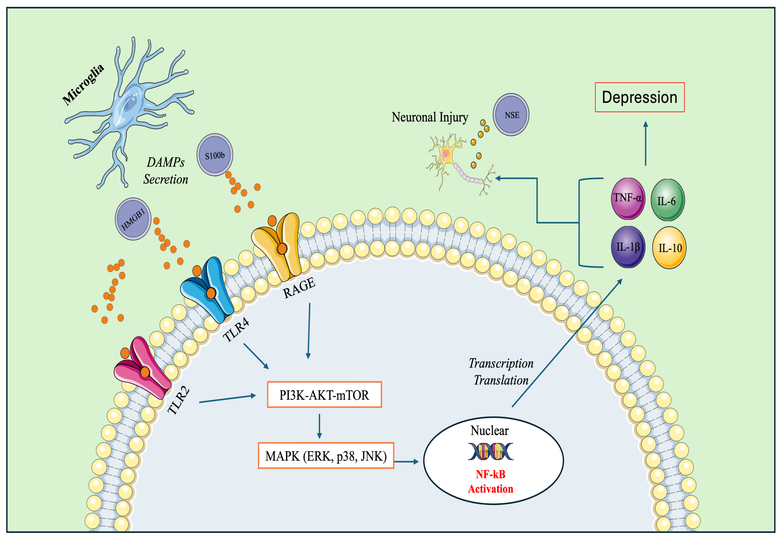

Figure 1. Potential Pathway of Modulation of ω-3 PUFAs on S100β, HMGB1, and NSE in Depression-induced Inflammation

Emerging evidence suggests that neuroinflammation and alterations in neuronal and glial cell function play crucial roles in the development and progression of MDD.[1] MDD induces pathophysiology changes in the brain. Microglia, the innate immune cells residing in the central nervous system (CNS), have been demonstrated to prominently generate inflammatory cytokines to uphold the neurobiological homeostasis.[2]

Damage-associated molecular patterns (DAMPs) released from damaged or stressed cells, like HMGB1 and S100 proteins act as danger signals that activate immune cells that leading to inflammatory responses.[3] Moreover, following chronic inflammation, the presence of elevated NSE levels can serve as an indicator of neuronal damage or injury.[4]

Methodology

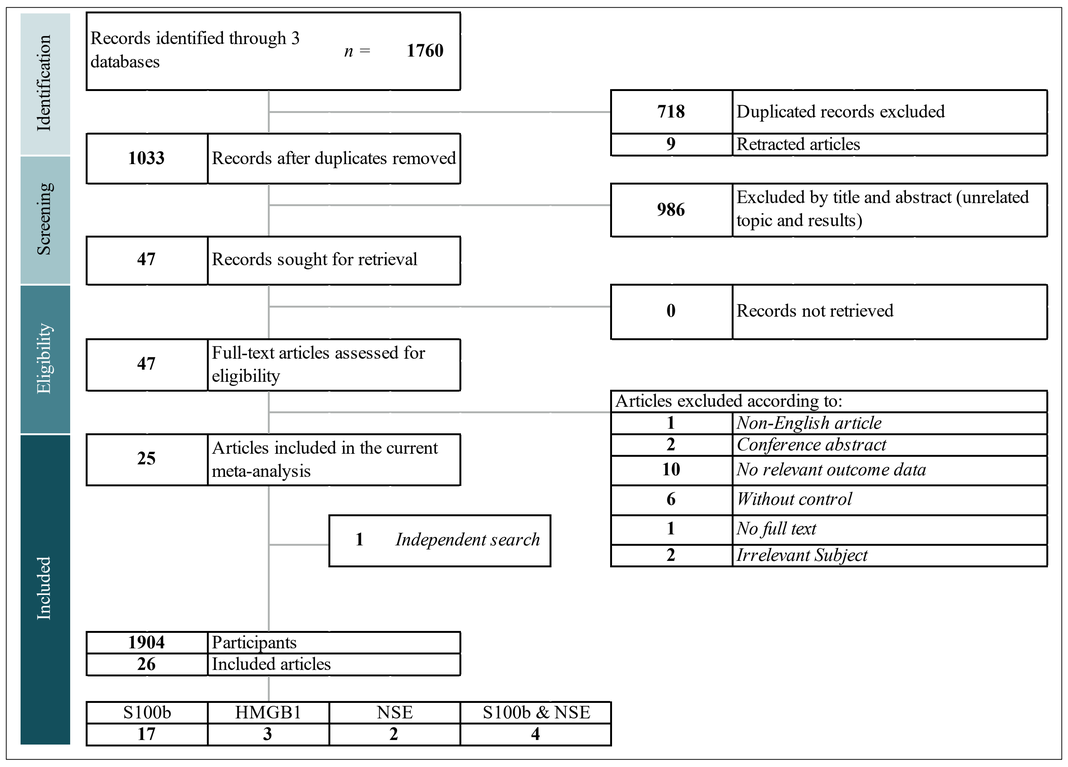

Figure 2. Potential Pathway of Modulation of ω-3 PUFAs on S100β, HMGB1, and NSE in Depression-induced Inflammation

Up to September 5th, 2024, we conducted data search on 3 electronic databases, including PubMed, Web of Science, and Embase. The inclusion criteria for inclusion were as follows: (**1**) Studies that compared relevant biomarkers between depressed patients and non-depressed patients; (**2**) Studies that included a comparison with a healthy control group; and (**3**) Studies that reported data on biomarkers, specifically mean values and standard deviations for each group. By adhering to these criteria, we ensured that the selected studies provided robust and comparable data, enabling a comprehensive analysis of the biomarkers' roles in depression as presented in **Figure 2**.

Results

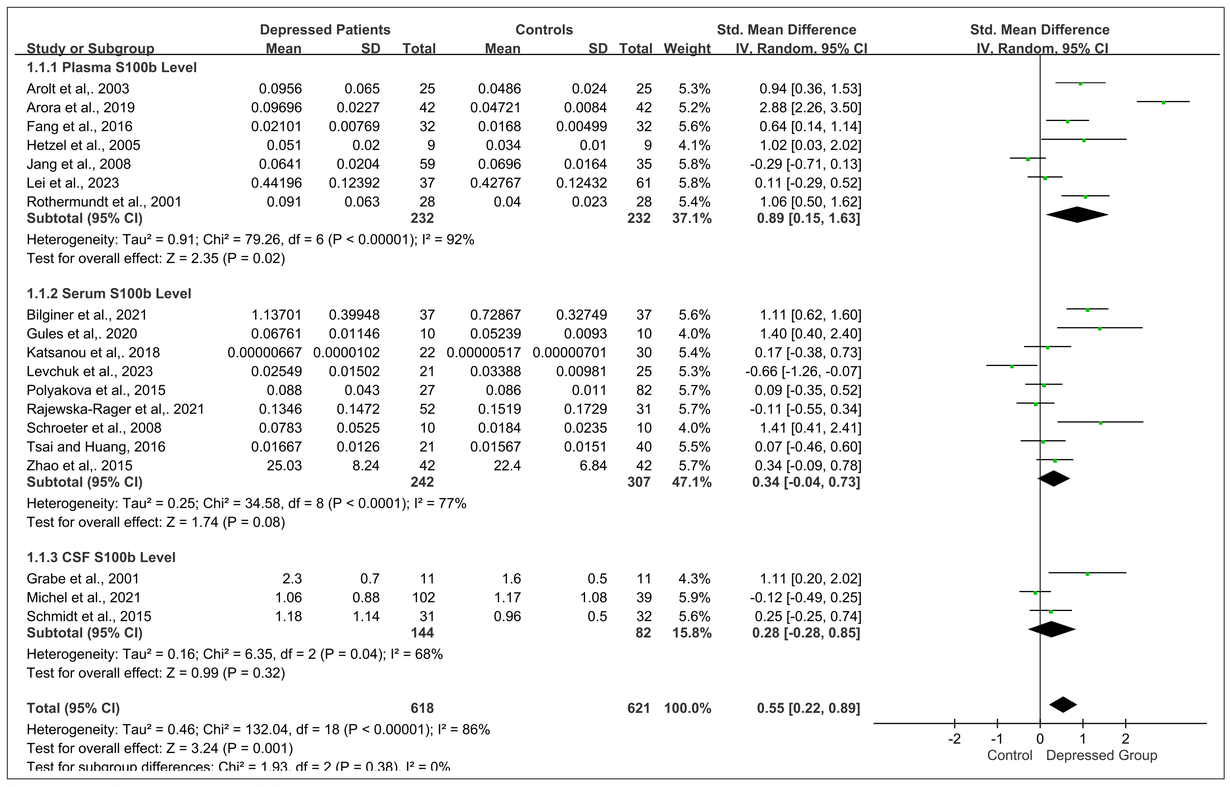

Figure 3. Comparison of S100b level in depressed group and healthy control

Results of meta-analysis show that Increased level of s100b found in depressed persons than healthy control over 20 included studies. Subgroup analysis shows that plasma s100b level is significantly higher compared with serum and CSF s100b level.

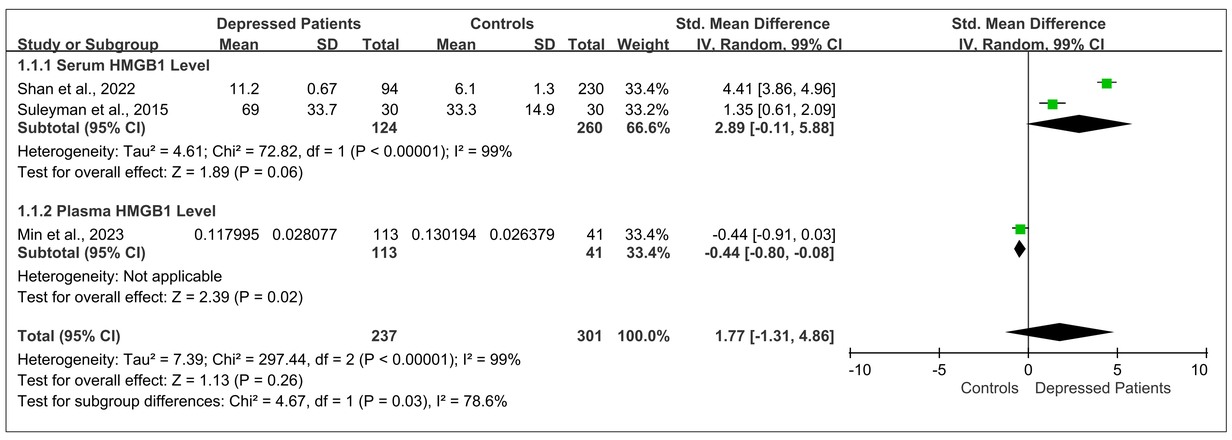

Figure 4. Comparison of HMGB1 level in depressed group and healthy control

Results of meta-analysis show that level of HMGB1 found not significantly higher in depressed persons than healthy control over 3 included studies. Moreover, high heterogenity is presented with >75%.

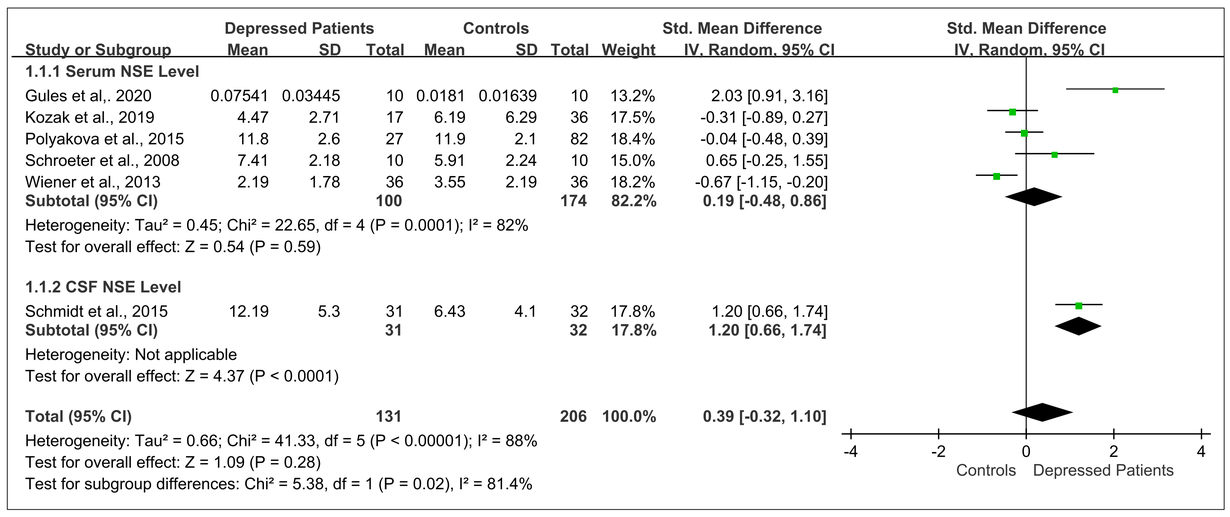

Figure 5. Comparison of NSE level in depressed group and healthy control

Results of meta-analysis show that level of NSE found not significantly higher in depressed persons than healthy control over 6 included studies. Subgroup analysis shows that CSF NSE level found to be significantly higher in depressed group. Moreover, high heterogenity is presented as >75%.

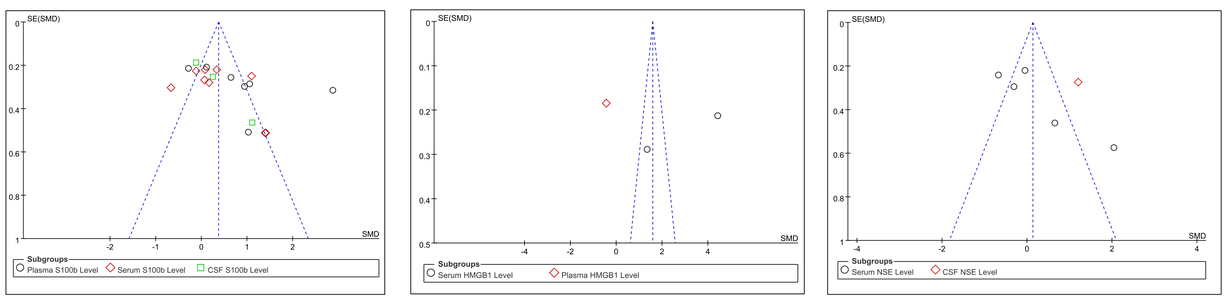

Figure 6. Funnel Plots of Publication bias of (a) S100b (b)HMGB1 (c) NSE

Funnel plots of three analyses present asymmetric distribution that reflect potential publication bias.

Conclusion

This meta-analysis highlights S100b as potential biomarker for MDD progression. Future research could explore their use in monitoring treatment effectiveness for MDD.

References

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