

LETTER TO THE EDITOR / EDİTÖRE MEKTUP

Serum or Plasma? A Methodological Blind Spot in Exercise–BDNF Research

Serum mu Plazma mı? Egzersiz-BDNF Araştırmalarında Metodolojik Bir Kör Nokta

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Dear Editor,

I read with great interest the systematic review by Birinci et al. [1] published in the *Turkish Journal of Sports Medicine*, which elegantly synthesized the effects of physical exercise on brain-derived neurotrophic factor (BDNF) in the elderly. Building upon their valuable evidence synthesis, I would like to highlight a critical methodological blind spot in exercise-BDNF research that affects how we interpret and pool such data. BDNF is widely used as a peripheral biomarker in exercise neuroscience; however, BDNF measured in serum and plasma should not be treated as interchangeable indicators of the same biological signal, particularly in systematic reviews.

Human platelets are a major peripheral reservoir of BDNF and release substantial amounts after activation [2]. Consequently, serum BDNF is strongly influenced by platelet degranulation during coagulation, whereas plasma BDNF depends heavily on residual platelet content and sample-processing conditions. Gejl et al. [3] showed that serum BDNF rose markedly during the first hour of clotting, plasma values varied with centrifugation strategy, and serum and plasma BDNF were not significantly correlated. These findings suggest that the two matrices may reflect analytically and biologically distinct BDNF pools.

This distinction becomes especially important during exercise. Acute exercise alters plasma volume, platelet count, and platelet activation, all of which can influence measured peripheral BDNF independently of neural production. Pareja-Galeano et al. [4] demonstrated that the apparent BDNF response to exercise depended on blood-processing method: after correction for hemoconcentration, increases were detected in whole blood and serum allowed to clot for 24 hours, but not in short-clotted serum or plasma. More recently, Tarassova et al. [5] reported exercise-intensity-dependent increases in serum mature BDNF and platelet counts without a corresponding increase in plasma mature BDNF; arterial-venous measurements also provided no evidence that the serum rise reflected net cerebral BDNF release. Thus, an exercise-associated increase in serum BDNF should not automatically be interpreted as increased brain-derived secretion.

The consequences extend to evidence synthesis. Pooling serum- and plasma-derived estimates without accounting for specimen type may introduce avoidable methodological heterogeneity and obscure biologically meaningful differences. Exercise studies should therefore report specimen type, anticoagulant used, clotting time and laboratory temperature, centrifugation conditions, platelet handling, sampling time relative to exercise, and whether exercise-induced plasma-volume

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shifts were considered. Meta-analyses should extract these characteristics systematically and, when data permit, analyze serum and plasma separately or evaluate specimen type through subgroup or sensitivity analyses.

The need for such standardization is timely. A 2026 scoping review identified substantial deficiencies in re-

porting preanalytical variables relevant to BDNF quantification, including clotting conditions, transport temperature, anticoagulant use, and platelet management [6]. Greater methodological transparency would improve reproducibility and help distinguish true exercise-related biological effects from variation attributable to specimen- type and sample processing.

Conflict of Interest / Çıkar Çatışması

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