

Is Treatment Resistance Sometimes a State Mismatch?

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Abstract

This concept paper examines is treatment resistance sometimes a state mismatch?. It develops an argument drawn from Applied Coherence Medicine, identifies the relevant biological or clinical mechanisms, and considers where that argument may fail. This is a narrative perspective, not a systematic review or an original clinical study.

The central problem

Treatment resistance is a clinical descriptor that can hide multiple phenomena: wrong diagnosis, inadequate dose or duration, nonadherence, comorbidity, drug interactions, severe disease and genuine nonresponse. The coherence framework proposes one additional contributor: an intervention may demand more cognitive, energetic or regulatory capacity than is currently available. This is a conditional hypothesis, not an explanation for every failed treatment.

Mechanisms and causal architecture

Consider a patient in severe insomnia and panic who is prescribed cognitively demanding psychotherapy homework. The intervention may be sound in principle but difficult to execute before attention and sleep improve. In rehabilitation, an excessive exercise load can similarly exceed current tolerance. By contrast, a patient with severe depression may benefit from immediate evidence-based therapy or medication despite poor energy; capacity rhetoric should never serve as a reason to postpone urgent care. The conceptual advance is matching treatment burden, sequence and supports to measurable limitations.

A discriminating example

A patient failing psychotherapy might need a different modality, improved access, higher-quality delivery, medication, treatment of sleep apnea or simply more time. State mismatch is one hypothesis among several. Its value emerges when it predicts a specific adjustment that succeeds without postponing necessary care. A framework that explains every failure after the fact has no meaningful predictive advantage.

Competing explanations and limitations

Existing stepped-care and personalized medicine frameworks already adjust treatment to ability, disease severity and patient preference. The Institute's proposal must be more precise than suggesting that all negative experiences prove state mismatch. Sometimes an intervention is ineffective, harmful, misdiagnosed or applied badly. Escalation can be lifesaving in psychosis, suicidality or acute organ dysfunction. A model that always blames the patient's state is unfalsifiable and ethically unsound.

What evidence would change the interpretation?

A useful comparison is whether baseline sleep, autonomic instability and cognitive load predict adherence and differential outcomes after adjusting for diagnosis. State matching should improve outcomes only if it changes the intervention appropriately, not simply because patients receiving more support do better for nonspecific reasons.

Implications for medical interpretation

For the website, this paper should invite a better clinical question: is the intervention wrong, premature, overly burdensome, insufficient or correctly targeted but genuinely ineffective? The answer is not determined by the framework alone.

Selected scientific reading

McEwen (1998), Protective and damaging effects of stress mediators, New England Journal of Medicine.
<https://doi.org/10.1056/NEJM199801153380307>

Barabási, Gulbahce & Loscalzo (2011), Network medicine: a network-based approach to human disease, Nature Reviews Genetics.
<https://doi.org/10.1038/nrg2918>

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