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EDITORIAL

New Horizons in Post-Traumatic Stress Disorder Treatment: From Current Status to the Future

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Throughout history, wars, disasters, and acts of violence have harmed not only bodies but also minds. Today, post-traumatic stress disorder (PTSD) is no longer merely an individual problem; it is a societal crisis that demands solutions for the future of humanity. The role of therapists, who serve as silent witnesses to trauma, should not be limited to mourning pain. Social solidarity, efforts to strengthen mental health, and the defense of human rights must be prioritized in PTSD interventions.

Post-traumatic stress disorder is among the most clearly defined disorders in psychiatry, owing to the specificity of its diagnostic criteria and the presence of a well-identified etiological factor—trauma. Unlike many other psychiatric disorders, PTSD is, by definition, precipitated by exposure to a traumatic event. This diagnostic precision has made PTSD easily identifiable in both clinical and easily identifiable in both clinical and research settings and has contributed to its status as one of the most intensively studied mental health conditions. Epidemiological studies estimate the prevalence of PTSD in the general population at approximately 3.9%.[1] However, this figure varies depending on several factors, with substantially higher rates—ranging from 17% to 28%—reported in populations exposed to severe trauma.[2,3]

Individuals with PTSD bear a significant personal, clinical, and economic burden. The disorder's etiology and phenotype are shaped by an interplay of factors such as genetic predisposition, the nature, severity, and recurrence of trauma, the age at which the trauma occurred, comorbid psychiatric conditions, substance use, and even cultural background.[4,6] This multidimensional framework highlights that PTSD is not solely an individual condition but also a complex phenomenon requiring evaluation within a broader societal context.

The observation that most individuals exposed to trauma demonstrate resilience, while only a minority develop PTSD, has led researchers to investigate individual defense and vulnerability mechanisms. Twin studies suggest that genetic inheritance may account for 30–40% of PTSD susceptibility, but the interaction between genetic predisposition and environmental risk factors appears to be critical.[7] Increasing evidence indicates that epigenetic mechanisms may mediate

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the relationship between trauma exposure and genetic vulnerability. Large-scale genetic and epigenetic studies offer the potential to illuminate the biological underpinnings of PTSD and to inform the development of novel mechanism-based therapies.[8,10]

In this editorial, we summarize current evidence-based treatments for PTSD that reflect the "spirit of the times" and evaluate the effectiveness of standard interventions recommended by current guidelines. We then explore emerging and innovative approaches likely to be integrated into future treatment protocols, including neuromodulation techniques, psychedelic-assisted therapies, individualized therapy matrices, epigenetic interventions, and artificial intelligence-supported psychotherapies. Accordingly, in this second issue of the *Turkish Journal of Trauma Stress*, we aim not only to assess the current landscape but also to invite our readers into a forward-looking scientific dialogue on the treatment paradigms of the future.

Current Evidence-Based Treatment Approaches

The current *zeitgeist* in PTSD treatment emphasizes the primacy and effectiveness of trauma-focused psychotherapies. International guidelines strongly recommend trauma-focused cognitive behavioral therapy (TF-CBT) and Eye Movement Desensitization and Reprocessing (EMDR) as first-line treatments for both PTSD and acute stress disorder (ASD).[11,16] These therapies are recognized for their robust efficacy in reducing traumatic stress symptoms and have become the cornerstone of evidence-based psychological interventions for trauma-related disorders.

Among trauma-focused CBT approaches, Cognitive Processing Therapy (CPT), Cognitive Therapy (CT), and Prolonged Exposure (PE) stand out as the treatments with the strongest evidence base.[11] Guidelines emphasize that trauma-focused therapies are more effective and should be preferred over non-specific or supportive interventions.[13,15]

For children, adolescents, and young adults, TF-CBT is recommended as a first-line treatment due to its broader evidence base; however, EMDR is also considered an effective alternative.[15]

Trauma-focused therapies have demonstrated efficacy when used as early interventions following trauma exposure, but only in individuals who exhibit significant symptoms or meet the diagnostic criteria for PTSD or ASD. In contrast, there is no evidence supporting the benefit of routine early intervention in asymptomatic individuals.[14,16]

Internet-based cognitive behavioral therapies (i-CBT) can be effective under specific circumstances; however, current studies on this topic are limited and of lower methodological quality, indicating a need for further high-quality research before establishing equivalence with conventional methods.[11,12,17]

Pharmacological treatments—especially selective serotonin reuptake inhibitors (SSRIs)—should be considered only when access to psychological therapies is limited. Guidelines consistently indicate that medication should not replace trauma-focused psychotherapy.[16,18]

Furthermore, *watchful waiting* and *psychological first aid* are recommended in the immediate aftermath of traumatic events, whereas routine psychological debriefing is not advised.[16]

In conclusion, all active psychological interventions are more effective than passive or standard care approaches; however, trauma-focused therapies remain the first-line treatments.[11,13,17]

Specifically, PE, CPT, and EMDR are trauma-focused psychotherapies whose efficacy has been demonstrated in numerous controlled studies. These modalities have been evaluated in patient samples with complex symptom profiles and comorbid conditions, compared to active control groups, and with long-term follow-up data. Their effectiveness has been consistently replicated not only by their developers but also by independent research teams.

Direct comparison studies of CPT, PE, and EMDR generally indicate that these treatments are similarly effective, with no one approach showing clear superiority over the others.[19,24] These findings

suggest that each of these validated therapeutic modalities is supported by robust evidence base and can be considered equally effective.

Efficacy and Limitations of Current Treatments

The effectiveness of trauma-focused psychotherapies is particularly notable in terms of effect size, as evidenced by meta-analyses and clinical trials. When classical TF-CBT methods are implemented, moderate to large improvements are generally observed in PTSD symptoms post-treatment.[25,32] In contrast, the impact of pharmacological treatments is relatively limited. Currently, the only approved pharmacological interventions for PTSD are SSRIs, such as sertraline and paroxetine, which typically yield only small symptom reductions (effect size d ≈ 0.3–0.5).[18,33–35] Indeed, the improvement rates achieved by SSRIs are approximately half those observed with trauma-focused psychotherapies or emerging treatments. For this reason, current guidelines frequently position pharmacotherapy as an adjunct or second-line treatment option. Some studies have also reported that the combination of psychotherapy and pharmacotherapy does not outperform psychotherapy alone.[18,36]

A significant limitation of current evidence-based therapies is that not all patients achieve full remission, and a notable proportion discontinue treatment prematurely.[21,37] For instance, in clinical trials involving trauma-focused therapy protocols, approximately one-third of participants drop out, and treatment response rates are generally lower among individuals exposed to military trauma compared to civilians. A substantial percentage of patients undergoing "first-line" therapies such as prolonged exposure and CPT remain symptomatic or discontinue therapy.[38,40] These findings indicate that even the most established treatments do not fully address the needs of all individuals.

Moreover, our ability to predict which patients will benefit most from which therapy remains limited. Although the underlying causes of these differences are not yet fully understood, it is evident that standard therapies may be less effective for individuals with histories of severe trauma or complex psychopathology. Consequently, significant therapeutic needs in PTSD treatment remain unmet. This reality continues to motivate clinicians and researchers to enhance existing modalities and to pursue novel treatment strategies.

Future Methods in PTSD Treatment

Emerging Approaches on the Horizon

Despite significant advancements in PTSD treatment over the past two decades, the fact that current methods are not universally effective has prompted scientists and clinicians to search for new solutions. The vision for future treatment involves not only relieving symptoms, but also transforming brain function, targeting the biological imprints of trauma, and addressing existential dimensions such as meaning and purpose in life.

1. New Pharmacological Approaches

Psychedelic- and Entactogen-Assisted Therapies

Compounds such as MDMA, psilocybin, LSD, ayahuasca, and ketamine are currently being investigated for their potential to enhance psychotherapy, reduce fear, and assist patients in processing trauma. In particular, MDMA-assisted therapy has demonstrated notable symptom reduction and a favorable safety profile in advanced clinical trials.[41,45]

In a multicenter Phase III trial conducted by the MAPS consortium, nearly two-thirds (67%) of chronic PTSD patients receiving MDMA-assisted therapy no longer met diagnostic criteria for PTSD after just three sessions.[46] In this study, the effect size was remarkably large (Cohen's $d \approx 0.9$) in the MDMA group, compared to a lower effect size (Cohen's $d \approx 0.3$–0.5, similar to SSRIs) in the group receiving the same psychotherapy with a placebo. These findings suggest that MDMA-assisted therapy may offer significantly greater benefits than current treatments, particularly in cases resistant to standard interventions.

This therapy enhances emotional resilience by allowing patients to access and process traumatic memories within a controlled therapeutic

environment. Additionally, the U.S. Department of Veterans Affairs (VA) is supporting studies investigating MDMA-assisted therapy for veterans with PTSD and co-occurring alcohol use disorder.

Ketamine is also being explored for its rapid-acting antidepressant properties, which may be particularly helpful for individuals experiencing the complex interplay of depressive and PTSD symptoms.[47,48] While other psychedelic substances show promise, further clinical evidence is needed before their widespread adoption.

What unites these psychedelic-assisted approaches is the notion that controlled administration during therapy sessions can lead to profound and long-lasting changes in how patients experience traumatic memories and perceive their sense of self.

New Drug Targets

Future pharmacological developments may focus on targeting the cannabinoid and oxytocin systems, glutamatergic signaling, neuropeptide Y, and neuroactive steroids. These mechanisms aim to directly modulate memory, stress responses, and emotional regulation more effectively than conventional antidepressants.[41,48,50]

Memory Modulation

Medications that impair the reconsolidation of traumatic memories or enhance fear extinction (e.g., glucocorticoid modulators, glycine agonists) are also under investigation.[41,49]

Adjuvant Agents

Agents such as D-cycloserine are being tested as adjuvants to enhance the efficacy of established interventions like PE.[51]

2. Psychotherapeutic Innovations

Technology-Assisted Therapies

Virtual reality (VR) and digital tools are increasingly being integrated into exposure-based therapies, enhancing accessibility, engagement, and personalization.[51] VR exposure therapy has garnered attention for its effectiveness in creating immersive and controlled environments where patients can confront trauma-related stimuli safely.[52,54] The interactive nature of VR enables customized treatments that can boost patient engagement and reduce symptoms. Ongoing research aims to further evaluate its comparative efficacy relative to traditional exposure methods.[55]

AI-assisted psychotherapies, including digital therapists, symptom-monitoring algorithms, and automated feedback systems, have the potential to significantly impact PTSD care—especially in terms of scalability and continuity during follow-up. These tools can facilitate real-time tracking of emotional states and offer adaptive interventions tailored to individual needs.

3. Neuromodulation Therapies

Brain Stimulation

Techniques such as transcranial magnetic stimulation (TMS), transcranial direct current stimulation (tDCS), and deep brain stimulation (DBS) have shown promise for individuals with treatment-resistant PTSD. Early studies generally report mild side effects and positive outcomes.[50] These interventions aim to alleviate symptoms by modulating neural circuits that are frequently dysregulated in PTSD.

For example, repetitive TMS (rTMS) targets the prefrontal cortex and limbic regions to reduce symptoms such as intrusions and hypervigilance.

Stellate Ganglion Block (SGB)

Stellate Ganglion Block (SGB) involves the injection of a local anesthetic into the stellate ganglion—a nerve cluster in the neck. Recent research (2025) has shown that SGB can disrupt fear memory consolidation and produce symptom relief lasting up to six months.[58] However, more longitudinal studies are needed to determine its long-term efficacy and safety.

Vagus Nerve Stimulation (VNS)

"In recent years, vagus nerve stimulation (VNS) has gained attention as a promising neuromodulatory approach for PTSD treatment. Researchers are currently exploring its simultaneous use with psychotherapy techniques. For instance, applying transcutaneous VNS during prolonged exposure

therapy sessions may enhance fear extinction learning and provide longer-lasting symptom relief. VNS potentially reshapes emotional and reward-processing pathways associated with traumatic memories by increasing norepinephrine release and promoting synaptic plasticity. Preliminary studies indicate significant clinical improvements in treatment-resistant PTSD cases utilizing this combined approach.[56,57] While these neuromodulation techniques are still in their early stages, they offer promising alternative or adjunctive options for individuals unresponsive to conventional treatments. Future large-scale clinical trials will be critical for validating their efficacy and identifying optimal patient profiles.

A 2025 feasibility study reported that short-term VNS applied concurrently with PE in patients with treatment-resistant PTSD significantly reduced symptom severity.[59] All participants no longer met PTSD diagnostic criteria post-treatment, and substantial reductions were observed in standardized measures.

These results suggest that VNS may enhance fear extinction through its plasticity-promoting effects, not only alleviating trauma-related memories but also reducing associated symptom clusters such as anxiety and hyperarousal.

4. Other Future Directions

Individualized Psychotherapy Matrices

Rather than applying CBT, CPT, or EMDR in isolation, future approaches are expected to prioritize appropriate triage and eclectic or integrative therapies. For example, Metacognitive Therapy (MCT) or Acceptance and Commitment Therapy (ACT) elements may be more beneficial for patients whose primary symptom is rumination, while behavioral strategies and value-based interventions may prove more effective for those whose main difficulty is avoidance.

Innovative therapeutic frameworks such as the Unified Protocol, which targets transdiagnostic emotional disorders, are gaining popularity—particularly in populations (e.g., veterans) where conventional trauma-focused treatments may be less effective or acceptable.[60] This trend highlights a shift toward inclusive and adaptive models tailored to the heterogeneous needs of individuals with PTSD.

There is preliminary evidence in the literature that different therapy modalities may be more effective for distinct symptom clusters. For instance, a recent study found that certain combinations of prognostic factors can predict better outcomes from supportive therapies (e.g., interpersonal therapy) rather than strictly trauma-focused interventions.[61] Such findings suggest that future treatment guidelines may adopt decision algorithms based on individual patient characteristics rather than fixed stepwise recommendations such as “start with PE.”

As part of this individualized treatment framework, the goal is to develop decision-support tools and therapeutic roadmaps to assist clinicians. In the near future, for example, an AI-supported clinical tool may analyze a new patient’s profile and generate predictions such as: “This patient has an 80% likelihood of benefiting more from an ACT + EMDR or MCT + EMDR combination than from PE alone.”

Although this vision remains in its early stages, it is anticipated that significant progress will be made toward personalized PTSD treatment in the coming years.

In summary, “individualized psychotherapy matrices” represent a holistic and future-oriented approach. Instead of viewing evidence-based therapies as competing models, this perspective seeks to match each approach with the right patient, at the right time, for the right purpose.

Family and Couple Therapies

Another promising development is the integration of couple- and family-based therapies that incorporate emotion regulation strategies.[62,63] These approaches acknowledge the social and relational dimensions of PTSD and aim to build a supportive therapeutic environment around affected individuals—enhancing treatment effectiveness and promoting sustainable recovery.

Epigenetic-Based Therapies

It is now better understood how epigenetic changes, such as DNA methylation, contribute to the pathophysiology of PTSD.[8,10] In the future, pharmacological agents that directly target these mechanisms may become viable treatment options.

Epigenetic modifications occur when environmental stressors—such as trauma—cause persistent alterations in gene expression. Various epigenetic signatures have been identified in both blood and brain tissues of PTSD patients. For example, methylation differences in genes associated with the immune system, along with changes in gene expression levels, have been reported, suggesting dysregulated inflammatory pathways in trauma-exposed individuals.[64,65]

Additionally, increased methylation in certain gene regions, such as HDAC4, has been observed in female PTSD patients. This may represent a mechanism contributing to gender differences in PTSD.[66] These findings not only highlight potential biomarkers, but also open new therapeutic avenues.

Could epigenetic modifiers be used to prevent or reduce PTSD symptoms in the future? While this remains speculative, preclinical and early clinical studies offer promising clues. For instance, in animal models, histone deacetylase (HDAC) inhibitors have been shown to alter patterns of fear-conditioned memories.[67,68] Such drugs may mitigate symptoms by disrupting or erasing trauma-related "fear traces" via epigenetic mechanisms.

Another future direction involves the use of epigenetic clocks or biological age indicators to assess PTSD risk and deliver prophylactic interventions to high-risk individuals. For example, some studies suggest that early administration of hydrocortisone post-trauma may prevent PTSD by inhibiting epigenetically mediated memory consolidation.[69,70]

Although these ideas are still under investigation, deeper understanding of epigenetic processes is expected to drive targeted molecular therapy development. It is important to note that epigenetic interventions must selectively target specific gene pathways, as broad-spectrum epigenetic modulation may carry unintended consequences. Therefore, pharmacogenetic and epigenetic data are increasingly being used to guide existing treatments in the framework of personalized psychiatry.

For example, a patient's unique epigenetic profile may help predict which treatment approach is most likely to be effective. Upcoming phenomic and epigenomic studies are expected to facilitate the development of both preventive strategies and novel therapeutic agents based on epigenome modulation.[8,10]

Artificial Intelligence-Assisted Psychotherapies

The growing presence of digital technologies in psychiatry indicates that AI-assisted psychotherapies will play a central role in the future of PTSD treatment. AI has the potential to enhance mental healthcare by providing clinical decision support for professionals and direct therapeutic tools for patients.

Recent advances have raised hopes that AI can optimize diagnosis, treatment planning, and therapy delivery, offering tailored solutions and expanding access to care. For instance, using machine learning algorithms, it is now possible to screen for PTSD using voice tone analysis or text data via natural language processing (NLP).[71]

Likewise, smartphone-based applications can collect daily symptom data, which AI can analyze to provide therapists with real-time feedback on patient progress, enabling dynamic treatment adjustments. When integrated with VR platforms, these systems can deliver personalized exposure therapies that monitor and adapt to the user's physiological stress responses.

In these settings, AI systems can detect signs of distress and alter the virtual environment in real time to match the patient's window of tolerance. Meanwhile, therapeutic chatbots—through text or voice—offer 24/7 support for individuals in crisis or between sessions. These bots can guide patients

through relaxation techniques, offer sleep hygiene recommendations, or even simulate basic cognitive techniques during high-stress moments.

Beyond the clinical level, AI contributes to health system efficiency through automated scheduling, treatment tracking, and follow-up systems, which can reduce therapists' workload and increase service capacity. Especially in settings with limited clinician availability, AI automation holds potential for expanding care and reducing costs.

However, AI-based interventions are not without ethical and institutional challenges. Issues related to data privacy, algorithmic bias, and emergency handling protocols must be rigorously addressed. Researchers emphasize that AI tools should be carefully trained and validated to avoid biased decision-making in vulnerable PTSD populations.

Despite these concerns, AI is poised to revolutionize PTSD treatment by enabling scalable, individualized, and evidence-informed care—particularly in underserved or rural areas. Therefore, AI-assisted psychotherapies represent a critical area of innovation and must be closely followed in the coming years.

The current and emerging treatment approaches summarized above indicate that PTSD therapy is undergoing continuous evolution. Although today's "first-line" therapies offer considerable benefits, they fall short for many patients, driving the need for novel solutions.

Some of the promising future modalities—such as psychedelic-assisted therapy and neuromodulation—are increasingly being conceptualized as adjuncts to standard treatments rather than as standalone solutions. For example, MDMA or ketamine administration enhances the depth and receptivity of psychotherapy, acting as a catalyst rather than a primary intervention. Similarly, vagus nerve stimulation aims to biologically support learning during trauma-focused sessions. These approaches suggest that integrative, hybrid models may dominate the future therapeutic landscape.

A critical topic of debate concerns the level of evidence and clinical scalability of these innovative treatments. Psychedelic therapies and neuromodulatory techniques have, thus far, been studied in relatively small cohorts, and their long-term safety and efficacy remain uncertain. While early results are promising, larger, well-controlled studies are needed to validate these findings and determine cost-effectiveness in real-world populations.

For instance, MDMA-assisted therapy—which may soon gain FDA approval—requires adherence to structured protocols, specialized therapist training, multidisciplinary collaboration, and strict ethical oversight (e.g., informed consent, safety planning). Similarly, the growing use of AI technologies in mental health demands the creation of new regulatory frameworks, guidelines, and monitoring mechanisms.

While some methods (e.g., individualized therapy matching) represent evolutionary progress in applying existing modalities more intelligently, others—such as psychedelics or AI—are disruptive innovations that challenge conventional paradigms and open new frontiers. The interdisciplinary collaboration of psychiatry, psychology, neuroscience, computer science, and bioethics will be essential to ensure the safe and effective integration of these advances.

Conclusion

PTSD occupies a privileged place in psychiatry due to its diagnostic clarity and the richness of scientific insight it offers. The trauma-focused therapies developed around this clarity continue to form the foundation of PTSD treatment.

However, the zeitgeist reveals that no therapeutic approach remains static. As science progresses, so do our treatment horizons. A wide spectrum of innovations—from neuromodulation to psychedelics, epigenetics to artificial intelligence—offers hope for patients living at the limits of current care.

Turning these possibilities into reality will require rigorous research and thoughtful clinical

application. This is precisely where platforms like the *Turkish Journal of Trauma and Stress* contribute: by disseminating knowledge about emerging trends and future research.

While the space constraints of this editorial prevent an in-depth discussion of every emerging modality, the overview provided here reflects a multidimensional and interdisciplinary future for PTSD treatment.

We invite our readers to actively contribute to this evolving perspective. Sharing clinical experience, research findings, and creative insights will be vital in advancing our collective efforts. Every trauma is unique—and so is each journey to recovery.

As a scientific community, our goal should be to diversify recovery pathways and strengthen the empirical foundation of each route. We extend our sincere thanks to all researchers and clinicians who are shaping the future by capturing the spirit of the times—and we encourage the readership of the *Turkish Journal of Trauma and Stress* to take part in this critical discourse.

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