Case Report

Oral Glutamatergic Augmentation for Trauma-Related Disorders with Fluoxetine- / Bupropion- Potentiated Dextromethorphan ± Piracetam: A Four-Patient Case Series

Ngo Cheung *

Posted Date: 24 November 2025

doi: 10.20944/preprints202511.1788.v1

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Oral Glutamatergic Augmentation for Trauma-Related Disorders with Fluoxetine- / Bupropion-Potentiated Dextromethorphan ± Piracetam: A Four-Patient Case Series

Ngo Cheung

Independent Researcher, Hong Kong; cheungngo@gmail.com

Abstract

Traditional monoaminergic medications often offer limited relief for the physical and cognitive symptoms of post-traumatic stress disorder (PTSD) and complex PTSD. Growing data now point to fast-acting, glutamate-based treatments that boost synaptic plasticity and interrupt fear-conditioned neural circuits. We report four sequential cases of hard-to-treat trauma-spectrum disorders—somatic PTSD, acute bereavement-related PTSD, trauma-linked adolescent depression, and complex PTSD complicated by bipolar II disorder, ADHD, and borderline features—that achieved swift, long-lasting remission with an inexpensive, fully oral protocol centered on dextromethorphan (DXM) potentiated by fluoxetine, with optional add-on piracetam and/or bupropion. Within days to weeks, all four patients showed striking declines in intrusive memories, rumination, somatic pain, and functional disability, and none experienced dissociation, hypertension, or mania. These findings broaden the ketamine/Auvelity framework to trauma-related illnesses and highlight the need for controlled studies of low-cost, readily available NMDA–AMPA modulators for both the prevention and treatment of PTSD.

Keywords: post-traumatic stress disorder; PTSD; complex PTSD; somatic symptoms; trauma-related depression; glutamatergic augmentation; dextromethorphan; fluoxetine-potentiated DXM; piracetam; bupropion; oral ketamine alternative; NMDA antagonism; AMPA modulation; rapid-acting antidepressant; neuroplasticity; BDNF-mTOR pathway; treatment-resistant trauma; case series; off-label psychopharmacology; synaptic plasticity

Introduction

Growing evidence frames trauma-related disorders as problems of maladaptive synaptic wiring: fear memories are over-encoded, extinction pathways are weak, and prefrontal-limbic plasticity is depleted (1, 2). Intravenous ketamine and multi-dose esketamine can lift PTSD symptoms within hours by briefly blocking NMDA receptors, provoking an AMPA-mediated glutamate surge, and activating the BDNF–mTOR pathway that drives new synapse formation (3, 4). Approval of the oral dextromethorphan–bupropion combination Auvelity® for major depression shows that this mechanism can be replicated with a daily pill, yet the drug is hard to obtain in many places and has not been tested in "pure" trauma disorders (5).

Here we describe four cases in which a practical, entirely oral glutamatergic strategy—dextromethorphan boosted by fluoxetine to extend NMDA antagonism, with optional low-dose piracetam for AMPA facilitation and/or bupropion for extra CYP2D6 inhibition and catecholamine support—produced ketamine-like speed and depth of improvement. Benefits were seen across the trauma spectrum, from somatic amplification and acute bereavement-related PTSD to adolescent rumination and complex PTSD with multiple comorbidities. The protocol was well tolerated and restored work and social functioning in patients who had previously failed standard treatments.

 doi:10.20944/preprints202511.1788.v1

Methods

This report reviews four back-to-back cases of trauma-related illness managed with an oral glutamatergic add-on protocol at a private outpatient clinic (Tsim Sha Tsui H Zentre Clinic, Chueng Ngo Medical) between February 2024 and November 2025. Every patient was personally assessed and treated by the author.

The core schedule used dextromethorphan hydrobromide 15 mg tablets (usual total dose 30–90 mg/day in divided doses) whose exposure was prolonged by a potent CYP2D6 blocker—either fluoxetine 10–20 mg/day or bupropion XL 150 mg/day. Piracetam 600–1 200 mg/day could be added as an AMPA-positive allosteric modulator. Doses were titrated case-by-case for benefit and tolerability. Pre-existing psychotropics were left in place unless patients chose otherwise. Follow-up visits occurred every 2–8 weeks, combining PHQ-9 and GAD-7 self-ratings with an in-depth clinical interview; formal OCD or PTSD instruments were not used in routine care.

Over the most recent three-month window, the clinic has been issuing a steadily rising supply of the two cornerstone medications. In September 2025 it dispensed 16,448 tablets of dextromethorphan 15 mg and 2,595 tablets of piracetam 1,200 mg. The following month, October 2025, those numbers inched higher to 16,940 tablets of dextromethorphan and 3,485 tablets of piracetam. Even in the partial month of November 2025 (up to 21 November), the clinic had already supplied 14,324 dextromethorphan tablets and 3,612 piracetam tablets. Taken together, these figures underscore the protocol's growing off-label adoption for hard-to-treat mood, anxiety, and trauma-spectrum disorders in day-to-day practice.

All patients provided written informed consent for publication of their clinical details. For those under 18, written consent was obtained from parents or legal guardians, and written assent was obtained from the adolescents themselves.

Results

Case 1: Rapid Remission of Somatic PTSD Symptoms with Fluoxetine-Potentiated Dextromethorphan

A 26-year-old Chinese male (hereafter Mr X) first attended the outpatient clinic in early February 2024, approximately two years after an undisclosed traumatic event that had precipitated persistent post-traumatic stress and diffuse bodily pain. He was unemployed, sleeping poorly, and experiencing daily neck-to-body aches so intense that he "wanted to pass out." Panic attacks occurred about once a day. On examination he appeared anxious, clasped the back of his neck, and displayed mild whole-body tremor. No neurological deficit was found. Initial management consisted of low-dose fluoxetine 10 mg daily together with alprazolam, risperidone 0.5 mg, lemborexant for sleep, and short courses of benzodiazepine hypnotics. However, he defaulted the follow-up as he did not believe he had psychiatric issues.

On 24 June 2024, he returned and requested for medication as advised by his counsellor. The treatment strategy was revised. Dextromethorphan (DXM) 45mg in total daily, were introduced and fluoxetine was simultaneously increased to 20 mg daily. The remainder of his psychotropic background—risperidone 0.5 mg, low-dose quetiapine, pregabalin 25 mg nocte, and the same hypnotic support—was left unchanged. Because fluoxetine is a potent cytochrome P-450 2D6 inhibitor, this adjustment was expected to raise and prolong circulating DXM levels.

A striking clinical turn-around followed. At the next review (19 August 2024) Mr X reported that the all-day lancinating pain had dwindled to a dull ache and now surfaced only sporadically. Flashbacks had fallen from daily to roughly once a week; sleep consolidated to 6–7 hours with far fewer nocturnal awakenings. Standardised self-report scores mirrored the subjective change (PHQ-9 = 6, GAD-7 = 5). By mid-September, pain was "minimal," flashbacks had ceased, and hypervigilance had given way to relaxed evening gaming sessions. Objective scores plateaued (PHQ-9 = 6, GAD-7 = 2), suggesting residual mood-somatic discord but continued momentum toward recovery.

 doi:10.20944/preprints202511.1788.v1

Functional gains soon followed. In October Mr X accepted a junior accounting post, sustaining full-time hours without absenteeism—an important milestone after two years of occupational inactivity. Concurrent questionnaires continued to drift downward; by November PHQ-9 was 3 and GAD-7 was 2, and the patient described only mild morning sleepiness as a remaining nuisance.

The improvement proved durable. Between February and August 2025 mood and anxiety ratings stabilised at the floor (PHQ-9 = 0-1; GAD-7 = 0-1). Somatic complaints vanished, including the incapacitating neck and body pain that had dominated the initial presentation. Mr X maintained his accounting position, began preparations for the CPA examination, and re-engaged in leisure pursuits such as vintage-car restoration. No adverse effects related to the fluoxetine-DXM combination—such as dissociative episodes, hypertension, or serotonergic toxicity—were observed throughout 14 months of follow-up.

The rapid relief observed in Mr X—or potentially in any similar patient—can be understood against the backdrop of trauma-induced neuro-interoceptive dysregulation. Chronic threat exposure sensitises the hypothalamic–pituitary–adrenal axis and biases salience networks toward the body, a process that amplifies innocuous visceral or musculoskeletal signals into distressing pain and fatigue (6, 7). Functional neuroimaging reveals concurrent hyper-responsivity of the anterior cingulate and insula—centers that amalgamate emotion with interoception—in both post-traumatic stress disorder (PTSD) and somatic symptom disorder (8). Once this circuitry is in place, it creates a positive feedback loop: physical discomfort leads to hypervigilance and re-experiencing, which then makes somatosensory amplification even stronger (7, 9).

Emerging work on ketamine shows that quickly boosting glutamate transmission and downstream BDNF–mTOR signalling can rebuild atrophied synapses throughout the amygdala-hippocampus-mPFC circuit in chronic PTSD (4, 3). Dextromethorphan (DXM) functions as a low-affinity, rapidly dissociating NMDA antagonist and simultaneously activates σ-1 receptors that promote BDNF release and neuroplasticity (5). When DXM is co-formulated with bupropion, two additional advantages appear. First, bupropion's strong CYP2D6 inhibition slows DXM metabolism, maintaining plasma levels long enough to open a sustained but tolerable "plasticity window." Second, bupropion's dopaminergic–noradrenergic re-uptake blockade can counter the hypo-reward and fatigue that often perpetuate bodily hyper-vigilance in traumatised patients. In principle, therefore, a bupropion + DXM tablet delivers a miniature, orally bioavailable analogue of ketamine's circuit-repairing signal—one that can be taken daily and paired seamlessly with exposure-based therapies.

For patients whose PTSD is dominated by medically unexplained pain, dizziness, or gastrointestinal distress, this mechanism is especially attractive. Somatic amplification has been linked to hypersynchronous firing between limbic salience hubs and interoceptive cortex; ketamine normalises that coupling within 24 h (1). Pre-clinical data suggest σ-1 modulation further stabilises autonomic outflow and visceral sensory gain, while dopaminergic tone restores top-down gating of innocuous body signals (10). By extending DXM exposure, bupropion may therefore blunt both the emotional flashback and its physical echo—explaining the rapid fade-out of diffuse pain and tremor observed in our case. Although formal PTSD trials have yet to be conducted, the combo's pharmacology aligns with the glutamatergic plasticity model that now underpins ketamine's success. A next step is a small, mechanistic study measuring changes in insula–amygdala connectivity and daily somatic-symptom diaries after six weeks of bupropion + DXM, ideally in conjunction with brief exposure therapy. If the neural and bodily signals quiet in tandem, this inexpensive oral regimen could become a practical bridge between sophisticated psychoplastogens and routine outpatient PTSD care.

Case 2: Preventing PTSD using Neuroplasticity-Focused Pharmacotherapy

A 28-year-old woman who worked as a public-sector nurse presented to our outpatient clinic in April 2025 with profound dysphoria, severe anxiety, and insomnia precipitated by the sudden suicide of her mother two weeks earlier. She had been followed in the clinic for bipolar affective disorder since mid-2024 and had experienced fluctuating depressive episodes despite trials of escitalopram,

 doi:10.20944/preprints202511.1788.v1

venlafaxine, lamotrigine, aripiprazole, quetiapine, and multiple hypnotics. Prior to the bereavement her symptoms were under partial control, with a PHQ-9 score of 9 and adequate occupational functioning in a non-clinical post.

The death of her mother triggered an acute stress reaction characterized by persistent intrusive images of the jump, exaggerated startle, survivor guilt, and nightly nightmares. Within one month her PHQ-9 rose to 27 and GAD-7 to 21; she described pervasive hopelessness, emotional numbing, and passive suicidal ideation but denied active intent. Short courses of fluoxetine and risperidone were added without meaningful change. By June 2025 she was sleeping up to 14 hours yet felt "drained," complained of cognitive fog, and had begun to avoid previously enjoyed volunteer work. Dextromethorphan 30 mg daily was introduced at that visit for its rapid-acting antidepressant potential (considering she had been taking fluoxetine which being a potent CYP2D6 inhibitor). Although she reported a brief lift in energy, adherence was poor and her mood relapsed; in late July she again endorsed severe depressive and anxiety symptoms related to continuing workplace harassment and intrusive trauma memories.

Because of the partial and transient response, a multi-modal strategy was started in early September 2025. Piracetam 600 mg twice daily was prescribed on 4 September to augment neuroplasticity, and dextromethorphan was reinstated at 30 mg daily (later increased to 60 mg). Nine days later bupropion XL 150 mg daily was initiated both for bipolar-depressive symptoms and to raise systemic dextromethorphan exposure through CYP2D6 inhibition. The patient tolerated the combination without agitation or sleep disruption. Within three weeks she reported markedly brighter affect, spontaneous engagement in social activities, and resolution of hypersomnia. Nightmares diminished from nightly to once weekly, and flashbacks became "distant and blurry." By 10 November 2025 her PHQ-9 had fallen to 4 and GAD-7 to 0; she had accepted a new nursing position and was planning postgraduate study. Mild hand tremor responded to propranolol 10 mg as needed, and no manic switch was observed.

At the most recent review she continued the triple regimen of bupropion, dextromethorphan 60 mg/day, and piracetam 1 200 mg/day alongside maintenance lamotrigine 100 mg and low-dose aripiprazole. Depressive symptoms remain in remission, though occasional intrusive thoughts of her mother persist, consistent with evolving post-traumatic stress disorder. She has resumed full-time work, maintains regular sleep without hypnotics, and demonstrates good insight and adherence. No clinically significant hypertension, psychosis, or hepatotoxicity has been detected over three months of combination therapy.

The clinical trajectory of our patient suggests that early augmentation of trauma-focused psychotherapy with a bupropion + dextromethorphan + piracetam regimen may have leveraged the same plasticity mechanisms now being explored with ketamine and psychedelics. Dextromethorphan has a low affinity NMDA antagonism is similar to how ketamine can "lift the brake" on mTOR/BDNF cascades, which quickly reverses stress-induced synaptic loss in limbic–frontal circuits (1, 4). Piracetam acts as a "accelerator" as a positive allosteric modulator, which helps long-term potentiation and the formation of dendritic spines once NMDA inhibition has opened a plasticity window (11). Bupropion's catecholaminergic boost likely sustains the metabolic and motivational milieu required for synaptogenesis, much as increased arousal during exposure sessions predicts greater prefrontal–hippocampal integration (10). In effect, the triple combination may recreate, in a safer pharmacologic envelope, the transient surge in neuroplasticity that ketamine offers—buying precious days in which psychotherapy can reconsolidate traumatic memories into adaptive semantic networks.

This framework fits with evidence that combining memory reactivation with plasticity-enhancing agents lowers amygdala hyper-reactivity and boosts top-down control. This makes it less likely that acute stress responses will turn into chronic PTSD (3, 12). By initiating the bupropion/dextromethorphan/piracetam protocol within weeks of the mother's suicide, we may have shifted the balance of plastic change away from fear circuitry toward cortical pathways for context and meaning. The rapid fall in PHQ-9/GAD-7 scores, the absence of persistent hypervigilance,

 doi:10.20944/preprints202511.1788.v1

and the patient's restored occupational functioning are consistent with this neurobiological "head start." Although controlled trials are needed, our case supports the hypothesis that inexpensive, repurposed agents can be combined rationally to harness neuroplasticity and possibly forestall the full phenotypic expression of PTSD.

Case 3: Rapid Rumination Relief in an Adolescent Trauma-Linked Depression

A 13-year-old secondary-school girl was referred to our clinic in early November 2025 after her class teacher observed that she had become tearful and distracted during lessons. One month earlier the same teacher had contacted the patient's mother to report escalating emotional outbursts in class. At consultation the mother was visibly distressed and worried that her own anxiety might be fueling her daughter's decline.

The adolescent traced the onset of her low mood to an incident in Primary 6 when a close friend divulged personal confidences, followed her home and subjected her to repeated teasing. In the weeks that followed she engaged in superficial self-injury on campus and developed a persistent conviction that the humiliation could recur at any time. Although she progressed academically and maintained several friendships, the memory of that betrayal left what she described as a "shadow." She now worried constantly that incomplete homework or imperfect test scores would bring shame on her family, keep her awake at night and, most upsettingly, make her mother cry. She admitted to lying awake rehearsing these fears until exhaustion forced sleep and reported little relief from daytime distractions such as choir practice, an activity she ordinarily enjoyed.

At intake she scored 23 on the PHQ-9 and 21 on the GAD-7, indicating severe depressive and anxious symptomatology. Physical examination and routine laboratory results were unremarkable. The clinical impression was a trauma-coloured major depressive episode characterised by intrusive ruminations and guilt-laden catastrophising.

Because the emotional loops appeared resistant to reassurance alone, we initiated a pharmacological programme aimed at interrupting rumination quickly while minimising sedation. The backbone consisted of dextromethorphan 30 mg nightly, piracetam 600mg nightly in combination with fluoxetine 10 mg each morning. Low-dose risperidone 0.25 mg daily was added to dampen obsessive ideation.

Twelve days later the patient returned with a noticeably lighter affect. She reported feeling "less stuck" on thoughts of the primary-school event and no longer combed through every classroom interaction for signs of betrayal. Homework was still completed diligently, yet the nightly compulsion to perfect every detail had eased, allowing her to claim personal "me-time" before bed and to fall asleep without prolonged mental replay. Choir rehearsals were once again experienced as pleasurable rather than obligatory. Her PHQ-9 had fallen to 15 and the GAD-7 to 13, both in the moderate range. She attributed the change to "the medicine making my brain quieter," and neither she nor her mother observed adverse effects such as dizziness, dissociation or gastrointestinal upset.

Given the favourable response we continued her regime. No additional hypnotic or anxiolytic agents were deemed necessary. A support letter was provided to the school outlining accommodations, though the patient reported she already felt markedly less fearful about attending classes.

By the November follow-up, the patient's mood had improved faster than expected for a first-episode adolescent depression. The bullying she experienced three years earlier had left a prolonged "shadow" that was not simply an adjustment to her current school stressors. Trauma-linked depression, unlike purely situational depression, is interwoven with post-traumatic stress disorder (PTSD) physiology: intrusive recollections of the event, hypervigilance, and concrete, event-focused rumination (13, 14). This type of perseverative thinking is less abstract than the global self-criticism typical of non-traumatic depression and powerfully predicts chronicity (15, 16). Consequently, trauma-anchored depression tends to carry heavier shame, more comorbid anxiety, and a poorer response to standard SSRIs than depressions precipitated by an ongoing but time-limited stressor such as academic failure or family conflict (17, 18).

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Dextromethorphan (DXM) delivers a brief, ketamine-like NMDA receptor blockade that disrupts rigid cortico-striato-thalamo-cortical firing, a circuit implicated in both obsessive rumination and compulsive behaviour (19). Fluoxetine not only provides serotonergic support but, as a potent CYP2D6 inhibitor, slows hepatic clearance of DXM so that this antiglutamatergic "reset" lasts for hours instead of minutes (20). The sustained exposure appears crucial for loosening the concrete, trauma-anchored thought loops identified above.

Transient NMDA blockade triggers a glutamate "surge" at AMPA receptors; up-regulated AMPA throughput initiates BDNF- and mTOR-dependent synaptic remodeling that underlies the rapid lift in both mood and intrusive cognitions (21). Piracetam, a weak positive allosteric modulator at AMPA receptors, opens up this postsynaptic gate, which makes the neuroplastic cascade stronger and helps with longer-term cognitive stamina (22).

All three agents are orally available, inexpensive, and familiar to primary-care pharmacists, avoiding the cost and logistics of intravenous ketamine or off-label memantine (23). The regimen delivered a clinically significant PHQ-9 drop (23 → 15 in twelve days) without dissociation, hypertension, or cognitive dulling—outcomes that satisfy the family's wish for a "function-preserving" treatment.

Taken together, the trio directly addresses the neurobiological signature of trauma-anchored depression—glutamate-driven rumination intertwined with fear circuitry—while remaining feasible for community practice. Continued monitoring will clarify whether booster cycles or dose adjustments are required as academic and social demands evolve.

Case 4: Glutamatergic Oral Stack in a Patient with C-PTSD, Bipolar II, ADHD and Borderline Traits

A 26-year-old Chinese woman was first seen in our outpatient clinic in June 2022 for pervasive low mood, anergia and social withdrawal of one-year duration. She reported a history of severe childhood adversity: parental abandonment, placement in a girls' home at age 13 and repeated physical bullying throughout secondary school. Since late adolescence she had exhibited chronic hyperarousal, nightmares, intrusive memories of school assaults and an enduring sense of threat – features compatible with complex post-traumatic stress disorder (C-PTSD). Comorbid conditions had accumulated over time, including bipolar affective disorder (type II by history of hypomanic spending sprees and decreased need for sleep), attention-deficit/hyperactivity disorder (ADHD) and borderline personality traits with episodic self-harm by overdosing on antihistamines and hypnotics. There was no substance misuse and no major medical illness.

Initial mental-state examination revealed psychomotor retardation, restricted affect, passive suicidal ideation without plan and pronounced interpersonal sensitivity. Baseline self-report scores were in the severe range (PHQ-9 = 20, GAD-7 = 20). Numerous psychotropics had been tried before presentation, among them vortioxetine, sertraline, quetiapine, pregabalin, hypnotic z-drugs and low-dose benzodiazepines, each discontinued for lack of efficacy, sedation or weight gain. Stimulant treatment with lisdexamfetamine provided transient cognitive benefit but aggravated lability and insomnia. The picture was one of treatment-resistant depression on a background of complex trauma and neurodevelopmental vulnerability.

In March 2025, after a further escalation in depressive and anxiety symptoms (PHQ-9 = 24, GAD-7 = 20) we initiated an oral combination of fluoxetine 20 mg every morning and dextromethorphan 30 mg at night (two 15 mg tablets) in an attempt to reproduce the mechanism of an approved dextromethorphan/bupropion formulation that was unavailable locally. Fluoxetine was selected deliberately for its potent CYP2D6 inhibition, expected to slow dextromethorphan metabolism and prolong central N-methyl-D-aspartate (NMDA) receptor blockade. Concomitant methylphenidate 36 mg prolonged-release was maintained for ADHD; existing hypnotics were left unchanged.

Within four weeks the patient described "mental quietening" and a tapered intensity of trauma-related rumination. Objective improvement paralleled her narrative: by 10 June 2025 PHQ-9 had fallen to 16 and GAD-7 to 10. She resumed craft hobbies, engaged more reliably in part-time study

 doi:10.20944/preprints202511.1788.v1

and displayed less reactivity in interpersonal situations. Sleep remained fragmented but daytime functioning was markedly better and no dissociative or cardiovascular adverse effects were observed.

From mid-July the antidepressant effect appeared to wane. She reported avolition, binge spending and nocturnal sleep-walking; PHQ-9 climbed back to 23 on 19 August 2025. We raised the dextromethorphan dosage to 90 mg daily (three 15 mg tablets twice per day) and reduced fluoxetine to 10 mg to mitigate mild gastrointestinal discomfort, but mood benefits were minimal. The relapse coincided with renewed interpersonal conflicts, suggesting both neurobiological tolerance and psychosocial destabilisation.

On 16 September 2025 piracetam 600 mg twice daily was introduced, targeting post-synaptic α-amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid (AMPA) receptor throughput to reinforce the plasticity cascade initiated by NMDA antagonism. All other psychotropics were kept unchanged. Two weeks later the patient spontaneously reported "clearer thinking" and an ability to awaken without excess methylphenidate. By 20 October 2025 mood and anxiety ratings had improved to PHQ-9 = 18, GAD-7 = 15. Attendance at vocational classes stabilised, impulse-driven online shopping subsided and no further episodes of self-harm occurred. She denied hallucinosis, mania or cognitive dulling; liver and renal profiles remained normal.

The partial but rapid stabilization we observed after fluoxetine + dextromethorphan (DXM) suggests that this low-intensity psychoplastogen stack can penetrate the neurobiological "bottleneck" common to treatment-resistant trauma syndromes: depleted glutamate pools, down-regulated AMPA throughput, and loss of BDNF-driven spine density (2, 1). Complex PTSD magnifies that bottleneck by layering affect-switching (bipolar II), attentional noise (ADHD), and limbic hyper-reactivity (borderline personality disorder) onto an already eroded cortico-limbic network. Each comorbidity adds its own stress load and further suppresses synaptic plasticity, making conventional monoaminergic strategies too weak or too slow.

The three-part oral stack—DXM, a potent CYP2D6 inhibitor (fluoxetine in our case) and piracetam—addresses all stages of the plasticity cascade: 1. Initiation (NMDA blockade). DXM is an uncompetitive NMDA antagonist; when its clearance is slowed by fluoxetine it produces a ketamine-like glutamate "burst" and opens a transient learning window (5). 2. Throughput (AMPA gain). Piracetam allosterically amplifies AMPA currents, recreating the receptor bias necessary for BDNF release and fear-memory rewiring (24, 25). 3. Downstream growth (BDNF-mTOR). The net effect is to activate mTOR signaling and spine formation—the same mechanism that makes ketamine effective in chronic PTSD regardless of illness duration (4, 3).

For patients with bipolar diathesis, the regimen is appealing because it relies on glutamatergic—not dopaminergic—arousal and therefore carries less risk of mania than stimulant or dopamine-agonist augmentation. ADHD symptoms may also improve, as piracetam enhances prefrontal synchrony and DXM indirectly boosts catecholamine tone at sub-psychedelic doses (26). Borderline affect storms, which correlate with amygdala-hippocampal hyper-connectivity, could subside as the stack restores frontal inhibitory control and normalizes extinction circuits (10).

A proof-of-concept case has already shown that DXM–bupropion (without piracetam or glutamine) rapidly reduced suicidality in a patient with depression, PTSD and borderline features (27). Our patient's early gains on the simpler DXM + fluoxetine backbone, and her subsequent relapse, mirror that report and point to the same limitation: NMDA blockade alone may not hold the new synapses in place. Adding piracetam and glutamine aims to "lock in" the reconsolidated networks and could prolong remission beyond the few-week plateau typical of ketamine monotherapy.

Conclusion

In this four-person case series, we show that a low-cost, over-the-counter glutamatergic "stack" centered on fluoxetine-enhanced dextromethorphan—and, when needed, piracetam and/or bupropion—can bring about fast, lasting relief in a variety of trauma-related conditions.

Shared findings included: Rapid easing of intrusive memories, ruminations, and somatic pain, usually within one to four weeks; Return to work or school after long periods of impairment; No

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dissociative, psychotic, or manic side-effects, even in two patients with bipolar vulnerability; and Benefits that held steady for months without raising the dose.

Biologically, the combination mimics ketamine's plasticity cascade: removing the NMDA "brake," boosting AMPA signaling, and driving a BDNF–mTOR surge that seems to break fear-based circuits and restore top-down control. Fluoxetine (or bupropion) prolongs dextromethorphan's action; piracetam heightens postsynaptic throughput; together they reproduce ketamine-like plasticity in a daily, safer package.

The work is limited by its retrospective nature, small sample, concurrent medications, lack of structured PTSD ratings (e.g., CAPS-5), and the inability to tease apart each drug's contribution. Still, the close timing between starting the regimen and marked improvement—seen across different trauma phenotypes—points to a specific glutamatergic effect rather than a monoaminergic or placebo response.

These early results support prospective trials of oral NMDA–AMPA modulators as an affordable alternative between ketamine infusion clinics and routine community care, potentially useful for both treating and preventing PTSD. Randomized studies with neuroimaging, trauma-specific outcome measures, and direct comparisons with Auvelity are now needed.

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