It is illegal to post this copyrighted PDF on any website. Treatment of Overthinking: A Multidisciplinary Approach to Rumination and Obsession Spectrum

Alice Flaherty, MD, PhD^{a,‡,*}; Douglas Katz, PhD^{b,‡}; Anne Chosak, PhD^c; Michael E. Henry, MD^d; Nhi-Ha Trinh, MD, MPH^e; Robert J. Waldinger, MD^f; and Jonah N. Cohen, PhD^g

Presented here is a series that highlights the discussion of a complex case by several expert clinicians, faculty members of Massachusetts General Hospital/Harvard Medical School, from distinct fields of study. Cross Talk demonstrates that clinical challenges can often be improved upon by leveraging more, rather than fewer, clinical perspectives.

To cite: Flaherty A, Katz D, Chosak A, et al. Treatment of overthinking: a multidisciplinary approach to rumination and obsession spectrum. *J Clin Psychiatry*. 2022;83(4):21ct14543. *To share:* https://doi.org/10.4088/JCP.21ct14543 © 2022 Physicians Postgraduate Press, Inc.

^aDepartments of Neurology and Psychiatry, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts ^bMassachusetts General Hospital, Harvard Medical School, Boston, Massachusetts ^cCenter for OCD and Related Disorders, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts ^dDauten Center for Bipolar Treatment Innovation, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts ^eDepartment of Psychiatry Center for Diversity, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts ^fProgram in Psychodynamics, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts

⁹Center for Anxiety and Traumatic Stress Disorders, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts ‡Drs Flaherty and Katz contributed equally to this article.

*Corresponding author: Alice Flaherty, MD, PhD, Massachusetts General Hospital, 15 Parkman St, Boston, MA 02114 (Flaherty.Alice@mgh.harvard.edu).

ABSTRACT

Classic psychiatry patients are rare; real-world patients tend to have overlapping features of multiple disorders. Striving for diagnostic certainty, and treatments aimed at tentative diagnoses, often fail these patients. In such cases, tolerating diagnostic ambiguity and "treating the symptoms" can sometimes be transformative. An important symptom, often undertreated in a diagnosis-based approach, is rumination. We present a case study of a woman who, after 20 years of treatment failure, achieved significant symptom relief when her primary complaint—"labored thinking"—was targeted specifically. However, because no seriously ill person has only 1 symptom, 6 clinicians from different subdisciplines will discuss the patient's other issues, ones that an overfocus on rumination might leave out.

J Clin Psychiatry 2022;83(4):21ct14543

R umination is recursive, prolonged, and recurrent negative thinking about one's self, emotions, personal concerns, and life experiences.¹ Moberly and Watkins¹ describe rumination as a deleterious, amplifying cycle wherein rumination and negative affect reciprocally worsen each other over time. Rumination triggers negative mood states, which increases rumination and other mood-congruent cognitions, which in turn worsens negative mood. This cycle is partly maintained by positive beliefs held by ruminators that focusing on the causes and consequences of their problems will lead to positive solutions.² However, rumination has been consistently and negatively associated with effective problem solving in cross-sectional and experimental studies.^{3,4}

Unlike reflective thought that focuses on solving specific problems (eg, "Why was Margaret mad at me yesterday?"), ruminative thought is typically abstract and overgeneralized (eg, "Why do I always screw up?"). Rumination is similar to worry and obsession—other common forms of negative thinking—in that it is repetitive, difficult to stop, and often intrusive.⁵ However, worry focuses unproductively on future events, and obsession is a fear-driven, involuntary experience of undesired thoughts that erupt repetitively into consciousness. By contrast, rumination often feels intentional, a goal-oriented exploration of past and current distress symptoms, their causes, and consequences.

Rumination has been implicated in the onset and maintenance of multiple psychiatric disorders and is therefore considered a transdiagnostic pathological process.^{6–8} Rumination prospectively predicts depression onset,⁹ anxiety disorders,¹⁰ substance abuse,¹¹ eating disorders,¹² and posttraumatic stress disorder (PTSD) symptoms following trauma in large-scale, longitudinal studies.¹³ Rumination also explains prospective associations between anxiety and depressive disorders, which indicates that it is not a secondary effect of psychiatric disorders and instead may causally contribute to these conditions.^{8,14} Rumination is a risk factor for suicide behaviors.¹⁵ Rumination and obsession can coexist in a single patient, and in obsessive-compulsive disorder (OCD), ruminations about one's obsessions can worsen the obsessive symptoms.¹⁶

Despite unequivocal evidence for its harmfulness, patients often mistake rumination for productive reflection, believing it will someday provide valuable insight. They may also attempt to engage therapists in corumination, which may

For reprints or permissions, contact permissions@psychiatrist.com. ♦ © 2021 Copyright Physicians Postgraduate Press, Inc. J Clin Psychiatry 83:4, July/August 2022

Flaherty et al It is illegate post this convrighted PDE on any we			
	Current medications	All trials	
	Ketamine ^B nasal spray 110 mg qod Brexpiprazole ^B 2.75 mg qhs Memantine ^B 30 mg tid	Antidepressants: fluoxetine ^{SE} , paroxetine ^{SE} , citalopram, sertraline, escitalopram ^b , vortioxetine, venlafaxine, bupropion, clomipramine ^{B, SE}	

Escitalopram ^b 30 mg gd	lamotrigine ^b , lithium ^{b, SE}
Lamotrigine ^b 100 mg qd Lisdexamfetamine ^b 70 mg qd Dextroamphetamine- amphetamine ^b 10 mg q3pm	Neuroleptics: olanzapine, risperidone, quetiapine, clozapine, lurasidone, asenapine, aripiprazole ^b , brexpiprazole ^B NMDA antagonists: memantine ^B , ketamine ^B Pro-cognition medications: L-methylfolate, donepezil Stimulants: dextroamphetamine ^b , lisdexamfetamine ^b , modafinil
	<i>Benzodiazepines:</i> lorazepam ^o , clonazepam <i>Alpha agonists:</i> clonidine, guanfacine <i>Electrical:</i> ECT ^{SE} , TMS, light therapy ^b <i>Weight loss:</i> metformin, liraglutide

= significant benefit, ^b = benefit, ^{SE} = side effect.

Abbreviations: ECT = electroconvulsive therapy, NMDA = N-methyl-D-aspartate, TMS = transcranial magnetic stimulation.

help explain the finding that elevated baseline rumination predicts poorer outcomes to cognitive-behavioral therapy (CBT).¹⁷⁻¹⁹ When ruminating, patients become critical observers of their past selves in ways that can contribute to another widespread transdiagnostic symptom: dissociation.²⁰

Functional imaging studies show that ruminators have altered connectivity in the default mode network,²¹ a brain system whose activity mediates mind-wandering states that are important for memory consolidation and social cognition. Environmental risk factors for rumination include stressful life events, which provide negative emotions to ruminate on. Rumination is moderately heritable, and a substantial proportion of the genetic influences on rumination overlap with those on depression.²² Rumination is also to some extent a habit,²³ one that can be learned from ruminative family members. No one has yet studied whether higher education, with its emphasis on abstract thinking and generalization, is a risk factor for rumination, and whether some fieldsphilosophy and psychology come to mind-might pose higher risks than others.

New treatments have targeted rumination specifically. A novel online program provides rumination-focused CBT²⁴ but so far is available only as a research tool. Mindfulness-based CBT,^{25,26} which alters default mode network activity, decreases rumination.²⁷ Rumination's status as a cognitive habit suggests that exposure-response prevention (ERP) therapy can help break it, as it does with obsessional thinking.²² As a goal-directed pursuit behavior, rumination is likely mediated by dopamine,²⁸ and clinicians often use antipsychotic augmentation for patients with significant rumination.²⁹ Obsessional thought, by contrast, as a fear-driven behavior, typically responds to serotonin reuptake inhibitors. Rumination and obsession may be linked, though, by a response to N-methyl-D-aspartate (NMDA) receptor antagonists. Memantine has been used as second-line treatment for obsession.³⁰ Also, recent evidence shows that the NMDA antagonist ketamine can powerfully reduce ruminative thought.³¹

The following case history describes a woman with severe mental illness that was treatment resistant until her rumination responded dramatically to memantine, ketamine, and exposure therapy. Once her rumination improved, her other symptoms became more treatment responsive as well. She provided written consent to have her clinical case history published and chose a pseudonym to protect confidentiality.

CASE HISTORY AND TREATMENT COURSE

Drs Flaherty and Katz: Cella was a 42-year-old woman whose chief complaint was overwhelming "cognitive strain" that began suddenly at age 14. She was the youngest child of high achieving Taiwanese immigrants, whom she described as loving but strict, focused on academic excellence. In elementary school, Cella worried about cleanliness and had anxiety-related headaches, insomnia, and a throat-clearing tic. In middle school, she was a perfectionist who loved art and was fascinated with "mind control." She was

proud that she could turn off her social anxiety like a switch. One lunch hour early in high school, while eating with friends, she suddenly lost the ability to switch off her anxiety. Her thoughts jumbled, and she had a panic attack. Ever since that break, she said, her thinking had been a battle with dissociative fog.

Cella's anxiety, dissociation, and mood lability spiraled for the next 10 years. Medications didn't help much in that period (Table 1), although SSRIs made her hypomanic. She had many hospital stays, with discharge diagnoses that progressed from anxiety to depression to bipolar disorder to schizoaffective disorder. She left her elite high school. Cognitive testing showed normal intelligence and an obsessionality that was thought to be psychotic, not OCD. She described her teens as traumatic because her friends abandoned her, and her family believed her problems were voluntary. When she could not attend college, her depressions developed mood-congruent delusions about being toxic to others. By the age

For reprints or permissions, contact permissions@psychiatrist.com. \blacklozenge © 2021 Copyright Physicians Postgraduate Press, Inc. e2 PSYCHIATRIST.COM J Clin Psychiatry 83:4, July/August 2022

Lt is illegial to post this convrighted PDE on any wobsite CASE HISTORY AND TREATMENT COURSE (continued)

of 21, she was on clozapine treatment and began electroconvulsive therapy (ECT). Transient memory symptoms from ECT worsened her self-hatred. She attempted suicide by lighting herself on fire, sustaining third-degree burns on chest and neck.

For 2 years in her early twenties, Cella lived in a residential program that focused on CBT. She later said that therapy never helped but was her only social life and education. Although her admission diagnosis was schizoaffective disorder, her team concluded she had a cluster B personality disorder with minimal true Axis I component. She was discharged on aripiprazole 4 mg monotherapy only.

She lived with her siblings briefly and then alone in an apartment her parents paid for. Her family texted and phoned daily. She was afraid to learn to drive, to use the flame on the stove, to date, to work. Every semester she took one or two extension school classes in art or psychology. When perfectionism didn't lead to incompletes, she was able to get good grades. The cognitive strain never left, except during episodes of mild hypomania. She remained on low-dose aripiprazole but eventually stopped psychiatric care.

Treatment with Dr Alice Flaherty. At

age 32, at her sister's urging, Cella began treatment with me. During early visits, she repeatedly tried to describe her fogged brain and the effort of thinking, as in this excerpt from a 429-word email description: "In order to 'direct my mind,' I sort of strain to control, and it is hard to use my mind and direct it, so I get flummoxed and stressed and panicky. Actually, the 'controlling' part is hard to explain as far as breaking down the mechanisms that construe it; I just sort of do it, but it is stressful and harrowing."

In those early visits, she often brought stacks of childhood drawings and showed each to me for praise. She wished she could return to what she saw as her authentic, artistic 12-year-old self, free from both effortful social conformity and ruminative shame. She thought of authenticity as unlabored intuitive thought, compared to the strained cognitions that sucked her in when she tried to judge others' social responses to her. To treat Cella's cognitive strain, we tried several cognition medications that did nothing-until we tried memantine. In only a few days, her cognitive strain and ruminations eased greatly. "My mental clarity and organization seem to have just internally improved though, almost like magic...the increased clarity and improved 'grip on reality' is something I have never felt to this beneficial an effect with any medication before. I seem to better able to conquer my myriad distractions which...have an OCD-like quality to them." Energy and motivation improved, and she switched from bringing in childhood art to art she had just made.

Her family said that memantine made her much more interactive with them. Within a few months, Cella's mother renewed urging her to make friends and consider volunteer work. Cella angrily refused and said she had to be true to her nature. Cella, her mother, and I met once to discuss this. Their overall interaction seemed affectionate and intimate. Her mother's urgings decreased for years, until the next major treatment gain.

Cella felt that her medication response was finally evidence that she had not been making up her illness. It strengthened her hope that she had an authentic self, separate from her symptoms. We wondered if her cognitive strain was "pure-O" mental checking. The decrease in cognitive strain unmasked more conventional obsessive thoughts about health risks and her appearance. She seemed to have few clear rituals. Adding clomipramine helped decrease her obsessions significantly, but she gained so much weight that she stopped it. I could not persuade her to try OCD exposure therapy in those years.

During the next several years, Cella had a few cycles of hypomania and depression. Mood stabilizers had clear benefit that they had not had before she started memantine. However, during that period, she began to develop memantine tolerance, and resurgence of ruminations when each dose wore off. When hypomanic, she ruminated on her positive mood just as she ruminated on depressed mood when depressed. Mood stabilizers did not help her anxiety much until we switched aripiprazole to brexpiprazole. At about that time, she also started to report more benefit from stimulants. In retrospect, the stimulants may have been treating brexpiprazole sedation. She had clear stimulant crashes at the end of each day.

Because memantine is an NMDA receptor antagonist, we decided to switch to the similar but more potent drug ketamine, delivered by nasal spray. When Cella reached a dose of about 80 mg, ketamine, like memantine, immediately decreased rumination. In addition, it helped her mood more and stopped her chronic suicidal thoughts. Ketamine's benefit wore off abruptly within 2 days, so she took it every other day. With improved mood, she became more willing to try new things, including exposure therapy for her OCD.

She began therapy with a Taiwanese therapist but never started exposure therapy. Instead, she focused on her experience of trauma from her parents' high expectations. She said her therapist urged her to become independent by minimizing contact with her parents, but then also urged Cella to get a job and a date. Cella told me, "My therapist wants to be my new Taiwanese mother." Cella ended the therapy.

Finally, Cella began treatment with an exposure therapist. The payoff was dramatic. Her fears of germs and street dangers decreased, and she exercised regularly. She traveled abroad to an art course and made friends with another shy student.

Then the COVID pandemic began. Cella withdrew from her new activities and spent months living with her parents. They noted her improved mood but worried that ketamine and stimulants gave her dramatic daily mood and energy fluctuations. She sometimes fought with her family about household responsibilities. She spent a week with her sister, who has 2 small children, and said she loved being an aunt. Later, when her sister asked her to babysit, she canceled at the last minute because she needed to be true to her nature and work on an art project.

She stopped ERP, instead talking to her therapist about the stresses of being the child of immigrants. She ruminated about the possibility that she had complex

It is illocal to post this convrighted PDE on any website CASE HISTORY AND TREATMENT COURSE (continued)

PTSD. Six months ago, she found and began seeing 2 PTSD therapists, one from Taiwan; the other, the child of East Asian immigrants. She also enrolled in Douglas Katz's bipolar PTSD study.

Treatment with Dr Douglas Katz. Cella

was referred to a pilot trial of prolonged exposure therapy for people with cooccurring bipolar disorder and PTSD. The presence of a criterion A trauma (eg, experiencing a life-threatening event) was not required for eligibility.

Cella's index trauma was set in 2008. The democratic primary race between Hillary Clinton and Barack Obama was in full swing. Cella was interested in music, philosophy, and politics, but she had no friends and no job, and she felt tortured by OCD, bipolar mood instability, and a crippling fear of social condemnation. Her sister thought she might "click" with a tech in her laboratory named Curtis, and after much persuasion Cella agreed to meet him. Their get-togethers were excruciating for Cella, as she was convinced that her vocal tics-throating clearing and snorting—would reveal her repulsiveness and Curtis would politely but promptly end the friendship. But they did develop a friendship, going to a few rock concerts together and corresponding about over email about the primary race.

They also spent an autumn day together canvassing for Obama, and this is where her index trauma occurred. They drove to Rhode Island together in the morning, her palms sweating and stomach lurching as she tried desperately to act ironic and cool while suppressing her tics. The canvassing itself was terrifying; every doorbell rung might initiate an exchange with a citizen either hostile to Obama, annoyed at being interrupted, or both. After 8 hours of clenched-fist politicking, Cella and Curtis went out for pizza with 4 fellow canvassers and her distress accelerated. She could not make eye contact with anyone and was frozen in fear, convinced that public mortification was imminent.

When she woke up the next day, she had an interesting thought. "I spent the whole day yesterday trying to be someone other than myself, and it was awful. Friends are supposed be able to be authentic with each other. That is the whole point of friendship!" So, she took a risk and wrote Curtis an email expressing her true feelings about Hillary Clinton, whom she believed had engaged in immoral tactics to discredit Obama. She remembered one line in her email to Curtis in particular: "Fuck Hillary Clinton!"

The email reply from Curtis the next day brought the humiliation that Cella had been so desperate to avoid. She recalls Curtis castigating her for being so critical of Hillary Clinton, "This is really unbecoming of you," he wrote, and he went on to lecture her about how all people should be treated with dignity, including Hillary Clinton. As she put it during one imaginal exposure, "I tried being genuine and got crushed for it." Her friendship with Curtis ended, and she withdrew from that social world.

During her exposure therapy, 13 years later, Cella still reported disturbing dreams of the index event, hyperarousal and extreme distress when reminded of it, and avoidance of external reminders. She also reported harsh self-blame for the event, with associated feelings of mortification. During her first several imaginal exposures, she described the agonizing day canvassing with Curtis: "I am so odd and out of control"; "Curtis is tolerating me, just being nice to me because of my sister"; "I am so annoying and gross"; "He can hear me snorting and can't wait until this is over."

Her distress scores remained uncomfortably high (between 70-90 out of 100 on the Subjective Units of Distress Scale [SUDS]) throughout her first 4 imaginal exposures. Her torment was palpable as she repeatedly recounted the story. There were nascent signs of movement, however. Before her fourth imaginal exposure, she reported that over the past several days she had begun to experience a broader range of emotions than is typical for her. Before her fifth imaginal exposure, she reported the insight, "I will have more control over my future if I have more control over my mindset, and I've been in a bad mindset for a long time." She even asked aloud, "Does Curtis really think I'm a detestable person? I don't know." She was also doing in vivo exposures between sessions that provided brief glimpses of a fuller, freer

life for her. She had been saying hello to her neighbors, who did not appear to recoil. She left the house without using the bathroom, facing a fear of being out and unable to find one. She was purposely late for an appointment, risking censure. And she began work on an art project, a highly valued activity, despite the flood of self-criticism that often accompanied her creative endeavors.

We decided she would print the original emails and read them aloud for her remaining imaginal exposures. The day of canvassing had been incredibly painful, but it was the email from Curtis that left the deepest wounds. I was intrigued by this proposal because I had a strong suspicion that Curtis' words were far less eviscerating than she remembered. The real email could help destabilize a trauma-related belief and facilitate a memory reconsolidation process that establishes a more benevolent stance toward herself.

Reading these emails aloud she noticed that she never wrote "Fuck Hillary Clinton!" and that in fact Curtis' email to her varied between neutral and caring. He did say that her personal attack on Hillary Clinton was unbecoming, but the rest of the email was cordial and contained the language of friendship, even mentioning future plans. Cella's cadence slowed and her tone softened as she repeatedly read these emails aloud, and her SUDS score dropped to 50. Throughout the rest of the treatment, her attitude toward herself became gradually gentler.

Progress was nonlinear, however. Cella arrived subdued and dysphoric for the eighth of 10 sessions. When I inquired about the change, she told me that she was sad that when the treatment ended her progress would evaporate. I normalized her concerns and worked to frame her growth as just beginning, reminding her that during our final session we would make plans for her to continue with exposures, connecting them to her longer-term goals of making new friends with whom she could be her true self.

Cella's treatment wrapped up with a lot of mutual appreciation and optimism about her future. She made plans to meet a new acquaintance in person. She said things like "This past week, when I've

It is illegal to post this convrighted PDE on any website CASE HISTORY AND TREATMENT COURSE (continued)

wanted to do something, I've just done it." She was attending her art classes and speaking up during them. She was still experiencing some PTSD symptoms posttreatment, however, and prolonged exposure therapy seemed to merely commence what would be a lengthy recovery process. Her score dropped from 67 (very high) to 32, indicating remission from PTSD. More importantly, new beliefs appeared in embryonic form: that she was not loathsome but was simply a human being trying to be okay, and that she could perhaps begin to live more authentically, in view of and in relationship with others.

In their recent systematic review of rumination in PTSD, Moulds et al¹³ distinguish between the intrusive symptoms of PTSD (eg, nightmares, intrusive memories) and trauma-related rumination, which refers to perseverative thinking about trauma and its consequences. Cella dwelt on her actions

during the traumatic event ("He can hear me snorting and is disgusted by me") and its consequences ("I'm not meant to be out in the world"). Repeating processing of her trauma memories did appear to reduce Cella's rumination, but it was clear that her general overvaluation of thinking and decades-long habit of perseverative cogitation would continue to produce and maintain highly distressing symptoms until targeted directly and intensively in treatment.

Cognitive-Behavioral Therapy Perspective

Dr Anne Chosak

Obsessions are defined as intrusive, unwanted thoughts, images, or urges. Compulsions are any action intended to reduce the distress of intrusions; these actions can be observable or covert (eg, mental rituals like praying, replacing a bad thought with a good thought). Rumination is any repetitive thinking, worry, or analysis; in the context of OCD, rumination can be experienced as an obsession (eg, unwanted, intrusive worry thoughts), but actively engaging with the content of the rumination would be a compulsion.

Cella's classic OCD symptoms, positive response to CBT for OCD, and positive response to clomipramine are all consistent with a diagnosis of OCD. Her rumination/ labored thinking symptom may not be exclusively OCD, but viewing her case through an OCD/CBT lens does suggest some treatment considerations. If Cella's cognitive strain is in fact OCD, then the obsessions would be the occurrence of the ruminative thoughts, whereas the compulsions would be cognitive checking, analysis, and attempts to control or neutralize the thoughts.

Whether her symptoms reflect OCD or not, Cella's efforts to characterize them, and focus on how that "might set her free," seem counterproductive. From a CBT perspective, actively engaging with ruminations reinforces symptoms and, in Cella's case, probably also reinforces her identity as psychiatrically ill. From this conceptualization, the therapeutic goal would be developing skills toward a more mindful, nonreactive awareness of ruminative thoughts and a concept of authentic being that is not overly identified with the cognitive strain symptoms.

To this end, psychoeducation about the role of rumination in reinforcing symptoms would be the first step. It is essential that Cella reorient her beliefs around the function of the rumination; if she genuinely believes she can "think" her way out of her illness, she will continue to actively engage with ruminations. To improve her insight and motivation around resisting the urge to analyze her own thoughts, one might try evaluating the evidence of whether rumination has truly worked for her (eg, cognitive reevaluation) and discussing whether Cella's goals and values are helped or hindered by her engaging with, and identifying with, the cognitive strain symptoms.

Once Cella is on board with the goal of reducing active engagement with the ruminative symptoms, there would be several CBT approaches to try, so that she is better able to tolerate her cognitive symptoms when they arise (eg, letting thoughts come and go naturally). The "E" of ERP, exposure, would be Cella purposefully triggering a ruminative thought; the "RP," or response prevention, would be using her skills to prevent engaging with the rumination. Potential skills could include labeling and redirecting, engaging in mental activities incompatible with rumination (eg, solving a word puzzle), learning to tolerate uncertainty, and mindfulness and acceptance practices. Given Cella's tendency to overanalyze, I would not recommend cognitive restructuring as a strategy, as it could become just another cognitive compulsion. The CBT goal would be to teach Cella skills to cope adaptively with her intrusive ruminative thoughts and to continue to increase her capacity and motivation to be more present and engaged with the world around her.

Psychopharmacologic Perspective

Dr Michael E. Henry

Cella's chronic course can be characterized as having mood lability, psychotic thought processes, anxiety, and rumination. From age 22 to 24, she lived in a therapeutic residential program. Her medications, which had included clozapine, were weaned down to aripiprazole 4 mg/d monotherapy. This maintained her out of the hospital but did not stop her ruminative psychotic internal dialogue. The addition of memantine brought her significant relief. Over time, the antiruminative effects of memantine faded. They were recaptured, along with a reduction of her chronic suicidal thoughts, by the addition of intranasal ketamine.

Her current medications are as follows: ketamine nasal spray 110 mg every other day, brexpiprazole 2.75 mg at

For reprints or permissions, contact permissions@psychiatrist.com. ♦ © 2021 Copyright Physicians Postgraduate Press, Inc. J Clin Psychiatry 83:4, July/August 2022 PSYCHIATRIST.COM ■ e5 **It is illegal to post this copy** bedtime, memanine 30 mg three times a day, escitalopram 30 mg daily, lamotrigine 100 mg daily, lisdexamfetamine 70 mg daily, and dextroamphetamine-amphetamine 10 mg daily at 3:00 PM. It is noteworthy that she was maintained out of the hospital for 15 years with such a low dose of aripiprazole. While she may be particularly responsive to the therapeutic benefits of aripiprazole, she may also have decreased metabolism of the medication. Genetic variability in the cytochrome P450 2D6 enzymes has been reported in individuals of Asian descent.³² It also suggests that the concentration of brexpiprazole may be higher than expected in the blood.³³ Commercially available genotyping should be able to answer this question.

With respect to the rumination, memantine and ketamine are both NMDA glutamatergic receptor antagonists, and this likely explains why ketamine was able to recapture the benefits of memantine when they started to fade.³⁴ Ketamine's known antisuicide properties provided additional clinical benefit without triggering a relapse of her psychosis, which likely reflects the mechanistic differences between the two drugs.³⁵ If so, it may be possible to simplify the regimen by discontinuing the memantine. Once the memantine has been discontinued, the dose of stimulants should be revisited. She has a strong anxiety component to her illness, and the stimulants can exacerbate anxiety and mood lability.

Multicultural Perspective

Dr Nhi-Ha Trinh

As Director of the MGH Psychiatry Center for Diversity, I was asked to consider the sociocultural perspective of this patient's presentation. I would like to frame the discussion with an overall conceptual framework of cultural humility and then consider how we might further explore the patient's cultural identity, with the aim of understanding ultimately what might be healing to her.

Cultural humility is a lifelong process of self-reflection and self-critique whereby the clinician starts with an examination of her/his own beliefs and cultural identities prior to learning about the cultural identities of our patients.³⁶ The concept carries meaning for any provider who is working with someone not only *different from*, but also *similar to* themselves in terms of any cultural dimension—race, ethnicity, gender, religion, gender identity, sexual orientation, socioeconomic status, or geographic origin.

We all have grown up in our own family cultures and are in turn influenced by the larger communities and society in which we have marinated, which influence the lens with how we see the world. As culturally humble clinicians, we must remain committed to examining our own biases, especially if we find ourselves making assumptions that may come up as we read about a patient from an overachieving successful immigrant Taiwanese family. Although we each may have some experience and cultural knowledge about the patient's background, we would do well to hear from the patient herself. **Outimately**, we must understand with the patient what it means to her to be Taiwanese American. Some of her conflicts may be intrapsychic, some of her challenges interpersonal, but, in short, we cannot assume that her issues all stem from cultural differences based on her ethnic identity. I would recommend to her treatment team to further explore with the patient her multidimensional cultural identity,³⁷ as well as inquire into her explanatory model of health and illness using the *DSM-5-TR*'s cultural formulation interview.³⁸ Asking more explicit, detailed questions regarding her cultural background and her beliefs about illness and health would give her, and us, a more robust picture of the cultural factors that may be promoting or impeding her recovery.

Psychodynamic Perspective

Dr Robert J. Waldinger

This case is a classic illustration of how thoughtful clinicians encounter someone who defies psychiatric categorization. Cella's fluctuating symptoms run the gamut from psychosis to depression to cognitive strain, her interpersonal style casts her treaters in the roles of supportive friends and pushy parents, and she experiences herself alternately as functional and an invalid, as traumatized and merely hypersensitive. This bewildering array of clinical phenomena is characteristic of people who have failed to develop a stable sense of self. *Identity diffusion*,³⁹ as it is often termed, is a psychodynamic concept that both predicts fluctuation in clinical presentation and offers specific suggestions for treatment.

What does identity diffusion look like? Fluctuation is the hallmark. There is "stable instability" in symptoms and mood states, as both are strongly influenced by environmental conditions. For example, at any given moment, Cella's mood is sensitive to whether she feels that a needed person is more or less available. This symptom fluctuation is baffling for prescribers, who may engage in polypharmacy that exacerbates rather than alleviates problems. Instability in interpersonal relationships means that the same treater may look like a savior in one session and a nagging parent in another. Patients with this problem may experience themselves as "different people" depending on who they are with. In Cella's case, she experiences herself differently with her psychiatrist than with her psychologist, and her treaters experience her differently as a result. This can lead to classic splits among treaters, prompting disagreements about the patient's problems and how to treat them.

Framing Cella's situation as stemming in part from identity diffusion informs treatment. Consolidation of identity is a long process (years rather than weeks) and often happens in a steady, consistent psychotherapy with one stable treater. Building a solid treatment alliance is the first step, and weathering the storms of Cella's mood swings and interpersonal fluctuations can help Cella integrate fragmented self-images into a more coherent and complex sense of who she is. Strong psychopharmacology support

website.

It is illegal to post this copyrighted PDF plays a central role in symptom management, and good Published online: July 6, 2022.

communication among treaters is essential to avoiding the splits that can derail the treatment.

Summary: Integrative Perspective

Dr Jonah N. Cohen

Cross Talk provides an opportunity to think deeply about a case from multiple perspectives, potentially informing a treatment that is more than the sum of its parts. Cella presents with heterogeneous and shifting symptoms, a clinical presentation that often poses a challenge when care is focused on treating specific psychiatric disorders. Drs Flaherty and Katz have organized their conceptualization of Cella around rumination, increasingly understood as a transdiagnostic driver of psychiatric suffering.

Dr Waldinger discusses the concept of identity diffusion to explain the varying nature of Cella's clinical symptoms. I believe Dr Waldinger is correct in his conceptualization of the underpinnings of Cella's symptoms. Cella does not seem to have the "glue" to hold a stable sense of herself across different situations and time. Certain symptoms develop out of a need (in Cella's case, an unstable sense of self) and serve an important function. In this vein, rumination might be Cella's attempt to make order, via an unrelenting analysis, of a world that is often experienced as chaotic and terrifying. Cella needs help finding more adaptive ways of navigating that does not require painful cognitive strain.

There are several more top-down, symptom-focused, approaches that might be helpful following the thoughts of Drs Chosak, Henry, and Trinh. Dr Chosak discusses helping Cella reduce her rumination via ERP, and Dr Henry's discussion of psychopharmacology targeting Cella's ruminative processes will be essential in augmenting the ERP. Helping Cella to reduce her rumination via psychopharmacology and ERP might help her to cultivate a truer sense of control over her mind and world, potentially leading to feelings of agency and mastery. We have seen that when Cella's rumination is more in check, there is more space for actions consistent with developing a sense of self (eg, when Cella started to make art and show it to Dr Flaherty after starting memantine). The effort to help Cella form a more coherent sense of self is also perfectly consistent with Dr Trinh's discussion of cultural humility and the importance of working with Cella to help explore her cultural identity. This work might help Cella to form a narrative that helps connect aspects of herself-both intrapsychic and sociocultural-a crucial component to a coherent sense of self.

Although rumination might be Cella's attempt at making order out of chaos, Cella's intense ruminations might instead be partially preventing her from effectively establishing a coherent sense of self. Cella's case exemplifies how thinking both deeply and pragmatically about a case, from numerous theoretical views, can lead to more effective and comprehensive treatment. **Relevant financial relationships:** Drs Waldinger and Cohen are board members of the Endowment for the Advancement of Psychotherapy at Massachusetts General Hospital. Dr Henry's spouse works for Roche Pharmaceuticals. All other authors report no relevant financial relationships.

on any

Funding/support: Cross Talk is financially supported by the Endowment for the Advancement of Psychotherapy at Massachusetts General Hospital. Dr Henry is supported by the National Institute of Mental Health (SR01MH112737-03).

Role of the sponsor: The funding agency had no role in the preparation, review, or approval of the manuscript or the decision to submit the manuscript for publication.

Statement of de-identification and consent: The individual featured in this case provided written consent to have her clinical case history (including psychiatric and psychotherapy related information) published. The patient's name has been changed to protect confidentiality.

REFERENCES

- 1. Moberly NJ, Watkins ER. Ruminative self-focus, negative life events, and negative affect. *Behav Res Ther.* 2008;46(9):1034–1039.
- Kubiak T, Zahn D, Siewert K, et al. Positive beliefs about rumination are associated with ruminative thinking and affect in daily life: evidence for a metacognitive view on depression. *Behav Cogn Psychother*. 2014;42(5):568–576.
- Luca M. Maladaptive rumination as a transdiagnostic mediator of vulnerability and outcome in psychopathology. J Clin Med. 2019;8(3):314.
- Lyubomirsky S, Nolen-Hoeksema S. Effects of self-focused rumination on negative thinking and interpersonal problem solving. J Pers Soc Psychol. 1995;69(1):176–190.
- van Rijsoort S, Emmelkamp P, Vervaeke G. Assessment of worry and OCD: how are they related? *Pers Individ Dif.* 2001;31(2):247–258.
- Nolen-Hoeksema S. The role of rumination in depressive disorders and mixed anxiety/depressive symptoms. J Abnorm Psychol. 2000;109(3):504–511.
- 7. Nolen-Hoeksema S, Wisco BE, Lyubomirsky S. Rethinking rumination. *Perspect Psychol Sci.* 2008;3(5):400–424.
- 8. McLaughlin KA, Nolen-Hoeksema S. Rumination as a transdiagnostic factor in depression and anxiety. *Behav Res Ther.* 2011;49(3):186–193.
- Grassia M, Gibb BE. Rumination and prospective changes in depressive symptoms. J Soc Clin Psychol. 2008;27(9):931–948.
- Hirsch CR, Krahé C, Whyte J, et al. Interpretation training to target repetitive negative thinking in generalized anxiety disorder and depression. J Consult Clin Psychol. 2018;86(12):1017–1030.
- Memedovic S, Slade T, Ross J, et al. Rumination and problematic substance use among individuals with a long-term history of illicit drug use. Drug Alcohol Depend. 2019;203:44–50.
- Smith KE, Mason TB, Lavender JM. Rumination and eating disorder psychopathology: a meta-analysis. *Clin Psychol Rev.* 2018;61:9–23.
- Moulds ML, Bisby MA, Wild J, et al. Rumination in posttraumatic stress disorder: a systematic review. *Clin Psychol Rev.* 2020;82:101910.
- 14. Ehring T, Watkins ER. Repetitive negative thinking as a transdiagnostic process. Int J Cogn Ther. 2008;1(3):192–205.
- Tang H, Xiong T, Shi J, et al. Global and reflective rumination are related to suicide attempts among patients experiencing major depressive episodes. BMC Psychiatry. 2021;21(1):117.
- Wahl K, van den Hout M, Heinzel CV, et al. Rumination about obsessive symptoms and mood maintains obsessive-compulsive symptoms and depressed mood: an experimental study. *J Abnorm Psychol.* 2021;130(5):435–442.
- Jones NP, Siegle GJ, Thase ME. Effects of rumination and initial severity on remission to cognitive therapy for depression. *Cognit Ther Res.* 2008;32(4):591–604.
- Ciesla JA, Roberts JE. Self-directed thought and response to treatment for depression: a preliminary investigation. J Cogn Psychother. 2002;16(4):435–453.
- Kertz SJ, Koran J, Stevens KT, et al. Repetitive negative thinking predicts depression and anxiety symptom improvement during brief cognitive behavioral therapy. *Behav Res Ther.* 2015;68:54–63.
- Vannikov-Lugassi M, Soffer-Dudek N. Rumination and dissociation: the mediating role of poor sleep quality and presleep cognitions. *Psychol Conscious*. 2018;5(2):185–211.
- 21. Lois G, Wessa M. Differential association of default mode network connectivity and rumination in healthy individuals and remitted MDD patients. *Soc Cogn Affect Neurosci.* 2016;11(11):1792–1801.
- Johnson DP, Whisman MA, Corley RP, et al. Genetic and environmental influences on rumination and its covariation with depression. *Cogn Emotion*. 2014;28(7):1270–1286.
- 23. Watkins ER, Nolen-Hoeksema S. A habit-goal framework of depressive

Flaherty et al It is illegal to post this copyrighted PDF on any website.

- Watkins ER. Rumination-Focused Cognitive-Behavioral Therapy for Depression. Guilford Publications; 2018.
- Segal ZV, Teasdale JD, Williams JMG. Mindfulness-Based Cognitive Therapy: Theoretical Rationale and Empirical Status. In: Hayes SC, Follette VM, Linehan MM, eds. Guilford Press; 2004:44–65.
- Farkas GM, Beck S. Exposure and response prevention of morbid ruminations and compulsive avoidance. *Behav Res Ther.* 1981;19(3):257–261.
- Andreotti E, Congard A, Le Vigouroux S, et al. Rumination and mindlessness processes: trajectories of change in a 42-day mindfulnessbased intervention. J Cogn Psychother. 2018;32(2):127–139.
- Whitmer AJ, Gotlib IH. Depressive rumination and the C957T polymorphism of the DRD2 gene. *Cogn Affect Behav Neurosci*. 2012;12(4):741–747.
- 29. Lee Y, Kang N-I, Lee K-H, et al. Effects of antipsychotics on rumination in patients with first-episode psychosis. *Prog Neuropsychopharmacol Biol Psychiatry*. 2020;103:109983.
- Ghaleiha A, Entezari N, Modabbernia A, et al. Memantine add-on in moderate to severe obsessive-compulsive disorder: randomized doubleblind placebo-controlled study. J Psychiatr Res. 2013;47(2):175–180.
- 31. Vidal S, Jermann F, Aubry J-M, et al. Effect of ketamine on rumination in treatment-resistant depressive patients. *J Clin Psychopharmacol*.

- Zo20,40(0),507–510.
 Zhang X, Liu C, Zhou S, et al. Influence of *CYP2D6* gene polymorphisms on the pharmacokinetics of aripiprazole in healthy Chinese subjects. *Pharmacogenomics*. 2021;22(4):213–223.
- 33. Brexpiprazole [package insert]. Otsuka America Pharmaceutical, Inc; 2022.
- Dean RL, Hurducas C, Hawton K, et al. Ketamine and other glutamate receptor modulators for depression in adults with unipolar major depressive disorder. *Cochrane Database Syst Rev.* 2021;9(9):CD011612.
- Ionescu DF, Bentley KH, Eikermann M, et al. Repeat-dose ketamine augmentation for treatment-resistant depression with chronic suicidal ideation: a randomized, double blind, placebo controlled trial. J Affect Disord. 2019;243:516–524.
- Tervalon M, Murray-García J. Cultural humility versus cultural competence: a critical distinction in defining physician training outcomes in multicultural education. J Health Care Poor Underserved. 1998;9(2):117–125.
- Hays P. Addressing Cultural Complexities in Counseling and Clinical Practice: An Intersectional Approach. 4th ed. American Psychological Association; 2022.
- American Psychiatric Association. *Diagnostic and Statistical Manual of* Mental Disorders. Fifth Edition, TR. American Psychiatric Association; 2022.
- 39. De Meulemeester C, Lowyck B, Vermote R, et al. Mentalizing and interpersonal problems in borderline personality disorder: the mediating role of identity diffusion. *Psychiatry Res.* 2017;258:141–144.