

# Clinical Remission of Treatment-Resistant Depression, Polysubstance Abuse, and Antidepressant Discontinuation Syndrome Through Engagement of Lifestyle Interventions

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## ABSTRACT

**Background** • This case illustrates the relationship between gut, hormonal, and brain function in that dietary changes, mindfulness interventions, and detoxification led to resolution of disabling psychiatric symptoms and protracted psychotropic medication withdrawal symptoms.

**Summary** • A 50-year-old partnered, unemployed, Caucasian female with a history of major depressive disorder, multiple suicide attempts, extensive trauma and abuse, and substance abuse presented for outpatient management. The patient reported limited benefit from over two decades of conventional treatment with psychotropic medications. She presented with depression and symptoms of protracted withdrawal after self-discontinuation of multiple psychiatric medications

and was prescribed a dietary, detoxification, and supplementation regimen by the primary author. Additional lifestyle interventions implemented included daily meditation, dry-skin brushing, and coffee enemas.

**Conclusion** • This case exemplifies dramatic clinical remission after cessation of medication treatment and engagement of lifestyle interventions, which include dietary change, meditation, and detoxification. As such, when limited results are achieved by psychotropic medication, tapering combined with dietary interventions as the first-line therapy should be considered. This case is also evidence of the role of lifestyle interventions in treating protracted withdrawal symptoms associated with discontinuing psychotropic medications. (*Adv Mind Body Med.* 2020;34(4):##-##.)

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## INTRODUCTION

This is a case of clinical remission of severe, treatment-resistant depression complicated by polysubstance abuse. After twenty-five years of conventional pharmacologic treatment without adequate response, the patient successfully attained remission of symptoms through cessation of medication treatment and engagement of lifestyle interventions. Her case represents a promising alternative therapy for patients whose symptoms persist in spite of conventional medication trials. In cases like this, tapering

medications in combination with dietary and lifestyle interventions should be considered. This case will also be informative for clinicians treating patients who prefer to attempt non-pharmaceutical therapy as a first-line approach before initiating medication.

In addition to the burden to the individual, depression is the single largest contributor of global disability, accounting for 7.5% of all years lived with disability worldwide.<sup>1</sup> Between 2005 and 2015, the disease burden of depressive disorders in the United States increased by 17.32%, with depression making up 2.72 million disability-adjusted-life-years in 2016.<sup>2</sup> During 2013-2016, over 8% of Americans over age 20 experienced depression during a given 2-week period, with women (10.4%) being almost twice as likely as men (5.5%) to be affected.<sup>3</sup>

Most adults diagnosed with major depressive disorder will not experience remission with standard pharmacological treatment. Among those who attempt multiple trials of conventional pharmacotherapy, at least half will fail to achieve and sustain remission.<sup>4</sup> Chronic treatment-resistant

depression is associated with persistent disability, higher suicide risk, greater medical morbidity and mortality, and higher rates of healthcare utilization and expenditures.<sup>5</sup>

The STAR\*D trial, the largest and most expensive antidepressant effectiveness study ever conducted, was designed to assess the efficacy of antidepressant treatment in “real-world” patients. According to the STAR\*D primary outcome measure, the 17-item Hamilton Rating Scale for Depression (HRSD), remission rates in this highly generalizable sample were about half that in typical clinical trials (25.6% vs 48.4%), with mean reduction of HRSD in the STAR\*D trial (6.6 points) also about half that reported in comparator trials (14.8 points), suggesting that strict exclusion criteria in clinical trials may lead to major overestimations of antidepressant efficacy.<sup>6</sup> Moreover, of the 4,041 patients initially enrolled in the STAR\*D trial, only 108 (3%) reported remission at one year, while the rest had failed to remit, relapsed, or dropped out of the study.<sup>7,8,9</sup>

All antidepressant medications are associated with withdrawal symptoms. For example, symptoms of withdrawal from selective serotonin reuptake inhibitor (SSRI) medications have been documented to include general flu-like somatic symptoms, sensory symptoms, sleep disruption, gastrointestinal symptoms, sexual symptoms, disequilibrium, and cognitive symptoms. Withdrawal can also manifest as affective symptoms such as depression, anxiety, or irritability that may be misdiagnosed as a recurrence of the disorder.<sup>10</sup> Many of the antidepressant medication withdrawal symptoms reported in the literature were corroborated by the patient of this case study.

Notably, this case shows that dietary changes, mindfulness techniques, and detoxification practices can resolve both the symptoms of psychiatric diagnoses and of antidepressant medication withdrawal. Overall, the dramatic symptom resolution of this patient illustrates the inextricable relationship between gut, hormonal, and brain health and suggests multiple entry points for clinical intervention.

### PATIENT INFORMATION

This is the case of RC, a 50-year-old partnered, unemployed, Caucasian female with a history of depression with multiple suicide attempts, extensive trauma and abuse, and substance abuse. She presented for outpatient management with symptoms of depression and protracted withdrawal after self-discontinuation of multiple psychiatric medications. She was referred to the main author through the “Mad in America” website. The results of her physical exam are included in Table 1, and a list of the supplements and medications she was taking at presentation are listed in Table 2.

### Social and Family History

RC was born and raised in Chicago as the second eldest of 5 sisters. She was born vaginally and was likely breastfed. Her mother was physically abusive, volatile, psychotic, and she displayed periods of schizophrenic behavior, narcissism,

**Table 1.** Physical exam

Physical Exam	
Height	62 in (157.4 cm)
Weight	130 lb (59.0 kg)
Age at first menses	12
Lifetime pregnancies	3
Dates of birth	0

**Table 2.** Current Medications and Supplements

GTA Forte-II (dessicated pork glandular)
Nerve Fix Homeopathic
Royal Maca for Menopause
Rhodiola Rosea
Tyrosine
Tryptophan
Magnesium

and personality disorders. Her father was a violent alcoholic who left when the patient was 5. Her household was intensely chaotic; strangers boarded in the home, her mother walked around nude and publicly masturbating, and the house was deliberately burned down for insurance money. One of her sisters was a drug addict with mental illness who lived in the streets or in jail, and another sister was a severe alcoholic with anxiety and depression.

When the patient was 13, her mother moved to California and the patient remained in Chicago, living with a variety of friends and siblings. RC suffered sexual abuse at 13 including sodomy by her “boyfriend” who was 22. She also struggled with corporal punishment at school, including a teacher who sat panty-less on her desk in front of the classroom. The patient dropped out of high school during sophomore year but later attained her GED. She had a brief marriage at age 17 that lasted one year. She attended college later in life starting at age 33 and graduated at age 36. At age 41 (2006), she moved to New York to live with her current boyfriend.

### Psychiatric History

RC struggled with feelings of depression throughout her early twenties, describing herself as “never stable or happy.” At age 19, she was treated for pelvic inflammatory disease with 3 weeks of an IV antibiotic. At age 24, she was treated for an ear and throat infection with an antibiotic. She reported “never feeling the same again” after the course of antibiotics and stated, “I believe that the antibiotics pushed me over the edge into a clinical depression.” RC’s first major depressive episode began at age 25 and became increasingly worse in intensity. She went to a holistic doctor for depression in 1992 and was treated with herbs and homeopathic remedies including horsetail tea, which were not helpful. She then went to see a psychiatrist and an endocrinologist, and she was diagnosed with depression and hypothyroidism. She

was started on fluoxetine, clonazepam, and levothyroxine. She reports that the levothyroxine helped “take the edge off” but did not improve her mood. The patient was hospitalized for the first time later that year at age 26 for depression with suicidal ideation.

From ages 26-31, the patient was hospitalized ten times for severe depression and suicide attempts. RC underwent trials of amitriptyline, sertraline, risperidone, depakote, clonidine, bupropion, and trazodone for periods lasting weeks to months. She describes that the medication resulted in severe discomfort, akathisia, and worsening suicidal ideation. She made three suicide attempts by overdose with prescribed and over-the-counter drugs during this period. These were very serious attempts with up to 160 pills ingested. She ultimately settled on pursuing long-term medication therapy with tranylcypromine. Despite treatment, she continued to struggle with daily suicidal ideation.

At age 33, the patient switched to a new physician who stopped the tranylcypromine and started her on venlafaxine. She experienced a reduction in her symptoms from ages 33-36, and she was able to attend and graduate from college during this period.

At age 37, the patient experienced a relapse of severe depressive symptoms. Venlafaxine was then increased to the maximum dose. At age 40, she began experiencing dark, intrusive thoughts and was started on lorazepam. At age 43, she was switched from venlafaxine to duloxetine at the maximum dose. She was trialed on lithium and bupropion, and ultimately methylphenidate was added to her regimen in order to “boost” her response to antidepressants from ages 43-48. At age 45, the patient was diagnosed with acne rosacea and prescribed low-dose doxycycline for 5 years. She was prescribed hydrocodone/paracetamol and methadone for migraines from ages 45-47, became addicted to the medications, and eventually tapered off them. During this time she had high cholesterol, acid reflux, and eczema, and she was treated with an unknown medication, which she did not take consistently.

At age 48 in 2014, RC visited a functional medicine physician to attempt to assess whether nutritional deficiencies were contributing to her depression, skin issues, and migraines. That physician prescribed ciprofloxacin for gut dysbiosis after a stool test, and she subsequently developed neuropathy, muscle weakness, and suicidality, leaving her unable to walk for 4 months. The patient reported that this experience triggered a critical examination of all the prescription medications she was taking.

Using diet, supplements, and daily coffee enemas, the patient was able to regain daily functioning. Later in 2014, she initiated a strict elimination diet protocol in an attempt to heal her gastrointestinal (GI) tract. The diet she implemented was based on a combination of the Gut and Psychology Syndrome (GAPS) diet and Wahls Protocol diet (See section Typical Day’s Diet below). She experienced some benefit from these dietary changes.

Reading the “Mad in America” website motivated her to take action, and she reports having used information found on Dr. Brogan’s blog and other online resources in the decision to self-taper and discontinue all medications. In 2015, she began a taper from duloxetine, lorazepam, and methylphenidate. She tapered duloxetine over 5 weeks and lorazepam at decrements of 0.25 mg per day.

Two weeks after her last dose of the psychotropic medication taper, RC experienced the feeling of being electrocuted, burning in her GI tract, bloating, fear, volatile moods, and low tolerance to exercise. Her menstrual cycle abruptly ceased upon medication discontinuation, never to return. She experienced loss of libido and weight gain. She reported continuing to experience depression, though less severe in intensity than while on medication. Since the taper, she has not experienced any suicidal ideation, which she reported was present every single day while on medication. She reported sluggishness, leg pains, very low energy, weakness, brain fog, mood swings, repetitive thoughts, and intrusive images.

In 2016, the patient was prescribed levothyroxine for hypothyroidism again and then switched to glandular thyroid supplements. Both medications interfered with her sleep.

Upon presentation on May 17, 2016, the patient reported depression, racing and intrusive thoughts, poor memory, brain fog, fatigue, and poor concentration. She also endorsed neuropathy, global pain, waves of intense pain centered in the legs and feet, and weakness, constipation, digestive flares, food and supplement sensitivity, loss of libido, weight gain, rosacea, and e-cigarette use. She believed that many of these problems were the result of the 25 years of medication use. The patient reported exercising at least five days a week and practicing meditation nearly every day. She endorsed beginning to volunteer and said she was feeling hopeful.

**Table 3.** Pharmaceutical treatment between 1978-2016

Fluoxetine
Clonazepam
Levothyroxine
Amitriptyline
Sertraline
Risperidone
Valproate
Clonidine
Bupropion
Trazodone
Tranylcypromine
Venlafaxine
Duloxetine
Doxycycline
Hydrocodone/paracetamol
Methadone
Lithium
Ciprofloxacin

**Table 4.** Substance Use History

	Age of First Use	Most Intensive Use	Current Use
Cocaine	14	1982-1987; 1994-1997	
Marijuana	11	Occasional	
Alcohol	11	1977-1987; 1993-1997	
Cigarettes	10	1978-present	✓ (e-cigarette)
Other	27	1994-1997 (heroin IV)	

**Personal History of Substance Use**

During her teenage years, the patient was a user of alcohol, marijuana, heroin, and cocaine. She engaged in Alcoholics Anonymous and maintained some periods of sobriety, but continued to relapse and was a polysubstance intravenous drug user throughout her 20s. The patient finally became sober at age 31. The patient started smoking cigarettes at age 10 and was still using e-cigarettes at presentation.

**Typical Day’s Diet**

The patient’s diet of the last 13 months has consisted of a Paleo/GAPS diet made up mostly of very clean protein and vegetables. She eats farmer’s direct pastured fresh meat, wild-caught fresh fish, organic cooked and raw vegetables, occasional eggs from a local livestock farm, weekly kefir shots, and some tree nuts and seeds. She ferments her own kefir and vegetables and tolerates a very small amount of sauerkraut. She drinks filtered water, bone broth, and turmeric tea. She does not eat grains, beans, starches, soy, corn, nightshades, fruits, inflammatory oils, sugar, processed foods, or desserts. She prepares all meals herself.

**Mental Status Examination**

The patient presented casually dressed with short grey hair, dyed purple in the front. Her interactions were friendly, animated, and appropriate. She had no gait disturbance, psychomotor retardation or psychomotor agitation. Her eye contact was good and speech was within normal limits. She characterized her mood as “generally better.” Her affect was reactive and full. Her thought process was logical and goal-directed. She did not reveal suicidal, homicidal, or persecutory ideation, auditory or visual hallucinations, or ruminations and preoccupations. She demonstrated good insight and judgment, and she was alert and oriented to person, place, and time.

**DIAGNOSTIC ASSESSMENT**

**DSM-IV Impression**

**Axis I.** Major Depressive Disorder, recurrent, severe, r/o substance-induced.

**Axis II.** Evaluation of axis II was deferred for continued observation.

**Axis III.** Medical conditions affecting the patient’s current psychiatric state include hypothyroidism, neuropathy, and gastritis.

**Axis IV.** Stressors in the patient’s life include recent health management issues.

**Axis V.** The patient’s global assessment of functioning at time of presentation was determined to be a score of 60, characterizing moderate symptoms or moderate difficulty in social or occupational functioning.

**Laboratory Testing**

A set of laboratory tests were ordered, and results of note are listed in Table 5. All other ordered lab results were within normal/functional limits including comprehensive metabolic panel, complete blood count, C-reactive protein, carnitine assay, copper, DHEA, ferritin, heavy metal screen, glycosylated hemoglobin test, homocysteine, lipid panel, MTHFR gene mutation analysis, RBC magnesium, RBC zinc, vitamin B12, selenium, free T3, free T4, TSH, T3 reverse, thyroid peroxidase antibody, thyroglobulin, ANA, pregnenolone, vitamin D, 25 hydroxy, B<sub>1</sub>, B<sub>6</sub>, histamine, and phosphorous.

**Table 5.** Laboratory Results of Note

Laboratory Test	Result	Reference Range
TSH	0.023	0.450-4.500
Sodium	146	134-144
Vitamin B <sub>12</sub>	1098	211-946

**Formulation**

The patient is a 50-year-old Caucasian female, domiciled with her boyfriend, unemployed with a history of extensive abuse depression/suicidal ideation developing after first exposure to antibiotics at age 24, now status post discontinuation of multiple psychiatric meds with resultant protracted withdrawal resolved through lifestyle interventions.

**Interventions**

The patient was recommended to increase hydration to two glasses of filtered water before each meal and three additional glasses throughout the day. She was recommended to measure out 0.5 teaspoons of salt per day to consume throughout the day and encouraged to take 30 seconds prior to eating anything to express gratitude for the journey the food took to get to her.

The patient was recommended a regimen of kundalini yoga exercises that included Kirtan Kriya (11 minutes), Sat Kriya (11 minutes), and Meditation for Prosperity II (3 minutes).

The patient was prescribed hypothalamus, thyroid, and adrenal support supplements. For detoxification, she was encouraged to start twice-daily skin brushing to stimulate and cleanse the lymphatic system. She was recommended to continue daily coffee enemas. Twice-weekly baths for 15 minutes with 1 cup of baking soda and 1 cup of Epsom salts were also encouraged.

After one month, a more intensive supplement regimen was introduced (summarized in Table 6). White rice and white potatoes were reintroduced at this time.

At 2.5 months follow-up, the patient was recommended to start the Donna Eden Five Minute Routine energy medicine practice daily. She was encouraged to start doing kundalini yoga as an early morning sadhana practice and was suggested to add the Brain Fatigue kriya to her practice. Thyroid supplementation was increased to two tablets twice daily.

### Outcomes and Follow-up

At the first follow-up on June 15, 2016, the patient reported mood as “generally better” and described that she has felt able to start thinking. She reported taking 2 GTA Thyroid because Allergy Research (2) left her feeling tired and unable to sleep. Constipation resolved with return to GTA thyroid. RC reported good energy and that she started taking a creative writing workshop.

Upon second follow-up on August 13, 2016, the patient reported practicing kundalini yoga regularly. She reported that she had 10-12 days of disability since June, compared with >50% of days prior to that, and she reports good sleep. RC said that she is angry and irritable at times, largely at the medical system, and she endorsed ongoing brain fog and chronic constipation, as well as trouble distinguishing right from left. She feels physical pressure at her third eye, has no sex drive or longing for contact, and reports being 5-10 pounds overweight and suffering negative effects from CoQ<sub>10</sub>. RC endorsed worse constipation with proburt that she used aloe to regulate. She has been adding sauerkraut to diet, which she wasn't previously able to tolerate. She reported eating raw heart, thymus, liver, and kidney five times weekly and that inclusion of potato and rice has helped with blood sugar.

## DISCUSSION

### Antidepressant withdrawal/discontinuation syndrome

In 1997, a group of experts convened to develop a clear conception of the phenomenon of adverse events following discontinuation of SSRIs that had previously only been described in case reports.<sup>11</sup> The newly conceptualized “antidepressant discontinuation syndrome” symptoms included “dizziness, lightheadedness, insomnia, fatigue, anxiety/agitation, nausea, headache, and sensory disturbance,” and it was purported to last up to 3 weeks.<sup>12</sup> The “FINISH” mnemonic was conceived to aid clinicians in remembering the symptoms, standing for Flu-like symptoms, Insomnia, Nausea, Imbalance, Sensory disturbances, and Hyperarousal (anxiety/agitation).<sup>13</sup> Somatic symptoms

**Table 6.** Supplements prescribed after 30 days of diet and lifestyle intervention.

Hypothalamus: 2 at night
GTA Thyroid
Adrenal: 1/4 to half a tab
Alpha lipoic acid (ALA): 600 mg daily
N-acetylcysteine (NAC): 600 mg twice daily
Ubiquinol (Coenzyme Q10): 400 mg daily
Progurt Probiotic Sachets

including myalgias, arthralgias, parkinsonism, and electric-like shocks, similar to the “feeling of electrocution” reported by RC, have been described in the literature.<sup>14</sup>

In 2013, the updated DSM-V added an entry on Antidepressant Discontinuation Syndrome (ADS), describing a set of symptoms commonly seen after discontinuation of an antidepressant taken for one month or longer that typically appear within 2-4 days.<sup>15</sup> The brief DSM-V entry acknowledges the paucity of knowledge on the clinical course of the syndrome, reports that symptoms resolve over time with gradual tapering, and notes “After an episode, some individuals may prefer to resume medication indefinitely if tolerated.”<sup>15</sup> Little is known about the long-term harms of antidepressants, and in a recent systematic review of 12 trials on SSRIs, all authors concluded that the drugs were not beneficial in the long term.<sup>16</sup> The argument has been made that using the term “discontinuation syndrome” with regard to antidepressant medications does not reflect current evidence, minimizes the associated risks, and should be replaced with “withdrawal syndrome.”<sup>17</sup>

In contrast to the current APA guidelines that suggest that ADS symptoms typically resolve without treatment in 1-2 weeks,<sup>18</sup> there is increasing evidence that the symptoms are not as time-limited or easy to manage as initially reported.<sup>17 19</sup> A recent systematic review of 14 studies found that withdrawal incidence rates averaged 56%, with 46% of patients rating the severity of their symptoms at the highest possible level.<sup>20</sup> Seven out of ten studies that assessed withdrawal duration found that a significant number of people experienced withdrawal for longer than two weeks.<sup>20</sup> A recent analysis of posts on an antidepressant withdrawal website found a mean duration of 90.5 weeks of withdrawal symptoms with SSRIs and 50.8 weeks with SNRIs.<sup>21</sup> While likely biased towards patients with difficult withdrawal syndromes, this report identifies a subset of patients with protracted withdrawal symptoms that may be missed if clinicians conceive of withdrawal as a brief, self-limited phenomenon. One of the largest direct-to-consumer surveys on withdrawal from antidepressant drugs found that 38% of respondents discontinuing antidepressant medication experienced withdrawal symptoms for more than a year, and that 66.5% of the respondents claimed not to have received any information from their doctors on potential risks and side effects of the prescribed antidepressants.<sup>22</sup>

The APA guidelines on depression suggest an antidepressant taper over “several weeks,”<sup>18</sup> and UpToDate recommends a taper over 2-4 weeks.<sup>23</sup> There is evidence that a brief taper does not eliminate the risk of ADS, and that there is no significant advantage of tapering over abrupt discontinuation.<sup>24 25</sup> However, evidence suggests that these short tapers over a few weeks are less likely to be effective at reducing withdrawal syndromes than gradual dose reduction over a period of months.<sup>10</sup> Tapering regimens have been proposed using stepwise 10% reductions in serotonin receptor occupancy while monitoring for withdrawal symptoms, with reduction intervals ranging from 1 week<sup>26</sup> to a more conservative 1 month recommendation.<sup>10</sup> Using risk factors for ADS to identify patients who require a slower tapering regimen has also been proposed; proposed risk factors include being prescribed a higher than minimum effective dose for therapeutic effect, having experienced withdrawal symptoms with a missed dose, or having a failed previous attempt to discontinue.<sup>26</sup>

RC tapered the maximum dose of duloxetine over 5 weeks and experienced the onset of withdrawal symptoms two weeks later, including severe fatigue, weakness, and prominent sensory disturbances, which persisted for approximately 4 years. As she was at 120 mg daily, above the minimally effective dose, she was at higher risk for ADS and would likely have benefited from a slower tapering regimen. Additionally, using a 10% reduction in serotonin transporter occupancy dosing regimen, the dosage steps from duloxetine 60 mg would be 30 mg, 15 mg, 10 mg, 6 mg, 4 mg, 2 mg, 1 mg, 0 mg over a minimum period of 9 weeks.<sup>26</sup> RC had already made up her mind to come off all psychiatric medication, and thus in her case it would not have been appropriate to treat her withdrawal by restarting the antidepressant.

To counteract her protracted withdrawal symptoms, RC self-initiated *Rhodiola rosea*, tyrosine, tryptophan, and magnesium based on online information. *Rhodiola rosea* has been shown in case reports to stabilize patients withdrawing from psychotropic medication, and it has been demonstrated to reduce depression, anxiety, and fatigue in clinical trials.<sup>27</sup> After seeing Dr. Brogan, she was prescribed further supplements including alpha-lipoic acid, n-acetylcysteine, and ubiquinol. Adrenal and hypothalamus support were also initiated. N-acetylcysteine and magnesium promote parasympathetic nervous system relaxation and modulate excitatory NMDA receptors, which can aid in mitigation of withdrawal symptoms.<sup>28</sup>

### **Kundalini Yoga and Relaxation Response**

The practice of kundalini yoga prescribed to RC can be understood as exercises that elicit the relaxation response, which was first described by Walter Hess, PhD in 1949. Specifically, Dr. Hess won the Nobel Prize for his description of the anatomy of the relaxation response by characterizing the ergotropic and trophotropic centers in the cat hypothalamus. When stimulated electrically, the ergotropic

center produced symptoms of the sympathetic stress response, popularly called the “fight or flight” response. Conversely, stimulation of the trophotropic center, associated with parasympathetic activation, was associated with symptoms including decreased heart rate, blood pressure, respiratory rate, and an increase in gastrointestinal motility.<sup>29</sup> Hess called this response as “a protective mechanism against overstress.”<sup>30</sup>

In 1974, Herbert Benson, MD, officially coined the phrase “relaxation response,” an integrated nervous system response that consists of changes opposite to the sympathetic “fight or flight” response. He described four basic elements necessary to elicit this response in humans:

- 1) **Mental Device** - In order to shift away from normal logical thought, a stimulus such as a word should be repeated silently or audibly, or attention should be fixed on an external object.
- 2) **Passive Attitude** - When distraction arises, the subject’s attention should be redirected to the technique without worrying about performing it perfectly.
- 3) **Decreased Muscle Tonus** - The subject should be comfortable.
- 4) **Quiet Environment** - The technique should be performed in a setting with decreased interruption and few stimuli.<sup>30</sup>

The laboratories at Harvard Medical School have studied the benefits of mind/body response interaction for decades, finding that when a person engages the relaxation response, a specific set of physiologic changes occur, including decreased metabolism, heart rate, breathing rate, and slower brain waves. As such, the relaxation response can be an effective component of therapy for diseases that have stress as an etiologic component. Benson describes, “to the extent that any disease is caused or made worse by stress, to that extent this physiological state is an effective therapy.”<sup>31</sup>

These findings, in addition to other scientific evidence in the literature, underlie the efficacy and recommendation of kundalini yoga that was prescribed to RC. A common kundalini yoga technique called Kirtan Kriya (KK) has been shown to benefit people with Alzheimer’s,<sup>32 33</sup> depressive symptoms,<sup>34</sup> and anxiety.<sup>35</sup> The KK consists of specific sounds, posture, hand position, finger movements, and a unique focus. The practitioner sits comfortably, breathes naturally, and closes her eyes before chanting the sounds “Saa, Taa, Naa, Maa” (which means “birth, life, death, rebirth”). The chant is sung for two minutes, whispered for two minutes, repeated quietly for three minutes, then whispered and sung again for two minutes each. Through the exercise, the sound is visualized coming in through the top of the head and out the middle of the forehead in an “L” shape.<sup>29</sup>

As the fingertips, tongue, and vocal cords are highly represented on the cortical homunculus, a representation of

the anatomical divisions of the motor-sensory cortex, it is hypothesized that engaging the coordinated sound and finger movement during KK may be responsible for the increased blood flow seen in SPECT scan studies of the practice.<sup>29</sup> Specifically, the frontal lobes, prefrontal cortex, posterior cingulate gyrus, and anterior cingulate gyrus have been shown to experience changes in blood flow in response to the KK practice.<sup>29</sup> Furthermore, other studies have demonstrated lower levels of depressive symptoms, improvement in cognitive function, and improvement in telomerase activity in participants practicing KK.<sup>36</sup>

### **Antibiotic-Related Toxicity and Disability**

Ciprofloxacin belongs to a widely-prescribed class of antibiotics called fluoroquinolones, which have recently been recognized by the Food and Drug Administration (FDA) to cause what's known as fluoroquinolone-associated disability.<sup>37</sup> In fact, from the 1980s to 2015, the FDA received reports from over 60 000 patients reporting "serious adverse events" and have noted 6575 related deaths.<sup>38</sup> The severe side effects of these antibiotics include tendon rupture, chronic peripheral neuropathy, nervous system dysregulation, cardiotoxicity, hepatotoxicity, nephrotoxicity, and onset of type 2 diabetes.<sup>37</sup>

More broadly, antibiotic exposure has been shown to increase the risk of psychiatric symptoms such as depression and anxiety. For example, a large-scale study of patients receiving antibiotics demonstrated that treatment with a single antibiotic course was associated with higher rates of depression and anxiety, and repeated antibiotic exposures increased patients' risk of psychiatric symptoms.<sup>39</sup> Other analyses have found that quinolone antibiotics are associated with increased suicidal behavior and suicide attempts, especially when compared to other antibiotics.<sup>40</sup> Although there are some studies that do not find any associations between antibiotics, specifically fluoroquinolones, and suicidality, there are several case reports detailing suicide attempts and severe psychiatric symptoms following antibiotic treatment and resolution of symptoms after cessation of antibiotics.<sup>41</sup>

The deleterious effects of antibiotics, including physical disability and acute mental health concerns, illustrate how these medications should be prescribed with caution and that some types should be avoided as first-line treatments, particularly when a patient has pre-existing psychiatric issues.

### **Nutritional Interventions**

As noted in this case report, growing evidence suggests negative side effects from psychotropic medications and from tapering and withdrawal of these medications. As a result, other therapies for resolution of psychiatric symptoms are being considered, including dietary changes and nutritional interventions. Several studies have evaluated the persistence of mental health disorders in individuals following traditional "Western" diets, defined by Jacka et. al

as diets including fried foods, refined grains, high-sugar products, and beer, versus healthier alternatives.<sup>42</sup> One such study concluded that individuals following diets of vegetables, fruits, meat, fish, and whole grains were more likely to score lower on assessments of depression, dysthymia, and anxiety than those following the "Western" diet.<sup>42</sup> Another study concluded that individuals with a "whole food" dietary pattern emphasizing vegetables, fruits, and fish had lower odds of depression at a five-year follow-up than those with high consumption of processed food.<sup>43</sup> A meta-analysis of 13 observational studies by Lai et. al suggests similar findings, reporting that a healthy diet with high intake of fruits, vegetables, fruits, and whole grains was significantly associated (OR: 0.84; 95% CI: 0.76, 0.92;  $P < .001$ ) with reduced odds of depression.<sup>44</sup>

For her dietary intervention, prior to her work with Dr. Brogan, RC followed the Gut and Psychology Syndrome (GAPS) and Wahls Protocol diets in addition to fermenting her own vegetables and kefir and eliminating sugar, processed food, and grains from her diet. In the GAPS diet, a person eliminates grains, sugar (except in fruit), soy, starchy vegetables, some dairy products, and all processed foods. Similarly, the Wahls diet, based on the work of Terry Wahls, MD, excludes gluten, processed food, eggs, dairy products, and sugar. These two diets emphasize the consumption of vegetables, healthy fats, fermented foods, fruits, and organic meats. By following these two dietary protocols, RC adhered to the types of healthy diets that, as indicated by the studies above, are associated with a reduction in symptoms of depression and anxiety. Additionally, other studies suggest that fermented foods are beneficial for cognition, which RC also incorporated into her diet regime.<sup>45,46</sup>

RC also reports using supplements such as probiotics and N-acetylcysteine (NAC), which are supported by scientific literature to mitigate psychiatric symptoms. In a placebo-controlled trial examining patients with major depressive disorder, researchers found that those receiving probiotic supplements had significantly decreased Beck Depression Inventory scores after 8 weeks when compared with placebo as well as lower serum C-reactive Protein (CRP) concentrations, an inflammatory marker associated with increased psychological distress.<sup>47,48</sup> Similar resolution of symptoms has been shown in placebo-controlled trials with NAC, with one study indicating that patients with schizophrenia treated over a 24-week period demonstrated improved scores on the Positive and Negative Symptoms Scale (PANSS) total, positive, and general scales as well as on the Clinical Global Impression (CGI).<sup>49</sup> A similar placebo-controlled study was conducted to assay the effect of NAC effect on depression symptoms in bipolar patients, in which researchers found that NAC treatment significantly improved patients' scores on the Montgomery Asberg Depression Rating Scale (MADRS).<sup>50</sup>

Overall, despite the lack of large-scale, long-term research and controlled trials analyzing the benefits of paleo-like diets such as the GAPS and Wahls protocols, anecdotal

evidence, including the experience of RC, suggests that these dietary protocols may be beneficial for resolution of mental health and medication-induced symptoms. Continued research in the area of dietary and supplemental interventions represents promising opportunities for new therapies for psychiatric healing.

## CONCLUSION

This case exemplifies dramatic clinical remission after cessation of medication treatment and engagement of lifestyle interventions, which include dietary change, supplementation, meditation, and detoxification. When medication demonstrates limited results, tapering combined with dietary interventions as the first-line therapy should be considered. This case is also evidence for the role of lifestyle interventions in treating protracted withdrawal associated with discontinuing psychotropic medications.

## PATIENT PERSPECTIVE

### Update from RC as of 2018:

"I'm going to be honest, this has been a hard road! I became disabled by depression from 1994-1999. Then starting around 2003 I became totally disabled for the second and final time, unemployable, socially unreliable, isolated and totally dependent on a significant other. My world became and was very small. I was a very wounded (barely) survivor of a totally chaotic, extremely neglectful, and abusive childhood. The medications caused a lot of physical problems such as chronic pain, fatigue and a myriad of inexplicable ailments and symptoms. In short, I was very very sick physically and psycho-spiritually.

Because of the nature of my withdrawal, I was forced to focus on the physical aspect of my well-being for a couple of years after discontinuation. I also had a lot of neurological damage that made it difficult to wrap my head around the smallest task. My executive functioning was highly impaired. I had to first get through the fire of all the pain, which took around 2 years and then the last year has been about building from scratch. I really had no foundation of even the most basic life skills.

Where I'm at now: Pain is very manageable through diet and meditation and my nerve pain is nearly healed. The neurological damage was slow to heal and happened in spurts, the past 4-6 months I've experienced an accelerated amount of healing in that area. My confidence in my ability to heal has never wavered no matter how hard it's been. I feel like I'm doing everything in my control and I'm going to be fully recovered. I am healing from the trauma of my childhood and all the other deep wounds I've accumulated, something that felt impossible for so long. There was a lot of injury and I've surpassed every health and spiritual goal and I keep making bigger goals.

The fundamental success markers: I follow a whole foods, paleo diet and lifestyle. I don't use mind or body altering medications or substances on any level. I am able to and enjoy exercise more than I ever have in my entire life, I

do some kind of exercise at least 5 days a week. I use nature and meditation practice as my "church." I started working part-time, something that I have not been able to do for 15 years. I have new friends and have strengthened my existing relationship. We (my husband and I) were in terrible debt for many years. I took a deep dive into personal finance, wrote a plan and the past two years, I got us out of \$80K of debt and increased our net worth by some insane amount. Our joint financial life is very stable.

I still struggle with self-expression. The neurological issues profoundly affected my language skills. It's been a huge struggle to put into language what I am thinking. I still have metabolism issues, or really slow motility with physical functions such as digestion, sex drive, lack of hunger and thirst, etc. I still don't feel much pleasure, can't tolerate or enjoy music much of the time, don't "get" comedy, and I don't taste food too much. This kind of sucks, but I can feel love (thank god) deeper than I ever have, so that has compensated for lack of pleasure. I would also like to be able to fully support myself financially. I think I am going to let go of or achieve these remaining issues/goals very soon.

As hard and as incredibly painful this has been, I would not change anything about my journey, and I never wanted to go back to one day of my life before this."

### Update from RC as of 10/2019:

"Since January of 2019, I have had a lot of healing. A lot of my executive functioning has returned, making it much easier to plan and execute regular life tasks. My CNS has really healed. I can handle stress, stress meaning any stress to the mind and body. My CNS was so fragile, I could not handle any surprises, fun was stressful, everything was a stress for me. Now I feel like, for the first time in decades, I can plan and actually have a life that I envision. I feel like I have the mental and physical wherewithal to achieve my goals. I also have the mental clarity and self confidence to make choices that are really good for me. I do still have a couple lingering symptoms that come and go, but I can be with those symptoms. I know I will heal 100% and beyond. I like experiencing my life from this perspective. I like my life, which is something I never experienced."

## INFORMED CONSENT

Patient has reviewed this document and consented to all of the information herein.

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