

Tapering Off Psychotropic Drugs: Using Patient Cases to Understand Reasons for Success and Failure

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Abstract *Over the past several years the author has helped a number of patients taper off psychotropic drugs (PDs). This emerging aspect of his clinical work arose when patients demanded such services. During the tapering process, a combination of orthomolecular and/or botanical medicinal extracts can assist patients by minimizing withdrawal reactions and mental instability. Fourteen cases are described. The results showed that eight patients were able to remain functionally well following PD discontinuation, whereas the remaining six cases were not. Reasons for these different outcomes are discussed, and include: (1) problems in overcoming pharmacological dependence; (2) being psychologically dependent on being psychiatrically labeled; (3) not having a sufficient life strategy; and (4) being potentially brain-damaged from PDs. This paper can assist and empower clinicians to better understand some of the reasons why patients remain functionally well following tapering while other patients do not.*

Introduction

Over the past several years, I have helped a number of patients come off psychotropic drugs (PDs). This emerging aspect of my clinical practice arose when patients demanded such services. The well-known critic of psychiatry, Dr. Peter Breggin (a psychiatrist himself), authored an op-ed piece, *Today's Greatest Mental Health Need: Psychiatric Drug Withdrawal Programs*¹, in which he remarked that we would do far more good if we had programs developed to assist patients in coming off their PDs. From working with numerous patients, it appears that when individuals are in psychological distress they are normally offered PDs by physicians or nurse practitioners as first-line or initial treatments. Moreover, my patients have informed me that they were seldom offered any alternatives to PDs (e.g., psycho-

therapy or lifestyle interventions) when they were initially evaluated. The implications of this are considerable since patients are seldom given sufficient information about the pharmacological effects of PDs when they are prescribed for them to consent,² nor are they properly informed about the difficulties that can and often do ensue when attempts are made to discontinue them.³

Here I present 14 cases in which patients were successfully tapered off PDs by using combinations of orthomolecular medicines and/or botanical medicines. In some cases withdrawal-associated problems were so extreme that patients either destabilized or were on the verge of destabilizing following tapering, and their only recourse was to resume PDs. In other cases, patients gradually destabilized following tapering and felt it necessary to resume PDs. When a patient

has destabilized or is on the verge of destabilizing, he/she has become mentally unstable and thus cannot experience consistent emotional and psychological well-being, and has also lost the ability to use his/her cognitive and emotional capabilities to function in society and meet the ordinary demands of everyday life. Some patients, however, were able to live productive lives without resuming their PDs. Possible reasons for these diverse outcomes will be discussed.

Case Reports

In Table 1 (p. 161-162) the salient details for 14 patients who successfully tapered off their PDs (January 1, 2011-October 15, 2013) are described. I did not include patients who tried to taper, but could not fully come off their PDs due to difficulties in maintaining their mental stability while undergoing the tapering process. Thus, I have only included patients who successfully tapered off their PDs, and noted whether or not they remained mentally stable following the tapering period. A total of eight patients did well following discontinuation whereas the remaining six patients were unable to maintain their mental stability following discontinuation.

For each of the 14 tapering successes, orthomolecular and/or botanical treatments were customized to minimize withdrawal and support each patient's capacity to emotionally regulate through the tapering process. I included several case descriptions to demonstrate how I integrated orthomolecular and/or botanical treatments into the tapering process, and to highlight the possible outcomes that can result after coming off PDs.

Case 5. This patient had been taking 25 mg of Paxil CR for the past eight years to control obsessive-compulsive symptoms. After I evaluated this patient and determined that she was mentally stable and understood the tapering process, I sent a detailed letter to her family physician where I outlined a tapering plan.

The first part of the plan involved the patient stopping the Paxil CR and substituting it with 20 mg/day of Prozac. Since

the patient's goal was to get pregnant and not be on any PD during her pregnancy, I also prescribed a prenatal vitamin/mineral supplement, 4 mg of folic acid, and 2,000 mcg of vitamin B₁₂. After being stable on the Prozac for four weeks, the next part of the tapering plan involved switching to a liquid form of Prozac. The liquid form allows for a more gradual tapering process, which helps to mitigate PD withdrawal.⁴ The patient was then tapered off the liquid Prozac while taking increasing doses of a combination botanical medicine containing extracts of St. John's wort, valerian, and passionflower.

- Week 1: 16 mg daily of liquid Prozac and one pill twice daily of the botanical medicine.
- Week 2: 12 mg daily of liquid Prozac and one pill three times daily of the botanical medicine.
- Week 3: 8 mg daily of liquid Prozac and two pills AM and two pills PM of the botanical medicine.
- Week 4: 4 mg daily of liquid Prozac and three pills AM and three pills PM of the botanical medicine.
- Week 5+: Discontinue the liquid Prozac and remain on three pills AM and three pills PM of the botanical medicine until stable enough to discontinue.

The patient tapered off the Prozac and the botanical medicine in approximately two months. She did not destabilize while tapering. The patient prolonged the tapering schedule according to how she felt, which meant that she decreased the liquid Prozac every two weeks instead of the planned weekly decrements. She remained on the micronutrients while undergoing *in vitro* fertilization (IVF).

After only one course of IVF she became pregnant, but felt that the hormonal treatments exacerbated her psychological state. As such, her obsessive-compulsive symptoms returned very intensely. She even sought out an expert on the use of SSRI

Table 1. Results of Psychotropic Drug Tapering

Case*	Demographic Information	Name and Class of Psychotropic Drug (PD)	Brief Patient History and PD Dose at Initial Clinical Evaluation	Outcome Details as of October 15, 2013
1.	Male 21 years old	Celexa (citalopram); selective serotonin reuptake inhibitor (SSRI)	Prescribed in 2004 for obsessive-compulsive symptoms; 20 mg daily	Patient tapered off in 2013; been off PD for approximately 6 weeks
2.	Male 64 years old	Cipralelex (escitalopram); SSRI	Prescribed in 2005 for symptoms of major depression; 10 mg daily	Patient tapered off in 2013; been off PD for approximately 3.5 months
3.	Female 34 years old	Cipralelex; SSRI	Prescribed in 2009 for symptoms of anxiety and depression; 5 mg daily	Patient tapered off in 2012; been off PD for approximately 18 months
4.	Female 32 years old	Prozac (fluoxetine); SSRI	Prescribed in 2011 for symptoms of anxiety and depression; 20 mg daily	Patient tapered off in 2012; been off PD for approximately 10 months
5.	Female 29 years old	Paxil CR (paroxetine controlled-release); SSRI	Prescribed in 2003 for obsessive-compulsive symptoms; 25 mg daily	Patient tapered off in 2012; been off PD for approximately 18 months
6.	Female 34 years old	a. Zoloft (sertraline); SSRI b. Seroquel (quetiapine) extended-release (XR); atypical antipsychotic	Prescribed PDs in 2006 for obsessive-compulsive symptoms and depression that arose post-partum; 100 mg of Zoloft and 100 mg of Seroquel	Patient tapered off both medications (consecutively) in 2013; been off PDs for approximately 5 months
7.	Female 17 years old	a. Cipralelex; SSRI b. Seroquel; atypical antipsychotic	Prescribed in 2010 for symptoms of anxiety and depression, as well as some symptoms reflective of episodic hypomania; 30 mg of Cipralelex and 50 mg of Seroquel	Patient tapered off Seroquel in 2012 and was prescribed 60 mg daily of Celexa; tapered off the Celexa in 2013; been off Seroquel for approximately 11 months and Celexa for approximately 7 months
8.	Male 33 years old	a. Seroquel XR b. Klonopin (clonazepam)	Been off and on PDs since the age of 19 for the treatment of bipolar spectrum and anxiety-related symptoms; 300 mg of Seroquel XR and 0.5 mg of Klonopin as needed	Patient began taper of Seroquel XR in 2012 and was completely off by August of 2013; been off Seroquel XR for approximately 2 months; has not used Klonopin since July 2013

Table 1. Results of Psychotropic Drug Tapering

Case*	Demographic Information	Name and Class of Psychotropic Drug (PD)	Brief Patient History and PD Dose at Initial Clinical Evaluation	Outcome Details as of October 15, 2013
9.	Female 28 years old	Ciprexil; SSRI	Prescribed in 2008 for symptoms of depression; 10 mg daily	Patient began to taper off the PD in June 2013 and was fully off by August 2013 (approximately, 2 months), then destabilized in September 2013, and resumed 5 mg of Ciprexil in October 2013
10.	Female 55 years old	a. Loxitane (loxapine); typical antipsychotic b. Imovane (zopiclone); sedative-hypnotic	Been on PDs for approximately 30 years; 5 mg daily of Loxitane and 7.5 mg at bedtime of Imovane	Patient tapered off Loxitane in approximately 5 months (June 2012–November 2012); destabilized July 2013 and unaware if has resumed PD again, but assume so based on psychiatric history
11.	Female 49 years old	Celexa; SSRI	Prescribed in 1997 for symptoms of anxiety and depression; 10 mg	Patient tapered off the PD within 24-hours; destabilized in about 7 weeks and resumed PD at a dose of 40 mg daily
12.	Female 27 years old	Effexor XR (venlafaxine extended-release); serotonin-norepinephrine reuptake inhibitor (SNRI)	Prescribed in 2008 (unknown if patient was on a PD prior to this date) for symptoms of depression; 75 mg	Patient began to taper off the PD in November 2011 and was fully off the PD in November 2012; destabilized in March 2013; resumed PD at a dose of 37.5 mg daily
13.	Female 25 years old	Zoloft; SSRI	Prescribed in 2008 for symptoms of anxiety; 50 mg	Patient began to taper off the PD in January 2013 and was fully off the PD by April 2013; destabilized in June 2013; resumed PD and the dose was escalated to 50 mg and patient became extremely suicidal 2 weeks later and went to the nearest hospital; PD switched to Prozac and patient currently taking 10 mg daily
14.	Female 26 years old	Seroquel XR; atypical antipsychotic	Patient has been on numerous PDs since 2006 for bipolar spectrum symptoms; 200 mg	Patient began to taper off the PD in December 2011 and was fully off the PD in April 2012 against medical advice; destabilized and was hospitalized in May 2012; PDs as of most recent appointment (July 2012) were the following: Epival (divalproex sodium) 1000 mg daily; Seroquel 600 mg at bedtime and 25 mg in the morning; and Klonopin 0.5 mg daily

*Case numbers were assigned arbitrarily and used to quantify the number of patients that successfully tapered off PDs while under my clinical supervision.

drugs during pregnancy since she was re-considering resuming the Paxil CR. She was erroneously told that she should take an SSRI drug during pregnancy since untreated anxiety might lead to pre-term birth, miscarriage, and post-partum depression. (The information this patient was given is completely inaccurate since the use of SSRI drugs during pregnancy is associated with increased risks of miscarriage, birth defects, preterm births, newborn behavioural syndrome, persistent pulmonary hypertension of the newborn, and possible long-term neurobehavioural effects⁵). She was being scared into resuming antidepressant medication, but was not thrilled by the prospect of doing so. Instead she worked through her psychological distress. She hoped that when the hormonal treatments ceased, her levels of anxiety would become more manageable. Approximately four months following PD tapering, the hormonal treatment part of the IVF procedure was stopped, and within five days, her levels of anxiety became completely manageable. She subsequently had an uneventful pregnancy and is now the proud mother of a healthy and robust 8-month-old boy. It has been approximately 18 months since being on a PD.

Case 7. Since 2010 this patient was taking 50 mg daily of Seroquel XR for symptoms of anxiety and depression, as well as some symptoms reflective of episodic hypomania. She was also taking 30 mg daily of CipraleX. After I evaluated this patient and determined that she was mentally competent and understood the tapering process, I sent a detailed letter to her psychiatrist where I outlined a tapering plan.

She was first switched to the non-XR form of Seroquel since it can be cut into quarters making it easier to taper. The patient was able (via a pill cutter) to break the 25 mg tablets into quarters (6.25 mg per quarter). The tapering process was done very gradually and very slowly to mitigate instability.

- Week 1-3: 43.75 mg of Seroquel, 200 mg of L-theanine, and 500 mg twice daily of niacinamide.

- Weeks 4-6: 37.5 mg of Seroquel, 200 mg of L-theanine, and 500 mg three times daily of niacinamide.

- Weeks 7-9: 31.25 mg of Seroquel, 200 mg of L-theanine in the AM and 100 mg of L-theanine in the PM, and 500 mg three times daily of niacinamide.

- Weeks 10-12: 25 mg of Seroquel, 200 mg of L-theanine twice daily, and 1,000 mg of niacinamide twice daily. Add 1.5 mg of prolonged-release melatonin (PRM) 60-minutes before bed.

- Weeks 13-15: 18.75 mg of Seroquel, 200 mg of L-theanine twice daily, 1500 mg of niacinamide breakfast and 1000 mg at dinner. Continue with 1.5 mg of PRM 60-minutes before bed.

- Weeks 16-18: 12.5 mg of Seroquel, 200 mg of L-theanine twice daily, 1500 mg of niacinamide breakfast and 1,000 mg dinner. Increase to 3.0 mg of PRM 60-minutes before bed.

- Weeks 19-21: 6.25 mg of Seroquel, 200 mg of L-theanine twice daily, 1500 mg of niacinamide breakfast and 1,000 mg at dinner. Continue with 3.0 mg of PRM 60-minutes before bed.

- Week 22+: Discontinue the Seroquel, continue with 200 mg of L-theanine twice daily, and 1500 mg of niacinamide breakfast and 1,000 mg at dinner. Continue with 3.0 mg of PRM 60-minutes before bed.

At the end of the Seroquel tapering, the patient's SSRI was switched to 60 mg of Celexa by her psychiatrist. Four months following the Seroquel tapering, the patient expressed the desire to taper off the Celexa. Against my advice, the patient tapered off the Celexa in about six weeks without my clinical supervision while she was away at University and out of province. I did follow up in person with this patient about two months later and she was doing fine and presented without any evidence of mental instability. She is currently doing very well. She has been off the Seroquel for approximately

11 months and off the Celexa for approximately seven months.

Case 10. This patient had been on antipsychotic medications for around 30 years. About five years prior to seeing me, she was switched to atypical antipsychotic medication. She had been on Zyprexa for about one year and then, due to objectionable side effects, was switched to 5 mg of Loxitane daily. She had mild schizophrenic symptoms. Her daily dose of Loxitane was well below doses typically used for more severe symptoms (i.e., normally 40-65 mg twice daily⁶). She attributed chronic stomach pain, fatigue, and dizziness to the PD and wanted to stop it. She was also taking 7.5 mg of Imovane at bedtime to assist with insomnia.

I corresponded with her psychiatrist and we agreed that the patient was stable enough and had the insight and judgement necessary to pursue my tapering plan. The patient was then tapered off the Loxitane while taking increasing doses of a combination botanical medicine containing extracts of St. John's wort, valerian, and passionflower. I further supported her mental health by adding therapeutic daily dosages of niacin (3,000 mg), vitamin C (3,000 mg), omega-3 essential fatty acids (1,500 mg of eicosapentaenoic acid and 500 mg of docosahexaenoic acid) and n-acetylcysteine (1,000 mg).

The patient tapered off the Loxitane in approximately five months (June – November 2012) and did not find the tapering too difficult. For about five months following discontinuation of the Loxitane she did not experience any auditory hallucinations and paranoid ideation. All of the physical symptoms that she ascribed to the Loxitane had ameliorated as well.

- Weeks 1-3: 5 mg Loxitane every other day and 1 pill daily of the botanical medicine.
- Weeks 4-6: 5 mg Loxitane every two days and one pill daily of the botanical medicine.
- Weeks 7-9: 5 mg Loxitane every three days and one pill twice daily of the botanical medicine.

- Weeks 10-12: 5 mg Loxitane every four days and one pill twice daily of the botanical medicine.

- Weeks 13-15: 5 mg Loxitane every five days and two pills of the botanical medicine in the AM and one pill in the PM.

- Weeks 16-18: 5 mg Loxitane every six days and two pills of the botanical medicine in the AM and two pills in the PM.

- Weeks 19-21: 5 mg loxapine every seven days and three pills of the botanical medicine in the AM and 2 pills in the PM.

- Weeks 22+: No more loxapine and three pills of the botanical medicine twice daily for a minimum of three months.

She began showing signs of destabilization at around seven months post-Loxitane discontinuation (June 2013). She started worrying about being followed by the police or some type of intelligence service. These worries escalated into delusions of having been poisoned by fumes and gases in her home. She became so worried that the local ambulance service visited her home on two occasions and the police came on one occasion. She fully destabilized about one month later (July 2013). She cancelled her last appointment, so I do not know if she resumed an antipsychotic PD again but I assume so based on her psychiatric history.

Supporting the Tapering Process with Specific Natural Health Products

I have found it helpful to prescribe specific natural health products during and after the tapering process to mitigate withdrawal, prevent potential relapses, and improve a patient's chances of not requiring his/her PDs any longer. While there is no guarantee that any of these natural health products will prevent a patient from eventually destabilizing, this small cohort of eight patients have not needed to resume their PDs following tapering. In part, their ongoing mental stability can be attributed

to their ongoing use of an individualized prescription of natural health products.

The clinician should always consider re-evaluating the patient and checking for underlying differential diagnoses since various factors, medical or metabolic disorders can also contribute to a patient's ongoing mental stability including hormonal excesses or deficiencies, blood sugar problems, infections and even food allergies and sensitivities.

Orthomolecular Treatments

Unlike PDs, which impose potentially harmful biological burdens upon the brain and body, orthomolecular substances support the brain and body and are less likely to disrupt normal biochemical and physiological processes.⁷ They can be combined safely with PDs making them ideal treatment options throughout the tapering process.

Melatonin

Melatonin works well for insomnia, which is common during the tapering process. The hormone is being formally studied among patients with schizophrenic symptoms withdrawing from long-term benzodiazepine use.⁸ Previous reports have shown some efficacy in reducing benzodiazepine-withdrawal-associated sleep disruption.^{9,10} Ideally, controlled- or prolonged-release preparations should be used, with doses varying from 1-5 mg at bedtime. If taken one or two hours before bedtime, these forms of melatonin enable a more sustained blood level of the hormone and they promote sleep that tends to be deeper and less fragmented. I tend not to prescribe quick-release melatonin preparations since they rapidly increase blood levels, but do not promote a more restful and longer sleep. On occasion, I will combine a small dose (1 mg) of quick-release melatonin with a controlled- or prolonged-release preparation (3-6 mg), to facilitate quick sleep onset with sustained hormone levels to offset a broad array of sleep issues (e.g., racing mind, restlessness, and waking too early) that patients tend to experience during the tapering process.

Niacinamide

Niacinamide (nicotinamide) can also be given to reduce withdrawal symptoms from all psychotropic drugs since it generally "calms" the nervous system and does not possess any concerning drug interactions. It is sometimes very useful among patients withdrawing from benzodiazepines since it possesses benzodiazepine-like effects.¹¹ One case report demonstrated its clinical effectiveness in allowing a patient to remain clinically stable while tapering off Klonopin.¹¹ The patient weaned himself off Klonopin in two weeks while increasing his daily amounts of niacinamide until he was taking 2,500 mg each day. When this report was published, the patient had been free of Klonopin for six months and had remained stable on only the niacinamide. A written correspondence from the late Dr. William Kaufman (January 10, 1998), noted the following about the vitamin's mechanism of action:

"Niacinamide has ungated access to the brain. When it enters the brain, it has a strong affinity for the benzodiazepine receptors and causes a desirable calmative effect which you have observed. But it also improves other functions of the central nervous system."

Effective daily doses of niacinamide range from 1,500-2,500 mg. It is rarely necessary to go higher than 2,500 mg since higher doses can be associated with nausea and potentially vomiting. The mean elimination half-life in human subjects given 3,000 mg of the vitamin was 5.9 ± 0.6 hours.¹² Since it has such a short elimination half-life, niacinamide must be administered several times throughout the day; otherwise, its therapeutic effects will be lessened.

Gamma-Aminobutyric Acid

Gamma-aminobutyric acid (GABA) is very useful to moderate mood instability while also decreasing anxiety if given during the tapering process. Since GABA can also promote sleep, it can be given several hours before bedtime to decrease sleep fragmentation and sleep-onset problems. For patients tapering from lithium, GABA works particularly well for mood regulation. It func-

tions as an inhibitory neurotransmitter in the central nervous system. The mechanism of GABA's neuroinhibition is mediated through an increase in the permeability of post-synaptic membranes to chloride ions, leading to hyperpolarization. There continues to be uncertainty if GABA can traverse the blood-brain barrier when administered orally. GABA might act on the central nervous system without crossing the blood-brain barrier.¹³ There are two forms of GABA available – crystalline GABA and PharmaGABA (produced by a fermentation process that utilizes *Lactobacillus hilgardii*).¹⁴ Both forms of GABA have the same molecular structure and presumed mechanism of action, and therefore it is illogical to contend that one form somehow traverses the blood-brain barrier while another form does not.¹³ GABA might have a therapeutic effect comparable to benzodiazepine medications and might be useful for patients addicted to them.¹⁵ In a case report, a 40 year old female patient with a history of severe anxiety was able to stop her Valium (diazepam) and reduce her Ativan with 200 mg of GABA four times each day.¹⁵ The optimal dose of GABA is normally 2-3 grams daily away from meals.¹⁵ I normally do not use PharmaGABA since it only comes in 100-200 mg pills.

Even though side effects are rare from GABA, there is one report of neurologic tingling, flushing, and transient hypertension and tachycardia in a subject taking very high oral doses (10 grams on an empty stomach).¹⁵ Smaller oral doses (1-3 grams daily) have been reported to cause neurologic tingling and flushing in several volunteer subjects.¹⁵ PharmaGABA has been tested in rats that were administered doses of 5000 mg/kg.¹⁴ There were no deaths and the lethal dose that would likely kill at least 50% of the rat population was determined to be greater than 5,000 mg/kg of body weight.

L-Theanine

I sometimes use the amino acid, L-theanine, since it can decrease symptoms of anxiety and improve focus and concentration. It

is not uncommon for patients to experience disturbances in cognition during the tapering process making this intervention potentially valuable. L-theanine presumably increases both dopamine and serotonin, although a study in rats showed that it might decrease serotonin.¹⁶ It also increases alpha brain-wave activity, which is associated with relaxation.¹⁶ In a study involving patients with schizophrenic and schizoaffective symptoms, the use of L-theanine as an augmentation strategy was associated with reductions in the following: anxiety ($p=0.015$), positive symptoms ($p=0.009$), and general psychopathology scores ($p<0.001$).¹⁷ In another study using the same 40 patients, the beneficial effects of L-theanine were coupled with circulating levels of brain-derived neurotrophic factor and the cortisol-to-dehydroepiandrosterone ratio.¹⁸ My clinical experience has shown L-theanine to limit destabilization that can result while tapering from typical and atypical antipsychotic drugs. The optimal dose appears to be 200 mg twice daily. There should be no side effects attributed to L-theanine, although caution might be warranted since one of my patients is certain that it caused her to feel temporarily manic.

Botanical Medicinal Extracts

Botanical medicinal extracts – non-orthomolecular substances – can stabilize mood lability and other unpredictable mood states that result from PD withdrawal during the tapering process. However, botanical medicinal extracts are psychoactive just like PDs and their use are best restricted to short-term treatment only. Once the patient has tapered off his/her PD and has been stable for 4-12 weeks or when the patient has been consistently and functionally stable, the botanical medicinal extracts should be tapered from. In the majority of cases this is not difficult and patients are pleased to not need even their botanical medicinal extracts any more. I have not had patients' exhibit intense withdrawal reactions from coming off them although it is theoretically possible. To the contrary, I have routinely observed that botanical medications tend to minimize

destabilization and facilitate successful outcomes from PD tapering.

Combination Botanical Extract

I sometimes use a combination of several botanical medicinal extracts, containing very low amounts of hyperforin, which appears to limit anxiety, depression, muscle tension, stress reactions, and other withdrawal reactions resulting from the tapering process. Each pill contains 60 mg of the dry extract of St. John's Wort (*Hypericum perforatum*), 28 mg of the dry extract of Valerian (*Valeriana officinalis*), and 32 mg of Passionflower (*Passiflora incarnata*). There have been approximately 10 company-sponsored clinical studies (i.e., two controlled and eight observational cohort studies) and two experience reports, which have shown this botanical combination to be safe and effective for symptoms of depression and anxiety.¹⁹ Each of the individual botanical extracts possess well-known postulated mechanisms of action.²⁰ The extract of *Hypericum perforatum* exhibits monoamine oxidase inhibition, GABA activity, monoamine reuptake, upregulation of 5-hydroxytryptamine 1A (5-HT_{1A}) and 5-HT_{2A} receptors, and modulation of cytokine production. Valerian is known to have GABAergic effects. *Passiflora* is a partial agonist to benzodiazepine receptors. Generally, my patients start with one pill once or twice daily, and over the course of many weeks, the dose is increased to three pills twice daily. Even though the elimination half-life is not known for this preparation, multiple daily dosing appears to yield more optimal therapeutic outcomes.

Clinicians should not be overly concerned about adverse drug interactions since this specific preparation contains a very low daily dose of *Hypericum perforatum* (i.e., 360 mg from 6 tablets) with a correspondingly low hyperforin content.²¹ Studies demonstrating significant pharmacokinetic drug interactions with *Hypericum perforatum* extracts typically involve daily dosages of 900 mg or more. At the recommended daily dose of six tablets, the mean amounts of hypericin and hyperforin delivered are 0.72 mg and 1.35 mg respectively. This small amount of hyperforin does not induce

the major liver drug-metabolizing enzyme, cytochrome P(CYP)450 3A4. *Hypericum perforatum* preparations containing much higher amounts of hyperforin do induce this enzyme, and those are believed to be the reason for numerous potential drug interactions.

A systematic review of 19 studies determined that *Hypericum perforatum* extracts that provide high daily doses of hyperforin (greater than 10 mg) resulted in CYP450 3A4 induction, whereas studies using *Hypericum perforatum* extracts that provide low daily doses of hyperforin (less than 4 mg per day) demonstrated no significant effect on CYP450 3A4 (thereby, limiting the potential of altered metabolism of many common drugs).²²

Rhodiola Rosea Extract

Rhodiola rosea extract can also stabilize patients during PD tapering. Clinical trials have shown it to attenuate mild and moderate depression, generalized anxiety, and burnout/fatigue,²³⁻²⁵ common withdrawal symptoms that many patients experience during tapering. It possibly works by inhibiting enzymes involved in the degradation of monoamine neurotransmitters (i.e., serotonin, dopamine, and norepinephrine) and this prevents the depletion of adrenal catecholamines following acute stress.²⁶ The therapeutic dose range is somewhere between 500-680 mg of a standardized extract containing 3% percent total rosavins and 1% salidroside. I normally recommend that *Rhodiola rosea* extract to be taken with breakfast, as it can cause considerable nausea and possibly vomiting on an empty stomach. I usually prescribe 500 mg at breakfast to stabilize mood and lessen anxiety, and I will increase the daily dose to 650-680 mg if the patient's response is not marked enough. Although a rat study determined the elimination half-life of salidroside in *Rhodiola rosea* extract to be 39.69 ± 21.02 minutes,²⁷ I have not found multiple dosing throughout the day necessary. I am doubtful that the elimination half-life from the rat study correlates to the elimination half-life in humans.

There is one published report of an in-

teraction between *Rhodiola rosea* extract and Cipralox.²⁸ The case involved a 26-year-old Chinese female who presented to the emergency department with a one hour history of heart palpitations and light-headedness. The patient was diagnosed with supraventricular tachycardia (SVT) as per electrocardiogram findings. Her pulse rate was 150 beats per minute, and her troponin I was significantly elevated (0.39 mg/L; normal < 0.06). All other investigations were normal. She was treated with 6 mg of intravenous adenosine, which normalized her sinus rhythm. No more SVTs happened at follow-up and her troponin I normalized in two days. While this case points to possible interactions between *Rhodiola rosea* extracts and SSRI drugs, I have not observed any untoward interaction when patients take them concomitantly during the tapering process. Therefore, it is important, to inform all patients of this possibility and instruct them to contact you immediately if they experience a sudden onset of heart palpitations and tachycardia.

Numerous other natural health products (both orthomolecular treatments and/or botanical medicinal extracts) could potentially be used alongside PDs during the tapering process. Clinicians knowledgeable in orthomolecular and botanical medicine must use their discretion during PD tapering while also monitoring patients' progress, mitigating potential interactions, and using available pharmacokinetic information to guide appropriate dosing.

Uncertain Patient Outcomes Related to Difficulties in Overcoming Pharmacological Dependence Associated with the Habitual use of PDs

Pharmacological dependence is an expected and biological adaptation of the body becoming long habituated to the presence of PDs.²⁹ Since PDs can induce unpredictable global reactions when used properly,^{30,31} there are no reliable ways to predict how patients will overcome pharmacological dependence once their PDs are tapered and eventually withdrawn. Every patient's withdrawal process is unique as is their susceptibility to de-

velop withdrawal symptoms.³² Patients can literally experience any symptom (e.g., anxiety, depression, electrical sensations or zaps, hypomania, mania, mood lability, muscle aches and pains, psychosis, sleep disturbances, and suicidality) during the tapering process. They need to prepare themselves with the notion that tapering will not be an easy or an uneventful process.

It is best to pursue tapering only when a patient is mentally stable and feels confident and ready despite the likely difficulties that he/she will experience during the tapering process. Better to pursue tapering from a position of strength (i.e., when the patient feels ready and confident) than when a patient might be feeling vulnerable and nervous. One helpful barometer of potential success involves the length of PD use. In one report, patients taking PDs for less than six months were more successful at tapering (81%), compared to patients on PDs for more than 5 years (44%), and patients on PDs between six months and 5 years (a little over 50%).³²

To improve the odds of a successful outcome, the tapering plan should involve one PD at a time and reduce the PD with the longest elimination half-life first.³ PDs with longer elimination half-lives (i.e., more than 24 hours) are easier to taper since their withdrawal reactions tend to be less severe than drugs with shorter elimination half-lives (i.e., less than 24 hours). PDs with short elimination half-lives can produce significant and quick withdrawal reactions. Considerations should be made to switching patients from PDs with short elimination half-lives to drugs with longer elimination half-lives (as was described in Case 5) prior to tapering, as this will increase the chances of a positive experience and successful outcome. A psychotropic drug like Paxil (has an elimination half-life of around 24 hours) can cause significant withdrawal and possible destabilization. A psychotropic drug like Prozac, on the other hand, can be used as a substitute for Paxil, allowing for a more successful tapering plan since the elimination half-life of this drug is around 4-6 days.³³

According to one report, for each unspec-

ified tapering period there should be a 10% reduction in dose, meaning that the PD gets reduced by subsequent 10% reductions until the patient is comfortably off the medication.³³ Another report suggests that the PD is tapered down every 2-3 weeks, so that after each 2-3 week tapering period, the dose is further reduced by 10% or less.³³ For example, if a patient, begins the tapering process on a PD that is 400 mg once daily, then the dose to take for the next two weeks would be 360 mg. After two weeks, the dose would be further reduced by another 10% to 324 mg and so on. This process would continue until the PD is fully discontinued. At any time during the tapering, if the patient feels that the reduction is too marked or if there are troublesome withdrawal reactions such as anxiety and sleep disturbances the patient should be told to remain on the previous tapered dose until he/she feels well enough to proceed.

Above all, discontinuing PDs is very difficult because it might not be possible for some patients to overcome the pharmacological dependence attributed to the habitual use of PDs. Part of the difficulty answering that question involves the complex mechanistic data on SSRI discontinuation that is still being studied. Some of the known potential molecular mechanisms might explain why four patients (cases 9, 11, 12, and 13) were unable to maintain their stability when off their antidepressant drugs. Animal studies have found that the mesolimbic dopamine system (possibly, through hippocampal dopamine-type 1 receptor upregulation) is involved in the behavioural effects following SSRI discontinuation, which likely has a role in the anxiety and agitation that patients experience.³⁴ Drugs of abuse also cause similar withdrawal effects due to their impact on the dopaminergic system,³⁴ but this might involve pathways that are distinctively different than those pathways involved in SSRI discontinuation. Animal research has also shown increased serotonin turnover rates (i.e., serotonin depletion marked by an increased ratio of 5-hydroxyindoleacetic acid to serotonin) following discontinuation.³⁴ The behavioural changes in relation to this have not been ad-

equately examined even though this might account for the increased incidence of anxiety experienced by patients following discontinuation of SSRI drugs.

Two other patients (cases 10 and 14) in the cohort failed to maintain their stability when off their antipsychotic drugs. In Case 10, the patient had a 30-year history of taking antipsychotic drugs, and in Case 14 the patient had at least a 5-year history of being on similar drugs. It is known that in the first 6-10 months following discontinuation of antipsychotic drugs after a prolonged period of time, some 25%-55% of patients with prior psychosis will relapse.³⁵ This relapse rate happens to be greater for patients that had been treated with antipsychotic drugs for prolonged periods compared to patients not on these drugs for prolonged periods.³⁵ Why is this so? Part of the increased rates of relapses has to do with the biological effects on the brain generated by the prolonged use of antipsychotic drugs. Reasons for this involve drug-generated buildup of supersensitive dopamine receptors prior to discontinuation, or from the buildup of excess dopamine receptors, or supersensitivity psychosis.³⁵ Thus, when antipsychotic drugs are withdrawn, the dopamine generated within the brain can stimulate the supersensitive or excessive number of dopamine receptors, leading to a hyper-stimulated, agitated, and destabilized mental state. Likely undiscovered genetic and epigenetic reasons for dopamine receptor dysregulation also contribute to significant withdrawal reactions following prolonged antipsychotic drug use. These issues await further study.

Uncertain Patient Outcomes Related to Difficulties in Overcoming their Psychological Dependence on being Psychiatrically Labelled

My clinical experience has shown that some patients cannot come off their PDs since they believe themselves to be inherently flawed. These patients lack the necessary confidence to live without PDs and cannot imagine this to be possible even though they felt confident and stable enough to try. On

some level these same patients have given in to the notion (whether implicitly, explicitly, or both) that their emotional regulation problems are the result of their broken brains and not the result of the choices they made, past or current life struggles, relationship problems, their lack of life purpose, and/or their difficulties in tolerating the emotional swings and hardships inherent to life.

Middleton and Moncrieff discussed this in their provocative article which questioned the merits of antidepressant medication. They noted the following:

“Symbolically, medication suggests that the problem is within the brain and well-being is dependent upon maintaining ‘chemical balance’ by artificial means. This message encourages patients to view themselves as flawed and vulnerable and may explain the poor outcomes of treated depression in naturalistic studies.”³⁶

Many such patients have placed so much of their “recovery” on the taking of PDs that to consider coming off them and taking responsibility for their own mental and physical health is terrifying and insurmountable.

Another piece of the puzzle relates to psychiatric labels that patients have been diagnosed with. Psychiatric labels are thought to provide rational reasons for misery. Patients often identify with their psychiatric labels. I have had many patients state that they cannot function without PDs because they have generalized anxiety disorder, major depressive disorder, attention deficit disorder, or some other psychiatric label. A patient might say out loud or think to him/herself something like: “How can I function if I have bipolar disorder and no longer take PDs?” Thus, a life without PDs might be difficult to accomplish for some patients since this “new” existence demands an adjustment to life without having the absolution that psychiatric labels provide. This might sound harsh, and yet it has been my experience that for some patients it is easier to put the blame on their psychiatric labels than on themselves for their ongoing struggles and interpersonal problems. Some patients believe that what happened in their lives have been the result

of being psychologically disordered and not the result of their own choices. I am always willing to partner with any patient who has been psychiatrically labeled. We can work on ways to overcome attachments to the label; however, some patients are so attached that they cannot or are not willing to entertain a life without maintaining their psychologically-disordered self.

Uncertain Patient Outcomes Related to an Insufficient Life Strategy

Patients have to be informed that going from PDs to natural health products are not “one-off” situations. It is not that a patient comes off his/her PDs and can remain well only taking natural health products. It is vital that patients develop a strategy of living so that when they are off PDs they will have enough activities to lessen ruminations, deflect negative thought patterns, and even reduce the unpleasant physical sensations that accompany emotional discomforts. Research has shown that psychological distress can be mitigated by regular work (whether paid or volunteer), counselling, exercise, relaxation, hobbies, support groups, and religious/spiritual practices;³⁷ endeavors that promote a nourishing, positive, and life-affirming existence.

Recall that the patient described in Case 10 had little difficulty tapering off the Loxitane. However, in the ensuing months, she became socially isolated, inward, and believed to be under surveillance by the police or authorities. She also thought there were gases and poisonous fumes in her home despite the fact that her husband was well and healthy. During several follow-up appointments with this patient (i.e., before she destabilized), I stressed the importance of having a life strategy, keeping busy and fostering productivity. Unfortunately, she did not keep busy during the day, so it was easy for her to continue her patterns of delusionary and persecutory thinking.

Similarly, in Case 13, the patient had little difficulty tapering and reported doing well for a couple of months following PD discontinuation. Prior to tapering, we had a fulsome discussion about successful tapering

and wellness. She was advised to revisit regular counselling, a regular exercise plan, and to participate in some form of relaxation. She destabilized two months following the tapering and neglected to take these additional steps that would have supported her and perhaps prevented the relapse. She is now on temporary leave from her full-time job. Following the relapse, she agreed that more resources were needed and that she also needed to address some very painful issues related to the loss of a close family member that occurred years earlier. She is currently participating in weekly psychotherapy, practicing mindfulness-based meditation, and regularly exercising, but felt the need to resume her PD. She continues to worry excessively and appears to place a certain degree of emphasis on being psychologically disordered.

Another patient, Case 14, tapered off her PD against medical advice. While we agreed to the initial tapering strategy, there was a point during the process when she was clearly destabilizing. At this juncture I advised her to stop reducing her PD since she needed the stability it was providing. Perhaps she even required a temporary increase. This information was also conveyed to her sister. She disagreed and opted to stop the PD against my medical advice. She did not welcome the help her sister was willing to provide. It was apparent that she was unable to emotionally handle any stress. Her employment contract ended, but she was not disciplined enough to secure another full-time job. She was also unwilling to engage in regular exercise, relaxation training, or eat a nutritional diet. A relative of hers had a medical incident shortly during tapering and this triggered lots of worry and concern about his prognosis. She also described her family as “all crazy” including herself, and she seemed to endorse the notion that she and her family members were all brain-disordered. She fully destabilized, required hospitalization for about 4–6 weeks, and is now taking three PDs. I am uncertain if she is working or if she is functionally well.

Despite ample clinical instruction, none of these patients were prepared to do the dif-

ficult work necessary to make their lives better. Natural health products are not enough to ensure ongoing stability unless their consistent use is met with an overall life strategy that promotes positive feelings, productivity, physical health, and keeps attentions aligned to the present and thoughts reality-based. My experience has shown that when patients let family members and/or friends know about being off PDs, they can receive much needed additional support. In these three cases, the patients did not use their social supports until they were on the verge of destabilizing or had destabilized. They would have been better off if their family members and/or friends had become involved when they started the tapering process. While some patients deny the usefulness of a robust social network, including supportive counselling, my experience has shown it to be among the most critical determinants of whether the tapering outcomes will be successful.

Uncertain Patient Outcomes Related to the Possible Brain-Damaging Effects of PDs

Prolonged use of SSRI drugs might lead to chronic depression (termed, tardive dysphoria) due to drug-induced changes to serotonergic transporter function.³⁸ When exposed to SSRI drugs, especially when the brain is still developing as in young animals, the neuroplastic changes within the brain can result in reductions or the elimination of serotonin transporter function, as well as alterations in serotonergic architecture and function, leading to anxious and depressive behaviours. The concerns raised about how these PDs influence the developing brains of young animals has led clinicians to speculate that these changes are likely occurring among adult humans exposed to SSRI drugs for prolonged periods of time. Also, these changes may be permanent if SSRI drugs were administered at a young age or if the individual has reduced serotonergic transporter function due to a genetic variant. Thus, it is possible and even conceivable that some patients cannot overcome their distressing psychological symptoms when

discontinuing SSRI drugs due to the potentially brain-damaging effects resulting from their prolonged use.

Similar concerns can be raised for the antipsychotic drugs since the published literature has shown numerous changes to patients' brain architecture that can permanently impair brain function and quality of life even after discontinuation. Breggin asserts that antipsychotic drugs shrink (i.e., atrophy) the brain, inhibit mitochondrial enzyme systems, chronically block dopamine neurotransmission (resulting in death to the striatal neurons), and cause tardive dyskinesia with "associated impairment of cognitive and affective functioning."³⁹ Robust analyses of the published data has shown global deficits in brain volume among patients treated with antipsychotic drugs. These effects are seldom excluded as the cause of reduced brain tissue volume among drug-treated patients in some studies.⁴⁰ In addition to the devastating tardive dyskinesia that antipsychotic drugs can cause in some patients, tardive dyskinesia is also associated with general cognitive decline, suggesting that antipsychotic drugs can induce generalized brain dysfunction.⁴¹

Given the fact that the very nature of antipsychotic treatment is to suppress or disable the nervous system as a means to create a state of psychological indifference,⁴² it is not surprising that this class of PDs can permanently injure the brain. It is possible that some patients become permanently brain-damaged from their prolonged exposure to these drugs, such that they remain permanently impaired following discontinuation, making it very difficult to emotionally regulate and acclimate to ordinary life stresses. Thus, these patients risk destabilizing following antipsychotic drug discontinuation even though the reasons for their difficulties adjusting are conceivably the result of being damaged by the very drugs given to "stabilize" them.

Conclusion

Tapering successfully is achievable and requires a coordinated effort that includes the judicious use of orthomolecular sub-

stances, botanical medicinal extracts, a slow tapering plan, knowledge of pharmacokinetics, close clinician-patient communication, and a fulsome understanding of the potential reasons for tapering success and failure. It is extremely difficult to predict which patients will function successfully once they have tapered off their PDs. They must have a certain level of readiness, confidence, and awareness so that once they are off PDs they can adjust to living without depending on the pharmacological and/or psychological effects that PDs possess. Some of the possible reasons why patients become mentally unstable following tapering involve pharmacological dependence, being psychologically dependent on psychiatric labels, not having a sufficient life strategy, and/or the possible brain-damaging effects of PDs. This paper can assist and empower clinicians to better understand some of the reasons why patients remain functionally well post-tapering and why other patients do not.

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Competing Interests

Dr. Prousky is a consultant for Pascoe Canada, the distributor of Neurapas[®] balance and other natural health products. Neurapas[®] balance is the botanical medicinal extract mentioned in this article. The author generates no income from the sale of this product, but does generate income from webinars and educational materials delivered to health professionals on behalf of Pascoe Canada.

Statement of Informed Consent

Written consent was obtained from all the patients described in this report.

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