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Use of Micronutrients Attenuates Cannabis and Nicotine Abuse as Evidenced From a Reversal Design: A Case Study

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Abstract — Prior research shows that micronutrients, particularly amino acids, can assist individuals with substance dependence to quit various drugs of abuse, including cannabis, alcohol, and cocaine. As part of a wider investigation of the impact of micronutrients (mostly vitamins and minerals) on psychiatric symptoms, such as Attention-Deficit/Hyperactivity Disorder (ADHD), depression, and anxiety, we observed that many participants reduced or eliminated use of alcohol, cigarettes, and cannabis. One case using a single-case reversal (off-on-off-on-off) design is presented and shows not only on-off control of psychiatric symptoms as micronutrients are consumed or withdrawn, but also simultaneous on-off use of cannabis and cigarettes, despite not directly targeting this substance use as part of the treatment protocol.

This case adds to a growing body of research supporting the use of micronutrients in the treatment of psychiatric symptoms and suggests it may extend to substance dependence. Micronutrients, by assisting with mood regulation and reductions in anxiety, may assist with successful cessation of drug use. Alternatively, they may directly impact on the brain reward circuitry believed to be involved in the expression of addictions, thereby providing the appropriate precursors and cofactors necessary for adequate neurotransmitter synthesis. This case should continue to stimulate researchers to consider the role of nutrients, in particular vitamins and minerals, in drug treatment programs and encourage more rigorous trials.

Keywords — addiction, cannabis, micronutrients, minerals, treatment, vitamins

BACKGROUND

Cannabis dependence occurs in 6.8% of 18-year-olds (American data; Office of Applied Studies 2000), with 10% reported as heavy users in New Zealand longitudinal development studies (Fergusson & Boden 2011), and it is the most common illicit drug of abuse among young people (Dennis et al. 2004). Its use is linked to emergency hospital admissions and has been identified as a significant and potent risk factor for psychosis (Arseneault et al. 2002; Fergusson & Boden 2011) as well as depression and anxiety (Patton et al. 2002). Chronic cannabis

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use is also associated with reduced educational attainment, greater welfare dependency, higher risk of unemployment, and reduced satisfaction with relationships and life circumstances, even controlling for socio-economic factors and adverse childhood experiences (Fergusson & Boden 2008). Use also exacerbates adult psychiatric symptoms such as Attention-Deficit/Hyperactivity Disorder (ADHD) (Fergusson & Boden 2008). The most well-researched options available for the treatment of cannabis abuse include pharmacotherapy, cognitive-behavioral therapy (group and individual), and motivational enhancement therapy (Dennis et al. 2004).

Over the last decade, interest in the impact of nutrients on mental illness has grown and micronutrients are being increasingly studied for the treatment of psychiatric conditions. Several studies have analyzed the effect of broad spectrum micronutrients (mostly minerals and vitamins) on mental disorders such as ADHD, autism, and bipolar disorder (Frazier 2012; Gately & Kaplan 2009; Mehl-Madrona et al. 2010; Rucklidge, Taylor & Whitehead 2011), on psychological symptoms such as stress and anxiety (Carroll et al. 2000; Kennedy et al. 2010; Schlebusch et al. 2000; Stough et al. 2011), and on physical illness such as infectious disease and stroke recovery (Barringer et al. 2003; Chen et al. 2011; Gariballa & Forster 2007; Sato et al. 2005), with generally positive outcomes reported (Rucklidge & Kaplan 2013).

In the treatment of addictions, Blum and colleagues have developed formulas they refer to as "neuronutrients" or "neuroadaptagens" that consist mainly of amino acids, although some earlier formulas contained minerals and vitamins (see Chen et al. (2011) for a review). For example, Tropamine™ contains minerals and vitamins and SAAVE™ contains amino acids and one vitamin (B_6), whereas Synaptamine Complex Variant KB220™ contains only amino acids. This line of research supports the use of nutrients to reduce drug hunger and withdrawal (Blum et al. 1988), reduce relapse rates (Blum, Chen & Chen 2009; Brown, Blum & Trachtenberg 1990; Guenther 1983), and improve psychological functioning (Poulos 1981). The comparison of SAAVE™ with Tropamine™ showed the additional benefit of micronutrients in reducing treatment dropout against medical advice as well as drug hunger (Blum et al. 1988). There is certainly a need to investigate the impact of micronutrients with a broader array of nutrients on substance abuse and dependence.

The micronutrient formula used in the present study, known as EMPowerplus (EMP+), consists of 36 ingredients: 14 vitamins, 16 minerals, 3 amino acids, and 3 antioxidants (see Table 1 for ingredients and Table 2 for published studies on the formula). We present here one case from the adolescent case control study where we documented on-off cravings and changes in the use of cannabis and cigarettes within the context of collecting data on psychiatric symptoms. The procedures were approved by the University and Health and Disability Ethics Committees. Written consent was obtained from the individual to participate in research, with the knowledge that his data may be reported as a single case but with his anonymity preserved.

TABLE 1
EMPowerplus Capsule Ingredient List

Ingredients	15 capsules
Vitamin A	5760 IU
Vitamin C	600 mg
Vitamin D	1440 IU
Vitamin E	360 IU
Vitamin B_1	18 mg
Vitamin B_2	13.5 mg
Vitamin B_3	90 mg
Vitamin B_5	21.6 mg
Vitamin B_6	36 mg
Vitamin B_9	1440 ug
Vitamin B_{12}	900 ug
Vitamin H	1080 ug
Calcium	1320 mg
Iron	13.74 mg
Phosphorus	840 mg
Iodine	204 ug
Magnesium	600 mg
Zinc	48 mg
Selenium	204 ug
Copper	7.2 mg
Manganese	9.6 mg
Chromium	624 ug
Molybdenum	144 ug
Potassium	240 mg
dl-phenylalanine	360 mg
Glutamine	180 mg
Citrus bioflavanoids	240 mg
Grape seed	45 mg
Choline bitartrate	540 mg
Inositol	180 mg
Ginkgo biloba	36 mg
Methionine	60 mg
Germanium sesquioxide	20.7 mg
Boron	2400 ug
Nickel	29.4 ug
Vanadium	1194 ug

METHOD

Participant

Brian (not his real name), a 20-year-old male of European descent, in a stable relationship for one year, completed a standardized assessment of his psychiatric functioning in February 2010 using The Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version (SCID-I; (First et al. 1997) and the Conners' Adult

TABLE 2
Intervention Studies with EMPowerplus

Sample	Sample size	Design	Measures	Length of Trial	Results	Reference
Adults with BD	$n = 14$, 11 completed	OL	HAM-D, BPRS & YMRS	6 months	Symptom reduction 55–66%, reduction in meds 50%, effect sizes >.8	Kaplan et al. (2001)
Clinician diagnosed individuals with BD	$n = 22$ (10 adults, 9 adolescents, 3 children)	OL	Clinician rated CGI	6–9 months	17/22 (77%) showed moderate to marked improvements	Popper (2001)
8-year-old with OCD, 12-year-old with PDD	$n = 2$	ABAB case studies	CPRS & CBCL	2 years	On-off control of symptoms	Kaplan et al. (2002)
Adults with treatment-resistant BD I and II	$n = 19$	OL	Clinician rated CGI	5–21 months (mean 13 months)	15/19 (78.9%) showed moderate to marked improvement	Simmons (2003)
Children with mood and behavioral problems; 63.6% boys (8–15 years)	$n = 11$, 9 completed	OL	CBCL, YOQ, YMRS	16 weeks	Significant improvement on 7 of 8 CBCL scales, including attention; significant improvement in measures of mood; effect sizes large	Kaplan et al. (2004)
12-year-old treatment-resistant male with BD-I, mixed, with psychotic features	$n = 1$	Case study	none	14 months	Resolution of all psychiatric symptoms	Frazier et al. (2009)
18-year-old male with OCD	$n = 1$	ABAB case study	Y-BOCS, BDI, BAI	32 weeks	On-off control of OCD symptoms with some improvement in mood	Rucklidge (2009)
Adults with BD	$n = 358$	Database analysis	DSM-IV based rating scale for mood	6 months	Symptom reduction of 45% from baseline, effect size .76, 53% experienced > 50% improvement and a reduction in medication use	Gately and Kaplan (2009)
Adults with ADHD and SMD	$n = 15$, 14 completed	OL	YMRS, MADRS, CAARS, CGI	16 weeks (8 weeks OL, 8 wks follow-up)	Medium to large ES for all measures, normalization of mood and hyperactivity	Rucklidge et al. (2011)
Children and adults (2-28) with ASD	$n = 88$ (44 in each group)	Naturalistic Case control study: patient preference for micronutrients or pharmaceuticals	CGI, Childhood Autism Impressions Scale, ABC, Childhood Psychiatric Rating Scale	Mean follow-up: 23 months, minimum 3 months	Both groups significantly improved but micronutrient group improved significantly greater than medication group on ABC, CGI change greater for micronutrient group	Mehl-Madrona et al. (2010)

20-year-old female with ADHD, BD II, and Panic Disorder with Agoraphobia	$n = 1$	ABAB case study	MADRS, YMRS, CAARS	1 yr	On off control of symptoms, symptom free at 1 yr follow-up	Rucklidge and Harrison (2010)
Children 7-18 years with BD and or ADHD	$n = 161$ (120 with BD, 41 with ADHD)	Database analysis	DSM-IV based rating scale for mood and ADHD symptoms	6 months	Mean change in bipolar symptoms from baseline 46% (large ES), 47% for ADHD symptoms, 52% drop in medication use	Rucklidge et al. (2010)
Adults with ADHD and SMD, 14 matched controls without ADHD	$n = 28$ (14 ADHD taking micro-nutrients, 14 controls not taking micronutrients)	Case control – comparison of those taking and not taking micronutrients	Neurocognitive battery including DKEFS, WRAML-II, CPT-II	8 weeks	Those taking micronutrients showed significant changes (large ES) in verbal abilities with no changes (none to small ES) in control group	Rucklidge et al. (2011)
Adults with ADHD exposed to a 7.1 earthquake	$n = 35$, 16 on micronutrients, 17 off micronutrients	Case control	DASS	N/A	Micronutrient group had significantly lower scores on stress and anxiety post-earthquake than non-micronutrient group (ES = .69)	Rucklidge et al. (2011); Rucklidge & Blampied (2011)
Children with bipolar spectrum disorder	$n = 10$ children with bipolar spectrum disorder (8-12 yrs); 7 completed	OL	KMRS, KDRS	6.5 months	Decrease in both depression and mania scores for study completers; intent-to-treat showed significant decrease in mania scores only	Frazier et al. (2012)

TABLE 2
(Continued)

Sample	Sample size	Design	Measures	Length of Trial	Results	Reference
Stressed adults exposed to the February 22 2011 earthquake in Christchurch, New Zealand	$n = 91$ adults with stress (>18 yrs) and 25 nonrandomized controls; 84 completed	RCT; 1) Berocca™ ($n = 30$); 2) low dose (4 pills) EMPowerplus™ ($n = 31$); 3) high dose (8 pills) EMPowerplus™ ($n = 30$)	DASS, PSS, IES-R, CGI	4 weeks plus 4 week follow up	All three treatment groups significantly better than baseline (large to very large effect sizes) across measures of depression, anxiety, stress, PTSD symptoms with EMP™ groups experiencing greater reduction in intrusive thoughts as compared with Berocca™, with no group differences on other measures of psychological symptoms. EMP8 group reported greater improvement in mood, anxiety, and energy with twice as many reporting being "much" to "very much" improved. Treated participants had better outcomes on most measures over four weeks as compared to controls.	Rucklidge et al. (2012)
11-year-old boy with a 3-year history of mental illness including psychosis, anxiety and OCD; borderline intellectual functioning	$n = 1$	Case study	ABAS, CGAS, DSM-IV based rating scale for symptoms of psychosis, anxiety/panic and OCD	4 yrs	Complete remission of psychosis; severity of anxiety and obsessional symptoms decreased significantly ($p < .001$); improvements sustained at 4-yr follow-up; cost comparison showed that micronutrient treatment was less than 1% of inpatient mental health care	Rodway et al. (2012)

OL = open label, DASS = Depression, Anxiety and Stress Scales, DKEFS = Delis-Kaplan Executive Function System, WRAML-II = Wide Range Assessment of Memory and Learning, CPT = Continuous Performance Task, MADRS = Montgomery-Asberg Depression Rating Scale, YMRS = Young Mania Rating Scale, CGI = Clinical Global Impression, CAARS = Conners Adult ADHD Rating Scale, Y-BOCS = Yale Brown Obsessive Compulsive Scale, BDI = Beck Depression Inventory, BAI = Beck Anxiety Inventory, CBCL = Child Behavior Checklist, ABC = Aberrant Behavior Checklist, YOQ = Youth Outcome Questionnaire, HAM-D = Hamilton Rating Scale for Depression, BPRS = Brief Psychotic Rating Scale, ES = Effect Size, BD = Bipolar Disorder, ADHD = Attention-Deficit/Hyperactivity Disorder, SMD = Severe Mood Dysregulation, ASD = Autism Spectrum Disorder, IES-R = Impact of Event Scale- Revised, PSS = Perceived Stress Scale, KDRS = Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present Episode-Depression Rating Scale, KMRS = Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present Episode-Mania Rating Scale, ABAS = Adaptive Behavior Assessment System, 2nd edition, CGAS = Children's Global Assessment Scale.

ADHD Diagnostic Interview for DSM-IV (CAADID; Epstein, Johnson & Conners 2002). He was then followed through to May 2011. Brian met DSM-IV criteria for ADHD Combined Type, Major Depressive Disorder, Panic Disorder with Agoraphobia and Substance Abuse (cannabis). He used cigarettes and cannabis on a daily basis and despite having tried to reduce, had been using these drugs for several years. In the past, Brian had been on various medications for his psychiatric symptoms, including methylphenidate, imipramine, fluoxetine, clonidine, amitriptyline, lorazepam, and clonazepam. He remarked that none of the medications had directly reduced his symptoms without him experiencing significant side-effects. At the time of the assessment and throughout the trial, Brian did not take any psychotropic medications.

Measures

Severity of symptoms of depression and ADHD were assessed bimonthly in the first eight weeks and then every few months thereafter by a clinical psychology graduate student alongside a clinical psychologist using: 1) The Clinical Global Impressions Severity (CGI-S) and Improvement (CGI-I) Scales (Spearing et al. 1997). The CGI severity and improvement were assessed separately for depression and ADHD symptoms. The score for the CGI-S ranges from 1 (normal, not ill) to 7 (among the most extremely ill patients). The score for the CGI-I ranges from 1 (very much improved) to 7 (very much worse); 2) The Global Assessment of Functioning (GAF; American Psychiatric Association 2000), a numeric scale (1 through 100) used by mental health clinicians and doctors to rate the general functioning of adults; 3) The Montgomery-Asberg Depression Rating Scale (MADRS; Montgomery & Asberg 1979), a 10-item scale administered by a trained clinician who assigns a severity rating for each item of depression based on a personal interview. At transition phases, the Conners' Adult ADHD Rating Scales (CAARS; Conners, Erhardt & Sparrow 2003) were used to assess changes in ADHD symptoms. Both a self-report version and clinician version were administered.

Measure of Nicotine and Cannabis Use

Given that cannabis and nicotine use were not primary outcome measures, a rating scale was developed based on information gathered on the frequency of use of cigarettes and marijuana. A weekly rating was assigned ranging from 0 (not at all over the last week) to 1 (once a week), 2 (several times a week), 3 (every day), and 4 (every day in conjunction with high dose) and used retrospectively to track substance use.

Procedure

The trial began with a baseline phase of four weeks, and then a first treatment phase (10 weeks), during which Brian consumed a standard dose of micronutrients every day. In a planned reversal of treatment, he stopped taking micronutrients for 10 weeks and then resumed consumption in a final treatment phase of four months. Assessments and interviews took place at bimonthly intervals in the first three phases and then monthly in the final phase. A final withdrawal (reversal) phase occurred when he left the city, but further assessment was possible after contact was reinstated one year post-baseline. Compliance was monitored with daily diaries and pill counts.

RESULTS

Phase 1: Baseline: Assessment and Diagnosis (Weeks 0–4)

Brian entered the initial baseline phase while depressed, confirmed by a MADRS score of 28. CGI-S ratings were "moderately" to "severely ill" for both ADHD and depression. His GAF score was 51, indicative of moderate symptoms and moderate impairment in functioning. In terms of his ADHD symptoms, the CAARS self-report and clinician ratings indicated clinical elevations on measures of both DSM-IV inattentive and hyperactivity/impulsivity symptoms (T-scores greater than 65). A drug screen indicated the presence of nicotine and cannabis in his urine (see Figures 1 and 2).

A second baseline was collected a month later as there was a delay in getting blood tests done (haematological and biochemistry measures were taken to monitor safety of the nutrients over time). Generally, Brian's symptom levels were stable over this baseline period. More specifically, his MADRS score increased slightly to 31. His GAF score remained the same, as did his CGI-S ratings.

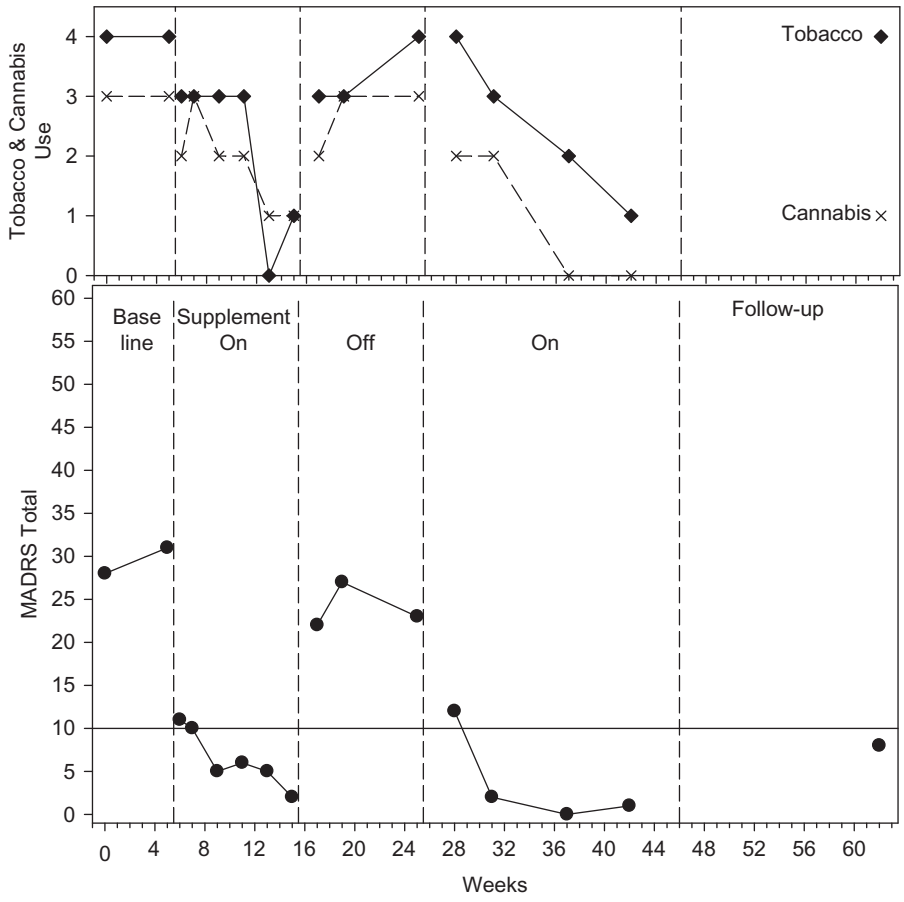
Phase 2: First Treatment with EMP+ (Weeks 5–14)

Brian's micronutrient consumption was titrated over a week up to the daily dose of 15 pills a day (taken as five pills three times a day with plenty of food and water). Only minor side-effects were reported, such as a mild stomach ache when the pills were not taken with food and "cramps" at the back of his head, reportedly worse than headaches, but these were transient and only occurred in the first couple of weeks. Brian's compliance was excellent in that he took the full dose of 15 pills most days, only missing a few doses on occasion.

Changes were noted after only a week on EMP+. Brian's mood lifted substantially, with a decrease in his MADRS score from 31 to 11. After two weeks on the pills, Brian remarked that he could sit through an entire movie, which he was unable to do previously, and he reported being able to "focus on one thing at a time." At four weeks, there was a further improvement in his mood, confirmed by a MADRS rating of 5. At six weeks on the micronutrients, Brian's partner reported on several changes in Brian including greater motivation, being less "on the

FIGURE 1

Time-Series Data Showing Change in Brian's Montgomery Asberg Depression Rating Scale (MADRS) Scores, Cannabis and Tobacco Use. B = Baseline, On = On Micronutrients, Off = Off Micronutrients. Solid Line Indicates Remission. Dashed Lines Represent the Different Phases of the Trial



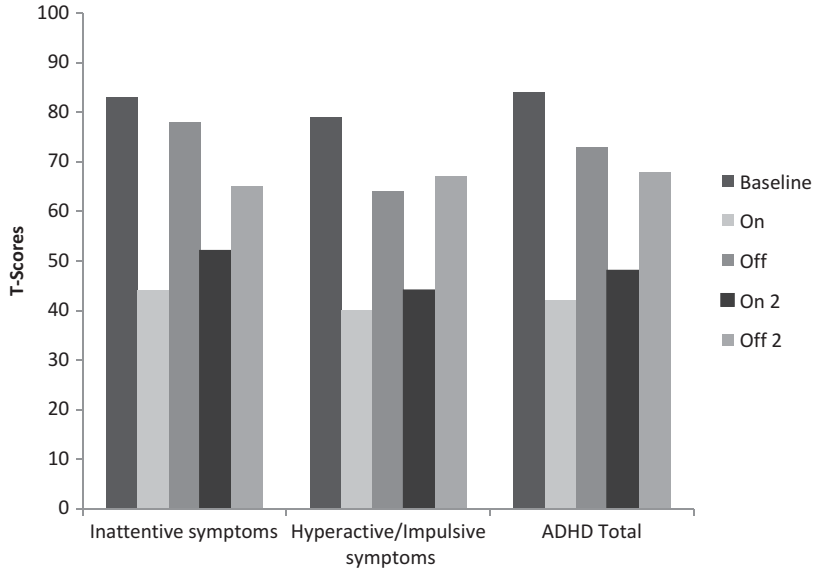
go," getting to work on time, less paranoia, less wound up, and slightly more "laid back." At eight weeks, Brian reported that he had quit smoking cigarettes the previous week and experienced cravings only every few days. He also reported no longer needing to use cannabis on a daily basis.

All outcome measures were repeated at 10 weeks. Brian was no longer in a depressed episode, confirmed by a MADRS score of 0. Brian's CGI-S ratings were "minimally ill" for ADHD and "normal/not ill" for depression. CGI-I ratings were "very much improved" for both ADHD and depression. His GAF score (80) was substantially higher than at baseline, reflecting a substantial reduction in symptom severity and improvement in functioning. Brian's ADHD symptoms reduced to the non-clinical range on both self-report and observer measures. He reported he had stopped smoking cigarettes and cannabis. Haematological and biochemistry tests were repeated; all tests fell in the normal range.

Phase 3: Withdrawal of Micronutrients (Weeks 15–24)

At the beginning of week 15, as per trial protocol, Brian was instructed to stop taking micronutrients entirely. After being off EMP+ for one week, a text message from Brian described himself as feeling more stressed out and having greater difficulty with quitting smoking. At two weeks off, Brian reported smoking one pack of cigarettes over the last week and using an increased quantity of cannabis on two occasions. Brian reported that he had been late to work a few times over the last week due to sleeping through his alarm. He reported feeling more stressed, having difficulties in focusing at both work and home, getting distracted by everything, quickly losing interest in things, being disorganized, fidgety, forgetful, and starting

FIGURE 2
Change in Brian's CAARS Observer-Rated (Screening Version) Scores Completed by Clinician



tasks but not finishing them. Depressive symptoms had also returned, although not as severe as baseline, confirmed by a MADRS score of 22. By four weeks off EMP+, Brian's cannabis use had increased again. He reported smoking cannabis every day and two packs of cigarettes over the last week (indicating heightened cravings). He was experiencing more mood swings in that he would get agitated every couple of days and annoyed at his partner and friends over small things. His sleep had also worsened; he was taking a long time to get to sleep, waking during the early hours of the morning, and struggling to get back to sleep. He described feeling tired during the day and had to "drag himself out of bed." He reported that he had been more fidgety, forgetful, restless, and "terrible sitting still." His partner stated that Brian was "more snappy, wound up and does not leave the house."

Outcome measures were repeated at 10 weeks off EMP+. Although his depressive symptoms did not return to his baseline severity level, they did increase substantially, confirmed by his MADRS score of 23 (see Figure 1). Brian's CGI-S ratings were "markedly ill" for ADHD, and "moderately ill" for depression. Brian obtained a GAF score of 60, indicating moderate symptoms. In terms of Brian's ADHD symptoms, both his self-reported inattention and hyperactivity/impulsivity returned to clinically elevated levels (T-scores greater than 65 – see Figure 2). He reported that he could not relax unless he smoked. Brian missed appointments due to sleeping in and forgetfulness. In addition, he appeared more stressed and disorganized.

Phase 4: Reinstatement of Micronutrient Treatment (Weeks 25–41)

EMP+ was reintroduced in week 25 and Brian was followed-up every few weeks over a four-month period. Appointments were either in person or over the phone. Brian again slowly titrated up to the full dose of 15 pills a day. At three weeks back on micronutrients, Brian's mood had improved, confirmed by a MADRS rating of 12. Furthermore, he obtained a GAF score of 65. Brian reported no difficulties getting to sleep. Further improvements were noted five weeks into the phase, confirmed by MADRS rating of 2 and a GAF score of 71. Brian described himself as not on edge anymore and having no difficulties with concentration. At this time, there was a 7.1 earthquake in Christchurch and Brian's reaction to this was monitored. He was reportedly coping well in the face of a potentially stressful situation and no changes were noted in his mood and anxiety.

Outcome measures were repeated when Brian had been back on EMP+ for three months. He obtained a MADRS score of 0, confirming that he was no longer in a depressive episode (see Figure 1). He obtained a GAF score of 81, indicating minimal symptoms and general satisfaction with life. Brian obtained CGI-S ratings of "minimally ill" for ADHD and "normal/not ill" for depression, and "very much improved" for both depression and ADHD. In terms of Brian's ADHD symptoms, there were no clinical elevations on either self-report or observer screening versions of the CAARS. He reported no anxiety, panic,

irritability, and edginess and that he had not been feeling tense. He also noted that he had stopped using cannabis.

At four months back on micronutrients, Brian's depression remained in remission, confirmed by a MADRS rating of 1 and a GAF rating of 81. He also reported that he had quit smoking again for the last week and had not used cannabis for about six weeks.

Phase 5: Natural Treatment Withdrawal (Week 42 to 62)

Brian failed to attend his monthly review at week 45. He was unable to be reached on his cell phone and no contact was possible until five months later. When finally contacted at week 62, he stated that he had left the city suddenly in order to help a relative following the Brisbane floods in January 2011. He then returned to Christchurch a few days prior to the February 22, 2011, 6.3 earthquake. Because the university was closed for three months following this second earthquake, we did not track Brian down until May 2011. By this point, he had stopped the micronutrients for about four months. Although his ADHD symptoms had returned to baseline levels, his mood remained remarkably stable and he obtained a MADRS score of 8. However, he reported that he was feeling tense and on edge all the time and having difficulties with concentration, his mind wandering off more and being more forgetful, and he described feeling more energetic and "hyper" than usual. In terms of Brian's ADHD symptoms, he obtained scores in the clinical range (see Figure 2). Brian reported smoking cannabis about once a month and was smoking cigarettes on a daily basis again (see Figure 1 for change in cannabis/cigarette use over time).

DISCUSSION

Brian is a 20-year-old male who presented with severe mood dysregulation, ADHD, Panic Disorder with Agoraphobia, and cannabis abuse. He responded to a micronutrient treatment with improvements in all his psychiatric symptoms including depression, ADHD, and anxiety. His positive response to treatment was replicated through a reversal design, demonstrating on-off control of symptoms when micronutrients were consumed and then withdrawn. The detection of these treatment-related changes is aided by the stable baseline observed over a one-month period. Of particular interest, both Brian's nicotine and cannabis use reportedly decreased while on the micronutrients and increased again while off, although an obvious lag did occur in that the mood and ADHD symptoms resolved first, followed a few weeks later with a reduction in substance use. It is relevant that on the final follow-up Brian obtained a low mood score and concurrently reported low cannabis use. This clear relationship that emerged between depression and cannabis use supports other research suggesting that cannabis can be used to self-medicate for depression (Grant & Pickering 1998).

Therapist contact is unlikely to explain the dramatic changes in Brian's symptoms, as therapist contact was gradually tapered off over time and contact was minimal (once a month) in the second reinstatement phase. Further, therapist contact occurred even when Brian was not taking the micronutrients. Perhaps more remarkably, Brian achieved these changes after a long and well-documented history of poor response to conventional treatments; one intervention (micronutrients) stabilized ADHD and mood symptoms as well as anxiety.

Many theories have been proposed as to why nutrients might effect positive change on psychiatric symptoms, including correcting in-born errors of metabolism (Ames, Elson-Schwab & Silver 2002; Kaplan et al. 2007), addressing dysfunction within the mitochondria (Parikh et al. 2009), improving energy metabolism (Arnold et al. 2007), and improving gut inflammation (Wärnberg et al. 2009). In the drug addiction literature, studies are showing that providing the precursors to key neurotransmitters via amino acids can alleviate withdrawal symptoms (Chen et al. 2012), suggesting that the administration of precursors of neurotransmitters leads to augmentation of those neurotransmitters responsible for symptom reduction. Based on this research, it is possible that EMP+ provides the essential cofactors and precursors required for neurotransmitter synthesis, including some amino acids (DL-phenylalanine, L-glutamine, and methionine), although vitamins and minerals are relevant too (Ames, Elson-Schwab & Silver 2002).

There is a specific interest in the role of dopamine in the development and maintenance of addiction, encapsulated in the latest definition by the American Society of Addiction Medicine (ASAM) as a brain disorder due to impaired reward circuitry (see www.asam.org). Blum and colleagues (2008) argue that not only addictions but also ADHD may be the result of a reward deficiency syndrome whereby defects in the dopaminergic genes lead to dysfunction in the "brain reward cascade." Neutraceuticals may correct this dysfunction by providing the necessary precursors to normalize dopamine and, in turn, reduce the need for addictive drugs. Indeed, research is providing evidence that neutraceuticals, at least amino acids, not only assist with withdrawal (Blum et al. 1988; Blum, Chen & Chen 2009; Chen et al. 2012), but may also normalize aberrant electrophysiological parameters of the reward circuitry site, providing support for the proposed biological mechanism explaining why these treatments might work (Blum et al. 2010; Miller et al. 2010). L-glutamate, in combination with B_6, synthesize γ-Aminobutyric acid (GABA), which may influence symptoms via an anti-dopamine effect (Schousboe & Waagepetersen 2010). Preliminary work has also shown that some B vitamins may share structural similarity with dopamine, thereby enhancing

dopamine concentrations via their competitive binding to the dopamine transporter-binding site and proposing another mechanism by which nutrients may be influencing the dopaminergic system (Shaw, Rucklidge & Hughes 2010).

While this study is limited in terms of generalizability and inferences may be limited by potential halo effects as well as bias from the researchers, it is important to consider that the researchers were not intending to reduce or eliminate use of cannabis and cigarettes. Indeed, at the beginning of participation, we ask that participants *not* make drastic changes in cigarette use and other substances or make changes to their diet in order to prevent drug withdrawal from impacting on treatment response. As substance abuse was not one of our primary targets of intervention, we did not assess it as systematically as could have been done, either using standard interviews or scales assessing more broadly not only use but evidence of abuse and dependence. Nevertheless, we hope this case underlines the possible importance in using nutrients as a treatment for withdrawal and/or reduction in cannabis and cigarette use. This case highlighted the potential of nutrient supplementation in treating a chronic and debilitating addiction and extends the literature using amino acids as treatment for withdrawal, justifying larger and more controlled trials with a much broader array of micronutrients.

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