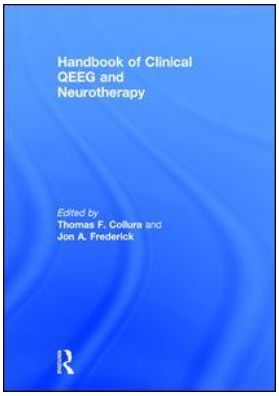

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THE USE OF SURFACE 19-CHANNEL Z-SCORE TRAINING TO AMELIORATE SYMPTOMS REMAINING OR APPARENTLY CAUSED AFTER WITHDRAWAL FROM THOSE MEDICATIONS

Kathy Abbott

Abstract

Medication influences brainwave amplitude and power (Meckley & Kaiser, 2012). Three cases are presented in which the clients developed symptoms when coming off their medications. In a third case, the client developed worsening symptoms that did not remit when they discontinued the drug. In one case a client developed a tic when trying to discontinue Strattera. In the second, the client developed more severe restless legs syndrome resulting is very poor sleep when coming off her last dose of Hydrocodone. In the third case use of Wellbutrin was associated with worsening of depressive symptoms which remained worse off Wellbutrin. After four to six sessions of surface 19-channel z-score training (19 ZNF), the first two clients were able to discontinue their medications without a resumption of their post withdrawal symptoms. The third client required 20 sessions. Possible reasons for the effectiveness of 19 ZNF are explored. 19 ZNF may be a way of treating post-withdrawal symptoms.

Introduction

Medications influence brainwave amplitude and power (Meckley & Kaiser, 2012). For example, Depakote is associated with a decrease in theta and an increase in alpha (Porras-Kattz et al., 2011), and benzodiazepines are associated with an increase in 12–18 Hz (Herrmann & Kubicki, 1981). In addition, it is known that medications sometimes cause side effects and that discontinuing a medication may be associated with physiological withdrawal symptoms.

Development of drugs for purposes such as psychiatric disorders can be difficult. According to Greden (1994, p. 33), the brain has neurotransmitters,

> many of them interacting with receptor sites that have two to ten subtype configurations, each producing different neurobiological actions. The process is further confounded by co-localization and co-release of selected neurotransmitters from certain synaptic junctions,

differing duration and extent of neurotransmitter actions at the receptor sites, different intracellular second-messenger systems, different signal transduction mechanisms, and different effects on gene expression and protein synthesis.

Thus, it is not surprising that medication problems emerged in these three cases.

The purpose of this chapter is to discuss the use of surface 19-channel z-score training (19 ZNF) in cases of clients who have a reaction either to the medication or to physiological withdrawal from the medication. Three cases are presented in which 19 ZNF training was used to decrease or remove these drug-related symptoms.

With this in mind, three clients who had a reaction either to the medication or physiological withdrawal from the medication were given 19 ZNF training with the purpose of returning their brainwave pattern closer to normal and probably closer to how it had been before developing their symptoms. One client experienced an increase in depression which remained subsequent to physiological withdrawal from the antidepressant, another had difficulty discontinuing a pain medication because she developed a worsening case of restless legs syndrome, and the third had difficulty discontinuing atomoxetine (Straterra) because she developed a tic when not taking the medication.

Surface 19-Channel Z-Score Training (19 ZNF)

Surface 19-channel z-score training (19 ZNF) is based on the following principles.

1. Z-scores assume a normal distribution (Thatcher, Biver, & North, 2004–2007) with a mean of zero and a standard deviation of one.
2. Normative databases have been developed using z-scores that are corrected for age, location, and frequency range. These databases include Neuroguide (Thatcher et al., 2004–2007) which was used in these cases.
3. The Neuroguide database specifically include measures of power for different frequencies (delta, theta, alpha, etc.) and measures of connectivity, such as coherence, phase, and asymmetry.

Method

A Brainmaster Discovery with Brainmaster software, version 1.5.9, was used for feedback and the normative database for the z-scores used was Neuroguide software, version 2.7.2. The Neuroguide database was developed from 625 people ranging from 2 months to 82 years of age (Thatcher et al., 2004–2007). The software includes norms for the following bandwidths: delta (1–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), beta (12–25 Hz), hi-beta (25–30 Hz), beta-1 (12–15 Hz), beta-2 (15–18 Hz), beta-3 (18–25 Hz), alpha-1 (8–10 Hz), and alpha-2 (10–12 Hz) (Thatcher et al., 2004–2007, pp. 7–8). At each of the 19 sites, the z-scores were trained for Absolute Power and Relative Power for each of the above bandwidths. Also, ratios between delta and theta, delta and alpha, and so on were trained for all 19 sites. In addition, z-scores for Asymmetry, Coherence, and Phase for every possible pair of sites was trained.

The 19 channels used were Fp1, Fp2, F3, F4, F7, F8, C3, C4, T3, T4, P3, P4, T5, T6, O1, O1, Fz, Cz, and Pz. These channels represent the 19 basic placements as measured using the 10–20 system (10/20 System Positioning Manual, 2012).

The protocol used was Z-Score Percent ZOKUL created by Mark Smith. As indicated above, all 19 channels/placements were used. PZOK is defined as "percentage of all trained z-scores that fall within a given target range" (Collura, 2014, p. 170). Upper and lower limits for z-scores were set around plus or minus 1.0 standard score. Training was done on 5700 z-scores. Clients were

challenged to make a Pacman-like image move when a certain percentage of the z-scores were within the z-score range. The percent of these numbers was set so that the client was being rewarded around 50–60 percent of the time.

Case Studies

Client G—A Case of Depression

Client G, an older adolescent, reported severe depression and ADHD. She had withdrawn to her bedroom and had stopped attending college classes. For her ADHD symptoms, she was given Adderall, which gave her panic attacks and extreme anxiety. Wellbutrin was added but the symptoms did not remit. However, when the Wellbutrin was increased from 75 mg to 150 mg, the depression worsened. The client became more depressed and significantly more socially withdrawn and unmotivated. After discontinuing both drugs, the panic attacks remitted. However, the client continued to report being more depressed. In addition, she remained in her room most of the time and did not communicate with her family. Motivation dropped. Following 20 sessions of 19 ZNF, her affect brightened and she became more talkative, more hopeful, and less depressed. She was able to return to school and hold a part-time job.

There are several EEG subtypes of depression (Johnstone, Gunkelman, & Lunt, 2005). One of these is the beta spindling subtype. However, Client G did not have any beta spindling. However, it has been noted that excess frontal beta may be associated with passive personality or avoidant personality, and may be associated with flat affect and hiding one's feelings (Soutar & Longo, 2011, p. 88). And Kupfer, Reynolds, and Ehlers (1989) found excess beta in people with depression, especially those with delusions.

Some antidepressants appear to cause an increase in depression and suicidal ideation in adolescents. Compared to a placebo, Wellbutrin (Buproprion) and other antidepressants may be associated with in increased risk of suicidal ideation and acts in children through young adult ages (Physicians Desk Reference, 2013). Side effects may include agitation, insomnia, allergic reaction, increased blood pressure, confusion, and seizures (Physicians Desk Reference, 2013). Of 1829 people from New Zealand who filled out an on-line questionnaire, 60 percent reported feeling more emotionally numb (Read, Cartwright, & Gibson, 2014). Forty-two percent reported a decrease in positive feelings. Fifty-two percent reported a loss of self-esteem. Five percent reported feeling less motivated. And 39 percent reported "Suicidality," which was more common in younger respondents. It should be noted that there was no control group. Also, people with negative responses may have been more likely to reply thus producing a self-selection bias.

In one study, it was found that a decrease in prefrontal theta cordance, after a one week of daily Buproprion (Wellbutrin), was a predictor of a positive response to four weeks of treatment in people who had not responded to other antidepressants (Bares et al., 2010). A drop in theta probably would result in a decrease in the theta/beta ratio with a relative increase in beta power. But the client had an excess of relative beta to begin with which may help explain how the medication may have contributed to Client G's depression.

Hunter, Leuchter, Cook, and Abrams (2010) studied 72 people with major depressive disorder who were given 20 mg of fluoxetine, 150 mg of venlafaxine, or a placebo. Of those, nine showed emergent suicidal ideation which was associated with a transient drop in right frontal and midline cordance as measured 48 hours after the people started the medication.

Why would excess beta along the cingulate be related to poor motivation and depression? The dorsal anterior cingulate and the striatum are involved in cost-benefit decisions (Schouppe, Demanet, Boehler, Ridderinkhof, & Notebaert, 2014). Activation of these areas may be associated with tendency to decide that effort is not worth the reward.

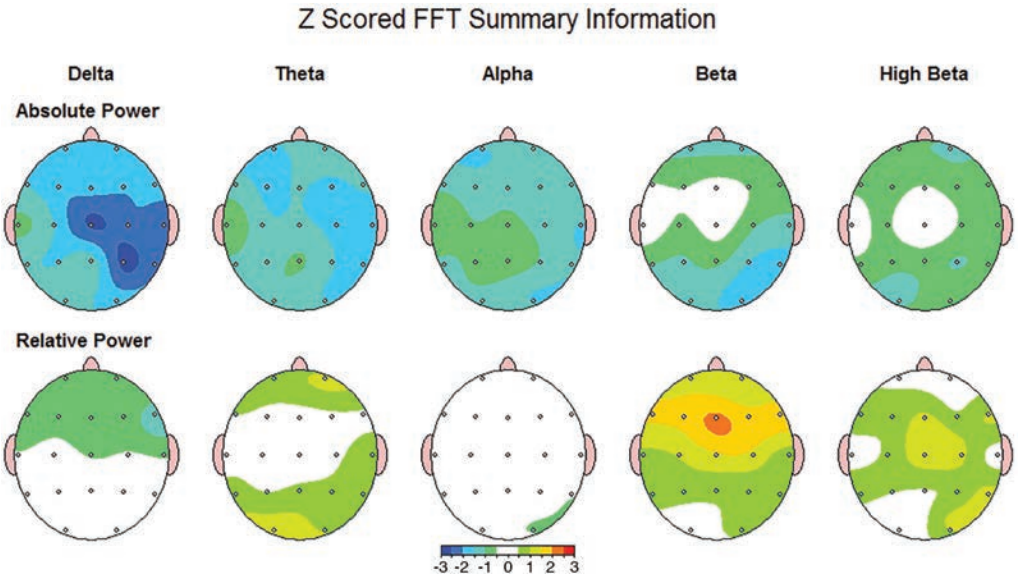

Figure 21.1 Client G z-scored FFT summary information showing excess beta at Fz.

Client P—A Case of Restless Leg Syndrome

Client P is an elderly woman who is mentally alert. She continued to play bridge, listen to books on tape and socialized until she suffered several compression fractures in her back. The compression fractures resulted in bed rest for three months. She moved to an apartment where she would get out of bed for short times. After the compression fractures had healed, she remained in a great deal of pain but was encouraged to discontinue her pain medications including Hydrocodone.

While on the pain medications she had experienced typical side effects including feeling sedated and nausea (Physicians Desk Reference, 2013). She was in favor of discontinuing the medications due to these side effects.

The symptoms of feeling sedated and nausea diminished as she went off her medications. Her thinking seemed clearer and she felt more like herself. However, she was unable to discontinue her nightly dose of 15 mg hydrocodone because without this dose she experienced restless legs syndrome (RLS); this resulted in her having difficulty getting to sleep and she would have to get up several times during the night. Client P had a history of RLS from before being on the medication, but she had been able to manage it by using heat and massage.

Following six sessions of 19 ZNF, Client P was able to sleep and to manage her restless leg symptoms which had returned to pre-medication levels. Sleep improved dramatically. Five weeks later, she had one night of excessive restless legs but otherwise she was sleeping well.

What is Restless Legs Syndrome (RLS)? Restless legs syndrome is characterized by the urge to move one's legs. The urge grows with rest and becomes worse at night or at evening time. The symptoms may be partially relieved through physical activity (Aurora et al., 2012). According to the National Institute of Neurological Disorders and Stroke (http://www.ninds.nih.gov/disorders/restless_legs/detail_restless_legs.htm#241543237), restless leg syndrome is a "neurological disorder characterized by throbbing, pulling, creeping, or other unpleasant sensations in the legs." It is an uncontrollable need to move. RLS disturbs sleep and inhibits falling asleep. It affects 5.5 percent of adults and it occurs more often in women than men (Ohayon & Roth, 2002). Occurrence of RLS is

associated with being female, older age, exercise closer to bedtime, smoking, drinking, snoring, shift-work, and stress (Ohayon & Roth, 2002).

The cause of RLS is unknown but may be genetic (National Institute of Neurological Disorders and Stroke). The cause may be related to dysfunction of the circuits of the basal ganglia (http://www.nhlbi.nih.gov/health/health-topics/topics/rls/causes.html). Also, there may a lack of iron or poor use of brain iron. The iron-related causes may be due to kidney failure, rheumatoid arthritis, diabetes, Parkinson's Disease, or iron deficiency (http://www.nhlbi.nih.gov/health/health-topics/topics/rls/causes.html; Woimant & Trocello, 2014). Client P does have rheumatoid arthritis but she has none of the other conditions that are related to RLS.

There is evidence of the effect of opiates on sleep (Brand, Lehtinen, Hatzinger, & Holsboer-Trachsler, 2010). Compared to people with Major Depressive Disorder who also have poor sleep, those with RLS had statistically significantly worse sleep including more difficulty getting to sleep, more waking up during sleep, and smaller amounts of slow-wave sleep.

Non-Drug Treatment for RLS

Treatment may include movement itself, heat and leg massage (which Client P was using), and exercise (National Institute of Neurological Disorders and Stroke). "Alerting activities" may also be useful (Silber et al., 2013).

Drug Treatment

Dopamine agonists used to treat Parkinson's Disease (PD) are also used to treat RLS. A study concluded that women with low normal or low ferritin levels showed similar decrease in International Restless Legs Severity Scale (IRLS) scores when treated with iron or with a Parkinson's drug called pramipexole and the improvement was moderate (Lee, Lee, Kang, Park, & Yoon, 2013).

The effects were studied of this dopaminergic drug, pramipexole, on the motor evoked potential (MEP) which was measured through transcranial magnetic stimulation (Scalise, Pittaro-Cadore, Janes, Marinig, & Gigli, 2009). The MEP amplitude increased in those with drug treatment following rest after a motor task. Increases in evoked potential amplitude may be associated with increased excitability (Misulius & Fakhoury, 2001).

Other medications used to treat RLS include opioids, anticonvulsants, and benzodiazepines (Aurora et al., 2012).

RLS and EEG/ERD/ERS

It has been noted that RLS is "characterized by closely interrelated motor and sensory disorders" (Tyvaert et al., 2009, p. 1090). Event-related beta and mu rhythm (de)synchronization (ERD/ERS) were measured while thinking about immobilizing their ankle dorsally and while flexing the ankle dorsally at 8:30 pm when symptoms were expected and at 8:30 am when symptoms were not expected in non-symptomatic people and those with primary RLS. The duration and amplitudes of the ERS and ERD were greater during the 8:30 pm (symptomatic) time for voluntary movement for RLS patients than for normal controls. Morning ERDS and ERS were similar for the two groups. It was concluded that RLS symptoms are related to a dysfunction of sensorimotor activity.

In addition, beta synchronization was measured after people with PD and a control group actively and passively moved their index fingers and in response to electrical stimulation of the median nerve (Tyvaert et al., 2009). In all three conditions, contralateral beta synchronization was lower in PD people than controls. (ERD can be interpreted as an electrophysiological correlate of activated

cortical areas involved in processing of sensory or cognitive information or production of motor behavior (Pfurtscheller, 1992).)

Degardin et al. (2009) reached a similar conclusion. They note that when people move, beta synchronizes, which reflects deactivation of the motor cortex. Following movement, people with PD show a decrease in beta synchronization which indicates idling of the motor cortex that is abnormal and may be related to the cause of akinesia. Perhaps this finding is consistent with the use of training up sensory motor rhythm (SMR) in people with PD. And since opiates tend to increase power of slower frequencies and an increase in beta power tends to lower those slower frequencies, it may be that an increase of this frequency was related to the decrease in symptoms of Client P.

Effect of Opiates on EEG

Shufman et al. (1996) found that compared to controls, addicts had a higher ratio of low alpha to high alpha (8.0–9.5 Hz to 9.5–12.0 Hz ratio). Those addicts who were abstaining also exhibited alpha slowing, more frequent delta waves, and a higher than average ratio of delta to low alpha which decreased over length of abstinence. Polunina and Davydov (2004) found that a high dose of heroin was associated with changes in alpha-2 and that the change was associated with length of use. Addicts studied had been using for from 6 days to 4.5 months. Phillips, Herning, and London (1994) studied 12 polydrug abusers. Their EEGs were tested following a placebo and two doses of Morphine. The 15 mg dose of Morphine was associated with a global increase in alpha-1, alpha-2, theta, and beta and improved mood. Increases in amplitude were global.

According to Greenwald and Roehrs (2005), a high dose of Fentanyl is associated with increases in amplitude of delta and theta. Delta waves are associated with sleep with 20 to 50 percent of the waves being delta in stage III sleep and 50 percent of the brainwaves being delta in Stage 4 sleep (Hughes, 1994).

Fingelkurts et al. (2006b) studied 22 opiate addicts and 14 controls. They found that the percentage of beta and fast alpha increased globally and for longer periods of oscillation but were more predominant in the occipital lobe, and in the right side of the frontal, temporal, and parietal lobes. On the other hand, Franken, Stam, Hendricks, and van den Brink (2004) found that compared to controls, chronic heroin users exhibited more beta-2 power and more left gamma coherence intrahemispherically.

In the Shufman et al. (1996) study, following 80 days or *more* of abstinence, the ratio of alpha-1 to alpha-2 gradually returned to match that of controls. However, the length of time of post-physiological withdrawal of RLS symptoms would have contributed to Client P's difficulty discontinuing her evening dose of the opioid.

There is evidence that long-term users of opiates have differences in their QEEGs. And there are differences between users with shorter term dependency of less than 6.5 years from addicts with 6.5 years or more of dependence. Those with less than 6.5 years of dependence exhibited more EEG fast beta power and less alpha than controls, and addicts with a history of 6.5 years or more dependency exhibited an average alpha power greater than controls but average fast beta compared to normal controls (Bauer, 2001).

Opiates may also impact connectivity. Fingelkurts et al. (2006a) found that compared to controls, long-term opiate users exhibited more disrupted connectivity. Short-distance connectivity increased and long-distance connectivity was lower. Using fMRIs, Ku et al. (2014) found a relationship between both decreased connectivity and increased connectivity between the thalamus and other structures in the thalamocortical circuit in patients with restless leg syndrome. Diminished connectivity between the thalamus and the right parahippocampal gyrus was most highly connected with severity of restless leg symptoms. 19 ZNF works on connectivity and may normalize these changes.

Neurofeedback Treatment of Parkinson's Disease (PD)

Since RLS and Parkinson's Disease are both movement disorders, neurofeedback that is effective with PD may also be helpful with RLS. Thompson and Thompson (2003) studied 15 patients with PD. All of them had a deficit of SMR—13–15 Hz (p. 120). The Thompsons report using heart rate variability (HRV) and SMR training with PD with dystonia and with people with Tourette's. Training up SMR also helps decrease hyperactivity in people with ADHD. Training up SMR is consistent with the sensorimotor dysfunction seen in PD and Tourette's. The presence of SMR is associated with a lessening of motor excitability associated with a decreased transfer of sensory information to the cortex (Sterman, 2000).

Training up SMR is also helpful for training down hyperactivity in ADHD. The residual slowing seen in opiate addicts may be ameliorated with SMR training. And 19 ZNF may help decrease the slow activity and increase beta in clients who have developed RLS when trying to discontinue a pain-relieving opioid.

Effect of QEEG-Guided Neurofeedback on Opiate Addicts

Evidence that QEEG-guided neurofeedback has positive results in opioid addicts was found by Arani et al. (2010). They followed the Cry Help methodology of Scott, Kaiser, Othmer, and Sideroff (2005) which included 10–20 sessions of SMR or Beta training followed by alpha-theta training. In the Cry Help study, the experimental subjects first trained up either SMR or Beta training until their TOVA scores normalized.

In the Arani et al. (2010) study, compared to a control group, the people with addiction improved in SCL-R scores on hypochondriasis (in those with this symptom), obsession, hypersensitivity to others, aggression, and psychotic symptoms. On the Heroin Craving Questionnaire, there were improvements on scores related to craving and expectation of a positive outcome. The post QEEGs showed improvement toward normalization in the following: (1) delta at central, frontal, and parietal areas; (2) theta in frontal and central regions; (3) parietal alpha; and (4) SMR at frontal and central areas. However, perhaps due to lack of symptoms of restlessness or to lack of assessment of this symptom, it is not known if one of the results of this training was a decrease of restlessness in this group.

RLS is a movement disorder. Opiates tend to cause slowing of alpha frequency in a patient's brainwaves and have long-lasting post-physiological withdrawal effects. In the case of Client P, the remaining side effect was worsening of RLS. QEEG-guided neurofeedback has been used to normalize physiological withdrawal effects from opiates. In light of the long-term frequency changes and long-term side effects, it is not surprising that the 19-channel z-score training normalized the client's brainwaves—assumedly moving them closer to their pre-medication levels, thus causing the RLS to return to pre-medication levels.

Client J—A Case of Tics in Response to Withdrawal from Buproprion

Client J had done neurofeedback six years previously for symptoms of Asperger's disorder. There was an improvement in social skills, empathy, and prosody. Six years later the client returned for neurofeedback for her ADHD symptoms.

More recently she had taken atomoxetine (Strattera) to help with her ADHD symptoms. The drug did not help. However, six hours after a missed dose she would develop a tic. The client was given two sessions of 19 channel z-score training and the tic resolved. Six weeks later her mother noted that the tic was returning. One more session of 19-channel training and the symptom resolved. Six months later the tic had not returned.

Tourette's Disorder is sometimes co-morbid with ADHD (Biederman, Newcorn, & Sprich, 1991). Therefore, it is not surprising that the client developed the tic since she may have been prone to developing this disorder.

So why did she develop a tic when discontinuing this medication? Atomoxetine has been used to decrease tics but also exacerbates them in some people (Sears & Patel, 2008). Somkuwar et al. (2013) found that in spontaneously hypertensive rats, inhibition of norepinephrine by atomoxetine indirectly decreased dopamine cell surface function in the orbital frontal cortex. This would explain how tics could be caused by this drug but not how they might be exacerbated.

It is possible that since atomoxetine is used to treat tic disorders, physiological withdrawal from the medication may cause tics in clients prone to the disorder if the client makes some adjustments to the medication.

According to a review on the involvement of norepinephrine in ADHD, atomoxetine modulates the level of dopamine in the prefrontal cortex which may be associated with a rebalancing of the dopamine system (Viggiano, Ruocco, Arcieri, & Sadile, 2004). The effect on the dopamine system may be related to the occurrence of tics in Client J.

In Tourette's Disorder, the motor cortex and lateral orbitofrontal circuits' activities may be coupled, which differentiates them from controls (Jeffries et al., 2002). PET scans were performed on 18 drug-free clients with Tourette's' syndrome and 16 controls matched for age and gender (Jeffries et al., 2002). They found significant differences between those with and without Tourette's syndrome especially in ventral striatum connectivity but to a lesser degree in the primary motor cortex, insula, and somatosensory association areas. Also, there was a difference between the two groups in the functional connectivity of the motor and lateral orbitofrontal circuits with over coupling in the Tourette's syndrome people in the motor and lateral orbitofrontal circuits. This is consistent with the hypothesis that there are abnormal interactions between the limbic and motor systems in Tourette's syndrome. If this interaction were reflected in coherence and/or power, it is likely that z-score training may be helpful when the brain was inadvertently made abnormal by a drug that had an impact on either functional area.

It turns out that atomoxetine increases absolute and relative beta (Barry et al., 2009). It is not known how the discontinuation of this drug would cause tics. It is also interesting that the drug can bring on tics or help stop them. If it helps stop tics, perhaps the mechanism of causing them is due to the person adapting to the drug such that physiological withdrawal takes away the person's natural mechanism for preventing them.

Conclusion

Although the reasons are not clear, 19 ZNF neurofeedback appears to help ameliorate symptoms related to side effects from being on medication that do not remit, and improves symptoms that occur when one discontinues medication. Part of the reason may be that the medications alter the relative power of various frequencies. This appears to be the case with Client P and Client G. In these two cases, it is logical to assume that moving their brainwave patterns closer to normal would have returned them to their pre-medication levels. However, the correlation does not appear to be present with Client J even though neurofeedback was effective in ameliorating her tics. However, there may have been some adjustment that was a response to the medication which when the medication was no longer present resulted in her symptoms.

Use of 19 ZNF to ameliorate symptoms caused by prescribed drugs, including symptoms following discontinuation of a drug, has not been studied. It may be that use of 19 ZNF has been underutilized for this purpose. Further study is needed.

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