T_3-Induced Recovery from Fibromyalgia by a Hypothyroid Patient Resistant to T_4 and Desiccated Thyroid*

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Abstract. The main purpose of this case report is to illustrate a clinical observation common to me: that fibromyalgia patients with central hypothyroidism who fail to benefit from T_4 or desiccated thyroid completely recover when they switch to T_3. Changing status in the patient was evaluated in three ways: a psychiatrist used a depression inventory, a physical therapist performed functional musculoskeletal assessments, and I performed algometer tender point exams and monitored symptoms. I hope the description of the management of this case provides a protocol that other clinicians will use with fibromyalgia patients similar to the one who is the subject of this report.

Keywords • Fibromyalgia • Hyperthyroidism • T_3 • T_4 • TSH • Desiccated thyroid • Algometry

Introduction

A number of researchers in the 1950s and 1960s reported that hypothyroid patients responded to T_3, the metabolically active thyroid hormone, after failing to benefit from T_4, desiccated thyroid, or thyroglobulin.[8][9,p.13][10,p.274][11][12][13][14] Many of the symptoms the patients in these reports recovered from are remarkably similar to those characteristic of fibromyalgia. The symptoms are listed in Table 1.

The fibromyalgia patient whose case I report here resembles the patients in the 1950s and 1960s case reports in two respects: first, she shares with them the same general symptoms; and second, she responded to T_3 afer failing to benefit from desiccated thyroid. The patient discussed in this report and other fibromyalgia patients may be modern day examples of those 1950s and 1960s patients.

Like fibromyalgia patients studied by Ferraccioli and coworkers[18] and Neeck and Riedel,[19] this patient had a blunted TSH response to TRH, and this, combined with her thyroid hormone profiles, indicates that she had central (probably pituitary) hypothyroidism. Her complete recovery from fibromyalgia may point the way to relief for other fibromyalgia patients with central hypothyroidism.

Methods

Patient. The patient in this case study was a 41-year old Caucasian female. She was a homemaker and mother of two children.

On March 2, 1993 the patient's automobile, traveling at 20 miles per hour, struck another that came into her path. Immediately after the impact, she experienced neck and left shoulder pain. Subsequently, she underwent treatment, seriatim, by a chiropractic physician, a medical physician, a physical therapist, two additional chiropractic physicians, and myself. I concurred with the other practitioners that the patient had a traumatically-induced regional cervical injury but also diagnosed her as having fibromyalgia. Apparently she had had fibromyalgia symptoms for many years.

At the beginning of the study, she indicated on body drawings that she had widespread pain according to the American College of Rheumatology 1990 criteria:[23] pain above and below the waist and on the left and right sides of her body. The body areas she shaded on the drawings included the anterior, posterior, and

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lateral neck, the upper posterior thoracic area, the supraspinatus muscles, the interscapular region down to about the T6 spinal level, and the low back and gluteal muscles. She described her pain as "throbbing, aching, burning, and sometimes shooting and stabbing." she stated that her muscles felt too tense. She also reported the symptoms listed in Table 2.

Previous Treatment. On March 25, 1988 her psychiatrist prescribed desiccated thyroid. The supplement was intended to increase her energy level and serve as an adjunct to the antidepressant Desyrel. She also took the antidepressant Wellbutrin. She continued the thyroid supplement until we began this study although it benefitted her only in one way: her coldness decreased in distribution. Before taking desiccated thyroid, her whole body was cold. After beginning the supplement, only her hands and feet were cold—the Raynaud's-like symptom of fibromyalgia.

After delivering a baby in March 1990, she experienced severe post-partum depression and started an estrogen supplement.

Table 1. Six sets of symptoms reportedly relieved by T_3 after T_4, desiccated thyroid, or thyroglobulin failed to relieve them.

1. Aching in both knees, skin pallor, facial puffiness, a dull feeling, and tiredness.[8]
2. Lethargy, easy fatigue, nervousness, irritability, sensitivity to cold, headache, musculoskeletal pain, diminished sexual potency, and menstrual irregularities.[9]
3. Chronic fatigue, muscle and joint aches, excess weight, bowel dysfunction, cold intolerance.[10]
4. Muscle aches, stiffness, chronic fatigue, excess weight, menstrual disturbances, dry hair and skin, brittle fingernails, nervousness, irritability, depression, mental apathy, puffiness of the face.[11]
5. In school children, poor school records, short attention span, lack of ability to concentrate, "don't care attitude," anxiety, restlessness, poor appetite, constipation.[12]
6. Muscle and joint pains, fatigue, irritability and mood swings, lethargy, decreased libido, premenstrual tension, GI disturbances, scalp seborrhea or hair loss, palpitations, and shortness of breath.[13]

Methods of Assessment. There were several forms of evaluation.

Musculoskeletal functional evaluation. A physical therapist performed functional musculoskeletal assessments of the patient on three occasions.

Psychiatric evaluation. The patient filled out a Zung's Self-rating Depression Inventory on July 23, 1994 at the beginning of treatment and on January 13, 1995 at the end.

Fibromyalgia evaluation. The patient's fibromyalgia status was assessed through three methods: weekly pain drawings, mean algometer scores (the average of the pressure/pain thresholds of the 18 tender points), and diaries of symptoms. Between July 2 and August 8, 1994, I performed five baseline algometer exams. Between August 14, 1994 and January 27, 1995, I performed 19 treatment-phase algometer exams.

Laboratory evaluation. The patient's laboratory profiles were available dating back to 1988. Each included a CBC, SMAC, lipid profile, and thyroid profile. At my request, on July 6, 1994, an internist performed a TRH-stimulation test to evaluate the patient's TSH response to TRH, the hypothalamic hormone. Between July 19 and 20, 1994, he also performed a dexamethasone suppression test to assess adrenal cortical function.

In the TRH-stimulation test, the internist drew a blood sample to establish the patient's TSH serum baseline level. Thirty minutes after injecting TRH, he drew a second blood sample to measure the change in the TSH level. The baseline level was 0.88 IU/ml; the second TSH level was 7.83 IU/ml. This was a blunted TSH response to TRH.

The internist also measured the patient's serum cortisol on July 19, 1994 which was 16.65 ug/dl. After he injected the patient with the synthetic glucocorticoid dexamethasone, he again measured the cortisol level on July 20, 1994. The value was 0.84 ug/dl. This constituted proper adrenocortical suppression.

Imaging procedures. The patient had cervical plain film x-rays that were taken on April 7, 1993. She had a cervical MRI on May 26, 1994. In the radiology report, dated May 27, 1994, the radiologist noted that the patient had a "small central disc bulge and small posterior osteophytes at C5-C6." The MRI study was otherwise unremarkable.

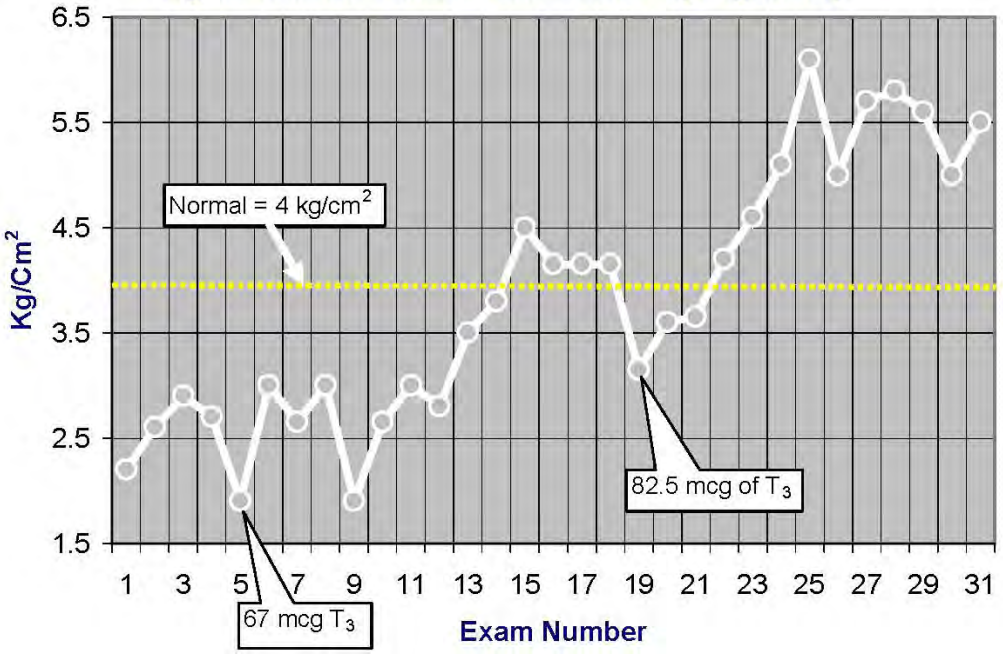
Treatment. After her automobile accident on March 2, 1993, the patient had treatment at intervals by two other chiropractors. Each performed directional non-force technique (a gentle manual spinal treatment procedure). She also received treatment several times by a physical therapist. The treatment involved exercise therapy and manual cervical traction. This treatment continued during the case study.

The patient took Armour desiccated thyroid from 1988 until the beginning of this case study. She was taking 2 grains when she first consulted me. Throughout the treatment phase of the study, she took various doses of T_3 prescribed by her psychiatrist. After the baseline period (the first five exams),

she abruptly stopped her desiccated thyroid hormone intake and immediately began taking T_3. Her starting dose was 67 mcg of T_3. On November 15, 1994, she increased her dosage to 82.5 mcg. She did so because of a brief reappearance of her symptoms and a drop in her mean algometer score.

Throughout the study, the patient held constant her intake of Ciba Estraderm patch, containing 4 mg

Figure 1. Mean Tender Point Scores by Algometry



of estradiol. On November 17, 1995 she stopped her previous 100 mg of Wellbutrin. She continued to take Desyrel on occasion. During the study, she received in my office treatment with ultrasound, soft tissue manipulation, moist heat, stretch and spray, and manual cervical traction.

RESULTS

Changes in Musculoskeletal Function. The patient's physical therapist performed three functional exams. On April 13, 1994, the therapist wrote: The patient "has two children, ages 4 and 13. She is unable to play games with them because of her symptoms. She has a housekeeper full-time and has not done significant housework, gardened, swum, or exercised since her accident. Sleeping is uncomfortable."

On June 10, 1994, the therapist wrote that the burning sensation in the patient's neck and shoulders had improved 75%. She still had dysfunction and trouble sleeping.

On September 23, 1994, the therapist wrote: The patient "has been seen weekly for chiropractic treatment and began taking T_3. She reports a dramatic improvement in her energy level. Now she has periods when she is pain-free. She states she is able to exercise now up to 1½ hours without feeling extreme fatigue as in the past." The patient's grip strength and shoulder flexor strength had improved bilaterally. She was able to sleep through the night most nights, and she had a marked increase in all ranges of cervical motion. Flexion and retraction were no longer painful. The patient did, however, still have regional pain and cervical spinal dysfunction associated with her cervical traumatic injury.

Changes in Psychiatric Status. On July 23, 1994, the patient's raw score on the Zung's Depression Inventory was 43. This converts to an SDS index of 54. The equivalent clinical global impression for the index is "presence of minimal-to-mild depression." On January 13, 1995, some six months later, her raw score on Zung's was 28. This converts to an SDS index of 35. The equivalent clinical global impression for this index is "within normal range: no psychopathology."

Changes in Fibromyalgia Status. By October 4, 1994–about two months after beginning T_3–the patient no longer met the 1990 criteria for fibromyalgia.[23]

Pain drawings. By September 21, the patient's pain decreased from widespread (according to the ACR 1990[23] criteria). She continued, however, to have re-

gional pain related to her cervical injury.

Algometer scores. On October 4, 1994, the patient's mean algometer score exceeded 4 kg/cm^2, the cut off point for normal.

Figure 1 shows the weekly mean algometer scores graphically plotted to show the change over a six-month period. The horizontal axis shows the number of each weekly measurement, and the vertical axis shows the pressure (applied with an algometer, registered in kg/cm^2) she could tolerate before experiencing discomfort at the tender point sites. When viewing the graph in Figure 1, keep in mind that the patient began taking 67 mcg of T_3 on August 8, 1994. On this date, I performed her 5th algometer exam and recorded the result on the graph. Because her symptoms briefly worsened and her mean algometer score dropped, she increased the dosage to 82.5 mcg on November 11, 1994 (the date of her 20th algometer exam).

Table 2. Symptoms reported by the patient at the beginning of the case study.

1. Sleep disturbance.
2. Prolonged morning stiffness (requiring 2-to-12 hours to loosen).
3. Occasional irritable bowel syndrome.
4. Daily headaches.
5. Depression.
6. Poor memory and concentration.
7. Cold hands and feet.
8. Chronic fatigue and sluggishness.
9. Husky voice.
10. Coarse, rough skin.
11. Puffy face and eyes.
12. Not sufficiently alert and attentive.
13. Difficulty losing weight.
14. Dry hair that fell out easily.

Visual inspection reveals an increase in the patient's mean algometer scores beginning the 13th week of the study. In the 19th week, the scores fell but not to baseline. But within three and a half weeks, they ascended again reaching and exceeding the normal value of 4 kg/cm^2. The scores remained above normal for the rest of the study and throughout follow-up.

Symptoms. At the end of the case study, the patient was completely free from all the symptoms listed in Table 2. Her pain was intermittent and limited to her posterior cervical and left upper thoracic regions.

She reported during several post-study follow-up contacts that her status had continued to improve. At follow-up on April 1, 1995, she maintained that she had remained free from all aspects of fibromyalgia for six months and thus considered herself completely recovered.

Changes in Laboratory Values. Four thyroid panels were available and are listed in Table 3. The profile performed in March 1988 shows that the patient's TSH, T_4 (RIA) and T_3 (RIA) were low normal. In July 1994, this same pattern prevailed, and the TRH-stimulation test performed on the same day shows a blunted TSH response. This indicated that she had central (probably pituitary) hypothyroidism.

The September 1994 and January 1995 profiles show that the TSH level decreased and the T_4 (RIA) decreased. In contrast to the March 1988 profile, however, the T_3 (RIA) increased above normal. This pattern indicates that her supplemental T_3 was inhibiting the pituitary glands's thyrotrophs so that they secreted a lower quantity of TSH. The lower exposure of thyroid gland cells to TSH apparently resulted in a reduced secretion of T_4.

Table 3. Four thyroid panels available on patient.

Date	Test	Value	Reference Range
03-28-88:	T_4 (RIA)	8.0	(5.5-11.5 µg/dL)
	T_3 (RIA)	133.00	(90-200 ng/dL)
	TSH	1.7	(0.4-4.3 µg/dL)
07-06-94:	T_4 (RIA)	6.4	(4.5-12.5 µg/dL)
	T_3 Uptake	25%	25% - 35%
	T_7	1.6	1.0-4.0 Units
	TSH	0.7	(0.4-6.0 µg/dL)
09-07-94:	T_4 (RIA)	1.8	(4.5-10.9 µg/dL)
	T_3 (RIA)	154.00	(60-181 ng/dL)
	TSH	0.89	(0.35-5.5 µg/dL)
01-19-95:	T_4 (RIA)	1.6	(4.5-10.9 µg/dL)
	T_3 (RIA)	199.00	(60-181 ng/dL)
	TSH	0.43	(0.35-5.5 µg/dL)

Discussion

Study Design. The format of this study was a single-subject design, also called a "functional design." Chiropractic and medical researchers currently most value another study design–one that tests hypotheses by comparing the responses of groups of subjects to therapeutic interventions. Such comparisons of groups are excellent for testing hypotheses. But investigators who use functional or single-subject designs are not so much concerned with hypothesis testing. Instead, they are concerned with quantifying a patient's response to a therapeutic intervention and measuring it repeatedly through the course of treatment. It is the *functional relationship* between the two variables (the therapy and the response) that interests them. Behavioral scientists–who typically are far better grounded in logic and the philosophy of science–make an argument that other clinical researchers could (were they to listen) profit from:

meaningful hypotheses seldom if ever derive from studies that compare differences between groups. By contrast, such hypotheses *do* tend to emerge inductively from the data derived from functional or single-subject studies.[24]

Most medical researchers measure groups of subjects' responses once before and once afer the therapy. By contrast, investigators conducting single-subject studies measure the subject's responses repeatedly throughout the course of the study. These repetitive measures provide a more detailed account of changes in the subject's responses over time. They show the *process* of therapeutic change plotted against the amount or intensity of therapeutic stimulus. This can reveal with clarity the functional relationship between the therapy and the patient's responses to it.[4,pp.29-37] We should use a functional design with single subjects when we aim for greater precision than group studies allow in determining the relationship between the independent variable (treatment) and the dependent variable (the patient's measured response).[4,p.14] I posit that the thorough failure of other fibromyalgia researchers to unearth the nature of or effective treatment for fibromyalgia is a direct outgrowth of their naive distrust of clinical observation and single-subject case studies.

Changes in Zung's Depression Inventory. The change in the patient's Zung's Depression Inventory indicates that she experienced a decrease from "minimal-to-mild" depression to "within the range of normal." This might be interpreted as reflecting an increase in serotonin secretion. The increase can be predicted to result from thyroid hormone stimulation decreasing the number of inhibitory á-adrenergic receptors and increasing the number of stimulatory â-adrenergic receptors on her CNS serotonergic cells. This would disinhibit their secretion of serotonin.[25,p.137] Also, increased numbers of â-adrenergic receptors in her CNS due to transcription regulation by T_3-thyroid hormone receptor complex may have increased the metabolism of CNS neuronal pathways that mediate a non-depressed mental state.

Interpretation of Laboratory Tests Results. In the TRH-stimulation test, the internist drew a blood sample to establish the patient's TSH serum baseline level. After injecting TRH, he drew a second sample after 30 minutes. The change from the baseline TSH level of 0.88 IU/ml to the 30-minute post-injection level of 7.83 IU/ml indicated a suppression of TSH response to TRH. There are several possible mechanisms for this blunted TSH response.

Was the patient's T_4 elevated and her TSH low because of her estrogen supplement? The patient used a transdermal estrogen patch. It is not likely that this accounted for her low TSH values. Oral estrogen supplements tend to increase the concentration of thyroid-binding globulin (TBG) in the blood. They do so by increasing sialylation of TBG, prolonging its biologic half-life.[1] This occurs because the liver clears a large percentage of the estrogen during its first passage through the liver, resulting in high liver estrogen concentrations. Even the low-dose estrogens in today's oral contraceptives increase TBG concentrations slightly. Only in occasional patients, however, does the serum total T_4 exceed normal limits.[2,p.336]Transdermal estrogen therapy allows the hormone to enter the circulation gradually rather than in the bursts characteristic of oral estrogen therapy. Because of this, estrogen does not accumulate in high concentrations in the liver. As a result, TBG levels may increase only a little.[3] It is unlikely, then, that suppression of TSH secretion by elevated thyroid hormone levels due to increased TBG levels would account for the patient's suppressed TSH response to TRH.

Was the patient's blunted TSH response due to hyperadrenocortical secretion? During the dexamethasone suppression test, the patient's serum cortisol level decreased from 16.65 ug/dl on July 19, 1994 to 0.84 ug/dl on July 20, 1994 after an injection of the synthetic corticosteroid dexamethasone. This was an adequate suppression of adrenocortical secretion of endogenous cortisol indicating that the patient did not have hypersecretion of endogenous cortisol. From this result, I concluded that the patient's blunted TSH response to TRH was not likely due to suppression of the pituitary thyrotrophs and obstruction of T_4-to-T_3 conversion by excess concentrations of cortisol. The result of this test is also inconsistent with the previous findings of failed adrenocortical suppression in some fibromyalgia patients.[18][20]

Comparative Doses of Desiccated Thyroid and T_3. When various investigators reported benefits from T_3 after patients had failed to improve with desiccated thyroid,[8][9,p.13][10,p.274][11][12][13][14] Jefferies objected that the doses of T_3 were higher than those of desiccated thyroid, and that the higher doses were responsible for the benefits rather than the form of thyroid hormone.[6] This is incompatible with many of my clinical observations. Many patients under Poo's and my care[22] took doses of T_4 and desiccated thyroid high enough to produce distinct thyrotoxicosis. When the patients stopped taking desiccated thyroid and switched to T_3, however, fibromyalgia symptoms dramatically improved or ceased completely without toxicity on doses that were proportionately lower than the thyrotoxic doses of T_4 and desiccated thyroid.

This indicates that in some way, T_3 corrects or

overrides the underlying mechanisms of fibromyalgia symptoms when T_4 or desiccated thyroid does not do so. One possible explanation for this difference is that T_4 (in desiccated thyroid and products such as Synthroid and Levothroid) is not effectively converted to T_3, the metabolically active thyroid hormone. If this were true, laboratory tests would show high cortisol output, low TSH, and high reverse T_3. Laboratory profiles I ordered have not shown this pattern in some two hundred of my patients who failed to respond to T_4 or desiccated thyroid but later, after the lab tests, responded to T_3. It is not likely, therefore, that a conversion problem is responsible for this therapeutic outcome.

Patient's Blunted TSH Response to TRH. Neeck and Reidel[19] found that 17 female fibromyalgia patients had a blunted TSH response to injected TRH. My patient also had a blunted TSH response. A blunted TSH response implies a deficiency of TSH, and secondarily, yet without certainty, a thyroid hormone insufficiency. The insufficiency can produce fibromyalgia symptoms.[15] Correcting the thyroid hormone insufficiency can relieve the fibromyalgia symptoms. If the patient's fibromyalgia symptoms were due solely to a thyroid hormone deficiency, conventional medical thought would be that T_4 or desiccated thyroid would relieve the symptoms. My patient, however, failed to respond for some seven years to two grains of desiccated thyroid (equivalent to 0.2 mg of T_4), a considerable dose.

The purpose of this case study was to determine whether my patient would respond to T_3 after failing to respond to T_4. She did, and this suggests that her symptoms were not due solely to a thyroid hormone deficiency. An alternate mechanism for her failure to respond to desiccated thyroid or T_4 is mutated thyroid hormone receptors.[21] It is possible that such mutations require that she take 86 mcg of T_3 to recover from fibromyalgia. T_3 probably was required at the cellular level to relieve her symptoms.

Possible Placebo Response of Patient. After numerous clinicians reported that patients improved on T_3 after failing to benefit from desiccated thyroid or T_4, Jefferies in 1961 argued that T_3 was probably a placebo and referred to the "suggestibility of many patients."[6,p.533] He wrote: "The practicing physician is, of course, often in a poor position from which to exercise critical judgement as to the relative efficacy of drugs in his patient. The patient consults a physician because he wishes to feel better, and the physician treats the patient with a sincere desire to oblige. Hence, the two together unconsciously conspire to produce a result pleasing to both."[6,p.534]

In the way of an answer, one must concede that double-blind studies are nonpareil in clinical science. When data from blinded studies are not available, however, it is clearly unreasonable to ignore other forms of evidence, although they are less rigorously derived than data from blinded studies. The issue brings to mind Carlton Fredericks' response to opponents of orthomolecular therapy.[7,p.97] Calling clinical observations "unblinded" is justified. But calling them "uncontrolled" is logically incorrect. In other published studies mentioned above and in this one, patients improved with T_3 *after they had failed to improve over a period of months or even years with desiccated thyroid or* T_4. Because of this, each patient was her own control. Patients' lack of response to desiccated thyroid and T_4 over a prolonged period provided a baseline against which to plot their degree of response to T_3.

The patient who is the subject of this report took substantial doses of desiccated thyroid for seven years without benefit, but she responded dramatically to T_3. Critics such as Jefferies warn that the response may be a placebo reaction. This is to say that the patient would have responded just as well if tablets contained an inert substance rather than T_3. The obvious reply is: Where was the placebo effect when she was taking desiccated thyroid or T_4? Why does T_3 cause a placebo response when other forms of thyroid hormone fail to do so? The likelihood that T_3 acted in this case report and other reports as a placebo is infinitesimally small.

Studies have shown no other therapies for fibromyalgia to be significantly effective,[16] while millions of fibromyalgia patients suffer non-remitting symptoms.[17] Because of this, clinicians and researchers should not ignore the possible benefits of T_3 therapy for their fibromyalgia patients.

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