

Reduced violent behavior following biochemical therapy

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Abstract

Reduced violent behavior following biochemical therapy. We conducted an outcome study to measure the effectiveness of biochemical therapy for 207 consecutive patients presenting with a diagnosed behavior disorder. The treatment protocols were based on clinical evaluation and our past experience in the treatment of 8000 patients with behavior disorders at the Pfeiffer Treatment Center (PTC) over a 10-year period. Each test subject was screened for chemical imbalances previously found in high incidence in this population, including metal-metabolism disorders, methylation abnormalities, disordered pyrrole chemistry, heavy-metal overload, glucose dyscontrol, and malabsorption. The clinical procedure included a medical history, assay of 90 biochemical factors, and a physical examination. Standardized treatment protocols were applied for each imbalance that was identified. The frequencies of physical assaults and destructive episodes were determined using a standardized behavior scale before and after treatment, with follow-up ranging from 4 to 8 months.

Results: Seventy-six percent of the test subjects achieved compliance during the treatment period. The remaining 24% were reported to have discontinued the therapy. A reduced frequency of assaults was reported by 92% of the compliant assaultive patients, with 58% achieving elimination of the behavior. A total of 88% of compliant destructive patients exhibited a reduced frequency of destructive incidents and 53% achieved elimination of the behavior. Statistical significance was found for reduced frequency of assaults ($t=7.74$, $p<0.001$) and destructive incidents ($t=8.77$, $p<0.001$). The results of this outcome study strongly suggest that individualized biochemical therapy may be efficacious in achieving behavioral improvements in this patient population.

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1. Introduction

Research studying the relationship between human body chemistry and human behavior has accelerated in recent years. Preliminary evidence suggests that chemical imbalances in the body may be as important an influence on behavior as are poverty, abuse, and other environmental factors that traditionally have been accepted as the root causes of aberrant behavior [1–4].

Many biochemical abnormalities observed in behavior-disordered (BD) populations have been documented to have an impact on brain chemistry. For example, copper

is an important factor in the conversion of dopamine to norepinephrine [5,6], zinc is needed for the efficient synthesis of GABA [7], Vitamin B-6 is required for the synthesis of serotonin, dopamine, GABA, and norepinephrine [8], and folates are required for the efficient production of catecholamines [9,10]. Neurotransmitters are synthesized in the brain from amino acids, vitamins, minerals, and other natural biochemicals. Genetic disorders that result in excessive or depressed levels of these nutrients may result in chemical imbalances in the brain.

Biochemical therapy is aimed at overcoming genetic or acquired abnormalities in neurotransmitter precursors and other important body chemicals. Over a 10-year period, the Pfeiffer Treatment Center (PTC) of Warrenville, IL, has amassed a large database of biochemical information for

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more than 8000 behavior-disordered (BD) patients, including measurements of 90 separate chemical factors in blood, urine, and hair tissue. An examination of these data reveals a high incidence of chemical abnormalities for the BD group compared with the general population, especially metal-metabolism disorders, methylation imbalances, abnormal pyrrole chemistry, elevated toxic metals, glucose dyscontrol, and malabsorption.

PTC has developed individualized biochemical therapies aimed at correcting these imbalances based on clinical studies of more than 8000 BD patients. This outcome study was designed to measure the efficacy of the PTC treatment protocol with respect to improving behavior in a census sample of patients.

2. Study population

The test subjects were selected from 258 consecutive outpatients who presented over a 4-month period with a prior diagnosis of attention-deficit disorder, conduct disorder, oppositional-defiant disorder, or other behavior disorder. Of the 258 patients, 28 had comorbidity of autism, bipolar depression, Tourette's Syndrome, or schizophrenia and were excluded from the study [11]. An additional 23 individuals whose initial behavior status had not been recorded prior to treatment were also excluded. The remaining 207 patients (149 males and 58 females) comprised the test population, which included residents of 35 states. The age range was 3 to 55 years, with a median of 11.5 years.

A total of 95.2% of the test subjects had received behavior modification, conflict resolution, counseling, and/or psychotherapy prior to seeking biochemical treatment, and 85.0% had a history of medication interventions (such as Ritalin, antidepressants, or tranquilizers). In all cases, serious behavior problems were still evident.

3. Study design

Diagnoses of chemical imbalances were based on 90 chemical analyses of blood, urine, and scalp hair conducted by independent accredited laboratories. The blood

assays and a routine urinalysis were performed by Smith Kline Beecham Laboratory (now Quest Diagnostics, Inc.). Blood assays included serum copper and ceruloplasmin, plasma zinc, whole blood histamine, lead, and manganese, along with panels used to assess status of iron/hemoglobin, electrolytes, and the functioning of the liver, kidneys, and thyroid. Urine kryptopyrroles were assayed by Norsom Medical Reference Laboratories. Hair trace metals were obtained by Doctor's Data, Inc.

The chemical analyses revealed chemical abnormalities, that clearly indicated specific chemical imbalances in a total of 179 test subjects. In the remaining 28 patients in which chemical analyses were less decisive, medical history and physical examination for traits and symptoms associated with specific biochemical imbalances were used to identify the imbalances present and assist in diagnosis. Each of the 207 patients was diagnosed with one or more chemical imbalances. The incidence of specific imbalances, their mean values, and reference levels are listed in Table 1.

Interviews by a primary care nurse with family members of the patients were conducted to document destructive and/or assaultive behaviors observed in the study population for periods ranging from 3 to 6 months before the initiation of the individualized biochemical therapy and 4 to 8 months after the onset of biochemical treatment. In each interview, the frequency (incidents/month) of physical assaults, destructive episodes, and/or verbal outbursts was recorded using the Walsh–Isaacson Behavior Scale (WIBS; [12]), a standardized behavior scale based on self-reports from patients and/or members of their families. The patient's compliance with the prescribed biochemical therapy also was recorded in the follow-up interview.

4. Chemical imbalances and biochemical treatments in the study population

Biochemical therapy may be defined as “correction of innate or acquired chemical imbalances using amino acids, vitamins, minerals, and other biochemicals naturally present in the body.” In this study, diagnoses of chemical imbalances were based on chemical analyses of dozens of

Table 1
Incidence of chemical imbalances in test population ($n=207$)

Imbalance	Number (%)	Mean value	Standard deviation	95% Confidence interval	Reference level
Elevated Cu/Zn ratio	156 (75.4)	1.86	0.49	0.88–2.84	0.8–1.2
Depressed blood histamine	61 (29.5)	26.7 ng/ml	9.5	7.7–45.7	40–70 ng/ml
Elevated blood histamine	78 (37.7)	99.7 ng/ml	22.6	54.5–144.9	40–70 ng/ml
Elevated urine kryptopyrroles	68 (32.9)	48.2 mcg/dl	38.5	0–125.2	0–20 mcg/dl
Heavy-metal overload	37 (17.9)	N.A.	N.A.	N.A.	N.A.
Glucose dyscontrol	63 (30.4)	N.A.	N.A.	N.A.	N.A.
Malabsorption	32 (15.5)	N.A.	N.A.	N.A.	N.A.

key biochemicals in blood, urine, and tissues, along with a comprehensive medical history and review of symptoms. A regimen of specific amino acids, vitamins, and minerals was developed for each subject based on his or her diagnosed imbalances [13–15]. Dosages were based on the severity of the imbalances, body weight, and the metabolic weight factor for each individual. In some cases, specific dietary restrictions were recommended. Each patient was given the option of taking the prescribed nutrients in the form of capsules, tablets, powders, or liquids that were divided into morning and evening doses. In most cases, the treatment plans involved 5 to 10 capsules, taken twice daily.

Test subjects receiving medication and/or counseling from other professionals were asked to continue these interventions (together with PTC nutrient therapy) for a minimum of two additional months after beginning biochemical therapy prescribed at PTC. In all cases, the management of medication and counseling was the responsibility of the patient's local health care providers.

The most common chemical imbalances observed in the test population and the biochemical therapy prescribed for each are described below.

4.1. Elevated copper/zinc ratio

A total of 75.4% of test subjects exhibited elevated serum copper and depressed plasma zinc [16,17], a chemical imbalance associated with an inadequate regulation of these metals by metallothionein. Behavior disorders associated with this imbalance include episodic rage disorder, attention deficit disorder, and hyperactivity [12,18–24]. Treatment involved metallothionein promotion therapy using zinc, cysteine, and manganese, together with augmenting nutrients such as pyridoxine, ascorbic acid, and Vitamin E.

4.2. Overmethylation

Of the subjects, 29.5% exhibited depressed blood histamine, which is a marker for overmethylation, elevated methyl/folate ratio, and elevated catecholamine levels. This imbalance is associated with anxiety, paranoia, and depression [13,14,24–27] and was treated using folic acid, cobalamine, niacinamide, and augmenting nutrients.

4.3. Undermethylation

A total of 37.7% of the patients exhibited elevated blood histamine, a marker for undermethylation, depressed

methyl/folate ratio, and low catecholamine level. This imbalance is associated with depression, seasonal allergies, obsessive-compulsive tendencies, high libido, and low levels of serotonin [13,14,24–27]. Treatment involved supplements of methionine, calcium, magnesium, and Vitamin D.

4.4. Pyrrole disorder

Pyroluria was exhibited by 32.9% of the patients. Elevated kryptopyrroles have been associated with an inborn error of pyrrole chemistry, but also can result from porphyria or exposure to heavy metals, toxic chemicals, and other conditions enhancing oxidative stress. This imbalance results in a striking deficiency of pyridoxine and zinc and is associated with poor stress control and explosive anger [13,14,16,28,29]. Treatment for this pyrrole disorder involved supplements of pyridoxine, pyridoxal-5-phosphate, zinc, and Vitamins C and E.

4.5. Heavy-metal overload

Elevated levels of lead, cadmium, or other toxic metals in the blood or scalp hair were exhibited by 17.9% of the subjects. Toxic metal overloads have been associated with behavior disorders and academic underachievement [30–35]. Treatment involved supplementation with calcium, zinc, manganese, pyridoxine, selenium, and the amino acid constituents of metallothionein, along with antioxidants to promote the excretion of the toxic metals.

4.6. Glucose dyscontrol

Among the test population, 30.4% exhibited a tendency for unusually low blood glucose levels. This imbalance appears to represent an aggravating factor, rather than a cause, of behavior disorders [36–42]. Treatment involved supplements of chromium and manganese, along with dietary modifications.

4.7. Malabsorption

A total of 15.5% exhibited a malabsorption syndrome involving generalized low levels of amino acids, vitamins, and minerals. This chemical imbalance has been associated with irritability, impulsivity, and underachievement [43–51]. Treatment varied, depending of the type of malabsorption (e.g., low stomach acid, gastric insufficiency, yeast overgrowth, or a brush-border disorder). The treatments included

Table 2
Posttreatment behavior outcomes: all test subjects

Behavior	Overall % improved	Behavior eliminated	Reduced frequency	Unchanged	Worsened	Noncompliant
Assaultive (<i>n</i> =137)	70.8	61	36	8	0	32
Destructive (<i>n</i> =146)	67.1	59	39	10	4	34

Table 3
Outcomes for compliant patients

Patient group	<i>N</i>	Average pretreatment incidents/month	Average posttreatment incidents/month	Average decline in incidents/month	Standard error	<i>t</i> ^a	<i>p</i> -Value
Assaultive patients	105	40.14	7.74	−32.39	4.08	−7.94	<0.001
Destructive patients	112	42.51	9.09	−33.43	3.81	−8.77	<0.001

^a Paired *t*-tests.

the use of nutrients for regulating stomach acid levels, digestive enzymes, biotin, and probiotics.

5. Compliance results

According to the reports of family members, a total of 76% of the patients remained compliant to the biochemical treatment regimen at the time of the follow-up interview. The remaining 24% of patients were reported to have discontinued treatment. About 50% of the noncompliant group was reported to have never successfully initiated treatment. The remainder were reported to have achieved compliance for more than 1 month but failed to sustain compliance. Overall compliance rates of 81%, 75%, and 71% were achieved for children, teenagers, and adults, respectively. The most common reasons for stopping treatment were reported to be refusal by the behavior-disordered test subject to swallow the supplements, chronic nausea, or emesis. Fewer than 50% of the noncompliant group supplied behavioral data during the follow-up interview.

6. Treatment outcomes

Among compliant test subjects, 105 had a history of physical assaults, 112 had a history of destroying property, and 90 had exhibited both behaviors. After treatment, 92% of the assaultive patients who achieved treatment compliance exhibited a reduced frequency of assaults, with 58% achieving elimination of the behavior. A total of 88% of compliant test subjects with destructive behavior exhibited a reduced frequency of destructive episodes, with 53% achieving elimination of the behavior. Table 2 presents the behavior outcomes for all test subjects, including non-compliant patients. Table 3 presents the outcome results for the subjects who complied with the prescribed biochemical therapy. Paired *t*-tests were used to compare the frequency of assaultive and destructive behavior before and after treatment. The compliant subjects tended to have significantly lower frequencies of both assaultive and destructive behavior ($p < 0.001$) after treatment. No significant difference in treatment outcomes was observed between males and females. Compliance and treatment effectiveness, however, declined with age. For example, reduced frequency of assaultiveness was achieved by 92% of compliant patients under age 14, compared with 79% for older compliant patients.

7. Discussion

The results of this study indicate that individualized biochemical treatment was effective in improving behaviors of compliant subjects. Statistical significance was found for reduced frequency of assaults ($t = 7.94$; $p < 0.001$) and destructive incidents ($t = 8.77$, $p < 0.001$). Complete elimination of these behaviors was reported in 58% of compliant assaultive patients and 53% of compliant destructive patients. Treatment effectiveness was highest for children under the age of 14. This finding may be due to the reduced incidence of serious drug/alcohol abuse and a less-ingrained negative self-image in this younger population.

Our results suggest that compliance may be the greatest barrier to successful treatment of behavior disorders using biochemical therapy. To enhance compliance, the PTC has recently developed a compounding capability that reduces the prescribed number of capsules by more than 50%.

For decades, researchers have debated the relative influence of nature and nurture in rage disorders, crime, violence, etc. The high incidence of biochemical imbalances in the behavior-disordered population and the major behavioral improvements following the correction of these imbalances suggest that individual biochemistry has a powerful influence on human behavior. Effective prevention of delinquency and crime may require early interventions aimed at normalizing the body chemistries of at-risk children.

To confirm these results and evaluate the potential of biochemical therapy as a crime-prevention measure will require (1) double-blind, placebo controlled studies to decisively measure treatment efficacy and (2) longitudinal studies to determine if the behavioral improvements seen in this study after 4–8 months of therapy are enduring. Future studies will also be required to assess the role played by previously prescribed medications taken concurrently with biochemical therapy by some patients.

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References

- [1] Reiss A, Miczek K, Roth J, editors. Understanding and preventing violence. Biobehavioral influences, vol. 2. National Academy Press; 1994.
- [2] Wilson JQ, Herrnstein R. Crime and human nature. New York: Simon and Schuster; 1985.
- [3] Gesch C, Hammond S, Hampson S, Eves A, Crowder M. Influence of supplementary vitamins, minerals, and essential fatty acids on the antisocial behaviour of young adult prisoners: randomized, placebo-controlled trial. *Br J Psychol* 2002;181:22–8.
- [4] Cloninger C, Gottesman I. Genetic and environmental factors in antisocial behavior disorders. In: Mednick S, Moffitt T, Stack S, editors. The causes of crime. New biological approaches. New York: Cambridge University Press; 1987. p. 92–109.
- [5] Ames B, Elson-Schwab I, Silver E. High-dose vitamin therapy stimulates variant enzymes with decreased coenzyme binding affinity (increased Km): relevance to genetic disease and polymorphisms. *Am J Clin Nutr* 2002;75(4):616–58.
- [6] Klinman JP, Brenner M. Role of copper and catalytic mechanism in the copper monooxygenase, dopamine beta-hydrogenase (DBH). In: King TE, Mason HS, Morrison M, editors. Oxidases and related redox systems. New York: Alan R. Liss; 1988. p. 227–48.
- [7] Prasad AS. Biochemistry of zinc. *Biochemistry of the elements*, vol. 11. Plenum Press; 1993. p. 153–64.
- [8] Dakshinamurti K, et al. Neurobiology of pyridoxine. *Vitamin B-6. Annals of the New York Acad of Sci* 2000;585:128–44.
- [9] Coppen A, et al. Depression and tetrahydrobiopterin: the folate connection. *J Affect Disord* 1989;16(2–3):103–7.
- [10] Alpert JE, Fava M. Nutrition and depression: the role of folate. *Nutr Rev* 1997;55(5):145–9.
- [11] Diagnostic and statistical manual of mental disorders: DSM-IV. 4th ed. Washington (DC): Amer. Psych. Assn; 1998.
- [12] Walsh WJ, et al. Elevated blood copper/zinc ratios in assaultive young males. *Physiol Behav* 1997;62(2):327–9.
- [13] Pfeiffer C. Mental & elemental nutrients. New Canaan (CN): Keats; 1975. p. 396–402.
- [14] Jaffe R, Kruesi O. The biochemical immunology window; a molecular view of psychiatric case management. *J Appl Nutr* 1992;44(2):1–15.
- [15] Pfeiffer C. Nutrition and mental illness. Rochester (VT): Healing Arts Press; 1987. p. 93–103.
- [16] Pfeiffer C, Audette L. Pyroluria, zinc and B-6 deficiencies. *Int Clin Nutr Rev* 1988;8(30):107–10.
- [17] Prasad AS. Biochemistry of zinc. *Biochemistry of the elements*, vol. 11. Plenum Press; 1993. p. 77–92.
- [18] Linder MC. Biochemistry of copper. *Biochemistry of the elements*, vol. 10. Plenum Press; 1991. p. 182–94.
- [19] Cunnane SC. Zinc: clinical and biochemical significance. Boca Raton (FL): CRC Press; 1988.
- [20] Ebaldi M, Murrin LC, Pfeiffer RF. Hippocampal zinc thionein and pyridoxal phosphate modulated synaptic function. *Vitamin B-6. Annals of the New York Acad of Sci* 1980. p. 189–201.
- [21] Kagi JHR, Schaffer A. Biochemistry of metallothionein. *Biochemistry* 1988;27:8509–15.
- [22] Pfeiffer C, Iliev V. A study of zinc deficiency and copper excess in the schizophrenias. *Int Rev Neurobiol* 1972;72:141.
- [23] Walwork J, Sandstead H. Effect of zinc deficiency on brain catecholamine concentration. *Fed Proc* 1981;40:939.
- [24] Chiang P, Gordon R, et al. S-adenosylmethionine and methylation. *FASEB J* 1996;10:471–80.
- [25] Walsh WJ, Rehman F. Methylation syndromes in mental illness. Abstract, Neuroscience Society. New Orleans; Nov. 1997.
- [26] Abou-Saleh MT, Coppen A. Serum and red blood cell folate in depression. *Acta Psychiatr Scand* 1989;80(1):78–82.
- [27] Pfeiffer C, Braverman E. Folic acid and vitamin B-12 therapy for the low histamine, high copper biotype of schizophrenia. In: Botez M, Reynolds E, editors. Folic acid in neurology, psychiatry, and internal medicine. New York: Raven Press; 1979. p. 483–7.
- [28] Irvine D, Bayne W, Miyashita H. Identification of kryptopyrrole in human urine and its relation to psychosis. *Nature* 1969;224(81):811–3.
- [29] Pfeiffer C, LaMola S. Zinc and manganese in the schizophrenias. *J Orthomol Psychiatry* 1983;12:215–34.
- [30] Goyer R. Toxic effects of metals. In: Klassen C, Amdur M, Doull J, editors. Casarett and Doull's toxicology. 3rd ed. New York: Macmillan Publishing; 1986. p. 582–635.
- [31] Neurotoxicity: identifying and controlling poisons of the central nervous system. U.S. Congress, Office of Technology Assessment, U.S. Govt. Printing Office, OTA-BA-436; 1990.
- [32] Needleman H. The long-term effects of exposure to low doses of lead in childhood. *New Engl J Med* 1990;322:83–8.
- [33] Nevin R. How lead exposure relates to temporal changes in IQ, violent crime, and unwed pregnancies. *Environ Res* 2000;83(1):1–22.
- [34] Needleman H. The persistent threat of lead: a singular opportunity. *Am J Public Health* 1989;79:643–5.
- [35] Thomson G, et al. Blood lead and children's behavior—results from the Edinburgh lead study. *J Child Psych* 1989;30(4):515–28.
- [36] Virkkunen M. Reactive hypoglycemia tendency among habitually violent offenders. *Nutr Rev* 1986;44:94–103.
- [37] Breakey J. The role of diet and behavior in childhood. *J Paediatr Child Health* 1997;33:190–4.
- [38] Venables P, Raine A. Biological theory. In: McGurk B, Thornton D, Williams M, editors. Applying psychology to imprisonment: theory and practice. London: Her Majesty's Stationery Office; 1987. p. 3–28.
- [39] Gray G. Diet, crime and delinquency: a critique. *Nutr Rev* 1986;44:89–94 [Suppl].
- [40] Bennett P, Brostoff J. The health of criminals related to behavior, food, allergy and nutrition. *J Nutr Environ Med* 1997;7:359–66.
- [41] Kruesi M, et al. Effects of sugar and aspartame on aggression and activity in children. *Am J Psych* 1987;144:1487–90.
- [42] Milich R, Pelham W. Effects of sugar ingestion on the classroom and playgroup behavior of attention deficit disordered boys. *J Consult Clin Psychol* 1986;54:714–8.
- [43] Kanarek R. Nutrition and violent behavior. In: Reiss A, Miczek K, Roth J, editors. Understanding and preventing violence. Biobehavioral influences, vol. 2. Washington (DC): National Academy Press; 1994. p. 515–39.
- [44] Black M. Zinc deficiency and child development. *Am J Clin Nutr* 1998;68:464S–9S [Suppl.].
- [45] Schoenthaler S, Bier I. The effect of vitamin–mineral supplementation on juvenile delinquency among American schoolchildren. *J Altern Complement Med* 2000;6(1):7–17.
- [46] Stevens L, et al. Omega-3 fatty acids in boys with behavior, learning, and health problems. *Physiol Behav* 1996;59(4–5):915–20.
- [47] Benton D, et al. Vitamin supplementation for one year improves mood. *Neuropsychobiology* 1995;32(2):98–105.
- [48] Anderson G, Hrboticky N. Approaches to assessing the dietary component of the diet behavior connection. *Nutr Rev* 1986;44:42–51 [Suppl.].
- [49] Virkkunen M. Serum cholesterol levels in homicidal offenders. *Neuropsychobiology* 1983;10:65–9.
- [50] Virkkunen M, Penttinen H. Serum cholesterol in aggressive conduct disorder: a preliminary study. *Biol Psychiatry* 1984;19:435–9.
- [51] Rumsey J, Rappaport J. Assessing behavioral and cognitive effects of diet in pediatric populations. In: Wurtman R, Wurtman J, editors. Nutrition and the brain, vol. 6. Raven Press; 1983. p. 101–62.