Treatment of attention deficit hyperactivity disorder with monoamine amino acid precursors and organic cation transporter assay interpretation

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Background: This paper documents a retrospective pilot study of a novel approach for treating attention deficit hyperactivity disorder (ADHD) with amino acid precursors of serotonin and dopamine in conjunction with urinary monoamine assays subjected to organic cation transporter (OCT) functional status determination. The goal of this research was to document the findings and related considerations of a retrospective chart review study designed to identify issues and areas of concern that will define parameters for a prospective controlled study.

Methods: This study included 85 patients aged 4–18 years, who were treated with a novel amino acid precursor protocol. Their clinical course during the first 8–10 weeks of treatment was analyzed retrospectively. The study team consisted of PhD clinical psychologists, individuals compiling clinical data from records, and a statistician. The patients had been treated with a predefined protocol for administering amino acid precursors of serotonin and dopamine, along with OCT assay interpretation as indicated.

Results: In total, 67% of participants achieved significant improvement with only amino acid precursors of serotonin and dopamine. In patients who achieved no significant relief of symptoms with only amino acid precursors, OCT assay interpretation was utilized. In this subgroup, 30.3% achieved significant relief following two or three urine assays and dosage changes as recommended by the assay results. The total percentage of patients showing significant improvement was 77%.

Conclusion: The efficacy of this novel protocol appears superior to some ADHD prescription drugs, and therefore indicates a need for further studies to verify this observation. The findings of this study justify initiation of further prospective controlled studies in order to evaluate more formally the observed benefits of this novel approach in the treatment of ADHD.

Keywords: attention deficit hyperactivity disorder, 5-hydroxytryptophan, tyrosine, L-dopa, organic cation transporter assay interpretation

Introduction

A large meta-analysis (n = 171,756) published in 2007 involving the review of 303 literature articles placed the worldwide pooled incidence of attention deficit hyperactivity disorder (ADHD) at 5.29%. However, this review suggested that geographic location plays only a limited role in the reasons for the large variability of ADHD/hyperactivity disorder prevalence estimates worldwide.1 This paper documents the results of a retrospective chart review relating to a novel serotonin and dopamine amino acid precursor treatment approach to ADHD which integrates organic cation transporter (OCT) assay interpretation.2–7 Our hypothesis was that this novel approach of admin-
istering amino acid precursors of serotonin and dopamine with OCT assay interpretation when indicated may have efficacy that is superior to some of the prescription drugs currently used in the treatment of ADHD.

The diagnosis of ADHD is dependent upon meeting the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria in the areas of inattention, hyperactivity, and impulsivity which negatively affect performance in school and work, as well as in relationships with others. It is a generally accepted premise that a primary factor in development of ADHD is the status of the monoamine system to include serotonin, dopamine, norepinephrine, and epinephrine. In response, the pharmaceutical industry has demonstrated, to the satisfaction of the US Food and Drug Administration (FDA), that certain drugs that impact the monoamine systems meet FDA efficacy standards. Examples of these drugs include neutral sulfate salts of dextroamphetamine and amphetamine, methylphenidate, dexamphetamine, atomoxetine, and lisdexamfetamine dimesylate.

Side effects and adverse reactions associated with ADHD prescription medications are significant, serious, and potentially life-threatening. The following is a limited list of these events associated with the ADHD group of drugs as a whole, which include, but are not limited to:

- Black box warning of increased risk of suicidal ideation
- Severe liver injury
- Sudden death in cases with pre-existing structural cardiac abnormalities or other serious heart problems
- Risk of stroke and myocardial infarction
- Exacerbation of symptoms of behavior disturbance and thought disorder in patients with a pre-existing psychotic disorder
- Induction of mixed manic episodes
- Treatment by amelioration of usual doses can cause emergent psychotic or manic symptoms, eg, hallucinations, delusional thinking, mania in children and adolescents without prior history of psychotic illness or mania
- Amphetamines may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or vehicles
- Higher incidence of infection, photosensitivity reaction, constipation, tooth disorders, emotional liability, decreased libido, somnolence, speech disorder, palpitation, twitching, dyspnea, sweating, dysmenorrhea, and impotence
- Integument disorders including, but not limited to, urticaria, rash, and hypersensitivity reactions, including angioedema and anaphylaxis; serious skin rashes, including Stevens Johnson syndrome and toxic epidermal necrolysis
- Lowering of seizure threshold
- Increased aggression and hostility
- Contraindicated in patients with marked anxiety, tension, and agitation, because the drugs may aggravate these symptoms
- Risk of drug dependence
- Development of leukopenia and/or anemia.

These drugs do not increase the total number of neurotransmitter molecules in the central nervous system. Their primary mechanism of action is thought to be reuptake inhibition which sets up conditions that move neurotransmitters from one place to another. However, previous writings suggest that the process of reuptake inhibition may deplete neurotransmitters throughout the body.

The administration of amphetamines stimulates another potential area of concern relating to neurotoxicity.

There has been no previous peer-reviewed literature published addressing the efficacy of amino acid precursors of serotonin and dopamine simultaneously administered in the treatment of ADHD. The immediate amino acid precursors of serotonin and dopamine are 5-hydroxytryptophan (5-HTP) and L-3,4-dihydroxyphenylalanine (L-dopa), respectively. They are freely transported across the blood-brain barrier and are then synthesized into serotonin and dopamine without biochemical feedback inhibition. L-tryptophan and L-tyrosine are immediate precursors of 5-HTP and L-dopa, respectively.

This study reviews the effects of a novel method of treatment involving the use of monoamine amino acid precursors that do what drugs are unable to do. This novel approach has the ability to increase the total number of neurotransmitter molecules in the central nervous system, leading to efficacy observations that appear greater than those of prescription drugs without the potential for neurotransmitter depletion, neurotoxicity issues, and severe potentially life-threatening drug side effects associated with prescription drugs.
Material and methods

The study included 85 children aged 4–18 years who had been diagnosed as having ADHD under the DSM-IV criteria by a licensed PhD clinical psychologist. The patients were then treated by a clinical psychologist. The medical charts and treatment results were reviewed retrospectively. Patients were evaluated twice during treatment with the ADHD Rating Scale (ADHD-RS). Other variables assessed via a questionnaire included: taking/not taking ADHD medicine; previous history of taking stimulant drugs; gender; age; perceived amount of improvement as noted by a conversation between the parent (or patient alone if an adult over 18 years) and the psychologist; and number of comorbid factors (eg, depression, cerebral palsy, chronic indigestion, hair pulling, seizures, autism, obsessive compulsive behavior).

The time period covered in the review was 18 months. The individual patients were treated for a period of 8–10 weeks with staggered starting of treatment. If no relief of symptoms was observed in the first 3–4 weeks of treatment, while administering the amino acid dosing protocol values of Tables 1 and 2, a urine sample was collected. Urinary serotonin and dopamine assay results were then subjected to OCT assay interpretation in order to define the needed change in amino acid dosing values. The goal of treatment was resolution of symptoms or achieving urinary serotonin and dopamine amino acid precursors in significant amounts. This three-phase model is the basis for OCT assay interpretation. Reported values were then subjected to OCT assay interpretation. Reporting of urinary monoamine levels as µg of monoamine per g of creatinine compensated for the specific gravity of the urine.

OCT assay interpretation

Peer-reviewed publications from 2009 and 2010 outlined a novel urinary “three-phase model” of urinary serotonin and dopamine response to simultaneous administration of serotonin and dopamine amino acid precursors in significant amounts. This three-phase model is the basis for OCT assay interpretation. A 2010 paper proposed a novel renal organic cation transporter model which potentially describes the etiology of the “three-phase response” of serotonin and dopamine during simultaneous administration of their amino acid precursors in varied daily dosing values.

Table 1 Pediatric protocol for patients aged 16 years of age and younger

| mg 5-HTP/mg L-tyrosine | Morning | 4 pm | 7 pm |
|-------------------------|---------|------|------|
| Level 1                 | 75/750  | 75/750 | –    |
| Level 2                 | 112.5/1125 | 112.5/1125 | – |
| Level 3                 | 112.5/1125 | 112.5/1125 | 112.5/1125 |

In addition to the basic amino acid dosing values, other daily cofactors generally required for synthesis of the monoamine and maximum benefit from the protocol were administered. These included vitamin B6 1000 mg, calcium citrate 220 mg, vitamin B6 75 mg, folate 800 µg, L-lysine 500 mg, L-cysteine 4500 mg, or for adults 12250 mg for children, and selenium 60 µg for adults and 200 µg for children. In general, L-dopa in the form of standardized mucuna pruriens 400 mg was added when the recommendation of the first urinary OCT assay interpretation demonstrated its need; this was a frequent occurrence.

Patients were seen weekly. The initiation of a treatment prescription with amino acid precursors of serotonin and dopamine was at the level 1 dosing values of Tables 1 and 2. If the symptoms persisted after one week of treatment, the dosing was advanced week to week to level 2, then level 3. Patients did not achieve relief of symptoms on level 3 dosing values had a urine sample collected after one week on that dosage; serotonin and dopamine levels were determined and reported in µg of monoamine per g of creatinine. Reported values were then subjected to OCT assay interpretation.
functional status interpretation. The flawed science behind
the urinary neurotransmitter testing model was discussed in
a 2010 paper.6

The serotonin and dopamine filtered at the glomerulus
are metabolized by the kidneys, and significant amounts
do not reach the final urine. Serotonin and dopamine found
in the urine, in patients not suffering from a monoamine-
secreting tumor, primarily represent monoamines that are
newly synthesized in the proximal convoluted renal tubule
cells of the kidneys and have never been in the central nervous
system or peripheral system. The fate of the newly synthe-
sized serotonin and dopamine inside the proximal convoluted
renal tubule cells is primarily dependent upon the interaction
of the basolateral monoamine transporters and the apical
monoamine transporters of these proximal tubule cells. The
basolateral monoamine transporter transports both serotonin
and dopamine to the renal interstitium where they ultimately
end up in the peripheral system via the renal vein. The apical
monoamine transporters transport the newly synthesized serotonin and dopamine not transported by the basolateral
monoamine transporter to the proximal nephrons and, from
there, ultimately end up in the final urine as waste.3,24

Serotonin and dopamine are found in two states. The
endogenous state is found when no amino acid precursors
are administered. The competitive inhibition state is found
when significant amounts of both serotonin and dopamine
precursors are simultaneously administered. Proper OCT
assay interpretation requires that the serotonin and dopamine
systems be simultaneously placed in the competitive inhibi-
tion state prior to OCT assay interpretation.5–7,24

The basis for OCT assay interpretation requires that two
or more urinary serotonin and dopamine assays be performed
while taking serotonin and dopamine amino acid precursors
at significantly varied dosing values. The results are then
compared to determine the change in urinary serotonin and
dopamine levels in response to the change in amino acid
precursor dosing values.3,7,10

A urinary serotonin or dopamine value less than 80 µg
or 475 µg of monoamine per g of creatinine, respectively,
is defined as a phase 2 response. A urinary serotonin or
dopamine value greater than 80 µg or 475 µg of monoamine
per g of creatinine, respectively, is interpreted as being in
phase 1 or phase 3. Differentiation of phase 1 from phase 3
is as follows. If a direct relationship is found between amino
acid dosing and urinary assay response, it is referred to as a
phase 3 response. An inverse relationship is referred to as a
phase 1 response. The phase 3 therapeutic range for urinary
serotonin is defined as 80–240 µg of serotonin per g of
creatine. The phase 3 therapeutic range for urinary dop-
amine is defined as 475–1100 µg of dopamine per g of creatine.5–7

Processing, management, and assay of the urine samples
collected for this study were as follows. Urine samples were
collected about six hours prior to bedtime, with 4 pm being
the most frequent collection time point. The samples were
stabilized in 6 N HCl to preserve the dopamine and serotonin.
The urine samples were collected after a minimum of one
week during which time the patient was taking a specific
daily dosing of amino acid precursors of serotonin and dop-
amine where no doses were missed. Samples were shipped
to DBS Laboratories (Duluth, MN) which is operated under
the direction of one of the authors (TU, hospital-based
pathologist, dual board certification in laboratory medicine and
forensic pathology). Urinary dopamine and serotonin were
assayed utilizing commercially available radioimmunoassay
kits (3 CAT KIA IB88501 and IB89527, both from Immuno
Biological Laboratories Inc, Minneapolis, MN). The DBS
laboratory is accredited as a high complexity laboratory by
CLIA to perform these assays. OCT assay interpretation
was performed by one of the authors (MH, NeuroResearch
Clinics Inc).

Results

The retrospective chart review of this pilot study covered the
treatment of 85 children aged 4–18 years diagnosed under
DSM-IV criteria to have ADHD. The age distribution of the
study group was 4–8 years (n = 7), 9–12 years (n = 36), and
13–18 years (n = 22). The mean age of the subjects was
12.2 years. There were 51 boys and 34 girls evenly distributed
across the three age ranges.

Of the 85 patients, 62 (72.9%) had previously taken a
stimulant drug for ADHD, and 23 (27.1%) had no history of
treatment with an ADHD stimulant drug. There were
28 patients (30.0%) currently taking an ADHD drug while
57 (70.0%) were not. The breakdown of drugs taken at
the start of treatment was as follows: 14 were taking amphet-
amine enantiomers; five were taking methylphenidate; five
were taking atomoxetine; three were taking other drugs not
specifically defined; and one was taking a combination of
amphetamine enantiomers with atomoxetine. Parents sought
treatment under this novel approach primarily due to concerns
over lack of drug efficacy and/or drug side effects.

The ADHD-RS inventory was administered at the start
and end of treatment. Results indicated that group

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scores (2 and 3) on the ADHD-RS scale (behavioral symptoms of ADHD) decreased significantly ($P < 0.001$) from the first to the second testing. ADHD-RS results are shown in Table 3.

The decrease in 2 and 3 scores shown in Table 3 occurred regardless of the variable being investigated, including age and gender. This reduction in symptoms is noteworthy. Prior to treatment, the number of significant ADHD behavioral indicators that were displayed as “often” or “very often” were in the 5–9 range. Only two post-treatment behavioral indicators were noted. The only variable that approached significance ($P < 0.08$) was gender. More males experienced a decrease in symptoms in the ADHD-RS (3) from 8.9 to 2.3 versus females in whom this score decreased from 7.1 to 2.2.

In addition to the statistical analysis parameters that were identified on the DSM-IV, the following observations were calculated relating to other issues. Some of the more compelling findings are included in the tables.

The results shown in Table 4 revealed that 63% of the participants achieved significant improvement with only monoamine amino acid precursors of serotonin and dopamine. Patients who achieved no significant relief of symptoms with only amino acid precursors represent a subgroup in whom urine samples were collected and OCT assay interpretation was utilized. In this subgroup, 38% achieved significant relief of symptoms following two or three urine assays. The total percentage of patients showing significant improvement was 77%.

Referring to Table 4, further 10% of patients who had taken stimulant drugs in the past reported complete symptom relief. There seems to be some advantage for the effectiveness of the amino acid supplement treatment when there is a history of having taken stimulant drugs in the past.

As noted in Table 7, a potential advantage was identified with the administration of amino acid precursors relating to taking ADHD drugs.

Urine tests did not typically occur until visit 4, and were indicated if the patient did not show significant improvement with relief of the majority of major ADHD symptoms after one week taking level 3 dosing values of Table 1 or Table 2. Those who experienced control of symptoms prior to or at visit 4 were excluded from urine testing. Results of the patients who had an OCT assay are shown in Table 8.

Therefore, it appears that urine testing with OCT assay interpretation was beneficial because urinary serotonin and dopamine assay interpretation defined the proper dosing values. To establish urinary serotonin and dopamine phases only requires two assays performed with varied amino acid precursor dosing values. The significant relief values of 64% prior to testing and 70% after two assays noted in Table 7 and Table 8 represent only one amino acid dosing change, with the confidence of knowing the serotonin and dopamine phases.

### Discussion

The data generated in the study were compared with data generated in double-blind, placebo-controlled studies. Tables 9 and 10 summarize the results of this literature search. It would appear that the placebo effect is strong in ADHD studies, because 28%–40% of placebo patients achieved significant relief of symptoms in the atomoxetine studies reviewed (Table 10), and 14%–31% had a placebo benefit in the methylphenidate study (Table 9).

To meet the criteria for approval under FDA guidelines, a drug has to demonstrate efficacy and safety. The amino acids and cofactors used in this retrospective study are classified by the FDA as generally recognized and accepted as

## Table 3: Changes in Attention Deficit Hyperactivity Disorder Rating Scale scores at initiation and end of treatment

| Group ADHD-RS changes | Pre-Rx | End-Rx | t-test | $P$  |
|-----------------------|--------|--------|--------|------|
| 2s                    | 4.6    | 1.2    | 8.42   | $<0.001$ |
| 3s                    | 8.3    | 2.3    | 12.26  | $<0.001$ |

**Abbreviations:** Rx, treatment; ADHD-RS, Attention-Deficit-Hyperactivity Disorder Rating Scale.

## Table 4: Percentage of the entire group ($n = 85$) achieving significant relief of symptoms by weeks 3 and 8 ($P < 0.05$)

| Significant relief | Week 3 | Week 8 |
|--------------------|--------|--------|
| No stimulant drug in past | 67% | 77% |
| Stimulant drug in past | 22% | 28% |

## Table 5: Percentage of the entire group ($n = 85$) achieving complete relief of symptoms by weeks 5 and 8

| Complete relief | Week 5 | Week 8 |
|-----------------|--------|--------|
| No stimulant drug in past | 30% | 33% |
| Stimulant drug in past | 32% | 35% |
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Table 7 Effect of taking and not taking a prescription ADHD drug on the endpoint of the study

| Week 5 Significant relief | Week 8 Complete relief |
|---------------------------|------------------------|
| Not taking a drug         | 64%                    |
|                           | 28%                    |

safe (GRAS), in the same category as supplemental vitamins and minerals. There are no safety concerns with the amino acids based on this FDA position. All of the amino acids and components used in the study are sold in the US over the counter without a prescription.

The drugs prescribed for ADHD have potentially controversial concerns associated with them, including neurotransmitter depletion, neurotoxicity, drug side effects, and adverse reactions; this amino acid approach in comparison has none of these concerns associated with it. This gives a significant advantage to this amino acid approach if studies continue to bear out that it is similar or superior to prescription ADHD drugs in its efficacy.

This retrospective study was performed in order to focus on the structure needed for a formal prospective study. In the course of this study, the following observations and considerations came to light. The administration of properly balanced amino acid precursors of serotonin and dopamine with OCT assay interpretation resulted in improvement that appears to be superior to methylphenidate and atomoxetine (Tables 9 and 10). This certainly provides encouragement to undertake further studies.

Even if the finding was that use of serotonin and dopamine amino acid precursors with OCT assay interpretation was equal to reported efficacy values in studies, this approach would be superior because it does not share the adverse reactions, potential depletion of neurotransmitters, and neurotoxicity concerns reported with the group of drugs prescribed for ADHD treatment.

There is variance identified and reported in children who were and were not taking drugs during this study. Future studies need to be designed to address the impact of amino acids on subgroups such as this. A further identified issue in this study that needs to be corrected in future studies is the timeline of the study. In response to the lack of amino acid efficacy at visit 4 (taking level 3 dosing values for one week from Tables 1 and 2), OCT assay interpretation was started. Further identified issue in this study that needs to be corrected in future studies is the timeline of the study. For children in the study for 10 weeks, three urinary tests were obtained. Experience leading up to this study suggested that a significant number of patients with ADHD do not achieve relief of symptoms until both urinary serotonin and dopamine are in the phase 3 therapeutic ranges. Data analysis revealed that it typically takes 2–8 urine tests with OCT assay interpretation to achieve this goal. Provisions need to be made in future studies to move away from rigid time guidelines and position the studies as a process independent of time where the endpoint is urinary serotonin and dopamine in the phase 3 therapeutic ranges or relief of symptoms, whichever comes first.

Table 8 Approximately 59% of patients in the group achieved relief of symptoms with administration of amino acids and no testing

| Urine test group | Week 5 Significant relief | Week 8 Complete relief |
|------------------|---------------------------|------------------------|
| Two tests        | 70%                       |
| Three tests      | 78%                       |

Notes: If no response was observed after treatment with the three amino acid dosing levels of Table 1 or Table 2, OCT assay interpretation was initiated leading to an increase in the number of patients in the study who experienced significant relief of symptoms.

Table 9 Retrospective study results, significant improvement in patients (Table 4) versus reported results in double-blind, placebo-controlled studies taking methylphenidate

| Pilot study results | Methylphenidate studies |
|---------------------|-------------------------|
| AA with OCT assay interpretation | Study 1\(^{24}\) | Study 2\(^{27}\) | Study 3\(^{28}\) |
| n                   | 85                      | 154                   | 97                    |
| % improved          | 77% (Table 4)           | 64%                   | 52%                   |
| % placebo improved  | N/A                     | 27%                   | 31%                   |
| % drug improvement over placebo | N/A | 37% | 21% | 44% |

Notes: The “% placebo improved” row represents percentage of subjects taking placebo who experienced significant remission of symptoms to the defined threshold of the study or greater. The bottom row is the advantage of the drug over placebo in the study cited.

Abbreviations: AA, amino acid; OCT, organic cation transporter.
Table 10 Retrospective study results, significant improvement in patients (see Table 4) versus reported results in double-blind, placebo-controlled studies of patients taking atomoxetine

|                  | Pilot study results | Atomoxetine studies |
|------------------|---------------------|---------------------|
|                  | AA with OCT assay   | Study 1²⁹          | Study 2³⁰          | Study 3³¹          |
|                  | interpretation      | n                   | % improved            | % improved          |
| n                | 85                  | 618                 | 36                   | 84                   |
| % improved      | 77% (Table 4)       | 71%                 | 54%                  | 59%                  |
| % placebo       | N/A                 | 59%                 | 40%                  | 31%                  |
| improved        | N/A                 | 28%                 | 14%                  | 28%                  |
| % drug improvement over placebo | N/A | 43% | 14% | 28% |

Notes: The “% placebo improved” row represents percentage of subjects taking placebo who experienced significant remission of symptoms to the defined threshold of the study or greater. The bottom row is the advantage of the drug over placebo in the study cited.

Abbreviations: AA, amino acid; OCT, organic cation transporter.

It is also suggested that the scrutiny of this retrospective study be expanded to identify more phenotype traits. Incorporation of expanded data fields such as this into further studies would facilitate more in-depth comparison with other studies and statistical evaluation of subgroups.

This analysis does provide some initial evidence of the efficacy of amino acids in significantly reducing symptoms associated with ADHD. Tables 9 and 10 reveal the efficacy of this treatment protocol to be potentially superior to results seen with prescription drugs. Future studies are necessary to investigate the reliability of these observed effects. If these results can be replicated in controlled studies, then such important issues as cause and effect for the change in ADHD symptoms, potential mediating variables, and long-term use can be further investigated and clarified.

Conclusion

Based on the FDA guidelines, the amino acid precursors of serotonin and dopamine, used in this study, are classified as GRAS, meaning no significant safety concerns exist about their use. The next question to ponder is whether the approach is effective. The FDA has set the bar very high in demonstrating efficacy of prescription drugs. There are numerous examples of drugs being approved that are only 7%–13% more effective than placebo.¹ Under these conditions, it would appear that the findings of this study have the potential to demonstrate at least that level of efficacy in a prospective study based on Tables 9 and 10.

The purpose of this paper was to document formally the results and findings generated during the course of this retrospective pilot study involving 85 children, and define parameters that allow focus on a future prospective study. It is the goal of this paper to spark interest, research, awareness, and scrutiny of these findings, and to raise awareness of potential neurotransmitter depletion and neurotoxicity issues relating to ADHD drugs.

Disclosures

This study was funded by an unrestricted grant from CHK Nutrition, Duluth, MN. MH discloses his relationship with DBS Labs Inc and NeuroResearch Clinics Inc. TU discloses his relationship with DBS Labs. The other authors report no disclosures.

References

1. Michelson D, Buittelaar JK, Danckaerts M, et al. Relapse prevention in pediatric patients with ADHD treated with atomoxetine: A randomized, double blind, placebo controlled study. J Am Acad Child Adolesc Psychiatry. 2004;4:896–904.
2. Trachte G, Uncini T, Hinz M. Both stimulatory and inhibitory effects of dietary 5-hydroxytryptophan and tyrosine are found on urinary excretion of serotonin and dopamine in a large human population. Neuropsychiatr Dis Treat. 2009;5:227–235.
3. Hinz M, Stein A, Uncini T. The dual-gate lumen model of renal monoamine transport. Neuropsychiatr Dis Treat. 2010;6:387–392.
4. Hinz M. Depression. In: Kohlstadt I, editor. Food and Nutrients in Disease Management. Boca Raton, FL: CRC Press; 2009.
5. Hinz M, Stein A, Uncini T. A pilot study differentiating recurrent major depression from bipolar disorder cycling on the depressive pole. Neuropsychiatr Dis Treat. 2010;6:741–747.
6. Hinz M, Stein A, Trachte G, Uncini T. Neurotransmitter testing of the urine: A comprehensive analysis. Open Access Journal of Urology. 2010;2:177–183.
7. Stein A, Hinz M. Uncini Amino acid responsive Crohn’s disease, a case study. Clin Exp Gastroenterol. 2010;3:171–177.
8. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorder IV; Fourth Edition. Text Revised. Washington, DC: American Psychiatric Association; 1994.
9. Shire US Inc. FDA approved prescribing information for neutral sulfate salts of dextroamphetamine and amphetamine. Available from: http://pi.shircontent.com/PDFs/AdderalIXR_USA_ENG.PDF. Accessed Oct 14 2010.
10. Concerta®, FDA approved prescribing information for methylphenidate. Available from: http://www.concerta.net/sites/default/files/pdf/Prescribing_Info-short.pdf. Accessed Oct 14, 2010.
ADHD: Risks and mechanism of action.

Ricaurte G, Mechan A, Yuan J, et al. Amphetamine treatment similar to that used in the treatment of adult attention-deficit/hyperactivity disorder: A randomized, placebo-controlled study. J Atten Disord. 2007;11:8–16.

Faraone S, Biederman J, Spencer T, et al. Efficacy of atomoxetine in children and adolescents with attention-deficit/hyperactivity disorder. Eur Child Adolesc Psychiatry. 2005;1:16.

Stein M, Sarampote CS, Waldman ID, et al. Acute response study of OROS methylphenidate in children with attention-deficit/hyperactivity disorder. Arch Pediatr Adolesc Med. 2006;160:82–90.

Svanborg P, Thernlund G, Gustafsson P, et al. Atomoxetine improves patient and family coping in attention deficit/hyperactivity disorder: A multisite controlled study of OROS methylphenidate in the treatment of adolescents with attention-deficit/hyperactivity disorder. Arch Pediatr Adolesc Med. 2009;163:725–735.

Michelson D, Allen AJ, Busner J, et al. Efficacy of atomoxetine in adult attention-deficit/hyperactivity disorder: A drug-placebo response curve analysis. J Clin Psychopharmacol. 2011;31:12–16.

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