

An Amino Acid Protocol for Attention Deficit Hyperactivity
Disorder: A Retrospective Study

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Abstract

Objective: The purpose of the present retrospective study was to provide initial information regarding the effectiveness of an amino acid protocol to reduce the behavioral symptoms resulting from ADHD.

Method: The records/charts of 85 children and adolescents (ages 4-18) covering an 18-month period were reviewed. All clients underwent a standard amino acid protocol that included weekly visits (8-10 weeks) with amino acid dosage and type remaining the same or altered depending on the severity of symptoms still remaining (also informed by urine analysis after week-4).

Results: Findings revealed a significant decline in the behavioral symptoms seen often or very often (3's and 4's on the 18-item DSM-IV checklist) from the first (near the beginning of treatment) to the second (near the end of treatment) administration. Results also revealed that most of the benefits of the amino acids were seen in the first 4-weeks of treatment.

Conclusion: It appears that amino acids were responsible for the changes observed in behavior, although controlled prospective studies are suggested to document this relationship and make formal linkages.

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According to the Centers for Disease Control, Attention Deficit Hyperactivity Disorder (ADHD) is the most commonly diagnosed behavioral disorder of childhood affecting 5% -25% of school-aged children. Recent data suggest that at least half of the children with the disorder continue to have significant symptoms throughout life (Biederman, & Faraone, 2005). People who are diagnosed with ADHD have a problem with inattentiveness, over-activity, impulsivity, or a combination, which negatively affect performance in school and work, as well as in relationships with others, according to the Diagnostic and Statistical Manual of Mental Health (DSM-IV, 1994). ADHD is clearly a real phenomena affecting millions of children, adolescents and adults every year.

The most common treatment prescribed for ADHD is stimulant medication, even though there is recent evidence of a relationship between use of ADHD stimulants in childhood and an increased prevalence of drug abuse as teenagers (Kulig, 2005). While using stimulant medication can relieve many ADHD symptoms, there are often side effects that include dizziness, loss of appetite, insomnia, and headaches (Spencer, 2004). In addition, long term use of these types of prescription drugs appear to deplete the neurotransmitters which can cause the drug to lose its effectiveness and allow all the symptoms of ADHD to return. Because of the serious health concerns related to prolonged use of stimulants, there is a growing dissatisfaction with the medical treatments of ADHD and a desire for safe, effective alternatives (Bilici & Yidirim, 2004;

Madaan et al., 2006; Rojas & Chan, 2005). For example, some of the alternative and complementary therapies include supplementation with essential fatty acids (e.g., Schmidt, Mocks, Lay, et al., 1997), dietary modification (Bateman, Warner, Hutchinson, et al., 2004) neurofeedback (e.g., Monastra, Monastra, & George, 2002) and homeopathy (e.g., Strauss, 2000). Unfortunately, the findings related to the efficacy of these approaches are mixed and controversial. However, alternative approaches to the treatment of ADHD continue to be advocated by the National Institutes of Health

One of the most recent attempts to find an alternative treatment of ADHD is with the use of amino acid supplementation (Bourre, 2006; Iverson, 2006; Purvis, Kellermann, Huisman, & Pennings, 2007). Amino acids are compounds that are left behind when proteins are digested, and are also the raw materials used to make neurotransmitters, among other substances. It is the neurotransmitter irregularities that appear to cause the symptoms of ADHD (Iverson, 2006). Given what is known about the mechanisms of effective ADHD medications, it seems reasonable to suggest that amino acids may affect the production of neurotransmitters. Furthermore it has been argued that amino acids can restore balance to these neurotransmitters by preventing further depletion typically seen with the use of traditional drugs to treat ADHD (Hinz, 2007). Despite anecdotal testimonials attesting to the positive effects of amino acids in reducing symptoms associated with ADHD, there has been little empirical research regarding the effectiveness of the use of amino acids as a treatment for ADHD.

Obviously, studies need to be conducted to document the effectiveness of amino acids in treating ADHD. Along these lines, a recently developed amino acid formula has received testimonial and other anecdotal support for its effectiveness in changing neurotransmitter levels and subsequently behavioral indicants of ADHD (Ross Stewart, personal communication, 2007). However, to date, there has been little empirical research investigating the effectiveness of this amino acid treatment. Thus, the current research project has been designed to test the effectiveness of an amino acid supplementation protocol on ADHD deficits by using a retrospective chart review protocol. This type of review, although not as powerful as a prospective controlled study, can begin to provide evidence as to the potential of amino acids in alleviating ADHD symptoms.

Method

Eighty-five children between the ages of 4 and 18 who had been diagnosed by a clinical psychologist of having ADHD (using the 18 criteria in DSM-IV) had their charts reviewed and analyzed. It should be noted that since this was a retrospective chart review, no variables were manipulated. The period that the charts were reviewed covered from May of 2005 to November of 2006. Participants were selected based on their age (4-18) as the study focused on children diagnosed with ADHD. All participants underwent a standard amino acid protocol (explained later in this section), which was informed by regular urine tests (typically starting after week-3) and analyses, although not all clients needed to have urine analyses conducted. In essence, the program of amino acid administration and subsequent urine tests was scheduled to be conducted

over an 8-10-week period, although based on the responses of the clients to the treatment, the protocol was often stopped before the 8-10-week period was reached. That is, due to the client becoming “regulated” (i.e., significant reduction in symptoms or total symptom relief) before the 8-10-weeks, the amino acids no longer needed to be changed and the client would simply continue to take whatever dosages and types of amino acids shown to be effective in significantly reducing symptoms of ADHD.

However, in general, amino acid type and amount given to clients was varied based on their reaction to these amino acids and then the urine analyses (when available). It was felt if the client was not regulated in the first 3-4 weeks, the urine analysis would begin and the urine analysis would provide important information concerning what should be the specific kinds and amounts of amino acids given to clients to maximize their relief from ADHD symptoms. That is, the exact kinds and amounts of amino acids given clients would be altered based on urine analyses. The amino acids that were used with the clients (and their specific ingredients) included NeuroReplete (Vitamin C 500mg -Ascorbic Acid, Calcium 110mg -Calcium Citrate, Vitamin B 37.5mg -Pyridoxine Hydrochloride, Folate 200mcg, L-Lysine 250mg, 5-Hydroxytryptophan 150mg, L-Tyrosine 1,500mg) , Cysreplete (Selenium 134mg, Folate133mg, L-Tyrosine 500mg), RepleteExtra (Folate 400mcg, L-Tyrosine 1,000 mcg, 5-Hydroxytryptophan 300 mg) , and TyrosineReplete (Folate 133mcg,L-Tyrosince 500mg, D5-40% Mucuna Pruienns 300 mg).

If there was no urine analysis and the client was not regulated, then a standard amount and type of amino acids was given weekly to each client. More specifically, on Step 1 (after diagnosis of ADHD was made) the following amino acid dosages were provided for a) adults (clients who were 16-18 years old received an adult dosage): 8 x NeuroReplete (e.g., 8 pills per day of NeuroReplete) and 6x CysReplete and (b) children (pediatric dose: 4 x Neuroreplete and 3 x CysReplete. After taking this dosage for one-week, clients returned to discuss their symptoms. If a majority of the worst persisted, the dosage was then moved to Step 2. Specifically the dosages were (a) adults: 12 x NeuroReplete and 6 x CysReplete and (b) children: 6 x NeuroReplete and 3 x CysReplete. The clients took this dosage for 1-week, and then returned again to discuss symptoms. If a majority of the worst symptoms still persisted, the dosage was moved to Step 3. These dosages were a) adults: 12 x NeuroReplete, 6 x CysReplete, and 3 x RepleteExtra, and (b) children: 9 x NeuroReplete, 3 x CysReplete, and 3 xTyrosineReplete. Once again, after taking this dosage for a week , the client (with parent) returned to discuss symptoms. If a majority of the worst symptoms still persisted, a urine analysis test was performed. The client stayed on Step 3 dosage until the laboratory results were reported. Then the dosage was revised based on this analysis, which averaged about 7 days. The client then took this revised customized dosage for 7 days. This procedure was continued for the next several weeks (unless clients became regulated, in which case they continued on the last revised dosage) and

dosages were revised and customized weekly until Step 8 was completed (which usually was approximately 8-10 weeks).

To assess the behavioral manifestations and signs of ADHD exhibited by the client, their parents twice completed the Attention-Deficit-Hyperactivity Disorder Rating Scale (ADHD-RS). This rating scale is symptom specific and targets problems related to the DSM-IV subtypes of ADHD. In essence, parents responded to 18 items that corresponded to the DSM-IV diagnostic criteria (toward the beginning and end of the treatment protocol). This provided an outcome measure of how well the treatment protocol (in this case amino acids) worked in alleviating typical behavioral symptoms of ADHD. For parents, the reduction in behavioral symptoms of ADHD children (e.g., inattentiveness, over-activity, impulsivity, or a combination, which negatively affect performance in school and work, as well as in relationships with others) is a central outcome they want to achieve through a treatment of ADHD. Using a 4-point scale, the numbers of 3's (often) and 4's (very often) that children displayed signs and symptoms of ADHD were noted by the parents across the treatment period. Other variables assessed by asking clients via a questionnaire included (a) taking/not taking ADHD medicine, (b) previously taking/not taking stimulant drugs, (c) gender, (d) age, (e) perceived amount of improvement as noted by a conversation between the parent (or client alone if an adult) and the psychologist, and (f) number of comorbid factors (e.g., depression, cerebral palsy, chronic indigestion, hair pulling, seizures, autism, obsessive compulsive behavior).

Results

First some demographic and frequency information was compiled to provide a more detailed look at the sample. Regarding age, the numbers for the different age ranges were 4-8 years old ($n = 27$), 9-12 years old ($n = 36$) and 13-18 years old ($n = 22$) and the mean was 12.2 years of age. Regarding gender there were 51 boys and 34 girls and these were evenly distributed across the three age ranges that were created. Twenty-eight of the clients were currently using an ADHD drug (57 were not) although 62 clients had previously used stimulant drugs for ADHD (23 never did). Thus, it appears that although the majority of clients had taken stimulant drugs in the past (approximately three quarters) to control the symptoms of ADHD, only approximately a third were currently taking some ADHD medication when they first visited the clinic. It is possible (and many parents of clients indicated this during their initial visit) that the parents were not finding relief of symptoms through the use of stimulant drugs and thus were seeking out an alternative treatment modality. This dissatisfaction by many parents regarding the effectiveness of stimulant medication for ADHD is one of the main reasons why this alternative of using amino acids is being tested. Regarding the frequency of comorbid factors, 28% had one comorbid factor and 16% had two comorbid factors in addition to the primary diagnosis of ADHD.

Due to the number of clients and missing data, the only parametric statistics that were meaningful were conducted on the Attention-Deficit Hyperactivity Disorder Rating Scale. It should be noted that the person conducting the statistical analyses had nothing to do with the charting of the clients and was

completed “blind” as to any a prior hypotheses or changes expected in the data. In addition, the researchers performing the charting also were blind to any hypotheses. Results indicated that scores (the numbers of 3’s and 4’s) on the ADHD-RS scale (behavioral symptoms of ADHD) decreased significantly ($p < .001$) from the first to the second testing. Specifically, overall, the number of 4’s on the ADHD-RS decreased significantly from 8.3 to 2.3 ($t = 12.26, p < .001$) and the number of 3’s decreased significantly from 4.6 to 1.2 ($t = 8.42, p < .001$). This decrease occurred regardless of the variable being investigated including age and gender. This reduction in symptoms is noteworthy since only approximately two behavioral indicators of ADHD were displayed often or very often, whereas before treatment approximately five to nine symptoms of ADHD were present. The only variable that approached significance ($p < .08$) was gender as males decreased more on the number of ADHD-RS 4’s (8.9 – 2.3) than did females (7.1-2.2).

Besides the parametric statistical analysis conducted on the DSM-IV- RS, percentages were calculated on a number of other relationships (low numbers in certain cells or missing data did not allow for a more complete statistical analysis). Some of the more compelling findings are included below. First, 77% of clients reported some relief from symptoms over eight weeks although 67% reported some relief by week three. Similarly, 33% reported complete symptom relief by the 8th week with 30% reporting complete symptom relief by week 5. Taken together, these two findings indicate that some or complete relief is usually attained fairly early in the treatment period. In essence, only a small

percentage of clients exhibited initial reductions in symptoms after the first three-five weeks of taking the amino acid supplements. Practically, most people who benefited from this amino acid treatment protocol did so within the first several weeks of treatment

When looking at the impact of previous stimulant drug use, (as noted above, 77% of clients in the present retrospective review had previously used some type of stimulant drug to help control ADHD symptoms) on current symptom relief, 35% of clients using stimulant drugs in the past reported complete symptom relief by week-8 compared to 26% of clients not on stimulant drugs in the past. Similarly, 32% of clients using stimulant drugs in the past reported full relief by week-5 compared to 22% of clients not on stimulant drugs in the past. Once again, these findings taken together indicate that most of the gains displayed by clients under the amino acid supplementation treatment were seen by week-5, regardless of previous stimulant drug use. Furthermore, there seems to be some advantage (about 10% more clients reported complete symptom relief who had taken stimulant drugs in the past) to taking stimulant drugs in the past on the effectiveness of the amino acid supplement treatment (of course this could have been due to a number of factors such as the severity of client's ADHD starting the program).

Further investigating stimulant drug use, 79% of clients currently taking an ADHD drug reported some symptom relief by week 8, whereas 64% of clients not currently taking an ADHD drug reported some symptom relief. Along these lines, 35% of clients currently taking an ADHD drug reported full symptom relief

by week 8, compared to 28% not currently taking any ADHD drugs. So there seems to be somewhat of an advantage to taking ADHD drugs while getting this amino acid supplementation although the success rate (as measured by degree of symptom relief) fell off significantly from partial relief to full relief.

Urine tests did not typically occur until week four when the client did not show significant improvement in the relief of the majority of major symptoms resulting from ADHD. In essence, not all clients received urine tests because many of them became regulated before week-4 and thus urine tests were not necessary to determine dosage and types of amino acids necessary. Results revealed that 78% percent of clients who had urine tests reported some symptom relief by the third week after testing, compared to 59% who did not have urine tests. After the first week of taking a urine test, only 33% reported some improvement in symptoms compared to 30% who did not receive a urine test. However, after the second urine test, 70% reported some improvement in symptoms compared to 58% who did not receive a urine test. Therefore, it appears that urine tests became more beneficial and accurate in regulating the proper types and dosages of amino acids over a 3-week period.

Discussion

It is important to understand that since these are retrospective data, conclusions should be viewed with caution as no cause-effect relationships can be made. In addition, besides employing parametric statistics on 18 items of the DSM-IV-RS, all other data comparisons are strictly based percentages and thus statistical significance could not be empirically tested. However, one of the

primary goals of a retrospective study, is to highlight and identify variables worthy of future investigation as well as help in designing a prospective study where key variables can be manipulated and/or controlled.

In general, with the data gleaned from the present study as well as recent hypotheses and theoretical formulations (e.g., Atilde, 2006; Bourne,2006; Iverson; Kinkead, Seiz, Owens, & Mandell, 2006), it appears that amino acids can play an important role in helping to reduce the symptoms normally associated with children suffering from ADHD. Most recently (Hinz, 2007) specific mechanisms have been proposed as to why and how amino acids may influence neurotransmitters in the body and thus provide an alternative treatment for ADHD. Specifically, Hinz argues that typical prescription drugs currently used to treat ADHD (e.g.,Ritalin, Concerta) are dopamine/nor epinephrine reuptake inhibitors. These drugs do not increase the number of dopamine and nor epinephrine molecules in the central nervous system. Rather, they appear to work by moving dopamine and nor epinephrine molecules from the vesicles of the pre-synaptic neuron to the synapse. When neurotransmitters are in the vesicles of the pre-synaptic neuron, they are safe from breakdown and metabolism. In the process, they facilitate a more effective firing of the electrical impulses across the synapse.

However, once outside the pre-synaptic vesicles, these neurotransmitters are exposed to different enzymes which cause an increase in the metabolism of dopamine and nor epinephrine. Thus, what eventually happens is that the number of dopamine and nor epinephrine molecules in the central nervous

system gets depleted. This leaves an imbalance in the neurotransmitters in the body, which can result in various side effects associated with ADHD drugs (it is these side effects of the typical drugs used to treat ADHD that concern many parents). In essence, long-term use of prescription drugs appears to deplete the neurotransmitters which can cause the drug to lose its effectiveness and ultimately causing the symptoms of ADHD to return. Such a depletion, could also cause a long list of secondary problems, including other mood disorders and chronic illnesses.

The amino acids used in the present retrospective study have received testimonial and anecdotal support regarding its effectiveness in changing neurotransmitter levels and subsequently behavioral indicators of ADHD (Ross Stewart, personal communication, 2007). In essence, amino acids (certain types in certain dosages) are hypothesized to restore balance to the neurotransmitters (i.e., prevent further depletion typically seen with the use of traditional drugs to treat ADHD). The results from the present retrospective study indicated the significant reduction in major symptoms of ADHD (as determined by the 18 item DSM-IV-RS for ADHD) seen often or very often after administration of an amino acid protocol. Due to the retrospective nature of the study, however, the underlying reasons or causes of this reduction are still unknown. A prospective study (which has been planned and scheduled to begin in Summer, 2008) needs to be conducted to empirically test if it is the amino acids per se that are responsible for the reductions in ADHD symptoms as well as investigating the

specific types and amounts of amino acids associated with changes in ADHD symptoms.

There were also a number of findings related to the reduction of ADHD symptoms over the 8-10 week period of using amino acids. In general, it appeared that clients became regulated (significant reduction of major symptoms) within the first few weeks of starting the amino acid treatment. Although some clients did significantly improve in the latter weeks of the treatment (generally weeks 5-10) most of the gains were made in the first month off treatment. This underscores the notion that improvements can be made before urine analysis begins. In essence, standard dosages and types of amino acids appear to produce significant improvements in ADHD symptoms and thus urine analysis most often not necessary. If this is proven to be consistent in subsequent studies, then the cost of this amino acid protocol would be significantly reduced if the use of urine analyses is unnecessary in many cases. However, it should be noted, that urine analysis could add to the success rate in reducing ADHD symptoms although it may not account for a majority of the clients.

Another interesting question concerns the effectiveness of this amino acid protocol in relation to previous or current stimulant drug use targeted to reducing ADHD symptoms. First, it should be noted that approximately one-third of the clients not currently taking any ADHD drugs and one-quarter of those not previously taking any stimulant drugs reported full relief by week 8. Therefore, the amino acids themselves as a treatment for ADHD appeared to be somewhat

successful (although there seemed to be a slight increase in symptom relief when ADHD drugs were used in conjunction with amino acids). It should be noted that the majority people (parents and their ADHD children) who came to this clinic had not had continued success with more traditional ADHD drugs and thus successful reduction of ADHD symptoms had not occurred in the past. Therefore, any gains realized here, in most cases, had not been realized with previous ADHD treatments.

Besides the limitation mentioned earlier in the use of retrospective data regarding cause-effect, other limitations should be noted. For example, there was no follow-up with clients after they left the clinic (usually after being regulated within 8-10 weeks). Therefore, it is unknown whether the clients continued to take the amino acids and if they were effective over a long period of time? In addition, would the dosage required to be regulated during the first 8-weeks continue to be the same over time? Furthermore, a prospective, controlled study would be able to determine if it was the amino acids that caused the change as opposed to some other mediating variable (e.g., diet, exercise habits, etc.). However, this retrospective analysis does provide some initial evidence for the efficacy of amino acids in reducing symptoms associated with ADHD. Future empirical studies need to continue to investigate this protocol to determine the reliability of these effects. If these results can be replicated in controlled studies, then such important issues as the causes/explanations for the changes in ADHD symptoms, potential mediating variables, and long-term uses (including any side effects) can be further investigated.

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