N-acetylcysteine (NAC) is a drug available over-the-counter in health food stores that seems to be effective for a variety of disorders, including depression and many different habits and addictions. Preventing relapse of cocaine abuse is one of its uses. Researcher Kathryn Reissner at the Medical University of South Carolina found that NAC increases the expression of a glial glutamate transporter (GLT-1) that helps clear excessive glutamate in the nucleus accumbens, and that this mechanism is critical to preventing the reinstatement of cocaine self-administration in rodents.

As we have previously described in the BNN, NAC also decreases cued release of glutamate in the nucleus accumbens by potentiating the cystine-glutamate exchanger. This initially increases extrasynaptic glutamate, but subsequently downregulates glutamate release in the nucleus accumbens through actions at an inhibitory presynaptic metabotropic glutamate receptor.

However, the new data indicate that this action at the cystine-glutamate exchanger is not required for NAC’s effects on cocaine reinstatement, but the induction of GLT-1 is. Furthermore, another compound, propentofylline, which increases glutamate GLT-1, is also effective in suppressing cocaine reinstatement. Cocaine decreases a marker of glial activity, glial fibrillary acidic protein (GFAP), in the nucleus accumbens, suggesting that deficient glial functioning and uptake of glutamate could be another target of therapeutics in cocaine addiction.

*Editor’s Note: There are also glial deficits in depressed patients, so it is conceivable that NAC’s effect on GLT-1 glutamate clearance is also involved in the antidepressant effects of NAC.*

**Editor Robert M. Post’s Personal Opinion**

With the usual caveat that all treatment strategies discussed in the BNN must be evaluated and administered by a physician, it may be useful to consider adding NAC to a treatment regimen for a patient struggling with recurrent unipolar or bipolar depression, and/or a comorbid substance use disorder. Using conventional treatments early in the course of these disorders for acute treatment and for long-term prevention would be the first approach. For less than satisfactory acute responses, conventional adjunctive treatments (as recommended in treatment guidelines elsewhere) might be considered along with NAC, which in some cases can have a delayed onset of action. (Three months may be required to see maximal effects in bipolar disorder.)
At the 65th Annual Scientific Convention of the Society of Biological Psychiatry, researcher Christian Carmeli reported that N-acetylcysteine (NAC, 2 gm/day for six months) increased electroencephalogram (EEG) synchrony over the frontal cortical and left temporal regions in patients with schizophrenia. The EEG measures the frequency and amplitude of electrical activity on both sides of the brain.

N-Acetylcysteine

Editor’s note: These data provide a neurophysiological mechanism that could explain the positive effects of NAC previously observed by researcher Mike Berk and associates in both schizophrenia and bipolar disorders and published in Biological Psychiatry in 2008. NAC is both a glutathione precursor providing antioxidant effects and a modulator of hyper-responsive glutamate reactivity in the n. accumbens or ventral striatum, the reward area of the brain. In placebo-controlled studies NAC appears effective in treating cocaine, heroin, and gambling addiction, as well as trichotillomania (compulsive hair-pulling). These effects are thought to be related to NAC’s dampening of glutamate responses in the n. accumbens, which, along with the dorsal striatum, appears to mediate habit memory.

Tags: <N-acetylcysteine, schizophrenia>
Antioxidants May Be Deficient in Patients with Bipolar Disorder, NAC May Help

February 8, 2012 · Posted in Potential Treatments · 2 Comments

In a poster at the 9th International Conference on Bipolar Disorder (ICBD) held in Pittsburgh in 2011, Guy Goodwin and colleagues reported that relative to controls, blood from patients with bipolar disorder contained more total glutathione, a potent antioxidant, and a higher ratio of oxidized to reduced glutathione. Measurements of blood glutathione could eventually serve as a biomarker, suggesting when a diagnosis of bipolar disorder is likely.

Editor’s note: Glutathione is one of the major antioxidants in humans. Oxidized glutathione is a less active form, so the higher levels of oxidized glutathione compared to reduced glutathione in patients with bipolar disorder suggests they may have a relative deficiency of the active form. These data are consistent with reports that patients in manic and depressive phases of bipolar disorder have increased oxidative stress and free radicals that impair cellular functioning.

Together, these results highlight the potential utility of treatments that increase antioxidant activity. One option is N-acetylcysteine (NAC), which the body converts into glutathione. As previously noted in the BNN, Michael Berk reported in Biological Psychiatry in 2008 that NAC (1000 mg twice a day) appears to exert greater antidepressant effects over a period of 24 weeks than placebo when added into previously ineffective regimens in patients with bipolar disorder.

In another poster at the conference, Magalhaes and colleagues reported on NAC treatment for a subgroup of the bipolar patients in the study by Berk who were in a major depressive episode at the time of the study. They found that NAC had highly significant acute antidepressant effects of large magnitude in this subgroup of patients.

The glutathione data by Goodwin et al. provide a further rationale for consideration of the use of NAC in bipolar disorder, particularly in the acute and longer-term treatment of the depressive phases. As we reported in BNN Issue 1 from 2010, NAC also exerts positive effects in many illnesses that commonly occur comorbidly with bipolar disorder. These include cocaine and heroin addiction, gambling addiction, obsessive compulsive disorder (as an adjunct to selective serotonin reuptake inhibitors (SSRIs)), and trichotillomania (compulsive hair-pulling).

Tags: <antioxidants, bipolar disorder, glutathione, N-acetylcysteine>
N-acetylcysteine (NAC), an antioxidant available without a prescription in health food stores, has shown remarkable effectiveness when added to regular treatments for schizophrenia, bipolar disorder, and the substance abuse that often accompanies these illnesses.

A 2008 article by Michael Berk and colleagues in the journal *Biological Psychiatry* reported that compared to placebo, 2 grams/day of NAC reduced both positive symptoms of schizophrenia (hallucinations, delusions) and negative symptoms (social withdrawal, difficulty planning and problem-solving). A 2013 study by Mehdi Farokhnia found that 2 grams/day of NAC improved negative symptoms in 42 patients with schizophrenia. Two other studies found that NAC improved deficits in auditory sensory processing in people with schizophrenia.

NAC also improves symptoms of bipolar disorder. A 2008 study by Berk and a 2011 study by Pedro Vieira da Silva Magalhães showed that NAC improved bipolar depression, and a small 2013 study by Magalhães showed that it improved mania in 15 patients. After 24 weeks, 60% of those who took NAC were in remission, compared to 15% of those taking placebo.

NAC is also effective at reducing habitual behaviors such as substance abuse, which is common in patients with schizophrenia and bipolar disorder. Studies have shown that NAC can reduce patients’ use of marijuana, cocaine, alcohol, and nicotine. It is relatively safe with minimal side effects, and fights oxidative stress, which is also common in severe mental illness.

NAC comes in 500mg or 600mg capsules. Dosing typically begins with one capsule twice a day for a week, followed by two tablets twice a day thereafter. As with any recommendations in the BNN, these should not be acted on without guidance from a treating physician.
At the 2014 meeting of the International College of Neuropsychopharmacology, researcher N. Miyake described the effects of the nutritional supplement N-acetylcysteine (NAC) on clinical symptoms in subjects with subthreshold symptoms of psychosis.

N-acetylcysteine, a glutathione precursor, has neuroprotective effects. In this case series, four patients with subthreshold psychosis were given 2000mg/day of NAC for 12 weeks. The patients’ symptoms improved to the point that three of the four were no longer considered at risk for psychosis.

*Editor’s Note: These promising anecdotal observations deserve careful follow up using a control group. Omega-3 fatty acids have been show to slow conversion to full psychosis and performed better than placebo in a controlled study. Both n-acetylcysteine and omega-3 fatty acids should definitely be studied for those with emerging symptoms of bipolar disorder.*

Tags: <bipolar disorder, N-acetylcysteine, psychosis, schizophrenia>
In 2008, Michael Berk and colleagues showed that N-acetylcysteine (NAC) is effective as an adjunctive treatment for bipolar depression. At the 2012 meeting of the International Congress of Neuropsychopharmacology, Berk reported that NAC (1000 mg twice a day) was also effective in unipolar depression, significantly beating placebo in a randomized double-blind 12-week study.

Editor’s Note: NAC has a broad spectrum of clinical efficacy in bipolar and unipolar depression, negative symptoms of schizophrenia (such as apathy and withdrawal), irritability in autism, trichotillomania (compulsive hair-pulling), gambling addiction, obsessive-compulsive disorder, and many substance-abuse disorders, such as cocaine, heroin, alcohol, and marijuana.

How can one substance do all this? NAC has antioxidant effects, it turns into glutathione (an antioxidant that is the body’s main defense against oxidative stress and free radicals), it has neuroprotective effects (causing neurite sprouting), and it re-regulates glutamate in the reward area of the brain, the nucleus accumbens. Berk believes it is NAC’s antioxidant properties that produce its positive effects in such a range of illnesses, while this editor (Robert M. Post) favors the glutamate mechanism (as discussed in BNN Volume 14, Issue 1 from 2010 and Volume 16, Issue 1 from 2012) as an explanation of NAC’s effects.

Whatever its mechanism turns out to be, NAC is worthy of consideration as an adjunctive treatment. It is readily available from health food stores without a prescription, relatively inexpensive (less than $20 for 100 pills), and relatively well-tolerated. Minor gastrointestinal upsets were the most common reported side effect in the Berk’s clinical trial. However, this editor has had one patient experience a worsening of psychosis.
N-acetylcysteine (NAC) is an anti-oxidant nutritional supplement that has been found to reduce a wide range of habitual behaviors, including drug and alcohol use, smoking, trichotillomania (compulsive hair-pulling), and gambling. It also improves depression, anxiety, and obsessive behaviors in adults, as well as irritability and repeated movements in children with autism. A new study suggests NAC may also be able to reduce non-suicidal self-injury, often thought of as “cutting,” in girls aged 13–21.

The open study, presented in a poster by researcher Kathryn Cullen at the 2015 meeting of the Society for Biological Psychiatry, compared magnetic resonance imaging (MRI) scans of 15 healthy adolescent girls to scans of 22 girls who had been engaging in self-injury, both before and after this latter group received eight weeks of treatment with N-acetylcysteine. Doses were 1200 mg/day for the first two weeks, 2400mg/day for the next two weeks, and 3600mg/day for the final four weeks. The girls also reported their self-injury behaviors.

Treatment with NAC reduced the girls’ self-injury behaviors. The brain scans showed that NAC also increased resting-state functional connectivity between the amygdala and the insula. Connectivity in this region helps people regulate their emotional responses. At baseline, the girls who engaged in self-harm had had deficient connectivity between the amygdala, the prefrontal cortex, insula, and the posterior cingulate cortices compared to the healthy girls, and this improved with the NAC treatment.

Tags: <amygdala, connectivity, insula, N-acetylcysteine, NAC, self-harm>
Cutting, or non-suicidal self injury, is a serious problem among adolescents, and few treatments are available. Researcher Kathryn Cullen and colleagues have found that **N-acetylcysteine (NAC)**, an antioxidant nutritional supplement that has been effective in the treatment of depression and many addictions and habit-related behaviors, can reduce cutting.

The study included 25 participants with a history of non-suicidal self injury, aged 13–21, and 12 controls. They participated in brain scans before and after treatment. Compared to the controls, the self-injurers showed greater overall psychopathology, greater activation in a few brain regions (precuneus, posterior cingulate, insula, and temporal lobes), and reduced lower left frontal activation. Patients who received NAC up to 900mg twice daily in weeks 5–8 of the study reduced their cutting and also showed reduced psychopathology. An increase in frontal activation in response to negative emotion was linked to the reduction in cutting.

*Editor’s Note: NAC improves mood in depression, many addictions, and many habits including trichotillomania (excessive hair-pulling), nail biting, and cutting. It may do this by increasing glial glutamate transporters in the nucleus accumbens, the brain’s reward center, which lessens the magnitude of the glutamate signal, mediating the compulsion to engage in the habitual behavior.*

**Tags:** <cutting, N-acetylcysteine, non-suicidal self injury>
New discoveries in neuroanatomy are helping clarify what addiction looks like in the brain. Peter Kalivas of the Medical University of South Carolina reported at the 2013 meeting of the Society of Biological Psychiatry that most drugs of abuse alter glutamate levels and the plasticity of synapses in the nucleus accumbens, the reward area of the brain. Glutamate is the main excitatory neurotransmitter in the brain, and compulsive habits may be associated with increased release of glutamate in this brain area.

During chronic cocaine administration, for example, the neurons in the nucleus accumbens lose their adaptive flexibility and their ability to respond to signals from the prefrontal cortex. Normally, low levels of stimulation would induce long-term depression (LTD) while high levels of stimulation would induce long-term potentiation (LTP). These are long-term changes in the strength of a synapse, which allow the brain to change with learning and memory. When long-term potentiation and long-term depression are no longer possible, memory and new learning in response to messages from the prefrontal cortex are diminished.

Given this absence of flexible responding, animals extinguished from cocaine self-administration (when a lever they had pressed to receive cocaine ceases to provide cocaine) are highly susceptible to cocaine reinstatement if a stressor is presented or if a signal appears that suggests the availability of cocaine. This cocaine reinstatement is associated with high levels of glutamate in the nucleus accumbens, so Kalivas reasoned accurately that lowering these levels would be associated with a lesser likelihood of cocaine reinstatement.

The drug N-acetylcysteine (NAC), which is available from health food stores, decreases the amount of glutamate in the nucleus accumbens by inducing a glutamate transporter in glial cells that helps clear excess synaptic glutamate. In Kalivas’ research, NAC prevented cocaine reinstatement, cocaine-induced anatomical changes in spine shape (bigger, stubby spines), and the loss of long-term potentiation and long-term depression in the nucleus accumbens.

The findings on NAC in animal studies led to a series of important small placebo-controlled clinical trials in people with a variety of addictions, and positive results have been found using NAC in people addicted to opiates, cocaine, alcohol, marijuana, and gambling. It also decreases hair-pulling in trichotillomania and reduces stereotypy and irritability in children with autism.

NAC also appears to be effective in the treatment of unipolar and bipolar depressed patients in placebo-controlled trials by Australian researcher Michael Berk. Thus, NAC could be useful for patients with affective disorders who are also having difficulties with comorbid substance use.
Some antibiotics (that are not commonly available) also induce the glutamate transporter and glial cells of the nucleus accumbens, offering a potential new approach to treating some addictions.

Tags: <addictions, cocaine, glutamate, N-acetylcysteine, nucleus accumbens>

High Risk of Suicide Attempts in Bipolar Disorder with Substance Abuse

October 7, 2014 · Posted in Potential Treatments, Risk Factors · Comment

At the 2014 meeting of the International College of Neuropsychopharmacology, researcher Rieva et al. reported that 60% of bipolar patients with comorbid alcohol abuse have attempted suicide, and 48% of bipolar patients with cocaine abuse have attempted suicide. Thus, both of these comorbidities deserve specific attention and treatment. Unfortunately there are currently no Federal Drug Administration–approved drugs for bipolar patients with these comorbidities. The most promising treatments, based on data in patients with primary addictions, are the nutritional supplement N-acetylcysteine and topiramate, which have both performed better than placebo in studies of alcohol and cocaine abuse disorders.

Tags: <bipolar disorder, comorbidity, N-acetylcysteine, substance abuse, suicide, topiramate>
It appears that the nutritional supplement n-acetylcysteine (NAC) may be useful for people who want to quit smoking. Researcher Eduardo S. T. Prado et al. reported that compared to placebo, NAC decreased the number of cigarettes a patient smoked per day and the amount of carbon monoxide they exhaled. Participants in the study took 1,500mg of NAC twice a day.

Editor’s Note: It looks as though NAC is effective in most addictions, including gambling, cocaine, heroin, marijuana, alcohol, and now smoking. Since it also helps depressed mood and anxiety in patients with bipolar illness (a finding first reported by researcher Michael Berk et al. in 2008), and can improve trichotillomania and obsessive compulsive disorder (OCD), it could be an important adjunctive treatment for many patients with bipolar illness who also suffer from many of these comorbidities. The usual dose in most of these studies was 500mg twice a day for one week, then 1,000mg twice a day thereafter, as opposed to the doses of 1,500mg twice a day that were used in the smoking study.

Tags: <addictions, N-acetylcysteine, nicotine, smoking>
The N-acetylcysteine Story: A New Potential Therapy for Bipolar Illness and Substance Abuse

April 29, 2010 · Posted in Potential Treatments · 2 Comments

N-acetylcysteine (NAC), a readily available substance from health food stores, is able to reestablish glutamate homeostasis (regulation and balance) in the reward area of brain (the nucleus accumbens), reported Peter Kalivas of the University of South Carolina at the “Staging neuropsychiatric disorders: Implications for idiopathogenesis and treatment” meeting in Mojacar, Spain this past November. Kalivas reported that NAC appears to be effective across a spectrum of addictions, including cocaine, heroin, alcohol, cigarette smoking, and gambling.

How NAC works in the brain

Even more remarkably, NAC also appears to have positive effects in placebo-controlled studies in the treatment of patients with bipolar illness, report Mike Berk and colleagues, who are studying the same substance in Australia. Compared with placebo, patients taking adjunctive NAC showed improvement in all outcome measures, especially depression, after 3 and 6 months. In another article, also published in Biological Psychiatry in 2008, Berk’s research group demonstrated that NAC improved some negative symptoms of schizophrenia. NAC has also shown positive effects in trichotillomania and on nail-biting, suggesting that it has a variety of potential clinical uses in conditions associated with pathological compulsive behavioral patterns.

Read more
Glutamate is the major excitatory neurotransmitter in the brain, while GABA is the main inhibitory neurotransmitter. Too much or too little of one or the other can lead to an imbalance in neuronal communication. In a 2012 study by Schmaal et al. published in the journal *Neuropsychopharmacology*, cocaine-dependent patients were found to have high levels of glutamate in the dorsal anterior cingulate cortex. A single administration of N-acetylcysteine (NAC) at a dose of 2400mg lowered these levels.

Healthy (non-addicted) participants who received the same administration of NAC did not show the same drop in glutamate levels.

The study also observed levels of impulsivity in the patients. Higher baseline levels of glutamate were associated with greater impulsivity, and both higher baseline level of glutamate and greater impulsivity were predictive of a larger drop in glutamate levels following NAC administration.

The researchers suggest that these findings may eventually be used in the treatment of cocaine-addicted people, since abnormal glutamate levels are related to risk of relapse. In drug-dependent rodents, NAC was found to normalize hyper-responsive glutamate release in the nucleus accumbens (the brain’s reward center) and prevent cocaine-reinstatement or relapse.

*Editor’s Note: When these data from the lab of Peter Kalivas at the Medical University of South Carolina were initially collected, it was thought that NAC’s effect on a cystine-glutamate exchanger in the nucleus accumbens explained its treatment success, but new data suggest that NAC may actually facilitate glutamate clearance by increasing the number of glutamate transporters in glial cells.*
Michael E. Hoffer et al. reported in the journal *PLosOne* in 2013 that **veterans with blast-induced mild traumatic brain injury had a better acute outcome when they were given the antioxidant N-acetylcysteine (NAC) within the first 24 hours after the trauma** versus when they were given placebo during the same period. Forty-two percent of those receiving placebo had a good acute outcome, while 86% of those receiving N-acetylcysteine had a good acute outcome. Memory loss, sleep disturbance, dizziness, and headaches all improved more in the N-acetylcysteine group. NAC’s benefits diminished when it was given 3 or 7 days after the trauma.

*Editor’s Note: These data add to the growing list of neuropsychiatric syndromes in which NAC has shown efficacy. These include schizophrenia, bipolar depression, unipolar depression, cocaine and heroin addiction, gambling addiction, trichotillomania (compulsive hair-pulling), obsessive-compulsive disorder (as an adjunctive treatment to SSRIs), and improvement in irritability and stereotypy (repetitive behaviors) in children with autism.*

*Given what appears so far to be a relatively benign side effects profile for NAC, and the potential for severe consequences from traumatic brain injury (TBI), a case for wider use of NAC (for example in emergency rooms) might be made.*

*The mechanisms of action of NAC in different syndromes remains to be clarified.* Researcher Michael Berk used NAC in schizophrenia and bipolar disorder and more recently in unipolar depression because it has antioxidant properties. Peter Kalivas found that NAC can normalize glutamate in the reward area of the brain through actions on the cystine-glutamate exchanger, and it also increases clearance of glutamate by increasing the glutamate transporter in glial cells. NAC decreases the amount of cued glutamate release in a part of the brain called the nucleus accumbens, which may be helpful in recovery from pathological habits. NAC also has anti-inflammatory and perhaps neuroprotective effects, and it increases brain-derived neurotrophic factor (BDNF), which protects neurons and is important for long-term learning and memory. Which of these many actions is important in the treatment of PTSD is not yet known.

Tags: <N-acetylcysteine, ptsd, trauma, traumatic brain injury>
We reported in 2014 that researchers Ahmad Ghanizadeh and Ebrahim Moghimi-Sarani had found that the over-the-counter nutritional supplement n-acetylcysteine (NAC) added to the atypical antipsychotic risperidone reduced irritability in autism more than placebo added to risperidone.

A randomized, double-blind, placebo-controlled clinical trial published by M. Nikoo and colleagues in *Clinical Neuropharmacology* in 2015 replicated these results. Forty children with autism disorders aged 4–12 years were randomized to receive either risperidone plus NAC or risperidone plus placebo. Risperidone doses were between 1 and 2 mg/day, and NAC doses were 600 to 900 mg/day. By the end of the 10-week study, those children who received NAC had significantly greater reductions in irritability and hyperactivity/noncompliance than those who received placebo.

*Editor’s Note: Three placebo-controlled studies have supported the efficacy of NAC in autism. One 2012 study, by A.Y. Hardan in Biological Psychiatry, evaluated monotherapy with oral NAC. In the other two, NAC was added to treatment with risperidone.*

Tags: <autism, irritability, N-acetylcysteine, risperidone>
In a 2013 study of 40 children and adolescents with autism spectrum disorders published by Ahmad Ghanizadeh and Ebrahim Moghimi-Sarani in the journal *BMC Psychiatry*, the combination of the over-the-counter nutritional supplement *N*-acetylcysteine (NAC) and the atypical antipsychotic risperidone alleviated irritability more than the combination of placebo and risperidone. Side effects were mild. The data extend 2012 observations by A.Y. Hardan et al. in which NAC improved irritability and stereotypy (repeated behavior) in autism more than placebo did.

The two studies taken together support the effectiveness of NAC prescribed either alone or in conjunction with an atypical antipsychotic for the treatment of autism.

Tags: <a>autism</a>, <a>irritability</a>, <a>N-acetylcysteine</a>, <a>risperidone</a>
The antioxidant N-acetylcysteine (NAC), which can be found in health food stores, seems to be effective for irritability and repetitive behaviors in children with autism. In a small controlled study that was published by Hardan et al. in the journal Biological Psychiatry in 2012, 33 mostly male children with autism (aged 3-12 years) received either placebo or NAC at doses of 900mg daily for 4 weeks, followed by 900mg twice daily for 4 weeks, then 900mg three times a day for 4 weeks. Beginning in week 4, the children receiving NAC showed significantly improved irritability scores, and a trend for improvement in repetitive behaviors.

Social responsiveness did not improve significantly, but the children receiving NAC did show some improvement in some areas of social behavior, such as social cognition and autism mannerisms.

There were few side effects associated with NAC. The most significant were gastrointestinal side effects, but these were mild, especially when compared with the side effects associated with FDA-approved treatments for autism, such as the atypical antipsychotics risperidone and aripiprazole.

The authors of the study plan to expand their research in a study of more than 100 children with autism.

Editor’s Note: It should we previously summarized this study in the BNN based on research presented by Fung et al. at a meeting of the American Academy of Child and Adolescent Psychiatry two years ago. The study has now been published.

Tags: <autism, children, irritability, N-acetylcysteine, stereotypy>
N-acetylcysteine Improved the Irritability Associated with Autism

November 1, 2011 · Posted in Potential Treatments · Comment

At the 57th Annual Meeting of the American Academy of Child and Adolescent Psychiatry (AACAP) in October 2010, Lawrence Fung of Stanford University reported that N-acetylcysteine (NAC), a compound sold over-the-counter in health food stores, improved irritability and other symptoms of autism in children aged 8 to 17. In this double-blind, randomized study of NAC compared with placebo, the children who received NAC were treated with 900mg once a day for four weeks, then 900mg BID (twice a day) for four weeks, and finally 900mg TID (three times a day) for the last four weeks of this three-month study. These doses significantly improved irritability and stereotypy (repetitive behaviors) compared with placebo. Side effects were minimal.

Editor’s note: The potential for a safe compound such as N-acetylcysteine to show efficacy in autism is striking. Currently only risperidone and aripiprazole are FDA-approved for effectiveness treating irritability in autism. There has also been a positive study of valproate compared with placebo in autism, although it is not FDA-approved for this purpose.

Most double-blind, placebo controlled clinical trials of NAC have been in adults, so this is the first report that suggests NAC can safely be used in children.

NAC’s ability to improve irritability in autism raises the possibility that this drug may be useful in the treatment of irritability and repetitive behaviors in bipolar disorder, particularly since N-acetylcysteine has also been reported to improve mood, especially depression, in adults with bipolar disorder in the studies of Mike Berk and colleagues published in Biological Psychiatry in 2008.

This study adds to the evidence that suggests N-acetylcysteine may reset the brain’s habit system in the ventral striatum (also called the nucleus accumbens), which is involved in the assessment of the reward value of a variety of substances of abuse and behaviors (as described in BNN Volume 14, Issue 1 from 2010). NAC improves a number of habit-related syndromes including cocaine, heroin, and gambling addictions, trichotillomania (compulsive hair-pulling), and now the irritability and stereotypic behaviors of autism.

In light of NAC’s profile of efficacy and safety, systematic exploration of the drug in childhood-onset bipolar illness is indicated. We are aware of at least one group that is planning such a study.

Tags: adolescents, autism, children, irritability, N-acetylcysteine, stereotypy>