THE AFIB REPORT
Your Premier Information Resource for Lone Atrial Fibrillation
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VIRTUAL LAF CONFERENCE

Proceedings of 23rd Session
January 26th, 2004 –

SUBJECT: Magnesium, NMDA Receptors & LAF

I'm new to the boards and relatively new to afib having been diagnosed about 9 months ago. I now realize I had my first episode in June 2001 and then went until March 2003 before a second episode, 5 weeks later in April a third, and two more just last month when I had the flu. I just read Hans Larsen's book and found it very informative. I've been taking Inderal since 1989 for high blood pressure and they added accupril about 2 years ago - well controlled, no other risk factors - all tests were good. They mentioned warfarin after the December episodes but I want to try the natural approach first. I do take an aspirin daily and have used vitamin E and selenium for several years. My question for those of you more knowledgeable and experienced than I concerns magnesium supplements. I have taken a calcium/magnesium supplement sporadically in the past but about 3 weeks ago, after all my research, decided to start taking 400mg. of magnesium (as oxide and gluconate). I have noticed an increase in ectopic beats and PACs since starting these and was wondering if anyone else has found magnesium to INCREASE palpitations, or perhaps this is some coincidence. I stopped them a couple days ago and the palpitations have calmed down. I have changed nothing else. From everything I have read, this doesn't make sense. I would appreciate anyone's advice or comments. Thanks alot.

Kay

Kay:

I too have also experienced dramatic increase of PACs which were constant for more than two weeks which I can only attribute to excessive overload of Magnesium. I was taking in excess of 2,500 mg for nearly three months. When cardio suggested I take magnesium he did not say how much. I was under impression any excess would be thrown off. I was wrong. Severe continual PACs resulted in trip to ER and Holter Monitor which confirmed no AF but PACs which I was told were not dangerous. Cardio disagreed that Magnesium overload could have caused, but see re excessive intake:

http://www.cc.nih.gov/ccc/supplements/magn.html#issues

Nevertheless, after I ceased magnesium for about four days and then took back up to 1,000 mgs a day PACs have decreased to very few a day and still no AF. So I am convinced I overdid it.

Stephen

Stephen - I'm glad you lowered your dose of magnesium.... but are you sure you are/were really taking 2500 mg....of elemental magnesium?

Most people can't tolerate much more than 800 - 1000 mg. of elemental magnesium without experiencing bowel intolerance.

It could be the form you were taking..... magnesium oxide is very poorly absorbed so it might be possible to reach the numbers you mention.

I'm not suggesting anyone take magnesium if it gives them more PAC's but most of us find magnesium very calming to the heart .... magnesium glycinate is specifically complexed to eliminate bowel intolerance yet provide the benefits of magnesium due to its bioavailability.

Some of us are now using another complexed form - magnesium taurate which can be taken at even lower doses...

Michael's post on the other minerals is very important..... we need the balance of the electrolytes involved in cardiac tissue function, although most afibbers do not do well with added calcium. Peggy, however, is reporting good results which points out once again, the biochemical individuality of us all. We are all at various stages of age, nutritional deficit, stress levels and a plethora of other influences that will change how these minerals work for us individually.

It is good to keep experimenting to find the balance that works for you, personally, by using the others' experience merely as a guideline.

It is also my experience that most doctors (unless holistic) will not recognize the benefit of any supplements such as minerals for heart function so it doesn't surprise me, the comments you're relayed here.

Magnesium overload will result in depression, lethargy, and other complications and is considered rare just because when we take too much, the body throws of the excess by producing diarrhea.... and everyone can recognize that symptom, and back off on their dosage.

If you aren't sure about the elemental magnesium portion.... here's a repeat of an old post I recently brought forward again....

Author: Theo (---.w81-249.abo.wanadoo.fr)
Date: 11-01-03 23:59

Magnesium oxide 1000 mg (1 g) = 550 mg elemental magnesium
Magnesium citrate 1000 mg = 100 mg elemental mg
Magnesium aspartate 1000 mg = 80.44mg elemental mg
Magnesium glycinate 1000 mg = 110.70mg elemental mg
Magnesium taurinate 1000 mg = 150 mg elemental mg
Magnesium arginate 1000 mg = 60 mg elemental mg

Jackie

Jackie, i think i need to clarify what i am doing with regard to calcium. Several months ago [maybe 4-5?] i jacked up my calcium intake in order to reduce my blood pressure, and was taking about double the suggested dose, and sure enough i was able to cut my lisinopril dose by half and still stay around 120/70, give or take a few points in either direction. I conveniently 'forgot' what i had read about calcium being bad for afibbers. When i told people here what supplements i was taking, i neglected to mention the calcium. I think i was classifying it as bp medicine and just not thinking of it when i thought about afib.

Then i got 3 mild episodes of afib, the first ones in some months. I did some wailing and gnashing of teeth here on the bulletin board, and then sat down and reassessed everything i had been doing, and it dawned on me that those calcium tablets might have something to do with this. I dropped them completely and had no more afib from that day to this.

Over the course of about a month, my bp began to climb so that i was forced to resume full 10 mg doses of the lisinopril, and even that was giving readings of 135/85 or so, and that is a little too high. Not really dangerously high, but too high. I added back one 600mg calcium tab, and kept that level for nearly a month, and got no afib out of it. During this time i added taurine to the mix too, the 6g a day dose that you and others felt was too high. As i have mentioned, i hoped it might reduce my bp and my cholesterol, while controlling the Mg runs.

Then i went to 2 of those calcium tabs, and cut back the taurine to 4g instead of 6. Still no afib. Gradually the bp dropped back to around 120/70, still with the 10mg lisinopril. This morning when i took my bp, it was 106/61. That's a little low, i get lightheaded at that level. I will try cutting back to 5 mg lisinopril and see what happens.

Comments are welcome, as i have said above. Probably there are too many ingredients to this soup to say what is doing what, but if the half dose of lisinopril works out, i will drop the calcium and see if the bp rises again, and get a little clue that way.

Peggy

Jackie:

Yes, I was taking Chelated Magnesium in groups of four to five tablets throughout the day and during the night for about three months with and without meals. Each four = 400 mg. And, this does not count the three Cal Mags I took every morning which represents another 500 mg a day of magnesium. So I may have easily exceeded 2,500 mg. I was ordering subject vitamins by the carton of 12 bottles of 100 tablets each. Yes, diarrhea was substantial and I in fact I lost nearly ten pounds. AF was held at bay but after three months PACs became permanent until a few days after I reduced dosage to present 900 mg a day. I can think of no other reason for reversal of PACs. Only med change was doubling of Diovan from 160 mg to 320 mg for BP control and use of Lexapro for anxiety. Whatever, PACs are now very few and acceptable,

Stephen

Jackie:

I should also mention the ER's blood test ($2,100 of total $5,290 for four hour ER visit) indicated blood level of magnesium in me at maximum level of 2.8. The more PACs I had which were continual with no breaks for more than a week were greeted by me downing even more magnesium. I ceased intake when I read on this website a posting by person who noticed far less PACs when she missed taking her magnesium daily dosage. That is when I researched and found over dosage can cause irregular heart beat which to me means PACs which were confirmed by ER and cardio but who both attributed to anxiety. But, how could anxiety sustain PACs during sleeping hours also.

Stephen

Stephen - diarrhea from the magnesium is a sure sign you are on overload....and with diarrhea, you are losing not only magnesium but other essential electrolytes such as sodium and potassium. With low electrolytes - you get more PAC's and often arrhythmia.

With the Cal Mag, you could have actually been getting too much calcium which tends to be excitatory for afibbers...I found when took Cal Mag, I would always have full blown afib.

Blood tests - serum magnesium - do not give a measurement of what is actually in the cell where the important work of magnesium is done. Serum evaluations are mostly meaningless.

In any event, I'm really glad to know it has slowed down. We each have to experiment and determine what works best for our own individual situation.

Stay healthy.

Jackie

Elsewhere on the BB there was a discussion of the need to take potassium as well as magnesium. My experience is that about 500 mg of magnesium supplement (other than magnesium oxide which is poorly absorbed) daily, in divided doses, plus 1500 mg of potassium daily, again in divided doses, works very well for eliminating PACs and afib. I depend on non-supplement dietary intake of calcium and sodium. All four of these alkaline minerals, taken in some balance, are required for proper cardiac function.

Michael in SF

It seems to me Michael is right about that. I take 800mg a day of magnesium glycinate from Carlson Labs, and currently 2g taurine for the diarrhea this can cause, but i also drink 2 cups a day of low sodium V8 juice which contains 900 mg potassium in an 8 oz portion, and have had no negative effects at all, and very few, very mild afib events. None at all since i cut out calcium.

Peggy

Hi Kay -

Welcome! Magnesium has caused a few to have increased PACs and other ectopics, but most, like myself have found the opposite to be true.

You mentioned that your magnesium is in oxide and gluconate form. Usually, when there are two forms of magnesium (or any element) in the supplement, the first compound mentioned on the label is the one that makes up, by far, the largest percentage of that supplement. Magnesium oxide is almost useless because it is not at all absorbable. Magnesium glycinate or magnesium taurate are the most absorbable forms and also don't cause loose bowels, if you've experienced that problem at all.

Good luck.

Lorraine

Hi Kay,

For me Mg glycinate increases the severity of my afib, whereas Mg taurate (thanks to Jackie who told me about Mg taurate) calms the afib.

I have been studying abstracts on Medline to try to find out why that is the case for me. As some of you may recall, I had my first attack of afib when the University in which I was a full (of it) Professor inadvertently sprayed methamidophos (an organophosphate pesticide affecting acetylcholinesterase) into the room in which I was teaching. I believe beyond all reasonable doubt that the pesticides caused the arrhythmia and even have a letter from Calkins (Hopkins EP) substantiating this inference (but then of course a doctor's letter is merely a summary with appropriate Latin labels of the patient's report). I bring up my etiology to explain why I have been reading a literature considering chemical sensitivity. By the by, organophosphate reactions (like afib) can occur 7-12 hours after exposure.
My search has led me to a recent article by Pall, M the abstract of which can be found in Medline. Basically, Pall, who is a biochemist, argues convincingly that chemical sensitivity involves excess NMDA activity and lo and behold I have found that Mg glycinate, but not MG taurate, increases NMDA activity.

I am very ill equipped to be a biochemist or cell biologist which is what is necessary to really understand the Pall

hypothesis. Maybe someone on this bulletin board can study the articles to see what an educated person would think of them. Meanwhile, I am trying to quell my college freshman attitude which consists of claiming that all my illness is due to excess NMDA activity (i.e. to a boy with a hammer, everything looks like a nail).

I hope to post more details before my surgery in February with Dr. Natale and meanwhile I hope this missive helps someone. Pardon my spelling- I am in a rush!

Lynn (known on medline a Penner MJ)

Lynne

Very interesting. Unfortunately I am not in any way equipped to be a biochemist either. What did pique my interest was the NMDA receptors you mentioned. I am also the boy with the hammer when it comes to NMDA channels. Everything to date that I have avoided as triggers affects the NMDA receptors.

The major ones are MSG and aspartame. By cutting out all forms of free glutamate I have stopped AF. I tried taking Mg but not as taurate but AF came back. Now they say that taurine is the supplement to take for MSG sensitivity - obviously because it does not work on the NMDA channels. WOW!!

As for organophosphate poisoning - in the past I have been exposed to sheep dip - it is only recently that the OP's in this have become widely talked about. When I helped dip sheep no one took any precautions and my clothes my hands my everything got covered in it - and what a smell.

My experience is that even if I get a small amount of MSG I will react with AF. So rather than blaming my AF on a genetic predisposition or something - it could be down to prior OP poisoning that has maladjusted the NMDA channels.

I am hoping Richard will pick up on this - he has a way with understanding biochemistry that totally escapes me.

All the best

Fran

Hi Fran,

It sounds as if you and I may have the same underlying cause for afib. We both need help with the NMDA channels and here is a summary of what Pall recommends for us:

1. inhaled glutathione. I am using this now having ordered it from Key pharmacy (1-800-878-1322 for the USA anyway).
2. Hydroxycobalamin injections (B12). I start this on Tuesday after my doctor teaches me how to inject myself.
3. General antioxidants
Vit C (250 mg once per day)
Mixed tocopherols 200 IU once per day
Selenium 200mcg once per day
COQ10 75 mg once per day in the morning
alpha lipoic acid 600 mg day
4. Components of SOD
zinc 15 mg per day
Copper 1 mg per day
Manganese 1 mg per day
5.Compounds related to peroxynitrite and its breakdowns
Mg 125 mg per day (I take 825 myself)
Betaine (methyl donor) 500 mg per day
6. Scavangers of peroxynitrate and its breakdown products

Gingko, 60 mg twice a day
Silymarin 70 mg twice oer day
Bilberry extract 60 mg twice per day
Cranberry extract 200 mg twice per day
Carotenoid mixture 5 mg lycopene, 5 mg beta carotene, 5 mg lutein once per day.

Key pharmacy has a pill with Pall's ingredients in it in case anyone is interested. As for me, on coumadin, I can't take the gingko so I have assembled all of the other ingredients except the cranberry as per a discussion on this chat group. For Fran and anyone who reacts to MSG, Pall's model and recommendations may be an important insight. Yes Fran, MSG is specifically discussed by Pall as increasing NMDA activity.

Again, I hope this helps someone.

Lynn

Thanks for the above Lynn

Do you know if this regime cures the underlying problem? By curing I mean do you take these supplements for a course then the NMDA receptors are back to normal - or do they work as short fix - to enable the NMDA receptor to normalise for as long as the supplements are in the body?

I will need to weigh up the pros and cons as to whether this specific supplement way is the way for me to go, or whether I am better off eating the way I do - which can get a bit of a pain when away from home.

I will need to check whether there is any way I can get a private Dr to treat me with this method (and how much it would cost) - there is no way in the UK I would get this on the NHS. Fantastic to get something new to work on with regards to a now obvious cause for AF.

Fran

Lynn - thanks for posting this. Important information here. I'm looking into the NMDA; complicated. I'm sure Richard will help out here.

As I've said before, I wish you well with your ablation. If anyone can help, Dr. Natale is the man.

I've lined up the angels and they are ready and waiting for you. I'll be sure to send them into action for you.

Thinking of you.

Jackie

Lynn,

Thank you for uncovering this subject of the role of sensitized NMDA receptors. I think it could be a very important clue. In the recent LAF Survey (LAFS V) I observed that 20% of 165 responding afibbers reported exposure to volatile industrial solvents, pesticides, crop-dusting chemicals or Agent Orange prior to their LAF diagnosis (The AFIB Report, September 2003).

What is perhaps even more important is the finding that afibbers who reported such exposure tended to have significantly longer episodes than did afibbers not reporting such exposure (median: 15 hours vs 6 hours); the difference was statistically significant. This observation would tie in with Pall's finding that the sensitivity of the NMDA receptors increase with continuing exposure.

Although only 20% of respondents reported exposure it is likely that many afibbers have been exposed without noticing it so the actual percentage of exposed afibbers could be much greater.

Hans

Hi!

Thanks to everyone who replied to my question - I stopped the magnesium a couple days ago and only a few palps. I think I'll try a different brand (other than the oxide which is the first ingredient on the label) I was only taking 400mg. a day so it seems like it wouldn't be over dosing, maybe just not the right one for me. I'm pretty convinced I need to take it though so I'll try a different one in a few days and see what happens. I did notice difference in bowels also so I'm pretty sure it was magnesium bothering me, for whatever reason. Thanks again.

Kay

Kay,

In some people, magnesium can cause problems. I am one of those. I didn't get full blown PACs or Afib, but it clearly gave me an uncomfortable feeling around my heart which went away very soon after I stopped. This was particularly disturbing for me as I have never had any heart related problems until the Afib started. So if you have had this problem or something similar, it was a good idea to stop taking the supplements.

Kerry

Hi Hans,
I agree with your insight that your 20% estimate of the number of people with afib affected by chemicals represents a lower bound on the number of us whose afib is actually triggered by VOCs and other chemicals. Pesticides are especially insidious in this regard because they are often applied without our knowledge and reactions typically occur many hours later. I read somewhere that about 80% of homes in the USA have been treated with chlordane, a potent neurotoxin, which the EPA has now removed from the market.

As to the source of afib, I do think that the mitochondria are very important and that is the thrust of Pall's arguments. I feel a bit uncomfortable though at using so many supplements which are based on ideas rather than on clinical data. Nonetheless, I am doing it. In this regard, Pall recommends 600 mg per day of lipoic acid. Apparently there are two forms, only one of which may be beneficial (the r form see http://www.rala.com for a discussion and then check out Medline). Does anyone know if the form of the ALA actually matters?

I do think that the inhaled glutathione recommended by Pall is helping me. I can measure my afib rate on my heart math before and after the inhalation and the heart rate does calm down quite a bit (about 5-10 bpm) after inhalation. However, I do not yet have enough data to be sure that this is a statistically significant effect rather than just episodic fluctuation in the afib (which I have all the time).

Best to all of you,
Lynn

Hello All,

WHOA!! I'm taken back by all this. I feel like I've been gone from planet Earth. It's really good to hear from you Lynn, and I certainly hope all the supplements help you. I'm amazed about the correlation you have made with the NMDA receptors, as well. I'll have to do an about face, and start looking into that. I got really involved in studying about lithium,

so I'll put that on the back burner for now.

How do you get to the study by Pall? Is there a direct link or did I miss it?

Fran, I'm humbled by your opinion of me, but I feel you have a much better understanding than I do about all of this. I really stumble through much of the material, especially PC's posts. I've been having to get my old college chemistry books back out and oil the rusty parts in my brain. Remember; If you don't use it, you lose it.

Lynn was the first one that helped me recognize that I could have a chemical sensitivity to organophosphates. On many occasions while playing golf, I would go out of rhythm, and my first episodes occurred while living on a golf course, and they are notorious for using this chemical. Since then, I do not golf when fresh chemicals have been put down. I also went out of rhythm when eating a nonorganic apple, and they are the worst for this, as well.

Anyway, I'll definitely get back, with what I find.

Richard

I wasn't absolutely sure of what I read, so I went back, and sure enough I find this very strange. I was very focused on lithium and inositol, because of thinking it was the inositol I had a reaction to. If you remember, I had a reaction to the supplement within 15 min., so there was no doubt it was either choline, inositol, or phosphatidylserine. Without getting too much into that topic tonight, here are a couple of studies that were in my saved data, for my future posting.

The therapeutic mechanisms of lithium for treating bipolar mood disorder remain poorly understood. Recent studies demonstrate that lithium has neuroprotective actions against a variety of insults. Here, we studied neuroprotective effects of lithium against excitotoxicity in cultured cerebral cortical neurons. Glutamate-induced excitotoxicity in cortical neurons was exclusively mediated by NMDA receptors. Pre-treatment of cortical neurons with LiCl time-dependently suppressed excitotoxicity with maximal protection after 6 days of pre-treatment. Significant protection was observed at the therapeutic and subtherapeutic concentration of 0.2–1.6 mm LiCl with almost complete protection at 1 mm. Neuroprotection was also elicited by valproate, another major mood-stabilizer. The neuroprotective effects of lithium coincided with inhibition of NMDA receptor-mediated calcium influx. Lithium pre-treatment did not alter total protein levels of NR1, NR2A and NR2B subunits of NMDA receptors. However, it did markedly reduce the level of NR2B phosphorylation at Tyr1472 and this was temporally associated with its neuroprotective effect. Because NR2B tyrosine phosphorylation has been positively correlated with NMDA receptor-mediated synaptic activity and excitotoxicity, the suppression of NR2B phosphorylation by lithium is likely to result in the inactivation of NMDA receptors and contributes to neuroprotection against excitotoxicity. This action could also be relevant to its clinical efficacy for bipolar patients.
http://www.jneurochem.org/cgi/content/abstract/80/4/589

Stress elevates cortisol, which in turn ups the excitatory neurotransmitter glutamate, which increases calcium influx into the neuron and activates certain calcium-dependent “death” enzymes. Cortisol may also reduce the neuron’s capacity to take energy-sustaining glucose into the cell so it doesn’t have the strength to deal with a subsequent crisis. Another casualty may be the glia, the “other” brain cell, once thought of as mere mind-glue but now recognized as an active partner of the neuron. One of its functions is thought to be clearing glutamate from the synapse.

Basically, Dr Manji explains, the cells can’t handle the load. Their atrophy and death tends to isolate neurons, affecting their ability to connect to and communicate with other neurons. The good news is that some of the meds we are taking may actually prevent and even reverse these processes

With new gene technology, Dr Manji and his colleagues started experimenting with lithium and Depakote (I believe this is valproic acid) on brain cell tissue, and found to their surprise these two completely different medications indirectly affected some of the same cell pathways associated with cell survival and death. One protective protein that utilizes these pathways is Bcl-2, which in one experiment was doubled by lithium and Depakote administration. Subsequent experiments on rats found lithium mitigated the effects of lab-induced stroke and led to the growth of new neurons in the hippocampus. When Dr Manji asked Dr Drevets to revisit his study, it was found that those patients on lithium or Depakote did not show brain atrophy. More recently, a study on human patients with bipolar found lithium increased

overall brain grey matter.
http://www.namiscc.org/News/2003/Newsletters/Spring/McManVol5-9.htm

I really find this a very odd coincidence, especially in light of the fact that 3 out of 3 of us were low in lithium. As you all may know, I started taking ConcenTrace ionic minerals several days ago. There is 1.5 mg of lithium that I get throughout the day, as I put drops in each glass of water that I drink. I can't explain it, and it could be a placebo effect, but I'm feeling even better, and have no activity of any weird beats. This is very interesting, to say the least.

Richard

Here's one other study:

Chronic lithium treatment robustly protects neurons in the central nervous system against excitotoxicity by inhibiting N-methyl-D-aspartate receptor-mediated calcium influx.

Nonaka S, Hough CJ, Chuang DM.

Section on Molecular Neurobiology, Biological Psychiatry Branch, National Institute of Mental Health, National Institutes of Health, 10 Center Drive, MSC 1272, Bethesda, MD 20892-1272, USA.

Lithium is the most commonly used drug for the treatment of manic depressive illness. The precise mechanisms underlying its clinical efficacy remain unknown. We found that long-term exposure to lithium chloride dramatically protects cultured rat cerebellar, cerebral cortical, and hippocampal neurons against glutamate-induced excitotoxicity, which involves apoptosis mediated by N-methyl-D-aspartate (NMDA) receptors. This neuroprotection is long-lasting, occurs at therapeutically relevant concentrations of lithium with an EC50 of approximately 1.3 mM, and requires treatment for 6-7 days for complete protection to occur. In contrast, a 24-h treatment with lithium is ineffective. The protection in cerebellar neurons is specific for glutamate-induced excitotoxicity and can be attributed to inhibition of NMDA receptor-mediated calcium influx measured by 45Ca2+ uptake studies and fura-2 fluorescence microphotometry. The long-term effects of lithium are not caused by down-regulation of NMDA receptor subunit proteins and are unlikely related to its known ability to block inositol monophosphatase activity. Our results suggest that modulation of glutamate receptor hyperactivity represents at least part of the molecular mechanisms by which lithium alters brain function and exerts its clinical efficacy in the treatment for manic depressive illness. These actions of lithium also suggest that abnormality of glutamatergic neurotransmission as a pathogenic mechanism underlying bipolar illness warrants future investigation.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?holding=npg&cmd=Retrieve&db=PubMed&list_uids=9482940&dopt=Abstract

Hans, being that lithium has to do with the NMDA receptors, I found it relevant to post here. Do you want me to post about lithium's effects on inositol and Ca influx in the heart here, or would you prefer me to wait and post on the BB?

Richard

Richard,

As there would seem to be a connection between NMDA receptors and lithium it would be OK to post your lithium observations in the Conference Room - but whatever you prefer.

Hans

Hi Richard,

In answer to your question, I started with the fact that I couldn't tolerate MG glycinate but could tolerate MG taurate. I wondered why. I assumed that it was some kind of chemical sensitivity because I know that the OP exposure started

my afib and led to other intolerances as well. Also, several years ago I paid (gasp) Clem Furlong at the University of Washington in Seattle $500 to test me and I have the Q-Q polymorphism which makes me more sensitive to OPs and other associated chemicals than do other polymorphisms.

Coincidentally, I have a friend with Parkinson's who worked in a building treated with pesticides. Apparently OP exposure increases the chance of Parkinson's by about a factor of 5. Anyway my friend and others are suing and as part of that episode, she went to see Kaye Kilburn, an MD ay USC medical school, and he (yes a he despite the name) mentioned the efficacy of inhaled glutathione. I had gone to Gersten, as you recommended Richard, and knew that I was low in glutathione. Anyway I searched Medline for glutathione and somehow came up with Pall's article on chemical sensitivity. It looked so good to me that I contacted a colleague at the U of Maryland who was also injured by the pesticide exposure there. He is a cell biologist and thought that Pall made a cogent argument. So I changed the Mg to the taurate form (thanks again to Jackie) and, when I tolerated it, I posted the NMDA information here for all to see. However, as I mentioned already, I am not really able to evaluate Pall's work. It is just not my field- I have no real fix on whether it is a brilliant idea or not.
Also let me reiterate that I spoke with Pall and his recommendations are not based on clinical trials but on the logic of how cells work.

I spoke with my GP about the Pall work and he mentioned that memantine (SP) is a NMDA channel inhibitor which was just approved for Alzheimer's. He is willing to prescribe it for me but as of now I have not taken it. I prefer to start with Pall's lists of supplements.

To see how pervasive the NMDA channels have become in the medical literature enter NMDA and heart and you will learn that NMDA excess activity is implicated in CHF, Alzheimer's etc. From an outsider's view NMDA is medically trendy right now.

Again, the leap from Pall's article to our afib is very large by NIH grant-getting standards.
I hope that someone on our chat group can determine whether the NMDA hypothesis is likely to help us or not.
I feel that I should end with a deep comment (well, well)

Lynn - whoseablationisFeb20withNataleinMarin

For those of you who would like to study Martin Pall's articles they can be found at:

http://ehpnet1.niehs.nih.gov/docs/2003/5935/abstract.html

and

http://www.fasebj.org/cgi/content/abstract/16/11/1407

you can print out both articles as a .pdf file.

I am still very intrigued by the possibility that LAF could be yet another manifestation of MCS (multiple chemical sensitivity). However, whenever a new hypothesis such as this comes up we still need to ask two fundamental questions:

1. What mechanism operates during the actual afib episode to reduce the sensitivity of the NMDA receptors to the extent that after an episode most afibbers (paroxysmal) are able to go for a while without another episode?

2. How does the NMDA hypothesis explain the very common phenomena experienced by paroxysmal afibbers that there seems to be a build up of something which eventually causes an episode and why do the episodes very often occur at very regular intervals?

By the way, in scanning through my book I came across the finding that excessive peroxynitrite is involved in atrial fibrillation (page 138) - this again fits in with the NMDA hypothesis.

Hans

The NMDA association that Lynn has raised is quite intriguing. We've discussed these receptors before. They bind glutamate and are integral in the vagal regulation of HR by the CNS (specifically the nucleus tractus solitarius or NTS in the medulla oblongata of the brainstem). We've also discussed peroxynitrite and lipid peroxidation of the cell membrane. The superoxide anion, peroxynitrite and hydrogen peroxide are the principle free radicals of reactive oxygen species (ROS). Please read Jackie's recent post in the BB on taurine.

Dr. Pall's hypothesis on multiple chemical sensitivity (MCS) incorporates the following:

Peroxynitrite depletes ATP
Peroxynitrite increases permeability of the blood–brain barrier
Peroxynitrite causes hypersensitivity of NMDA receptors
Nitric oxide stimulates release of the neurotransmitter glutamate
Pesticides and organic solvents may act via muscarinic stimulation

Assume for a moment that there is no MCS to initiate the above process.

Mg++ is known to block the NMDA-receptor
Mg++ is required for the production of ATP
Mg++ is an antioxidant
Mg++ is critical in maintaining cell membrane integrity
Many experts consider Mg deficiency to be the cause of chronic fatigue syndrome (CFS), including no less a luminary than Mildred Seelig
http://www.mgwater.com/clmd.shtml

ROS produced during the inflammatory process result in lipid peroxidation of cell membranes
Muscarinic receptors in the heart are responsible for vagal tone

I think a strong argument can be made to include at least a subset of LAF within the group composed of CFS (?=fibromyalgia or FM), MCS, post traumatic stress disorder (PTSD). Dr. Pall's hypothesis has been invoked to explain all of these.
http://molecular.biosciences.wsu.edu/Faculty/pall/pall_cfs.htm

PC

PC,

Thank you for that link. I agree that we should look at CFS as a possible learning tool, but I don't fall into some of the categories and some are simply not known, as to whether I do or not. I picked out the ones that I know to be relevant, at least to CFS, based on my testings. I'll paraphrase at the end of the quote.

Both cis-aconitate and succinate levels are reported to be elevated in CFS and the enzymes that metabolize these two compounds are known to be inactivated by peroxynitrite (1). (Succinic Acid result 2.6 range <=20 - Cis-aconitate result 13.3 range 1.4-76.8)

Polyunsaturated fatty acid pools are reported to be depleted in CFS and such polyunsaturated fatty acids are known to be oxidized by oxidants such as peroxynitrite.
(Polyunsaturated Fatty Acids according to Laboratory Evaluations:
n6
Linoleic (LA) result 11.8 range 10.5-16.9
Gamma Linolenic (GLA) result .09 range .03-.13
Dihomogamma linolenic (DGLA) range result 1.23 range >=1.19

Arachidonic (AA) result 16 result 15-21 show in yellow range not green
n3
Alpha linolenic (ALA) result .10 range >=.09 show in yellow not green range
Eicosapentaenoic (EPA) result 1.16 range >=.16 shows top of green range
Docosahexpentaenoic (DPA) result 2.95 range >=1.14
Docosahexaenoic (DHA) result 6.7 result >=2.1 high green range)

Biochemical similarities â€“ depletion of glutamine and cystine pools â€“ have been reported in CFS and several diseases characterized by elevated peroxynitrite levels, suggesting a similar biochemical basis for all of these conditions (1). (Glutamine result 68 range 50-70 high green range - Cystine result 5.4 range 4.9-8.0 low green range)

Possibly the most intriguing such mechanism relates to the widespread use of vitamin B12 injections in treatment of CFS (3). (I do take drops of hydroxycobalamin and 2000mcg methylcobalamin, yet my levels of B12 were good intracellularly. I believe that the problem is that I don't have enough sulfur (methionine) to use up my pools of B12 and folate.)

I did show low (red range) in glutathione and lipid peroxides were high (red range) on my oxidative stress panel.

I may be different in that I have flutter and not AF, so my results may not reflect others here. I just don't know. If we think about all the different pathways of diseases, whether it be Alzheimer's, Parkinson's, ALS, or CFS, to name a few, and then we connect some of the dots to AF, it seems that the problem is more to do with the brain connection, rather than atrophy of the heart. The brain just took a bit of a different route in regards to us.

Richard

Hi all, and thanks Lynn for the interesting new topic.

I've stated before that - as is the case for a few others here - mag glycinate INCREASES my ectopy rather than decreasing it. And this after I tested mildly mag-deficient (24hr urine-loading test) a year ago. I'm now about to try mag taurate. Will report in due course.

Mike F.

PC - thanks for bring this to the CR as well.

I've not read any of the articles yet...just printed out now to study....but your last paragraph is intriguing to me since I was diagnosed with FM before afib and eventually CFS after the afib began. And early on in the afib scene, I was contaminated on the golf course with Dursban. While I didn't have afib on the spot... my heart rate and respiratory rate were extremely elevated for a time after.

I'll be reading with interest.

I am pleased that you are continuing to list the positive cellular involvement of Mg++ ..... I also think it is appropriate at the same time to list the magnesium depleters....since most likely, the other reactions are enabled by the depletion factor.

I still think that when it is all said and done, Magnesium Deficiency will be at the core of the etiology for afib.

Diehard,

Jackie

Hello All,

I just want you all to know that I am not advocating lithium, only presenting what I find in my studies. As stated before, I am taking trace mineral drops in my water (30 per day) to achieve a balance of minerals. Here's a couple of links I found of interest.

It is of particular relevance in this context to consider the therapeutic actions of lithium, which has been shown to be effective in the treatment of mania28 and to have a prophylactic action in patients prone to attacks of frequently recurring depression or mania.5 The mechanism of action of lithium is being actively investigated. It is possible that its action is on monoamine metabolism,30 but it may also affect water and sodium metabolism. The action of this salt has a very interesting and unique influence on sodium metabolism and sodium transport across biological membranes. Keynes and Swan (1959) have shown that during an action potential, when sodium normally enters the cell, lithium and sodium enter with equal facility, but lithium is removed from the cell at about one-tenth the rate of sodium. Coppen and Shaw12 investigated the effects of lithium carbonate given in prophylactic doses over a week (on water and electrolyte distributio). They found an average increase of 1.5 liters in TBW and increases in both intracellular and extracellular water. Since we see that total body water, extracellular water and intracellular water increase with clinical recovery and since it is possible that lithium salts alter the physiological mechanisms responsible for these changes in water, this effect may be related to the therapeutic and prophylactic actions of lithium.

http://www.mgwater.com/mental.shtml

"Lithium has the lightest density of all minerals. Lithium is a soft, silvery, highly reactive substance. Lithium is a heat transfer medium, or a medium that transfers energy or exchanges energy. The presence of lithium in the body is "required" in order for the body to manufacture serotonin, which is also "required" for the manufacture of melatonin, which is a crucial neurochemical for brain function and energy exchange. Lithium by its very nature has the capacity to move energy, transfer energy and facilitate a shift, a balance in the polarities of the physical body." (from "Healing Waters Sacred Springs", page 34-35)

Fibromyalgia-chronic fatigue patients tend to also have a magnesium deficiency in the red blood cells. To correct this imbalance, clinical medicine procedures have been to give the patient injections of magnesium. Manitou's Medicine Waters contain a high concentration of magnesium that is already totally dissolved in water and ready to go to work in the blood to balance that which is not in balance.

http://www.healingwaterssacredsprings.com/fcfs.htm

Richard

Brilliant.

I would just like to add that I am just learning that the opiates found in dairy and grain (esp wheat) probably also act on the NMDA receptors. And maybe why a near paleo diet helps so much. It is so strange that most of us find that eliminating items that work on the NMDA receptors help our AF in some way. I haven't got much time just now but will be researching a lot more on this in the near future.

http://www.autisme-montreal.com/congres/2002/Laidler_en.html

More recent investigations have suggested that casomorphin and gliadomorphin may be active at another type of receptor, the NMDA (N-methyl-D-aspartate) receptor. This hypothesis is supported by the similarities between the symptoms of NMDA receptor blockade and the behaviors seen in autism.

Fran

Just wondering

Is there any specific test that can check the NMDA receptors for any damage? This is the one test I would get a mortgage for, as I am so sure this is where my problem lies.

Fran

Hi Fran and all,

Again, I did note the similarity of afib triggers and triggers which increase NMDA activity and posted it here because it is intriguing. But correlation does not mean causation although correlation does not preclude causation.

So, Fran and Hans and all, here is an idea. Key pharmacy has a pill (for $109 per month) that incorporates all of the Pall's supplement suggestions for damping NMDA response. How about doing a placebo controlled double blind experiment using the pill and a placebo on say 10 of us for a month or two and checking to see if the afib frequency decreases. This is a way to back into Fran's question of how to test for NMDA hyperactivity- do it by seeing of your symptoms improve when taking supplements which are supposed to dampen NMDA activity.

Alas though, please note that Pall has NOT tested this supplement on people. Thus far, we have a testable theory but without data. Maybe in fact the supplements do nothing for NMDA activity even though the NMDA hyperactivity is the culprit.

Lynn

Lynn

I'm not sure how I could get hold of Pall's pills living in the UK. We have very tight restriction on some supplements that are OTC in US, eg for melatonin we need Dr's prescription.

Would these pills not act like antiseizure meds made to block the NMDA receptor. I took antiseizure meds for 20 years and when I stopped them I have to admit it was the first time I could tell that I had eaten free glutamate without knowing. The symptoms were a lot worse after stopping antiseizure meds but I still had AF when I was taking them.

It might be difficult for me to join a double blind study if I got hold of the pills - as my diet is geared towards very little that works on the NMDA receptor and because of this I am AF free. And I am too scared to eat anything with MSG as a trial - as in the past the symptoms have led to near death experiences. After the last one I knew that this would be the way I would die for good and why I am so afraid and not tempted nearly as much as everyone else when it comes to eating processed food.

For the record though I did get in touch with an NMDA researcher living in Canada. I posted a link to his research a while back. I told him my theory regarding MSG, NMDA and AF and asked if he knew any research from others working in this particular field. He asked a few more question of me and promised to get back to me in time as he was very busy at this moment in time. This must have been over a year ago and I have not heard anything. I think I will try to chase him up in case he lost my email. But maybe it was to far removed from his own interest....

Fran

Fran and All,

I don't begin to profess that I completely understand this study, but it was interesting what I did try to derive from it. For anyone interested here's the link and title.

Neuronal Glutamate transporters limit activation of NMDA receptors by neuronal spillover on CA1 pyramidal cells.
http://www.jneurosci.org/cgi/reprint/21/21/8328.pdf

Richard

Lynn,

As you suggested, there appears to be a "glycine site" on the NMDA receptor that is a glutamate co-agonist (as opposed to antagonist). Furthermore, it appears that glycine can diffuse across the blood brain barrier.

http://www.ibogaine.org/lit-nmda.html

Since
1) neurons in the brainstem that control vagal tone have NMDA receptors that require the neurotransmitter glutamate
2) vagal tone is directly related to PACs and AF.

This would certainly explain why magnesium glycinate (but not magnesium taurate) might be problematic.

This would be another reason (in addition to that forwarded by Jackie in her BB post on taurine) for preferring the taurate form over the glycinate form. Perhaps those that had adverse reactions with Mg using the glycinate chelate might revisit Mg supplementation.

PC

I am taking "Losec" or omeprazole Mg - 20mg - for GERD problems that are the root cause of my LAF. I have also started taking Mg glycinate 500mg again.

My question is this:
I know the omeprazole Mg is a proton pump inhibitor but does the Mg glycinate "complement" the omeprazole Mg to do its job? Are these 2 types of Mg based drugs related?

Taking the omeprazole Mg and the Mg glycinate together have now virtually eliminated my LAF and pac's etc.

Dean

Dean,

I personally wouldn't monkey with what appears to be a good thing for you. Furthermore, I must plead ignorance on the function of Mg in your PPI med. However, I wouldn't classify magnesium glycinate as a med. Both components are items we obtain through diet. It's just that in this day and age it's hard to get enough Mg.

If your apparent success begins to go south, I'd switch to magnesium taurate. The fact that a GERD like condition is associated with your episodes suggests that your LAF is at least partially vagal in origin. In that case the glycinate could be enhancing vagal tone.

PC

PC,

Thanks for the post offering some clarification as to just why Mag Glycinate might make matters WORSE for some rather than better. I am one of those folks who find Mag Glycinate makes things worse not better. I have just today started Mag Taurate (each tab has 81mg Mg and 900mg Taurine). I'll gradually ramp 'em up to 2 tabs three times a day.

Mike F.

Lynn,

Some time ago I read that one of the types of lipoic acids had the sulfur removed, which caused it to not be as effective. I would guess it could be alpha lipoic. I'll do some checking, as I'm about to order more, and I want to make sure I get the one with the sulfur still in it.

Richard

Lynn,

It would seem to be that alpha lipoic acid is the one with the sulfur atoms attached, so that would be the one to take.

The chemical structure of alpha-lipoic acid gives it very unique capabilities. It consists of a relatively small, eight-carbon atom chain having two attached sulfur atoms, one attached to the sixth carbon atom and the other sulfur atom attached to the eighth carbon atom, with the sulfur atoms also linked to each other.

http://www.healthy.net/asp/templates/interview.asp?PageType=Interview&ID=160

Richard

Hi Richard

I started to read your link (I haven't got very far yet) but suggest that what they talk of could be related to why I still had AF whilst on a glutamate and hence NMDA blocking drug. The spill over. I will read more on this article tomorrow but I am really harassed for time tonight.

Soon,
Fran

I was wondering about triggers and NMDA receptors and how many of them seem to work on the NMDA receptor. This prompted me to do a search to see if the stress hormone also worked through the NMDA receptor. From the abstracts I have found this seems to be the case. So now we might have a reason why stress causes AF too. Sorry I had to use the cached version as the PDF file could not be found.

http://216.239.59.104/search?q=cache:GNB0qvLvgX8J:webex.lib.ed.ac.uk/abstracts/howe01.pdf+NMDA+receptor+and+cortisol&hl=en&ie=UTF-8

In the chronically cannulated late gestation sheep fetus CGP 37849, a competitiveNMDA receptor antagonist, significantly decreased the ACTH and cortisol response toinsulin hypoglycaemia stress on day 130 (term=145 days), and also reduced basal plasmaconcentrations on day 138, confirming that endogenous excitatory amino acidneurotransmitters acting through the NMDA receptor regulate ACTH secretion in the lategestation fetus. The coupling of the NMDA receptor to CRH and AVP secretion at themedian eminence was investigated by a microdialysis approach. Pre-treatment with CGP37849 attenuated the ACTH and cortisol responses to insulin hypoglycaemia, but notAVP secretion at the median eminence. It was not possible to detect CRH in thedialysate from any of the fetuses, but the failure of CGP 37849 to suppress AVP releasesuggests that NMDA receptors regulate ACTH secretion through CRH neurons. Thepotential for placental steroids to regulate the HPA axis response to NMDA was alsoinvestigated. Infusion of estradiol from day 120 for 96 h did not alter basal plasma ACTHor cortisol concentrations, pituitary sensitivity to AVP and CRH, or ACTH or cortisolresponses to NMDA, despite there being a significant suppression of

plasma folliclestimulating hormone concentrations and an increase in plasma prolactin concentrations.

There is also a couple more abstracts with regards to cortisol.

http://www.jneurochem.org/cgi/content/abstract/83/6/1441

http://www.memantine.com/en/studies/further_literature/2001/hergovich/

Fran

I find this drug of interest, only because of its actions. I also find it interesting that it is not as effective as lithium. It seems that what we are focusing on, strangely parallels bipolar disorder and epilepsy, if we're correct in our thinking.

Quote:
Topiramate in Bipolar Disorder

Topiramate (Topamax®), a new novel anticonvulsant, is increasingly being used in the treatment of refractory mood disorders. A number of recent open, add-on studies have suggested that topiramate is an effective adjunctive treatment in bipolar disorder. A recent excellent review by Chengappa et al. (2001)1 points out many of the unique structural, pharmacological, and clinical properties of topiramate that have led to its increasing use in bipolar illness. We will summarize these unique characteristics of topiramate, review the published studies of topiramate in mood disorders, and note the adverse side effects that may occur when using this new treatment. We highlight the conundrum that topiramate looks promising in open adjunctive studies, but three recent placebo-controlled studies in mania have shown the drug to be ineffective in monotherapy and less effective than lithium.

I. Structure and Pharmacology2

Topiramate is a sulfamate-substituted monosaccharide that was FDA-approved in 1996 for use in the United States in refractory partial-onset seizures as an adjunctive treatment. Absorption of topiramate is rapid, with peak plasma concentrations occurring at approximately 2 hours following a 400 mg oral dose. The relative bioavailability of topiramate from the tablet formulation is about 80% compared to a solution. The bioavailability of topiramate is not affected by food. Topiramate is not extensively metabolized and is primarily eliminated unchanged in the urine (approximately 70% of an administered dose).

The precise mechanism by which topiramate exerts its anti-seizure effect is unknown; however, electrophysiological and biochemical studies of the effects of topiramate on cultured neurons have revealed three properties that may contribute to its antiepileptic efficacy.

First, action potentials elicited repetitively by a sustained depolarization of the neurons are blocked by topiramate in a time-dependent manner, suggestive of a state-dependent sodium channel blocking action (shared by valproate, carbamazepine, and lamotrigine).

Second, topiramate increases the frequency at which (gamma)-aminobutyrate (GABA) activates GABAA receptors, and enhances the ability of GABA to induce a flux of chloride ions into neurons, suggesting that topiramate potentiates the activity of this inhibitory neurotransmitter (like valproate).

Third, topiramate antagonizes the ability of kainate to activate the kainate/AMPA ((alpha)-amino-3-hydroxy-5-methylisoxazole-4-propionic acid; non-NMDA) subtype of excitatory amino acid (glutamate) receptor, but has no apparent effect on the activity of N-methyl-D-aspartate (NMDA) at the NMDA receptor subtype. These effects of topiramate are concentration-dependent within the range of 1 µM to 200 µM.

Topiramate also inhibits some isoenzymes of carbonic anhydrase (CA-II and CA-IV). This pharmacologic effect is generally weaker than that of acetazolamide, a known carbonic anhydrase inhibitor (and used as a treatment for mania in some case reports), and is not thought to be a major contributing factor to topiramate's antiepileptic activity.

Topiramate is also a calcium channel inhibitor at the L-, N-, and possibly T-type channels as well.
http://www.bipolarnews.org/Research%20News%20102202.htm

Richard

This was a bit interesting, and this link also describes various diseases and their effects:

Nicotine addiction – nicotine activates nicotinic Ach receptors - effects of nicotine seem to be through pre-synaptic facilitor of glutamate.
Caffeine addiction – does not reach level of physical addiction, but does act as competitive antagonist for adenosine and dopamine GPCRs.
http://www.med.unc.edu/wms/firstaid/Nb-dz.doc

Richard

I found this of interest:

The prevailing electrophysiological effect of ethanol is the reduction of excitatory glutamatergic neurotransmission. It has been observed that low concentrations of ethanol can inhibit the stimulating actions mediated by NMDA upon hippocampal cells in culture.

In concentrations associated to "in vivo" intoxication, ethanol inhibits NMDA receptor current.

These findings could also explain part of the genesis of physical dependence to alcohol, through a process that is the opposite to that of GABA. That means that when ethanol is interrupted, glutamatergic pathways induce overexcitement of the central nervous system, causing convulsions, anxiety, and delirium.

Calcium influx into the cells has an important function in the release of neurotransmitters in the synaptic cleft, as well as in the activity of cellular second messengers. Ethanol, in concentrations of 25mM, seems to inhibit calcium flow through ionic channels, thus decreasing neurotransmitters release. This could also be one of the mechanisms responsible for dependence and tolerance, because when alcohol-intake is stopped these ionic channels would increase calcium influx and, consequently, neurotransmission, giving rise to signs and symptoms of withdrawal syndrome.
http://www.epub.org.br/cm/n08/doencas/drugs/abuse07_i.htm

Lynn, do you ever drink any alcohol, and if so, what have been the effects?

Richard

Hello all,

As Hans has mentioned, one could be exposed to pesticides and not know it. The reactions to OPs (organophosphates) in particular are many hours removed from the exposure and, in the USA, pesticides are routinely applied without notice.

So here is an idea for you folks to consider. If Pall is correct, then free glutamate should precipitate an attack of afib at least in those of us with lipophilic deposits of pesticides in us. So, how about drinking a glass or two of tomato juice and seeing if that precipitates an afib attack? I have permanent afib, and upon so imbibing, I had an increase in heart rate to 102 BPM from my usual 60-80. I tried again with the same result (i.e., replicability holds the key). Why perform such a test? First, the results indicate which diet to follow, and, second, if Pall is correct the results also govern which supplements to take.

Just a thought,

Lynn

Glad to know about that test. I routinely drink low sodium v8 juice for the potassium content [800mg /8oz] and it is mostly tomato juice, so I guess I can conclude that my afib does not have to do with OP poisoning. A good thing, altogether.

Peggy

In searching about my reaction to either phosphatidylserine, choline, or inositol, I came upon this discovery, even though it occurred in 2000. My reaction happened within 15 minutes of this combo supplement, so I'm not sure if the p-serine could have reacted that fast, however. Anyway, here's the article.

"This is an exciting discovery because serine racemase represents a novel way to potentially block the harmful effects of glutamate over-stimulation," remarks Solomon H. Snyder, director of neuroscience at the Johns Hopkins University School of Medicine. His lab was responsible for isolating and cloning serine racemase.

The overproduction of glutamate has been implicated in a large number of acute and chronic degenerative conditions, including stroke, epilepsy, peripheral neuropathies, chronic pain and Parkinson's, and Alzheimer's and Huntington's disease. During stroke and other degeneration conditions, excessive glutamate is released, which is highly toxic to neurons. The harmful effects of excessive glutamate are believed to occur principally through activation of a subtype of the glutamate receptor called the NMDA receptor.

NMDA receptors have two sites that must be activated in order for neurotransmission to take place. Previously, it was thought that glycine, working in tandem with glutamate, was the only activator of the second site. Recently, scientists at Johns Hopkins, led by Snyder, discovered that the D- isomer of the amino acid, serine (D-serine), was the principal activator of this site (as reported in the November 9, 1999, issue of the Proceedings of the National Academy of Scientists).

"Since glutamate is so abundant in our bodies, nature developed a failsafe mechanism to prevent over-excitation of NMDA receptors by glutamate. It's very much like a lock that requires two separate keys," explains Snyder.

http://www.findarticles.com/cf_dls/m0DED/8_20/60967571/p1/article.jhtm
http://hdlighthouse.org/see/brain/dserine.htm

Richard

Lynn,

This information might be of interest to you. This doctor is located close to Knottsberry Farm, and has a different way of handling sensitivities. I wonder if organophosphates would fall into this category of treatment.

http://www.truthinlabeling.org/NAET.html

There is a link from this site, directly to this doctor.

Richard

The NMDA receptor on nerve cells is unique in that it has various properties not found in other types of receptors. First, the NMDA receptors have the special ability to let in large amounts of calcium ions (Ca^{2+}), an important mediator of glutamate's toxic effects in HD patients. Non-NMDA receptors do not allow the entry of Ca^{2+}. We will talk more about the destructive effects of Ca^{2+} later in this section. A second important property of the NMDA receptor is that its

opening is blocked by a single magnesium ion (Mg2+). An Mg2+ ion is removed only when the electrical charge inside the cell rises to a specific value. While non-NMDA receptors open any time glutamate binds to them, the NMDA receptor needs both the binding of glutamate and an increase in cell charge before it opens.

Normally, as glutamate is released by “messenger-sending” nerve cells, it binds to the NMDA and non-NMDA receptors of the receiving nerve cell. Because the non-NMDA receptors are not blocked, the binding of glutamate alone opens these receptors and allows positively charged ions to flow into the cell. Ion pumps present in the cells remove some of the positive ions, preventing the charge inside the cell from rising too quickly. These ion pumps will only work if there is sufficient amount of energy in the cell. Because of the activities of these ion pumps, a lot of glutamate molecules have to bind to the non-NMDA receptors before the cell’s charge rises to the value that will allow the Mg2+ ion of the NMDA receptor to be removed. Once the Mg2+ ion is removed, the NMDA receptor allows Ca2+ ions to flow in.

In HD nerve cells, in contrast, the lower amount of energy available reduces the ability of the ion pumps to prevent a rapid increase in cell voltage. As a result, fewer glutamate molecules binding to the non-NMDA receptors are needed to increase the cell charge to the value needed to remove Mg2+. The premature unblocking of the NMDA receptor causes an increase in the entry of Ca2+ ions into the cell. As Ca2+ comes rushing into the cell, it activates various molecules that are capable of degrading essential proteins and cellular membranes, increasing the number of free radicals inside the cell, and causing further increases in the amount of Ca2+ inside the cell. Cell death eventually results from the combination of these effects that result from the increased Ca2+ entry.

In summary, the altered huntingtin protein causes a decrease in the nerve cell’s energy supply. This lack of energy results in an increase in the sensitivity of NMDA receptors to glutamate molecules. As the NMDA receptors become over-activated, more Ca2+ ions are able to enter the cell. The entry of Ca2+ results in the activation of various molecules that are capable of causing cell death.

Anti-glutamate therapies include drugs and supplements that are capable of reducing these various effects of glutamate in cells. These compounds either block glutamate receptors or reduce the amount of glutamate being released by other cells. These compounds may also reduce the amount of glutamate present in the junction between glutamate-releasing nerve cells and glutamate-accepting nerve cells.

http://www.stanford.edu/group/hopes/treatmts/antiglut/l1.html

Richard

Curative action of ascorbic acid on MSG toxicity:

http://www.unu.edu/unupress/food/8F071e/8F071E09.htm

Richard

Experiments performed on dissociated rat cortical cell cultures examined how ascorbic acid alters the neurotoxic effects of two agents, ascorbic acid and nitric oxide (generated from the breakdown of sodium nitroprusside). Ascorbic acid enhanced toxicity of nitric oxide, but it reduced that of NMDA. The results indicate that ascorbic acid produces neuroprotection by an action at the NMDA receptor, probably by antagonizing Ca 2+ influx starting the cascade of biochemical events that lead to the production of NO. *JA Bell, C Beglan, and ED London. Interaction of Ascorbic Acid with the Neurotoxic Effects of NMDA and Sodium Nitroprusside. Life Sci., 58: pp. 367 371, 1995*.

http://www.drugabuse.gov/DirReports/DirRep296/DirectorReport6.html

Richard

I could not take niacinamide, as it caused me tension headaches, as did tryptophan, even though my test results indicated very low. These two supplements didn't cause me to go out of rhythm, however. Beta blockers caused me to go into AF rather than flutter, which block adrenalin. This hypothesis was interesting, by Drs Osmond and Hoffer:

The Doctors tried to counteract a possible role of adrenochrome in schizophrenia by slowing down adrenaline production with vitamin B3, niacin, which was hypothesized to inhibit methylation in adrenaline formation.
The article goes onto to say:

Glutamatergic Underactivity:

A More Complete Theory of Schizophrenia

Because the NMDA receptor site antagonists PCP and ketamine mimic a psychosis researchers find to be more closely related to schizophrenia than the states induced by typical psychedelic drugs, underactivity at the glutamate receptor NMDA has been hypothesized as a cause of schizophrenic psychosis. Experiments with the atypical antipsychotic clozapine, which exhibits agonist effects at the NMDA receptor site, further shows that NMDA hypoactivity may be the causation of the disease.

The hypoactivity of NMDA may be an expression of reduced arachidonic acid. As previously mentioned, arachidonic acid is a second messenger in NMDA glutamatergic activity. The availability of free arachidonic acid is the rate-limiting factor in the activity of PGH synthase-and as mentioned, a depletion of arachidonic acid is hypothesized to be involved in the underactivty of NMDA receptors associated with schizophrenia. The depletion of NADPH from glutamatergic neurons due to redox cycling may limit the rate of fatty acid synthesis, and thus a depletion of NADPH, related to redox cycling of dopachrome, may ultimately decrease NMDA activity through decreased synthesis of arachidonic acid.

The irreversible binding of toxic o-semiquinones to active sulfhydryl groups on either the NMDA receptor itself, or the calcium ion mediating translocase, which is critically dependant on thiol groups, may also play a role in NMDA activity. Because of the concentration gradient of calcium ions across the cell membrane, continuous influx of calcium ions must be counteracted, if the mechanisms for doing this are not functioning correctly, then calcium ions enter the cell, decreasing the concentration gradient, but taking additional ions with it, drawing excessive water into the cell to come to an osmotic equilibrium, and in the process, cell membrane hemorrhaging may cause what is called exitotoxic.
http://sulcus.berkeley.edu/mcb/165_001/papers/manuscripts/_582.html

Richard

Hi Richard,
I did try NAET years ago. It was of no help, but of course all depends on the practitioner. At the moment, I think of NAET as mumbo jumbo but I could be wrong.

Lynn

Hi Richard,
The closest I ever got to alcohol (since I had afib) was in echinacea extract and I did react and now take the water-soluble herbal extracts.

Lynn

Richard, what do you mean when you say that caffeine 'does not reach level of physical addiction'? Caffeine most definitely causes a physical addiction with physical withdrawal symptoms. Please explain.

Peggy

Peggy,

I'm just quoting what a link said. Maybe they're considering the level of addiction as compared to heroin or PCP, on a cellular level. By that I mean the alterations of the cell's response to certain drugs can cause irreversible damage. I'm just assuming that.

Lynn,

Interesting that you tried that protocol. It sounded a bit hokey to me, as well, but thought it could be a last resort. Good to know it doesn't work. Did alcohol bother you at all, before the organophosphate incident?

Richard

This was interesting:

NMDA-evoked calcium transients and currents in the suprachiasmatic nucleus: gating by the circadian system
Christopher S. Colwell

Abstract

A variety of evidence suggests that the effects of light on the mammalian circadian system are mediated by glutamatergic mechanisms and that the N-methyl- d-aspartate (NMDA) receptor plays an important role in this regulation. One of the fundamental features of circadian oscillators is that their response to environmental stimulation varies depending on the phase of the daily cycle when the stimuli are applied. For example, the same light treatment, which can produce phase shifts of the oscillator when applied during subjective night, has no effect when applied during the subjective day in animals held in constant darkness (DD). We examined the hypothesis that the effects of NMDA on neurons in the suprachiasmatic nucleus (SCN) also vary from day to night. Optical techniques were utilized to estimate NMDA-induced calcium (Ca2+) changes in SCN cells. The resulting data indicate that there was a daily rhythm in the magnitude and duration of NMDA-induced Ca2+ transients. The phase of this rhythm was determined by the light-dark cycle to which the rats were exposed with the Ca2+ transients peaking during the night. This rhythm continued when animals were held in DD. -Aminobutyric acid (GABA)ergic mechanisms modulated the NMDA response but were not responsible for the rhythm. Finally, there was a rhythm in NMDA-evoked currents in SCN neurons that also peaked during the night. This study provides the first evidence for a circadian oscillation in NMDA-evoked Ca2+ transients in SCN cells. This rhythm may play an important role in determining the periodic sensitivity of the circadian systems response to light.

http://www.blackwell-synergy.com/links/doi/10.1046/j.0953-816x.2001.01517.x/abs/

Richard

I just ordered this book, "Tuning the Brain", by Dr. Goldstein, and think you all might find the preface quite interesting. Lynn this doctor is in your area, and there is a chapter on ketamine, as well as many other issues that could pertain to us. I believe this book mostly applies to CFS and fibromyalgia, but I believe it could be very enlightening. It's publication date is 2004. Pls. read the interesting preface and introduction.
http://www.haworthpressinc.com/store/sampletext/5004.pdf

Richard

And from the opioids in milk angle. Note also PLA2 and PLC release arachidonic acid. The rest is good reading in my view.

http://physrev.physiology.org/cgi/content/full/81/1/299

5. Activation of protein kinase C

A long-term, selective augmentation of N-methyl-D-aspartate (NMDA)-mediated glutamate currents by activation of μ-opioid receptors was observed in brain slices of trigeminal nucleus (80). This augmentation was mimicked by phorbol esters and blocked by the peptide inhibitor of protein kinase C (PKC). It was concluded that opioids activated PKC, which then increased the conductance activated by NMDA receptor agonists. This was the first and remains the strongest evidence that opioids augment postsynaptic glutamate currents by a mechanism involving the activation of PKC. There have, however, been more recent studies showing augmented NMDA receptor-mediated excitatory postsynaptic currents (EPSCs) by μ-opioid agonists in both the nucleus accumbens and hippocampus (312-314, 384). This augmentation was not observed in the locus coeruleus (LC) (359), suggesting that it may be dependent on the makeup of NMDA receptor subunits and/or the isoforms of PKC present on any given cell type.

The activation of PKC by opioids appears to result from the activation of phospholipase C and/or phospholipase A2, which is thought to result from an interaction of /-subunits of pertussis toxin-sensitive G protein and may require coactivation with the -subunits of pertussis toxin-insensitive G proteins (144, 342, 358, 441). The results suggest that in order for opioids to have a robust effect, coactivation with Gq subtype G proteins is required. A similar pathway is also thought to mediate the release calcium from inositol 1,4,5-trisphosphate (IP3)-sensitive stores (see sect. IIB6).