Guildford ME/CFS Support Group
(& West Surrey)

Newsletter

Spring 2012

Future dates

The following ME meetings are open to all members and carers.

27th June (Wednesday) 2.30pm The Anchor
Pyrford Lock, Wisley, GU23 6QW

23rd July (Monday) 7.30pm The Boatman
Millbrook (A281), Guildford GU1 3XJ

20th August (Monday) 11am Holiday Inn
Egerton Road, Guildford, GU2 7XZ

19th September (Wednesday) 4pm Home of Mair Ellis (Member)
Willowhayne, Barnett Lane, Wonersh, Surrey, GU5 0IU
Mair has kindly offered to host a meeting at her home. Those who want to can join in on a take-away meal (e.g. Chinese/Indian)

Annual General Meeting (AGM)
15th October (Monday) 7.30pm The Seahorse
The Street, Shalford, Guildford, GU4 8BU
Everyone is welcome at the AGM, which includes a review of the group over the last year and a future direction

Benefits and work guides

Our last newsletter asked if members would be keen for the group to purchase benefits guides for the group from the company called benefits and work. Because only a few members expressed an interest we will not be purchasing the guides. Instead we will keep available funds for future events.

Business cards for GPs

We have started a process of giving business cards for our group to GPs in the area. The business card shows our email address and website address. Our intent is for those diagnosed with ME/CFS to be informed of the existence of our group so that they have the opportunity to join.

Magtein - (Magnesium L-Threonate)

Source: www.magtein.com

The role of magnesium in memory and cognitive function has long been suggested, but not proven. Only recently, a unique compound called Magtein® was discovered by a group of scientist from MIT including a Nobel Prize laureate. It was hypothesized that brain synapse density correlated to age dependent memory loss. The animal research included the following three phases:

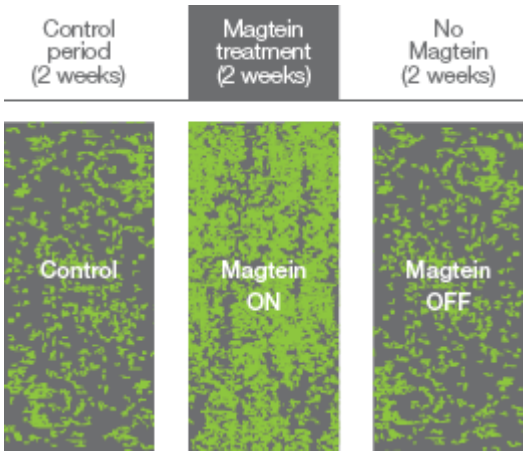
- Phase I: Evaluation of Magnesium forms
- Phase II: Uncover the mechanisms underlining Magtein's functions
- Phase III: Magtein increases memory via increasing synaptic density

The study showed that by increasing the brain's magnesium level, Magtein® could increase the learning ability, working memory, and short- and long-term memory in young and aged rats. It also showed that common magnesium compounds do not effectively improve brain magnesium levels, which is required to improve memory and cognitive functions.

A human study for memory and cognitive function has just started at University of Southern California, Department of Psychology, with a leading expert in cognitive health. It is a double-blind, placebo controlled study with 40 individuals. Preliminary results will be available by mid 2012.

On-going Magtein research is continuing to uncover a variety of new discoveries. This unique form of magnesium is being evaluated by research communities for Alzheimer's, dementia, insomnia and other aging conditions.

In animal research, Magtein was shown to increase total brain synapses vs. control. Increased brain synaptic density is correlated with improved memory. The study also found that when Magtein was no longer administered, brain synapse density reversed back down.



Magtein (Magnesium L-Threonate) is available on amazon uk. Example products and prices are included below.

Magnesium tends to cause sleepiness so best taken at night before bed.

Swanson Ultra Magnesium L-Threonate
(90 vegetarian capsules)
£31.99

Neuro-Mag Magnesium L-Threonate
90 vegetarian capsules
£28.95

Chronic pain control basics for ME/CFS and Fibromyalgia

Source: www.prohealth.com/library/showarticle.cfm?libid=16770
January 25, 2012

Of the symptoms of chronic fatigue syndrome (CFS) and fibromyalgia (FM), chronic pain is rarely treated adequately. Headaches, lymph node tenderness, muscle pain and joint pain cause considerable long term discomfort – sometimes mild, sometimes severe. There may be fluctuations in the severity of pain.

If pain remains one of your most important symptoms of CFS/FM, be sure to address it specifically.

General principles

There are several general principles of pain management that should be understood by the patient:

1. Always use the least amount of pain medication. These drugs have side effects and may cause intolerance, and do nothing to cure the underlying cause. Don't use them if they are not necessary.

2. Do not treat general malaise with pain medication. Sometimes, you may feel rotten but the pain is not that bad. Using pain medication is unlikely to be of help.

3. Communicate the pain clearly to your physician. There are many symptoms to address in CFS & fibromyalgia, and if [as your physician] I do not know that pain is the worst symptom, I may not attempt to address it. That is, if pain is one symptom listed among 20, I will not pay special attention to it.

4. Be patient and observe patterns. If the pain is mild and tolerable for two months, then bad for one week, do not go to the "big guns" right away. If the pain eases off after a week, you will not know if it is the medication or just the fluctuations of the illness. Once you understand the pattern, it may be reasonable to have a strong pain medication on hand for the bad episodes, then stop it when possible.

5. Assess the response to one class of medications well before moving to the next class. Many persons do not use ibuprofen correctly, and thus reject it thinking it doesn't help.

6. Do not jump to strong pain medications early in the morning if the pain and stiffness usually ease off after an hour. It will take the medications that long to work, and then your are left with the heaviness of pain medications for the next few hours without needing it. You can approach it by taking a longer acting medication at bedtime, or by stretching or showering in the morning.

Medications for pain by class

1. Non-steroidal anti-inflammatory drugs (NSAIDs)
This class is the standard pain relievers, many of them over the counter. If the response is not enough, make sure you are using them effectively and at the right doses. For example, ibuprofen may be effective taken three times daily to prevent severe pain, but may not appear to work if used only at crisis times. All can cause upset stomach, and even ulcers.

2. Acetaminophen (Tylenol® and others)
This medication has no effect on inflammation but can be useful for headache and muscle-joint pain. It is a reasonable first attempt. It can cause liver problems if used in very high doses and should never be taken excessively. If the regular dosage does not help either add an NSAID or move to another medication. Do not push the dose.

3. New NSAIDS.
For reasons I do not understand, sometimes other NSAIDS work better than ibuprofen and can be taken regularly and less frequently during the day. It is reasonable to attempt others in this class, usually by prescription, before going to strong medication.

These would include:

- Diclofenac (Voltaren®)
  50mg three times a day, or the long acting Voltaren® XL 100mg once daily.

- Sulindac (Clinoril™)
  100 to 200mg twice daily. Do not exceed 400mg daily.

- Naprosyn and many others.

- Arthrotec® is a brand that combines diclofenac with the drug misoprostal to protect the stomach (50mg/200mg up to four times daily). Do not take if pregnant or even if pregnancy is likely.

4. Tricyclics
These drugs are the old fashioned antidepressants and improve pain, but must be taken regularly to be effective. They should be used to prevent pain, and never be taken just when the pain is bad. This is one type of medication that must be taken regularly, good days and bad. CFS patients are usually sensitive to them and lower starting doses should be used.

[Note: SSRIs are another type of antidepressant, which may be prescribed off label for chronic pain, see attached sidebar.]

5. Tramadol (Ultram™ – 50 to 100mg three times daily).
I like this medication partly because the name sounds like Kurt Vonnegut designed it. It should be used with caution in conjunction with Prozac™ and tricyclics. It is a cousin of the NSAIDS and has some effect on the serotonin and norepinephrine systems as well as being a very weak opiate. While it is unlikely to cause dependence, some persons say it is unlikely to be of value. But it is worth a try.

6. Baclofen®.
This is a nifty drug; cheap, and when it works – great. Unfortunately, it does not work very often. It is best when the muscle pain is of a cramping or spasm quality, which is why it is used in multiple sclerosis. It is related to the benzodiazepines such as clonazepam or alprazolam and should be used cautiously with these. Some sedation is likely, and the dose should not exceed 10mg three times daily.

7. Seizure medications.
These must be used with caution, as the side effects may be significant. But when they work they are great. Not casual medication.

a. Neurontin (Gabapentin™ 900 to 1800mg daily). This medication was developed for seizure disorders and may cause dizziness or increase fatigue. The mechanism of pain relief is uncertain. Significant side effects are possible and it should be reviewed carefully before use.

b. Carbamazepine (Tegretol® 100mg twice daily to a maximum of 1200mg a day. Tegretol® XR 100mg twice a day.) This seizure medication can cause excitation, bone marrow problems and allergic reactions, and should not be used with erythromycin, Prozac and other drugs. It is a cousin of the tricyclics and sometimes gives good pain relief.

8. Narcotics (opioids)
While these drugs always have the potential for addiction, it is said that addiction rarely occurs when used to treat severe pain. Intermittent use is best if possible. Doctors are usually reluctant to use narcotics because of the risk of addiction; you don't need any more problems than you already have. Propoxyphene (Darvon™) is my least favourite drug because it may have a high addiction potential yet wimpy pain relief.

A note in Conclusion

When people hear the side effects of medications, they frequently become afraid and unwilling to try medications. If you were to see the side effect profile of acetaminophen (Tylenol®) you would probably never take it because it includes death, not just because it gets laced with cyanide.

When 280 million people use a drug, side effects are bound to occur. Keep in mind that if you saw the side effects and dangers of taking a shower (i.e., slipping in the bathtub, etc.) people would not bathe. That, however, also has its side effects (loss of friends, physicians, etc.).

Use common sense. Any medication that does something will have side effects. Some of the safest medications are only safe because they do nothing at all. Consider medications as you would consider driving a car. They are both inherently dangerous, but are helpful if used properly.

David S Bell, MD, FAAP

Further information

For the latest evidence-based findings regarding "off-label" use of drugs in chronic pain management, see www.postgradmed.org/doi/10.3810/pgm.2011.11.2504

Notes on Lyrica, Cymbalta, Savella & SSRIs prescribed for Fibromyalgia pain (by the FDA in America)

Source: www.prohealth.com/library/showarticle.cfm?libid=16770
January 25, 2012

Lyrica® (pregabalin) and Cymbalta® (duloxetine)
Both Lyrica (pregabalin) and Cymbalta (duloxetine) have been FDA approved for fibromyalgia. They both help most people with their fibromyalgia pain; the studies have shown that the majority achieve at least 30% improvement in pain.

They have different mechanisms of action. Lyrica works on the calcium channels, which are specialized parts of the nerve that conduct pain signals. Lyrica blocks the pain signal conduction through the sensitivity of the calcium channels. Cymbalta works on the nerve pathway that inhibits pain. It works by increasing the concentration of both serotonin and norepinephrine, two neurotransmitters in the spinal cord that activate nerves that block pain.

So Lyrica works to decrease pain intensity and Cymbalta works to increase the inhibition of pain. Lyrica can cause sedation, swelling and weight gain, and one starts at a low dose usually in the evening and tries to increase the dose to achieve pain-relief.

Don't get discouraged if you're not noticing any improvement on a low dose; the main reason for starting "low and going slow" is to make sure you're tolerating the medicine. Sometimes you need to get to a higher dose, perhaps 300 mg/day or more total before you get pain-relief.

Cymbalta works best when taken in the morning and usually starts with a 30 mg dose for the first week and then increase to 60 mg in week two. It can cause nausea, dry mouth, increased sweating and decreased appetite, but is usually very well tolerated.

In my opinion, Cymbalta has the better mechanism of action and is better tolerated. It's not uncommon to be on both medications, so check with your physician and see if you're a candidate to take one or both of these medicines.

Savella® (milnacipran)
A third FDA approved drug for fibromyalgia, Savella, is similar to Cymbalta in that it works to concentrate and increase the effect of serotonin and norepinephrine in the brain, though exactly how is not known. It would not be taken with Cymbalta owing to risk of serotonin syndrome (excess serotonin, a serious drug reaction). It may generally help mood and fatigue more than pain.

SSRIs prescribed off label for pain
SSRI stands for selective serotonin re-uptake inhibitor and refers to the class of medicines called antidepressants. They work by blocking the breakdown of serotonin (a hormone found to be low in FM and depression), thus making more serotonin available which can improve mood.

An off-label use of SSRIs is the treatment of chronic pain, and it is felt that the increased serotonin helps the body reduce pain. That's why a lot of people may notice some benefit with their fibromyalgia pain when taking an SSRI. The potential side effects can include weight gain, sexual dysfunction, and making you feel too "numb."

By Dr. Mark J Pellegrino, MD

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Note: This information has not been evaluated by the FDA. It represents the personal research and opinions of the authors, is for general informational purposes only, and is not meant to prevent, diagnose, treat or cure any condition, illness, or disease. ME/CFS/FM is an extremely complex illness, and advice in a newsletter may not be appropriate for a specific individual. Therefore, should you be interested or wish to pursue any of the ideas presented here, please discuss them with your personal physician.

DVD of the 7th Invest in ME conference

The 7th Invest in ME conference took place on the 1st June 2012 at One Birdcage Walk, Westminster, London

A DVD of the event is available to order.

Benefits of watching the DVD of the conference include:

- increase your understanding of diagnosis, treatment and management of ME/CFS
- explore current and future biomedical research into ME/CFS
- assess the status and role of immunological markers in ME/CFS
- learn about on-going clinical trials to treat ME/CFS, including Rituximab
- learn about Inflammation in the CNS and its contribution to Neurological Disease
- learn about the function of the immune response in the gut

The price is £14, which includes postage.

How to order
Send a cheque for the £14 to Invest in ME, PO BOX 561, Eastleigh, SO50 0GQ
Make cheques payable to Invest in ME
Please include your name and address and that you require a PAL version for the UK.

Online orders can be made at the following link (look for DVD option on the left side/bottom):
www.investinme.org/IiME%20Conference%202012/IIMEC7%20Registration.htm

Herpes viruses proliferate in the nervous system by taking over proteins the mitochondria need

www.prohealth.com/me-cfs/library/showarticle.cfm?libid=17015
May 31, 2012

Findings suggest that other neurotropic viruses (e.g., West Nile or polioviruses) could corrupt mitochondria in the same way.

Herpes and other viruses that attack the nervous system may thrive by disrupting cell function in order to hijack a neuron's internal transportation network and spread to other cells. [A process that stops mitochondrial energy generation in the cells.]

Princeton University researchers made the first observation in neurons that common strains of the herpes virus indirectly take control of a cell's mitochondria, the mobile organelles that regulate a cell's:

- energy supply;
- communication with other cells; and
- self-destruction response to infection.

The team reports in the journal Cell Host and Microbe [May 17, “Alpha-herpes virus infection disrupts mitochondrial transport in neurons”] that viral infection elevates neuron activity, as well as the cell's level of calcium - a key chemical in cell communication - and brings mitochondrial motion to a halt in the cell's axon, which connects to and allows communication with other neurons.

The authors propose that the viruses then commandeer the proteins that mitochondria typically use to move about the cell.

The pathogens can then freely travel and reproduce within the infected neuron and more easily spread to uninfected cells. When the researchers made the mitochondria less sensitive to calcium the viruses could not spread as quickly or easily.

These findings reveal a previously unknown and highly efficient mechanism that some of the most common strains of herpes viruses in humans may use to proliferate in the nervous system, said lead author Tal Kramer, a doctoral student in the lab of the paper's co-authorLynn Enquist, the Henry L. Hillman Professor of Molecular Biology and chair of Princeton's molecular biology department.

Kramer and Enquist used rat neurons to study two herpes viruses in the alpha-herpes virus subfamily: pseudorabies virus (PRV), a model alpha-herpes virus that infects animals, andHerpes simplex virus 1 (HSV-1), an extremely common human virus that causes cold sores and other lesions.

Other human alpha-herpes viruses are responsible for causing diseases such as chicken pox and shingles.

"No one before has looked carefully at mitochondrial motion during alpha-herpes virus infection in neurons. We provide new insight into how these viruses damage cells in the nervous system in ways that are important for the virus to propagate," Kramer said.

"If mitochondria are stopped in their tracks and can't go anywhere, that is potentially very bad," he said.

"They are not only the power plants of the cell, but regulate important processes. The virus likely acts to interfere with many of those processes."

Beyond herpes, the Princeton findings present a possible explanation for how otherneurotropic viruses such as rabies, West Nile and polio attack and disrupt the nervous system, Kramer said. [By invading the nervous system, these viruses “largely evade” immune cells which are active in the bloodstream.]

Although these viruses are different from the herpes family, the fact that HSV-1 and PRV had a similar effect on mitochondrial motion and function suggests that other pathogens could corrupt mitochondria in the same way, he said.

In addition, the paper lays out the implications of distorted mitochondrial function on neuron health.

Mitochondrial malfunction is a known factor in non-infectious neurodegenerative conditions such as Alzheimer's disease and Parkinson's disease, Kramer said, though the pathway to this disruption is not entirely known.

"Our model raises some new and exciting possibilities for future research on other important human viruses that can invade the nervous system and cause disease," Kramer said.

"And the fact that alpha-herpes infection damages the same key cellular function as neurodegenerative disorders also is striking," he said. "Understanding how viral infection damages neurons might give us insight into how diseases like Alzheimer's do the same. The viruses we study hijack well-studied cellular pathways that might make an effective target for future therapeutic strategies."

- In a healthy neuron, mitochondria move throughout the cell's elongated, tree-like structure to provide energy for various processes that occur throughout the cell.

- For the strenuous task of long distance intercellular communication, mitochondria move along the axon and synapses, sites of cell-to-cell contact where signaling occurs.

Calcium plays a key role in this cell communication, Kramer explained.

- A neuron experiences a spike in calcium levels in the axon and synapses when it receives a signal from another neuron.

- Though a natural rover, mitochondria contain a protein called Miro that detects this rush of calcium and stops the organelles in the synapse. [See for example "Moving or stopping mitochondria: Miro as a traffic cop by sensing calcium."]

- The mitochondria then provide energy as the cell passes a signal along to the next neuron.

Through live-cell imaging of neurons grown in the Enquist lab, Kramer and Enquist observed how this process becomes corrupted by HSV-1 and PRV - and how the viruses need the process to spread.

The chaos begins when the virus ramps up the neuron's firing of electrical signals, as was first reported in a 2009 paper published in the journal PLoS Pathogens by Enquist; first author Kelly McCarthy, a past member of Enquist's lab who received her doctoral degree from Princeton in 2011; and David Tank, the Henry L. Hillman Professor of Molecular Biology and co-director of the Princeton Neuroscience Institute.

In the latest research, Kramer and Enquist found that this spike in electrical activity floods the axon and synapses with calcium. As a consequence, the Miro proteins detect the increase in calcium and stop mitochondrial motion. [A live cell imaging video of uninfected nerve cells shows mitochodria busily zipping along the axons, compared with infected cells, where they do no more than twitch.]

The virus' control over the cell immediately dropped off, however, when Kramer and Enquist interfered with Miro's ability to respond to the uptick in calcium levels.

Though the viral infection was not completely disrupted, it could not spread within or to other cells with the same efficiency.

Based on these observations, Kramer and Enquist suggest that viruses such as HSV-1 and PRV may bring mitochondria to a standstill in order to hijack their transportation. Mitochondria move about the neuron on the backs of motor proteins dynein and kinesin-1. During viral infection, mitochondria shed these proteins to stop moving when Miro detects an upsurge in cellular calcium.

Previous research has shown that HSV-1 and PRV also use kinesin-1 specifically for transport within an infected cell. Thus, Kramer said, his and Enquist's work suggests that it is very likely that the viruses disrupt mitochondrial motility so that they can hitch themselves to the now available kinesin-1 proteins and move through the nervous system more efficiently.

James Alwine, a University of Pennsylvania professor of cancer biology, said that the Princeton research is a significant contribution to a growing body of research that describes how viruses seize cellular motor proteins such as kinesin-1.

While the findings have therapeutic potential - particularly in helping show how balancing cellular calcium might subdue viral infection - the demonstration that viruses can move through an infected cell with the ease of something as essential as mitochondria is notable in itself, said Alwine, who is familiar with the research but had no role in it.

"Determining the specific mechanism by which Miro function is abrogated may provide additional therapeutic avenues, but this also is marvelous basic research that does not have to be justified by its therapeutic potential," he said.

"To disrupt the loading of mitochondria to motor proteins so that virions [complete virus particles] can load instead is a clever way for a virus to be transported and is a great new idea provoked by this data," Alwine said.

"While other neurotropic viruses would have to be tested specifically, movement in nerve cells is required by all of them. Thus, this observation provides a starting place and a model mechanism for research with those other pathogens."

This research was published May 17 in the journal Cell Host and Microbe, and supported by the National Institutes of Health and a National Science Foundation Graduate Research Grant.