Guildford ME/CFS Support Group
(& West Surrey)

Newsletter

December 2019

Future dates

Open to all members and carers

For meeting details please email guildfordme@hotmail.co.uk

Coffee alternative boosts mental focus

Source: www.prohealth.com/me-cfs/library/coffee-alternative-boosts-mental-focus-92201
By Michael Downey 12th November 2019

Our ME group aims to bring supplement options to your attention that may be useful and should be harmless to try however everyone has unique health difficulties and such supplements are taken at your own risk.

Sometimes you need a way to clear afternoon brain fog. Coffee can do the trick, but for many people, drinking coffee later in the day can interfere with sleep, upset the stomach, lead to a jittery feeling, and result in a later "crash." There is an herbal alternative. Scientists have identified a unique spearmint extract that, like coffee, helps the brain focus. It even boosts short-term working memory. But it's stimulant-free and won't cause any of coffee's common side effects.

Available in a convenient, instant spearmint tea, this extract contains high levels of phenolics, health-promoting compounds found in plants, particularly rosmarinic acid. And this spearmint extract goes beyond offering a mental boost. A recent, clinical study demonstrated that it also enhances the ability to quickly initiate unplanned changes in direction or speed. This can help performance during exercise or sports, and lead to fewer falls in the elderly.

Supporting mental focus
Scientists have demonstrated in various studies that spearmint extract enhances the underlying elements of mental focus. It can:

- boost alertness, mood, and vigour;
- improve working memory and spatial working memory;
- improve one's ability to get to sleep at night; and
- in animals, promote the creation of new brain neurons, protect existing neurons, and boost neurotransmitter levels.

A recent study found that spearmint extract also boosts reactive agility, the ability to react rapidly when quick, sudden changes in direction or speed are needed. This type of agility can help prevent falls in the elderly and improve participants' sports and exercise performance.

Spearmint extract's effects for cognitive support have been verified in a range of studies.

Attention, concentration, and brain function
Scientists found that just a single 900 mg dose of spearmint extract led to significant improvements in attention and concentration in human subjects in as little as 2.25 hours. With longer-term use, over 30 days, they continued to show these same cognitive benefits.

In one study, 11 healthy adults who were experiencing typical age-related problems with memory took 900 mg of spearmint extract with breakfast for 30 days. The volunteers were given a battery of computerised cognition tests one hour before taking the initial dose. These tests were repeated after four hours, and again after 30 days.

Four hours after the first dose of spearmint extract, average scores showed:

- 46% improvement on a task requiring attention and concentration;
- 121% improvement on a second task requiring attention and concentration; and
- 39% boost in planning ability.

Thirty days after the initial dose, average scores demonstrated:

- 35% improvement on a test of reasoning;
- 125% improvement on a test of attention and concentration; and
- 48% boost in planning ability.

These findings show that supplementation with spearmint extract has both immediate and longer-term benefits for cognitive function.

Next, scientists investigated this extract's effects on a healthy, young, and active population. In a double-blind study, 142 healthy, recreationally active men and women were enlisted, who took either 900 mg of a proprietary spearmint extract each day for 90 days, or a placebo.

Improvements in sustained attention were measured at day 30 and day 90. Scores on cognitive tests requiring complex attention were improved at day seven. Response times for correct answers were also faster.

The study authors concluded that this spearmint extract enhances attention and "improves cognitive performance in a young, active population."

Improvement in working and spatial working memory
Turning to effects on memory, scientists enlisted 90 people, averaging 59.4 years of age, who had age-associated memory impairment.

Participants in this randomised, double-blind, placebo-controlled study took either 900 mg or 600 mg of spearmint extract or a placebo every day at breakfast for 90 days. The extract was standardised to contain 24% total phenolics and 14.5% rosmarinic acid, one of spearmint's brain-protecting components. After 90 days, the 900 mg of extract led to an improvement in working memory of approximately 15% and a 9% improvement in spatial working memory, compared to the placebo.

This suggests, "that this extract could improve working memory equivalent to that which may have diminished over a decade of life," the study's authors wrote.

What you need to know
Phenolic compounds in spearmint extract have been shown in human studies to significantly improve focus and attention, as well as concentration, plus working memory and ability to get to sleep at night.

Preliminary data suggest that spearmint phenolics like rosmarinic acid promote the creation of new brain cells and protect existing neurons.

Recent research on humans shows that spearmint extract also improves reactive agility, the ability to rapidly respond physically.

Spearmint extract does all this without caffeine or other stimulants, making it a natural and healthy alternative to coffee.

A spearmint extract delivering high phenolic levels, especially of rosmarinic acid, is now available in an instant, sugar-free spearmint herbal tea. It comes in one-cup, convenient grab-and-go packets for a quick boost in cognitive performance. (see page 5 of this newsletter)

Making it easier to fall asleep
The results of this study also demonstrated beneficial effects on sleep and mood, both of which help support daily attention, concentration, and focus. Participants in the 900 mg spearmint group reported improvements in their ability to fall sleep. And they were more alert when they woke up.

The improvements were so pronounced that they were similar to those seen with commonly used sleep aids, researchers noted, but without the negative side effects that often come with them. In addition to boosting daytime alertness and concentration, these effects might halt the longer-term decline in cognitive health associated with reduced sleep.

Using a standard psychological-rating scale, improved mood was observed in those taking 900 mg of spearmint extract. Taken together, all these effects can make a huge difference in an individual's mental focus and function.

Promotes brain neuron formation
Beyond improving cognition, the phenolics present in the extract promote neurogenesis, the formation of new brain cells. In cultures of cells from the hippocampus, the brain's centre of working memory, spearmint's rosmarinic acid significantly enhanced the growth of new cells.

Not long ago it was believed that people stop growing new brain cells after adolescence. But a 2018 study in the journal Cell Stem Cell found otherwise. Postmortem examination of the brains of people who died at various ages revealed that healthy, older individuals without cognitive impairment or neuropsychiatric disease maintain neurogenesis well into old age.

This has changed medicine's view of brain aging. Now that scientists know new brain cells are being formed, the focus has shifted to learning how quickly an individual produces them. A person's neurogenic rate may be vital in determining how well the brain functions and focuses.

Research suggests that spearmint extract provides the brain with support to optimise its potential for neuron creation. This can lead to improved focus and long-term cognitive function, and may help those at risk for age-associated memory impairment.

Increases neurotransmitter levels
Spearmint has also been shown to protect existing brain cells and the blood vessels that nourish them. Phenolics in spearmint inhibit the enzyme acetylcholinesterase, which breaks down the memory-associated neurotransmitter acetylcholine.

These phenolic compounds also inhibit harmful oxidative stress. One specific phenolic, rosmarinic acid, was shown to protect key memory centres of animal brains—such as the hippocampus and cortex—against cellular damage from this stress.

Improves reactive agility
In a double-blind study that appears to be the first of its kind, scientists recently assessed the effects of spearmint on a connection between mental and physical performance.

They gave 142 healthy, active volunteers, aged 18 to 50, either a placebo or 900 mg of spearmint extract daily for 90 days. Subjects avoided caffeine for 10 hours before and during the study. Using a special audio-visual device and footplates, researchers evaluated reactive agility, the physical ability to quickly react to a stimulus.

At days 30 and 90, the spearmint group demonstrated significantly greater reactive agility than the placebo group, showing a faster association between cognition and physical response with spearmint supplementation.

The study's author concluded that the spearmint extract appeared to be safe and have potential benefits for athletic performance.

Another study demonstrated that participants subjectively experienced energy improvement. This double-blind experiment involved 10 healthy individuals who had been sleep-deprived for 24 hours, during which time they had participated in very stressful, antiterrorism training.

Unlike the placebo group, those taking 900 mg daily of the proprietary spearmint extract containing rosmarinic acid reported increased feelings of energy. They also reported experiencing greater attention and focus. However, the researchers found that the overall results were less than conclusive, and called for further study.

A quick mental boost
All these successful, human studies employed 900 mg of a spearmint extract containing more than 50 phenolic compounds, standardized to 24% total phenolics and 14.5% rosmarinic acid.

This same dose of the extract is now available in just one serving of a sugar-free, instant spearmint tea.

Researchers achieved this high phenol concentration by using a gentle water-extraction process and an innovative drying technology. This preserves the phenolics and the rosmarinic acid more fully than typical steam-extraction methods.

This herbal tea comes in grab-and-go packets that make one cup of tea in seconds. Just pour the contents into a cup, add hot water, and stir—no steeping required. (see further below for details)

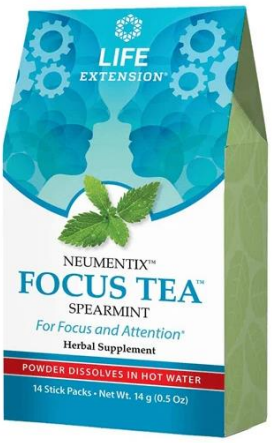
This instant refreshment delivers an immediate boost in mental focus and working memory without caffeine, and without the potential for a later “crash.”

Summary
People seeking an alternative to coffee can now get a quick boost in focus, attention, and concentration with a spearmint herbal tea. Human studies show that phenolics like rosmarinic acid, abundant in spearmint, enhance mental focus and working memory during the day, and improve one’s ability to get to sleep at night.

Early lab data suggest spearmint compounds may promote the creation of new brain cells.

A human study found that a spearmint extract can also increase reactive agility, a brain-muscle reaction that can benefit athletic performance. Another study showed that the extract enhanced feelings of energy.

In human trials the spearmint extract has been shown to be safe, without any adverse side effects.



Available in one-cup, grab-and-go packets that deliver a high concentration of rosmarinic acid and other phenolic compounds, this sugar-free, instant spearmint tea provides an ideal, caffeine-free way to quickly increase mental focus while improving cognitive health.

For references see original article here:
www.lifeextension.com/magazine/2019/9/coffee-alternative-boosts-mental-focus

Neumentix Focus Tea, Spearmint - 14 stick packs
Available to buy in the UK from:
www.powerbody.co.uk/life-extension/neumentix-focus-tea-spearmint,35854.html
£13.67

Finally found – a Natural Killer Cell enhancer for ME/CFS?

Source: http://simmaronresearch.com/2019/12/naltrexone-natural-killer-cells-chronic-fatigue-syndrome/
By Cort Johnson 19th December 2019

For several years now, researchers at the National Centre for Neuroimmunology and Emerging Diseases (NCNED) at Griffith University in Australia have been leading the research on natural killer (NK) cells in chronic fatigue syndrome (ME/CFS). In fact, they recently published an overview on NK cells and ME/CFS:

https://systematicreviewsjournal.biomedcentral.com/articles/10.1186/s13643-019-1202-6?fbclid=IwAR2-72rgdfOlR11WXgJxdnKFl35uKWu8DoyxRGbaaImp6PuyU2hh7NVjeoY

NK cells play a critical role in the innate immune response which kicks in first to fight off an infection. NK cells do just what their name implies: after alerting the immune system that trouble is ahead, they jump in and kill as many infected and damaged (cancer) cells as possible. The goal? To keep a pathogen in check long enough for big guns of the adaptive immune system (T and B cells) to rev up and ultimately destroy the invader.

For some time now, the Griffith group has focused on an unusual subject for ME/CFS – ion channels – the very, very small channels in our neurons and cells – which play a big, big role in nerve and cell activation. Ion channels are getting a lot of interest in pain research but except for the Griffith team – not so much in ME/CFS.

The problem with NK cells in ME/CFS is that they're just not killing very well. When given the chance to wipe out some infected cells, they pretty much poop out – not good news for anyone wanting to quickly knock down infections or remove cancerous cells.

NK cells, like many cells, require intracellular calcium to function properly, the levels of which are regulated, at least in part, by the ion channels the Griffith group is studying. These TRPM ion channels are found in a wide variety of cells and tissues, and play a particularly important role in sensory processing – a big concern in ME/CFS.

The ion channel that the Griffith group has been particularly interested in – TRPM member 3(TRPM3) – appears to be a jack of all trades. The fact that it can be activated by everything from temperature, natural chemicals, and toxins to synthetic compounds suggests it plays a fundamental role in the body, and, indeed, TRPM3 dysfunction has been implicated in inflammatory and neuropathic pain disorders.

Ion Channels and ME/CFS
The Griffith group's findings in ME/CFS stretch back almost four years. In 2016, they showed that both TRPM3 and intracellular concentrations of calcium were reduced in the NK cells of ME/CFS patients. These findings suggested that in ME/CFS, the signal to kill the pathogens wasn't getting through to the NK cells.

That same year, Griffith introduced a potential explanation: the genes that governed TRP ion channel functioning – in particular, TRPM3 ion channel functioning – were loaded with mutations in ME/CFS. That same year, the group reported they'd found similar mutations in the B cells of ME/CFS patients.

2017 brought another study validating the TRPM3 channel reductions. Further testing indicated something had gone wrong with the TRPM3 receptors themselves. When stimulation tests found a reduction in Ca2+ mobilization was occurring, the researchers proposed something startling: that TRPM3 channels across the body could be malfunctioning.

“As TRPM3 receptors are expressed throughout the human body, the current findings suggest that impaired TRPM3 function may play a significant role in the multisystemic pathomechanism of CFS/ME.”

Given how ubiquitous TRPM ion channels are, the loss of them body-wide could be responsible for many of the multitudinous symptoms associated with ME/CFS.

2018 and 2019 brought further validation of their previous findings (in small studies). Just this month, the group published evidence that a related ion channel, TRPM2 – perhaps in a compensatory response – is over-expressed on ME/CFS patients’ NK cells. Despite its increased levels, it too was not functioning well.

Then in October of this year came a potential fix for the NK cell problem in ME/CFS.

Naltrexone hydrochloride (NTX) is best known in its low dose form in ME/CFS. It was referred to in this paper, though, simply as naltrexone. NTX in its normal dose functions as an opioid antagonist which reverses the effects of opioids. While it’s doing that, it also happens to activate the same TRPM3 channels that have been found inhibited in ME/CFS.

The Australian researchers used something called a whole cell patch clamp technique to assess the functioning of NK cells from people with ME/CFS. This technique, which was developed in the 1970’s/80’s, enabled researchers to assess the functioning of single ion channels on cells for the first time. (It also won its creators the Nobel Prize.)

The study again found that low levels of TPRM3 channels were present in ME/CFS. It showed that stimulating the NK cells from healthy controls worked – the NK cells sprang into action. The NK cells from the ME/CFS patients responded to the stimulation by remain dead as a door nail. That stimulation test suggested that whatever TPRM3 channels were present simply weren’t working.

ME/CFS patients, then, appeared to have two problems: they were losing TRPM3 ion channels and those that were still present were not working well. Incubating the healthy controls’ NK cells in naltrexone had no effect on them, but the ME/CFS patients’ NK cells responded dramatically: they now appeared to be acting normally.

Besides presenting a possible treatment for the NK dysfunction in ME/CFS, the finding suggested the Griffith researchers’ original hypothesis could be correct: the mysterious NK cell dysfunction problem could derive from problems with the TPRM3 ions.

This was a laboratory study – a proof of concept study. It’s a long way from testing naltrexone in humans but it did hold out the potential of a treatment for the low NK functioning in ME/CFS.

Given that NK cells ferret out infected and cancerous cells and remove them, getting the NK cells functioning properly again in ME/CFS would be a big step forward.

The leader of the group, Professor Sonya Marshall-Gradisnik, was clearly enthusiastic: “This world-first discovery suggests new potential pharmaco-therapeutic interventions in ME/CFS.”

Opioid drugs and Immunosuppression

The study also raised the question of what effects opioid drugs could be having on the immune systems of people with ME/CFS. No studies have attempted to assess that issue, but this study and others suggests it could be negative.

Opioid drugs have been found to impair the functioning of macrophages, natural killer cells and T-cells and weaken the gut barrier. A 2013 review asserted that, given the prevalence of opioid use, “opioid-mediated immune suppression presents a serious concern in our society today”.

The effects of opioids are complex, however. Immune cells also secrete endogenous opioid peptides which relieve inflammatory and neuropathic pain.

Conclusion
The studies have generally been small, but the results have been consistently positive. They suggest that poorly functioning TRPM3 and perhaps related ion channels could be causing the reduced NK cell cytotoxicity commonly found in ME/CFS. This study found that the opioid antagonist Naltrexone was able to reverse the TRPM3 and calcium mobilisation problems in ME/CFS patients' NK cells.

Reversing the poor NK cell cytotoxicity functioning to normal would be a major step forward. Further studies will be needed, however, to determine if the results seen in the laboratory apply to people with ME/CFS – which is often a perilous step. I couldn't find any clue as to what the effective dose would be or whether the low dose form of naltrexone might help.

It bears mentioning that the Griffith group has evidence that another ion channel may not be working properly in ME/CFS, that these channels are widespread throughout the body, and a systemic dysfunction with them, if present, could cause many problems.

Powerful models accurately predict response to exercise and treatments in ME/CFS

Source: www.prohealth.com/me-cfs/library/powerful-models-accurately-predict-response-to-exercise-and-treatments-in-me-cfs-92194
By Cort Johnson 9th November 2019

How close are we to understanding chronic fatigue syndrome (ME/CFS) when we can accurately predict how the greatest stressor of all – exercise – affects ME/CFS patients' physiology? Nothing, after all, whacks a person with ME/CFS like exercise. That's a nice question to ask.

We're not there yet – the models being produced aren't comprehensive enough – but the fact that they're successfully incorporating important elements of two of the major systems (immune/endocrine) of the body suggests we're on our way to teasing out major factors in this disease.

It's taken an unusual approach to get to this point. It's pretty clear that ME/CFS arises out of the dysregulation of numerous systems, yet too often researchers approach these systems as if they exist in isolation from each other. That approach, these two research groups – Gordon Broderick's group based at the University of Rochester and Dr. Klimas's group based at Nova Southeastern University – believe is a big mistake.

Hypothalamic model of ME/CFS
A possible model of ME/CFS explains why. This model proposes that a stressor, such as an infection, triggers one stress response system (hypothalamus/pituitary/adrenal [HPA] axis) to activate the other stress response system (ouch!) (the sympathetic nervous system or fight/flight system) to create a positive feedback loop (an ongoing disease situation) kept alive by an inflammation in the hypothalamus.

It makes sense that the hypothalamus might be involved. In fact, a couple of years ago, Dr. Bateman concluded that everything in ME/CFS could begin with inflammation in the hypothalamus.

Located deep within the brain's limbic system, the hypothalamus is tasked with maintaining the body's internal balance – or homeostasis. The link between the endocrine and nervous systems, the hypothalamus produces the hormones which regulate the other hormones in the body. It directly regulates:

- heart rate and blood pressure (autonomic nervous system);
- temperature;
- fluid and electrolyte balance;
- appetite and body weight;
- glandular secretions in the stomach and intestines;
- production of substances that influence the pituitary gland to release hormones; and
- sleep.

Inflammation in the hypothalamus could be sustained by increased levels of just three cytokines (interleukin (IL)-1b, IL-6, and tumor necrosis factor-a (TNF-a). Put all these factors together and you could have the ongoing inflammatory/hormonal/autonomic nervous system mess that is ME/CFS.

Adding women into the equation
That HPA axis/immune model works, but it has a glaring hole – women. It can't explain the much higher ratio of women who have ME/CFS. It's possible women's greater susceptibility to infection and/or autoimmunity plays a role, but even then, any model of ME/CFS has to take into account women's complex hormonal situation.

In fact, researchers have for years shied away from including the complexity that women's hormones add into the equation. So few female mice studies were being done at the NIH, for instance, that in 2014 Francis Collins mandated that NIH-funded mouse studies include female mice.

However, there's been no shying away with this team. Instead, they've embraced the complexity of the female hormonal system and its manifold effects in a way no one else has done. The new model incorporates the HPA axis (corticotropin-releasing hormone [CRH], adrenocorticotropic hormone [ACTH], and cortisol), the hypogonadal [HPG] axis (estrogen, follicle-stimulating hormone [FSH], GnRH 1, luteinizing hormone [LH], and progesterone), norepinephrine, dopamine and immune factors (IFN-g, IL-1a, IL-1b, IL-2, IL-4, IL-6, IL-10, IL-13, IL-15, IL-17, IL-23, TNF-a, B-cells and NK functions).

It may be the first of its kind. It may be that no other model has so comprehensively incorporated sex hormonal findings into its results. The good news is that it appears to have worked.

The big test
Once they had their model, they gave it the big test: could it predict what happens in ME/CFS before, during and after exercise?

The study collected blood 10 times before, during and after (up to 24 hours) a maximal exercise test in 88 women (43 ME/CFS / 45 healthy controls). It measured frequencies of B cell (CD19+) and natural killer (NK) cell (CD3-CD56+) populations, cytokines (IFN-g, IL-1a, IL-1b, IL-2, IL-4, IL-6, IL-10, IL-13, IL-15, IL-17, IL-23, TNF-a) as well as estrogen (estradiol) and progesterone (at 4 time points).

Success!
"This finding suggests that the set of candidate mechanisms embodied in the endocrine immune circuitry model offer a framework for accurately reproducing the immune response to exercise." Authors.

The methodology is way beyond me and the authors do note several issues including a lack of data for some elements of the modelling, but a remarkable thing happened: the model was able to predict what happened to the immune/endocrine systems in ME/CFS both during rest and exercise.

Consider how difficult it must be to characterise the complex interactions in these systems at rest – something no one else to my knowledge has done – and then to throw in the huge impact that exercise must have on these systems – and get that right as well. This is clearly a robust model and a remarkable achievement.

The model found, if I'm reading it right, no less than 26 different ways to tweak these systems so as to arrive at an ME/CFS-like state. All the simulations, interestingly, involved "widespread endocrine dysfunction".

Immune hits
The exercise part of the study found that exercise does, indeed, whack the immune systems of people with ME/CFS quite hard: the levels of almost half the immune markers (IL-1b, IL-2, IL-4, IL-5, IL-6, IL-13 as well as the NK cells) were significantly altered in the ME/CFS group.

As noted above, the immune test results suggested the group's crazily complex models were right on; i.e. the modelling actually predicted perfectly the immune findings the testing revealed at rest and were within 5% of the immune findings during and after exercise.

Sex hormones
The modelling predicted the women with ME/CFS would have significantly higher estrogen levels ($p<.002$) at rest and throughout the exercise study – and they did. It also predicted transient up-spikes in progesterone would occur and a trend ($p<.07$) towards elevations in progesterone was found as well.

Predicting the future
Once they knew the modelling worked, the researchers pushed it to predict what the heck else was going on in ME/CFS. It turned out that the immune and endocrine dysregulations found were just a prelude: the modelling also predicted that a host of other markers (ACTH, cortisol, estrogen, GnRH1, IL-17, IL-23, LH, and TNF-a, IL-1a, B-cell activation, CRH, and dopamine levels) would be thrown off by exercise.

The models suggested, then, that exercise was massively altering many areas of ME/CFS patients' physiology – which would come as no surprise to anyone with this disease. All in all, the model/exercise study indicated exercise was triggering the following processes in women with ME/CFS…

- Inactivation of the HPA axis
- Overactivation of the HPG axis
- Heightened sensitivity to inflammatory stimuli, driven primarily by three cytokines (IL-1b, IL-6 and TNF-a) (particularly in the brain).

The model also predicted that:

- Inflammation in the brain is present (via the upregulation of chemokine (C-X-C motif) ligand 8 and IL-23).
- Dysregulation of the female hormone system has impacted the blood brain barrier, allowing immune cells to infiltrate the brain (Jarred Younger is exploring the possibility of an impaired blood/brain barrier now. A blog on that is coming up.)

Neuroinflammation
Neuroinflammation is clearly a topic Dr. Klimas is very interested in, and the paper suggested that the Epstein-Barr virus and/or mitochondrial issues in the hypothalamus in connection with mast cell activation could be causing it.

With Jarred Younger and another Univ. of Alabama at Birmingham researcher (McConathy) diving into a large brain imaging study, and with Ron Tompkins at the Open Medicine Foundation-funded Harvard ME/CFS Collaborative Research eager to use Harvard's brain imaging facilities, and with Dr. Klimas apparently interested in modelling neuroinflammation in ME/CFS, we will hopefully learn much more on the role neuroinflammation plays as time goes on.

Context matters
We often think of the body in terms of test results or data points, but single data or even multiple data points are hardly able to capture what's going on in a complex, dynamic system like the body. The upshot of modelling studies like these is that more traditional studies, with their focus on identifying "abnormal levels" of a factor, may be missing something vital: biological context.

Several ME/CFS studies, for instance, which appeared to fail to find evidence of significant alterations in female hormone levels, may be missing the forest for the trees. These studies didn't account for the outsized roles some female hormones could play once put into the altered endocrine-immune networks the models suggest are present in ME/CFS.

The fact that the models put forward in this paper suggest that overactivation of the HPG axis (estrogen, progesterone, etc.) is a major driver in women with ME/CFS indicates how stark the differences between a systems and non-systems approach to ME/CFS can be.

Predicting responders
The modelling efforts – which can assess how all kinds of inputs will tweak ME/CFS patients' systems – are also being used to predict the effect of different drugs – in this case, Rituximab and Ampligen.

We know that Rituximab didn't work out in ME/CFS and Ampligen is still up in the air – and the computer simulations largely bore this out. They suggested Ampligen would either work really well or have no effect at all. A return to health, however, occurred in only a "small fraction of the simulations run".

The Rituximab simulations did not suggest the drug would return ME/CFS patients to health, but that it might help ward off some "highly pathologic states" and offer a partial remission for a small number of patients.

The modelling effort also predicted which type of patient might benefit from each drug. It suggested, for instance, that ME/CFS patients with a certain biological profile (low levels of IL-1a, IL-17, and cortisol, intermediate levels of progesterone and FSH, and high estrogen levels) might benefit from Ampligen, while those with another biological profile (low norepinephrine, IL-1a, chemokine (C-X-C motif) ligand 8, and cortisol levels; intermediate levels of FSH and GnRH1; and high TNF-a, LH, IL-12) might benefit somewhat from Rituximab.

The potential of these kinds of models – to create personalized drug treatment regimens for people with ME/CFS based on their particular endocrine, immune and autonomic nervous system results – is clearly huge. That's a good thing, as the authors noted that the great heterogeneity found within ME/CFS ("the multiple disease phenotypes") presents real challenges.

Dysregulation, not irremediable damage
The good news was that, again if I read it right, the models suggest that ME/CFS is a disease of altered endocrine-immune regulation, not overt or irredeemable damage (i.e. to the basic circuits).

Those circuits have just been, as the authors have asserted in the past, pushed into a kind of altered reality. The circuits are functioning abnormally, but are not in themselves damaged: they just need to be pushed, prodded, and enticed back to normal functioning.

Conclusions
For me, this is all fascinating stuff, but what I'm really excited about is the process underway.

It's encouraging that the newer, more extensive model rested on – and ultimately validated – their earlier, less sophisticated model; they've had it right since the beginning. It's more than impressive that their models are actually able to predict the changes that occur when people with ME/CFS are put under the greatest stressor ever – exercise.

Even more encouraging is the fact that these models are being used to predict helpful treatments which are now being tested. It seems too much to ask, quite frankly, that any treatments at this stage will be a complete success. I would never expect the answer to come tomorrow, but a 30% improvement would be life altering – and if they can get that far, that success should lay the foundation for more.

Plus, even in the worst-case scenario (were the current drug trials to fail), the results will be fed back into the program and help them produce better, more accurate models of this disease. So long as Klimas, Broderick, Morris, Crawford et. al. can continue to get funding – and Dr. Klimas just got a major GWI grant – they should be able to keep improving their models of GWI and ME/CFS. (Next up, there appear to be models which incorporate mitochondrial metabolism, mast cells and neuroinflammation.)

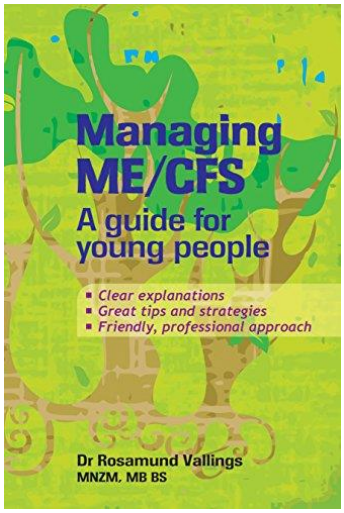
There's no doubt that this is cutting-edge stuff, with all that implies – potential breakthroughs as well as considerable risks. Consider how powerful, though, it would be to be able to put your immune and hormonal results into a computer and have it spit out a series of possible treatments that might shift your health back towards normal.

Some member recommended books

A few of our members have mentioned certain books at recent ME meetings that may be of interest.

Managing ME/CFS: A guide for young people (Kindle Edition), by Rosamund Vallings
Currently only available as an electronic book, the following link is for the kindle edition from Amazon UK, £9.60
https://www.amazon.co.uk/Managing-ME-CFS-guide-people-ebook/dp/B0118NVEBG

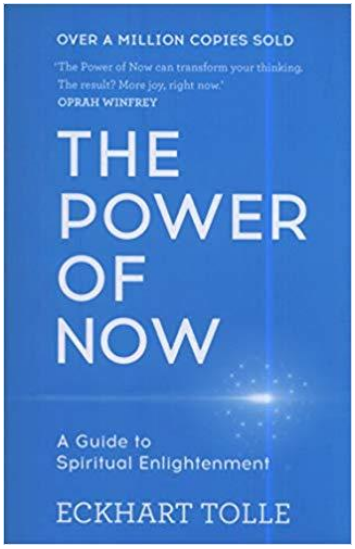
A review from the authors website reads…
"She explains this complicated illness in a way that is easy to understand. The book is full of great suggestions for managing everyday tasks and working through the ups and downs of the illness, and there are lots of tips on how to create the best chance of recovery. Dr Vallings has even included stories from young people who are managing this illness. Her message to young people is to learn as much as you can about ME/CFS and to actively take charge of your health."



Our group member adds…
"although this book is aimed at young people from about 10 to 16, it is a good summary and introduction to ME/CFS. Dr Vallings covers the medical side, explaining how areas such as the brain, circulation, and digestion are affected. There are practical tips on how to cope with school, college, friends, and holidays. I

recommend this book as a good introduction to the illness."

Further information about the Managing ME/CFS book can be seen here:
http://calicopublishing.co.nz/book/managing-me-cfs



The power of now: a guide to spiritual enlightenment, by Eckhart Tolle
£6.49 (paperback) from Amazon UK

Our group member comments that…
"It is very useful for anyone suffering anxiety, especially where they are worrying about the past or future."

Some worthy article mentions

In order to keep our group newsletters to a friendly size we are not able to include all of the interesting ME/CFS related articles of the moment. So as links some other articles that may be of interest include:

Under pressure: large spinal study finds intracranial hypertension common in ME/CFS
www.healthrising.org/blog/2019/12/22/chronic-fatigue-syndrome-intracranial-hypertension-craniocervical-instability

A large spinal study involving over 200 MRIs found:

- High rates of fibromyalgia (96%), joint hypermobility (49%) and Ehlers Danlos Syndrome (EDS) (20%) in ME/CFS. High rates of increased spinal fluid pressure (intracranial hypertension) (55-80?) – a condition which can produce many symptoms associated with ME/CFS
- Apparently normal rates of spondylolisthesis, osteophytes and spinal cysts
- Possibly high rates of bulging or herniated discs (which could interfere with spinal flows)
- Most normal clivo-axial angles – suggesting that cranialcervical instability may not be common in ME/CFS

The fact that the study was not published in a medical journal severely limits its impact.

Latest from Ron Davis: more evidence of "something in the blood"
https://mecfsresearchreview.me/2019/12/10/latest-from-ron-davis-more-evidence-of-something-in-the-blood

Something in (or missing from) the blood plasma of ME/CFS people seems to be affecting cells, making ME/CFS cells act abnormally. And finding the something responsible for that could provide a big clue to understanding ME/CFS. Davis has previously talked about his team's work to home in on the presumed "factor" in the blood. They start by splitting the blood, physically or biochemically separating its components into separate fractions. Then, they test to see which fraction of the blood contains the mystery factor. This work is being held up because the existing nanoneedle set-up is very slow. Davis's team have had problems making the nanoneedle chips that take the blood samples. And the machine that processes the chips can only process two samples at a time. The team have just built a prototype for a new machine that can process 200 samples simultaneously, which cost just $200 to build. And they now have more and better nanoneedle chips.

Chocolate cake

Quite a few ME/CFS people find themselves on dietary restrictions that make them feel better or which avoid certain additional symptoms, such as digestive symptoms.

The following is a diary free chocolate cake that maybe of Interest to some and has been provided by a group member
Cathy Gould.

The cake can be made both Dairy and Gluten free with the Use of gluten free flour.

Ingredients

225g plain flour
1 and a half teaspoons bicarb of soda
75g cocoa powder
300g soft dark brown sugar
375mls of hot water from recently boiled kettle
90mls rapeseed oil
1 and a half teaspoons of cider vinegar or white wine vinegar

Method

Put the flour, bicarb and cocoa powder into a bowl and mix together.
Put the sugar, water, rapeseed oil and vinegar into a pan, gently warm and mix together and then mix into the dry ingredients.

Pour the mixture into a 20cm springform cake tin with a paper cake liner inside the tin to prevent mix leaking out as it is a very wet mix.

Bake in oven at180 degrees Celsius for 35 minutes in an ordinary oven, or at 160 degrees Celsius for 55 minutes to an hour if you have a fan oven.

Test the cake with a skewer 5 minutes before time is up to see if it is cooked. If the skewer comes out wet, then cook for a bit longer until the skewer comes out clean.
Take the cake out and cool on a rack.

To avoid dairy in the icing, use icing sugar, cocoa powder and water. Mix together until runny and pour over the cooled cake.

I have never tried baking this with gluten free flour, but worth a try.

Delicious with dairy free ice-cream.