Solving The Riddle of Multiple Chemical Sensitivity: The Importance of TRP Channels

By Teena Booth

Introduction (Or, Houston we have a problem)

The closer one looks at the human body, the more one marvels at the intricacy of its design. Especially marvelous is our capacity for sensation, and how the body is able to perceive its environment through a delicate dance of energy. The sense of smell for example: Molecules of a scent rush into the nose as we breathe in, the molecule binds to a receptor (a protein) of a sensory neuron/cell at the top of the nose, the protein then changes shape, opening a channel and allowing an influx of ions that reverse the polarity the cell, firing off an electric signal that travels to the brain, which then interprets that signal as a sensation. It is a beautiful system, this translating of energy into conscious, perceiving life. Our sensory system connects us to the world and to the moment so seamlessly, so reliably, it never once crosses our mind that something could go wrong with it. But this delicate and finely balanced system gets bludgeoned every day by chemical onslaughts in the environment, in our homes, and in the food we eat. And once this system skews out of whack, and innocuous sensation suddenly leads to crippling pain -- what a shock! It feels as if the impossible is happening, our wonderful sensitivity turned against us.

It was August of 2013, in the middle of my ordinary life, that I began experiencing inexplicable headaches, heart palpitations, strange neurological symptoms and facial swelling. I thought at first I might have a food allergy, but eventually I worried I was afflicted with a brain tumor, or going crazy, or both. It took two months of fear and confusion -- along with visits to several doctors, numerous blood tests and a negative CT scan -- before I was given all the pieces of my medical puzzle. I was suffering from two related conditions: Multiple Chemical Sensitivity (MCS), and a food intolerance called Salicylate Sensitivity.

Essentially, whenever I breathed in chemicals from scented products like shampoo or detergent or cleaning solutions (beware of Swiffer), or when I ate spices or fruits or vegetables high in the natural food chemical salicylate (beware of cayenne), I experienced wretched headaches, a racing heartbeat, and a feeling like a shutter had been flipped shut in my brain. When I avoided those scents or foods, I felt pretty much normal. But of course, avoidance of those things was a

near impossible task. I quickly became a neurotic hermit, scared to be around other people, scared to eat. Worse, I felt life had become hostile to me. When the air you breathe and the food you eat effectively becomes poisonous to you…. Well, to say it was a rough mental road to travel is an understatement.

Although I'd previously never heard of such a condition--nor was anyone I personally knew familiar with MCS (including my doctor)--sensitivity to the chemicals in perfumes, scented detergents, cleaning products and air fresheners is actually surprisingly common. A 2004 prevalence study published in the American Journal of Public Health found that 12.6 percent of the population of the Southwestern U.S. reported "hypersensitivity to common chemicals," with 3.1 percent having been officially diagnosed with MCS .(1) Similarly, a survey sponsored by the California Health Department found that 15.9 percent of Californians said they are "unusually sensitive to everyday chemicals," with 6.3 percent receiving a diagnosis of MCS or environmental illness.(2) That means millions upon millions of us live with sensory systems overwhelmed by the swirling soup of chemicals that are so pervasive in our lives.

On one hand, I was lucky in that MCS is not life-threatening (although in the beginning, I did experience several anaphylactoid reactions that made me feel I might die). On the other hand, there were several uniquely cruel aspects of the condition. First, while most sick people can count on the comfort and support of their loved ones, MCS isolates one from other people. Merely sitting next to my child made me sick until I figured out the problem was the scent in his hair gel. I could no longer see friends because of the laundry scent on their clothes. Going into any public place – from the movie theater, to the grocery store and even the doctor's office – meant a fierce headache and racing heartbeat from whatever cleaning products might have been used there. I felt trapped in my house. Yet even there, the particle board in my kitchen and bathroom cupboards outgassed something (formaldehyde?) that gave me headaches, so I'd stay hunkered down in my air-purified bedroom, honing a prisoner mentality.

Not only did people disappear from my life, but a dismaying number also had little compassion for my dilemma, with several openly mocking me or suggesting the problem might be "all in my head." Ultimately, the most upsetting aspect of MCS is that is so little known and even less understood. It has never been recognized as a legitimate illness by the American Medical Association. (3) The condition does not show up as an abnormality in the usual diagnostic tests, it only presents itself in the subjective experience of the patient. This leaves those of us who suffer from chemical sensitivity caught in a Catch-22: Mainstream medicine will not recognize MCS without objective evidence, but in order to investigate and find that objective evidence, they must first be willing to recognize that the

condition exists. Thus, we suffer from this life-changing malady with little understanding and support from our loved ones, and even less validation or help from our doctors.

A scattering of alternative doctors affiliated with the American Academy of Environmental Medicine do specialize in "treating" MCS. But those doctors are few and far between, and often operate on a cash only basis as insurance companies don't recognize the condition, let alone pay for treatment. Furthermore, most of these doctors seem not have any true knowledge of what causes MCS, merely a vague web of theories that the body is suffering from a detox pathway impairment. The few existing books on Multiple Chemical Sensitivity tout the "bucket theory" of MCS, an idea made popular in the 1980s and 1990s, which says that one's system becomes increasingly overloaded with chemicals and toxins and stress until it reaches a tipping point that tilts them into the condition. But that theory never made sense to me. If it was true, then a combination of detoxing, chemical avoidance and clean diet should eventually reverse the condition. But I could find few accounts of people claiming to be 'cured' from MCS by detoxing. Many MCS sufferers had been living clean and detoxing for decades and yet continued to suffer reactions when exposed to chemicals.

Still, despite a lack of solid results, the standard treatments from MCS specialists typically focus on detoxing measures such as saunas, and/or managing symptoms in a way that may or may not actually worsen the condition. For example, "provocation and neutralization" is an involved and often traumatic process that purposely elicits reactions to a substance in order to find the so-called "neutralizing" dose of the substance. But in a survey of 917 MCS sufferers published in 2003, only 45 percent of those who'd tried it said the treatment was helpful to them, while 28 percent said it had no noticeable effect, and another 25 percent experienced it as actively harmful to them.(4) My visits to the one specialist in my state were comforting in that the staff at least validated my experience and confirmed my diagnosis, but those visits rapidly depleted my bank account and did absolutely nothing to relieve the severity of my symptoms.

I felt hopeful when I discovered a supplement protocol for MCS from Dr. Martin Pall, a professor of biochemistry and medical science, who in 2007 published his theory of a possible mechanism underlying MCS, as well as fibromyalgia and CFS, or chronic fatigue syndrome (5). He hypothesized that in this commonly co-occurring cluster of conditions, the body became trapped in a feedback loop he called the "NO/ONOO Cycle," in which too much nitric oxide (NO) in the body degraded into peroxynitrite (ONOO), causing oxidative stress and inflammation, which then created more nitric oxide and so on. Although I was taking a good number of the supplements he recommended (including

magnesium, which I had started taking in the month before I started going haywire), I immediately ordered everything else on his list, and was soon swallowing up to 25 pills a day. But after several months, I found no improvement in my symptoms. Internet searching turned up only a few accounts of benefits from the protocol, but many more forum posts that it hadn't made a difference. Even Pall himself wrote in 2010 that, while he still believed in the merit of his theory, his supplement protocol hadn't led to many reversals of MCS. (6)

Almost all of the stories of MCS reversal I did find online had been posted by the few people who claimed absolutely certainty about the cause of MCS. Ashok Gupta, the director of a clinic in the U.K. (7), and Annie Hooper, a counselor from Canada (8), both contend that MCS -- as well as fibromyalgia and CFS – results from faulty wiring in the brain, either in the amygdala (Gupta) or limbic system (Hopper). Both describe a "trauma loop" in which the brain incorrectly perceives threats, then releases stress chemicals into the body which then trigger more symptoms and reinforce the loop. Both market programs for brain rewiring and limbic system or amygdala retraining, and both have passionate advocates. And Dr. Claudia Miller, one of the few authorities on MCS (which she calls Toxicant-Induced Loss of Tolerance or TILT), seemed to confirm the brain impairment theory in a November 2013 article in Discover magazine.(9)

I didn't hesitate to order both Gupta and Hopper's brain retraining programs and as I watched the DVDs, I was already planning my own giddy testimonial of how I'd been cured of my malady. But while I definitely found their techniques helpful in dealing with my symptoms (especially Gupta's), and even lessening them to a degree, I was not able to completely reverse my symptoms.
The temptation was to blame myself, to scold myself for not doing it "right," but I found online accounts from others who could report similar improvements, but no complete reversal after many months of effort.

Ultimately, I found the brain impairment theory did not particularly match my experience. If my brain was mistakenly repeating a trauma loop that was triggered by the smell of harmless chemicals, then why did I experience symptoms from chemicals I couldn't smell at all? And why did I experience my worst symptoms from certain foods? I might not even know I had eaten an offending food until my headache and swelling face made me pay attention and go figure out what the culprit was (it was always some form of salicylate). That indicated to me that the "mistake" began before my brain took over the interpretation of it. However much faulty brain wiring might indeed be exacerbating or perpetuating my symptoms, I felt certain there had to be a deeper physiological cause and dysfunction in my body.

Sensing Chemicals (Or, Teena Gets a Clue)

Four months after the onset of my MCS, I stuck an air purifier in my car and drove up to Zion National Park to celebrate my 50th birthday in the most "safe" place I could imagine. However, an hour into a hike to the bottom of a gorgeous canyon in a remote area of the park, I had one of the worst MCS reactions I'd ever had – a complete headache-exploding, head-swimming, heart-slamming, throat-swelling, mouth-tingling reaction that sent me stumbling, panicked, back the way I came. Once I got away from the canyon bottom, I felt fine again. But it made no sense to me to have a reaction there, I was far away from any other human beings and their scents and chemicals, I had eaten nothing but bland salicylate-free food that day. I was surrounded by nothing but pristine protected nature, and hiking at home in the Arizona desert always took away my reactions, not caused them. I had been feeling happy and easygoing in the preceding hour, so I simply couldn't bend my mind to believe it was a stressed, hyperalert amygadala that had triggered the reaction. So what on earth had happened?

Later, I would go online and google "flora and fauna of Zion canyon" and read that trees of the *Salicilae* famiy (willow trees) thronged the park's canyon bottoms. There it was: salicylate, my nemesis. It never would have occurred to me that a tree could outgas a chemical that would set off an MCS reaction. I was horrified by this (I might never be able leave Arizona again!), but also fascinated by this. Exactly how had my body sensed that chemical was in the air?

I finally began asking myself questions I probably should have been asking months earlier. How does the human body 'sense' chemical irritants? Why and how might that sensing become dysfunctional? And, how was it possible that eating certain foods could evoke the exact same reactions as inhaling unrelated chemicals?

My questioning led me to revisit a post I had earlier seen on the Salicylate Sensitivity forum, but hadn't really paid attention to at the time. Dated January 2011, the message posted by someone identified by "marieling," said: "Basically people with food intolerance and quite a few other diseases have an over-expression of Transient Receptor Potential Cation Channels (TRP's) - particularly TRPV1 and TRPA1."(10) Another poster identified as "black wizards" agreed and followed up with numerous links to studies on TRP channels – a group of ion channels in the surface membrane of sensory neurons. One of those links was to a 2004 paper by Martin Pall which asserted that the TRPV1 channel is the "target" of chemical irritants in MCS.(11)

According to the paper, the TRPV1 receptor/channel is "a critical component in the 'common chemical sense,' located in the small C-fibers of the trigeminal

nerve, which innervates a large part of the face, eyes, and upper airways, and provides an early warning for sensory irritation, telling the organism it has entered a zone of irritant chemicals." As I read those words, I felt that jolt of excitement one feels when one discovers the key that will crack a long mysterious code.

Those posts and that paper launched me into months of research through the most recent studies on TRP channels. Though nearly all of the hundreds of TRP channel studies published over the past decade have looked at the channels in the broad context of chronic pain rather than the narrow context of MCS, chemical sensitivity is nothing if not a chronic pain condition. And as the pain is triggered by exposure to compounds which expressly activate TRP channels, I believe these pain studies also shed remarkable light on the most likely physiological mechanism underlying the development of many cases of MCS and salicylate sensitivity.

What follows is my best understanding of how TRP channels work, and my own interpretation of the theory, occasionally hinted at in a few places on the internet, that Multiple Chemical Sensitivity is basically a TRP channel problem. Which doesn't mean it is not a brain wiring problem as well; as I will explain below, faulty brain wiring almost certainly contributes to the intractability of the condition. However, it has become clear to me that overly abundant or otherwise malfunctioning TRP channels are the primary cause of onset.

Of course, I'm no medical professional, have never even studied science beyond compulsory classes in school, so I am not any kind of authority on this subject. My lack of credentials has made me hesitant to make my thoughts public. We are trained by our culture to believe that, when sick, we are supposed to submit ourselves to the proper medical authorities and let them tell us what is happening to us. But what are we to do when the medical professionals refuse to recognize the condition from which we suffer? The lack of scientific curiosity on this debilitating condition, which afflicts millions, is appalling to me. The hard truth is: those of us who live with MCS have literally been left to our own devices.

Fortunately, we live in the age of the internet, and have access to resources that would have been unthinkable only a decade or two ago. If one has the patience to comb through those resources, one's own devices can lead to a fairly well-informed theory that can then be tested against one's own unique experience. And so I am putting my theory "out there" for discovery and testing by others left to their own devices in the hope it might help move our common knowledge of this condition forward. I can say this theory was remarkably helpful to me in working my way through the pain and confusion of a life turned upside down, and in turning it right side up again.

The Stages of MCS

In my earliest days of knowing I had chemical sensitivity, I ran across the web page of environmental engineer Rabin Prusty, which described MCS as advancing in stages.(12) It made sense to me that my problem did not just come from 'out of nowhere.' Although I have found no other sources which delineate particular stages of MCS, it is widely recognized that the condition impacts different people with varying degrees of severity. I find it very helpful to understand MCS as a spectrum in which one may perhaps move back and forth between stages.

Stage One: A dislike for perfumes and/or an aversion to strong smells and chemicals. Mild headaches from scented products like candles or air fresheners, or feeling ill walking down the laundry aisle in a supermarket. This is the stage likely experienced by those 12 to 16 percent of Americans who say they are unusually sensitive to chemicals.

Stage Two: This is the stage where MCS becomes suddenly obvious and reactions "spread" to other chemical irritants, such as gasoline fumes, or outgassing from many other normally-tolerated items such as computers, carpets or cupboards. Reactions worsen from mild headaches to more severe headaches and brain fog, and may begin to include other bodily systems such as the cardiovascular (racing heartbeat and palpitations), skin (hives, rashes, itching, swelling), lungs (asthma like reactions), or gastrointentestinal upset. This is also the stage in which food intolerances begin to appear, such as getting a headache or diarrhea when eating strawberries or drinking tea. One's sense of smell becomes bizarrely heightened, and leaving the house becomes increasingly difficult. This is undoubtedly the stage experience by those 2 to 6 percent of Americans who have reached the point of being diagnosed with MCS.

Stage Three: Leaving the house becomes a nightmare during this debilitating stage. The slightest hint of fragrance chemicals can lead to frightening symptoms in which it feels as if every system is going haywire (from a surge in histamine). It especially hits the brain – not only punishing headaches, and dizziness, but one may burst into tears for no reason, or have trouble navigating normal tasks. Reactions may also include extreme tachycardia (racing heartbeat), blood pressure sharply rising or crashing, all-over skin itching, facial edema, throat swelling, a metallic taste in one's mouth, or other anaphylaxis-type reactions. Some may experience sudden diarrhea or a constant need to urinate (again, due to excess histamine). Many medications and almost all foods can trigger the same reactions, especially processed chemical-laden food, and many trapped in this stage live on a diet consisting of only five or six foods (such as low-salicylate unseasoned meat, rice, potatoes, pears). This is also the stage where face masks

become indispensable and many people feel they have no choice but to give up their lives and go live isolated and alone in a trailer or tent in the woods.

Stage Four: This extremely advanced and life-threatening phase is apparently rare, and most likely caused by catastrophic chemical injury. In this stage, it is impossible for the sufferer to breathe almost any air without an oxygen mask, and any exposure to chemicals can cause seizures, brain damage, or even death through anaphylaxis. This stage is life made impossible.

When I first encountered the idea of stages, it was clear to me that I had been experiencing the early stage of MCS for years, even decades. I'd long since quit wearing perfume or using scented laundry detergent as they always made me feel "yucky." The smell of scented candles or air fresheners in someone else's house always seemed overpowering and unpleasant.

It was also clear to me that in August 2013, I had suddenly progressed into Stage Two of the condition. And in the first two months, when I was still clueless about MCS and didn't know enough to avoid scented cleaning products, my reactions continued to worsen week by week, and I'm sure that for a short time I had actually advanced into Stage Three. In fact, late one evening I called 9-1-1 because I was certain I must having a stroke or heart attack or both. (Later, after several bad reactions to food coloring, I realized my paramedic-diagnosed "panic attack" had actually been an anaphylactoid reaction to the dyes coating a Benadryl capsule.)

Once I figured out what was happening to me and began practicing chemical avoidance, I moved back into Stage Two and life became more manageable. But I stayed in Stage Two for another four dark and depressed months, feeling sure I was "stuck" that way forever, and desperately searching for the answer to my problem.

Today, I am mostly back in Stage One; I still have a strong aversion to perfumes and chemical scents, but in what feels like a miracle, I can go many days without the symptoms of reactions. I can once again eat (most) any food I like without a crippling headache. Although I still have MCS, I believe my "recovery" back to the more normal life of Stage One was due to measures I took once I understood the nature of TRP channels, and how they might malfunction, and then changed my habits accordingly.

But before I get to TRP channels, I'd like to take a closer look at the onset of MCS and the possibility that there are actually two different paths to developing chemical sensitivity, or two different etiologies for the condition. If that is the case, then understanding which path one traveled to develop the condition could be vitally important for figuring out a way to reverse it.

The "Two Path" Theory of MCS

In 2001, Pamela Reed Gibson, author of *Multiple Chemical Sensitivity*, published the results of a survey of 917 people with self-reported MCS.(4) In answer to the question about how the condition developed, 20 percent of those with MCS could identify a single chemical exposure event which triggered onset, while 58.5 percent said onset came on gradually, after a "series of low level exposures." (The rest didn't know or blamed things such as stress). Most everyone familiar with MCS acknowledges that there are two different "speeds" of onset, some quite sudden, some gradual. This was the first fact that made me wonder, could there be two "types" of MCS?

In reading other people's accounts of their MCS experiences, I also noticed that a certain number of people complained about food intolerances (such as salicylate sensitivity), while others didn't. While I I didn't find a lot of curiosity about this common co-occurrence between the two conditions, I myself felt it had to be a key clue to the problem. Especially attention-getting to me was that so many people reported that going on a low salicylate diet actually exacerbated their MCS, which is exactly what happened to me. My sensitivity to scented products dramatically increased within a week of starting a low salicylate diet. Indeed, Anne Swain, the scientist who first established salicylate levels in food, almost casually acknowledged this in her book, Allergy Friendly Food. In one small warning paragraph, she wrote that going on a low food chemical diet makes many people suddenly "more sensitive to smells."(13)

Why the fact that a low salicylate diet could actually induce a higher stage of multiple chemical sensitivity wasn't being highlighted and hotly debated in MCS circles puzzled me. The usual explanation of MCS being the result only of chemical injury or chemical exposure was clearly not true; for at least some sufferers it was impacted by diet. Here again, I saw evidence for two different paths types of, or paths toward, MCS.

Another striking difference in people's experience of chemical sensitivity was their responsiveness to the brain rewiring techniques of Ashok Gupta and Annie Hopper. Many people with even the most long-standing MCS had apparently been able to dramatically and completely recover from the condition in a fairly short time with limbic system or amygdala retraining techniques. But many others, like me, had been unable to fully recover from the condition through even the most persistent effort at brain retraining. Again I wondered, was this because there are actually two types of MCS?

It was while researching TRP channels that I came across a paper published

in a pain journal which talked about different types of hyperalgesia, or the experience of pain in response to innocuous or low level stimuli (an apt description of MCS). This paper described two different paths in the development of hypersensitivity to stimuli:

"Hyperalgesia arises either from peripheral and/or central sensitization. *Peripheral* sensitization occurs by enhanced excitability [due to TRP channel activity] of nociceptive C-fibres in sensory neurons." Meanwhile, *central* sensitization results from "in an increase in nociceptor synaptic efficacy and enhanced responsiveness of neurons."(14) In other words, peripheral hypersensitivity is a phenomenon that happens at the local cell level, while central hypersensitivity develops throughout the nervous system and, because of our brain's plasticity, it becomes "wired" into the brain.

This same paper also pointed out that sensitivity that develops gradually over the long-term is often due to "expression and/or silencing of specific genes," whereas more sudden and short-term sensitivity is likely due to "covalent modification of the receptor," meaning something has happened to change (or injure) the TRP channels on the surface of the cell.

Reading this, I found confirmation that there must indeed be two different paths to developing MCS: 1) the sudden onset from a chemical exposure and/or injury which set in motion the process of **central sensitization**; and 2) the more gradual result of ongoing cell-level **peripheral sensitization** which could be as much the result of genetic susceptibility as chemical exposures.

If my "two path" theory was correct, it would explain why only some, and not all, of MCS sufferers could be cured through brain retraining techniques. For those who experienced a chemical exposure leading to temporarily malfunctioning TRP channels, that cell-level injury would heal over time, and normal cell-level TRP channel functioning would eventually return. However, because the brain had been so quick to rewire itself through central sensitization, one would be left stuck in the trauma loop of MCS, even when there was no longer a reason for it at the cell level. Those 'sudden onset' sufferers would therefore be the people most likely to completely recover through brain retraining.

On the other hand, 'gradual onset' MCS sufferers (nearly 60 percent of us, remember) were more likely to be afflicted with a cell-level problem -- such as a genetic tendency to overexpress TRP proteins -- resulting in ongoing peripheral sensitivity that simply could not be healed over time. While central sensitization almost certainly played an exacerbating role in this second path to MCS, no amount of brain retraining would lead to full recovery as long as that ongoing cell-level peripheral sensitivity was an issue.

The Sensitive TRP Channel

Once upon a time, we humans roamed the earth in small hunter-gatherer bands, looking for sustenance. In order to keep ourselves alive and find food that would nourish us, we acquired an acute sensitivity to our environment, allowing us to perceive different temperatures, tastes and smells. This is where the handy dandy Transient Receptor Potential (TRP) ion channel came in.

Technically, TRP is a protein manufactured inside human cells according to instructions from specific TRP genes in our DNA. Once assembled, the protein moves to the surface of the cell, where it sits embedded in the cell membrane, ready for stimulation. Upon activation by the particular molecules it is designed to respond to, the TRP protein changes its shape and opens a channel,' allowing mineral ions (usually calcium ions) to flow from extracellular fluid into the cell. These ions excite the cell, reversing its polarity and causing it to fire off an "action potential," an electrical signal that moves through the nervous system to the brain, which then interprets this signal as a sensation. Meanwhile, the activation of the TRP channel has also released a flood of neurotransmitters and other chemical compounds like histamine that instruct different parts of the body how to respond to that particular molecule.

It is chemosensory TRP channels that protected our hunter-gather ancestors from the extreme-tasting chemicals in different plants and foods that could be harmful to us. As one researcher explains, plants try "to discourage predators by the unusual sensory quality of spices. [Yet] by some strange perversion, humans have learned to enjoy low doses of these deterrent chemicals," and over time the naturally occurring chemicals in spices have greatly contributed to our "gustatory pleasure."(15) That's human nature all right, to love what is bad for us.

Out of 28 different TRP subtypes distributed throughout the body, several are found primarily on our sensory neurons, the specialized nociceptive cells located in the sensing apparatus (ganglia) of the central nervous system. Specifically, TRPV1, TRPA1 and TRPM8 are the body's temperature and "spice" sensors, activated by hot and cold as well as certain compounds in plants and foods, such as the "hot" in spicy cayenne, or the "cool" in mint or menthol. TRPA1 in particular is activated by pungent compounds like cinnamon, garlic, ginger, and also *the salicylate in spices and foods*. (16)

When I first read that, I jumped off my couch with a loud, "Aha!" Surely, TRPA1 was the culprit in my salicylate sensitivity. I sat back down to dig deeper into studies on this particular ion channel and found this:

"TRPA1 channels respond to a multitude of irritants with diverse origins and

chemical structures… [and] may bind to a large variety of irritant molecules to induce sensory neural excitation. "(17)

Another "Aha!" ensued. I finally understood why someone with MCS could experience the exact same reaction after eating a high salicylate spice like thyme, or while standing next to someone reeking of Downey fabric softener. Both activated TRPA1 and, to a lesser degree, TRPV1. (Both are co-expressed in sensory ganglia.)

Of course, the MCS reaction is not a "normal" response to TRP channel activation. In the normal way of things, activation is quickly followed by desensitization. Once the TRP channel opens to the influx of calcium ions, the increased intracellular calcium quickly shuts down the sensitivity of the receptor, and calcium influx basically stops. (18) This allows the body to quickly adapt to various stimulants the body is exposed to without chronic overstimulation, and explains why, when one first walks into a room with a funny smell, it can seem overwhelming at first but then quickly becomes barely noticeable. It also explains how when one first gets into a hot bath, it feels very hot at first, but the body quickly adjusts. (TRPV1 is literally the heat-sensing system of the body, and in laboratory tests, TRPV1 "knockout" mice have problems sensing heat stimuli.)

The process of TRP desensitization explained to me why going on a low salicylate diet could possibly advance or exacerbate MCS. With strict avoidance, perhaps one no longer regularly desensitized TRP channels, so that they became more or less 'virginal' again, sensitive to the slightest stimulation. It also possibly explained why saunas were often experienced as helpful in reducing MCS symptoms. Perhaps it wasn't the sweaty detoxification aspect after all, perhaps the heat served to desensitize thermal-sensing TRP channels.

But this begged the question, if TRP channels are normally supposed to desensitize themselves, then what exactly is happening in MCS?

Studies have shown that TRP channels can not only be desensitized, they can also become unusually hypersensitized, a process by which the cell causes TRP channels to increase in number and/or become more easily activated. Since TRP genes are responsible for how many TRP proteins the cell makes, there are genetic reasons one can overexpress the proteins (for which I could see a lot of evidence in my own family). Or, one could engage in a lifestyle which turns TRP genes on or otherwise encourages overexpression, such as a spice-heavy diet (I was a cayenne pepper freak, put it on everything). Or, a high-fruit and -vegetable diet rich in TRP-stimulating salicylates (like my two years of vegan and Paleo eating). Or, the frequent drinking of alcohol (um yes, that was me, too; I drank wine with dinner probably 4 or 5 nights a week). Indeed, the ethanol in alcoholic drinks is known to be such a potent TRP sensitizer that ethanol is sometimes

used specifically for that purpose in laboratory studies.

Once overexpressed and/or hypersensitized, TRP channels release all kinds of pro-inflammatory chemicals into the body, including substance P and calcium gene-related peptide (CGRP), a well-known trigger of headaches, the most common MCS symptom. These chemicals also cause mast cell degranulation throughout our tissues, which releases a flood of histamine into the body and triggers most of the other heart-pounding MCS symptoms. This excess of chemicals not only creates the reactions so well known to MCS sufferers, it also creates what is known as an "inflammatory soup" in the body, causing neurogenic inflammation, which in turn releases still more chemicals into the body that ratchets up the sensitivity of TRP even more. It is a vicious loop inflammatory cycle that once turned on, is very difficult to turn off.

How To (And How Not To) Address a TRP Problem

Once I had a basic grasp of how TRP channels work, and felt I understood how I had become so chemically sensitive, I was in a hurry to start addressing the problem by trying to assertively 'desensitize' my own TRPV1 and TRPA1 with my own self-fashioned 'spice protocol.' Why spices? Well, I was very focused on the fact that desensitization of a channel first required the activation of the channel. Plus, I had read on the Salicylate Sensitivity forum that some people felt they could increase their tolerance for high salicylate foods by first ingesting cayenne pepper, the well-known TRPV1 agonist that efficiently initiates the activation necessary for desensitization. And so, I began eating cayenne for TRPV1 and mustard for TRPA1 at the beginning of every meal, and waited excitedly for 'normal' TRP function to return.

Unfortunately, instead of heading toward normal, within 10 days or so I had relapsed back into Stage Three of MCS, and was experiencing the worst reactions to detergent scents I'd had in months. I was beyond disappointed. But the experiment made me think more carefully about all the possible ways TRP channels might be dysfunctional in MCS.

Was my problem primarily the vicious feedback loop of inflammation overactivating TRPs? That seemed plausible; for years, my blood test results had showed highly elevated C-reactive protein levels, a well-known marker for inflammation. To address whatever inflammatory soup might be swirling through me, I started taking high doses of fish oil each day, and making sure I kept to a low histamine diet.

Was my problem simply the result of an overexpression of too many TRP channels? Looking at a family history of allergies and aversions to scented prod-

ucts, it seemed likely that I might have a genetic reason for making too much TRP protein. Of course, there wasn't much I could do to change my genes; but, perhaps a TRP gene defect had been epigenetically turned 'on' through a lifestyle which included a TRP-activating spicy diet or frequent alcohol use. If that was the case, I could work to change my habits, and perhaps over time the defect would turn 'off.' And so, I drastically cut down on alcohol and tossed my spices into the trash.

I thought again about my failed spice protocol experiment. If activation was necessary for desensitization, why hadn't specifically activating the relevant TRP channels led to desensitization? It dawned on me that maybe my primary dysfunction was not merely in the overexpression of TRP proteins, but also in the desensitizating of, or closing of, the channel. Perhaps some people with MCS had TRP channels stuck "open" in activation mode, and so continually churned out cascades of the inflammatory compounds that created the symptoms of a reaction. Perhaps my entire problem was that *my ion channels were not desensitizing properly*.

I knew from my research that TRP channel desensitization was the result of an influx of calcium into the cell, and, at least in normal functioning, once a certain level of intracellular calcium was reached, the channel would close to avoid a toxic overload of calcium. So if my TRP channels were not closing, was it because calcium ions were somehow not properly flowing into the channel?

The only reason this question occurred to me was because for the past decade, I had been taking the calcium channel blocker Norvasc, prescribed for unexplained hypertension I'd had since my 20s. (Turns out TRP channels are involved in blood pressure regulation, but that's a different story). Back when I first discovered I had MCS, I had of course wondered if my daily dose of Norvasc might have anything to do with it, but I had been taking it for over ten years without noticeable side effects, so I doubted it had suddenly triggered the onset of MCS. Plus, not once, in any article or forum or message board, had I come across any mention of calcium channel blockers in relation to chemical sensitivity or food intolerance. Still, I wondered whether I should try to wean myself off the pills, just in case.

I then looked back at my journal to see what I might have been doing differently in the weeks before onset that might have influenced the flow of calcium ions into my cells. I was reminded that I'd started taking magnesium a month before the onset of MCS; I had read that it helped to lower blood pressure and combat stress with a calming effect on mind and body. Indeed, I'd found that magnesium dramatically helped relieve my muscle tension and improve my sleep, and I'd felt pleased with the discovery. Once I was sick, and saw that it was on

Martin Pall's list of supplements, I upped my intake still more, to 400 mg a day.

But despite my confidence that magnesium was nothing but beneficial to me, the time correlation between starting the supplement and the onset of MCS sent me back to the computer to research magnesium. After a few google searches, I found the mineral described as… (drumroll please)…. "nature's calcium channel blocker." Another Aha! moment. I read some more and discovered that calcium ions are "antagonized" by magnesium ions in the nervous system, and that supplemental magnesium has been shown to enhance the effects of calcium channel blockers like Norvasc.(19)

I immediately stopped taking magnesium. And, *in less than a week*, I noticed I was no longer having reactions when I left the house. I also noticed I no longer got an instant headache when someone wearing detergent-washed clothes walked into my house. I thought maybe I was imagining it. So I went out to buy some scented detergent and washed a shirt in it in the sink to better test it. I sat with the shirt for an hour, less than a foot away from my nose, and no reaction. None. I was stunned. Just like that, I had moved out of Stage Two of MCS, back into Stage One, and life as I once knew it was returned to me. At least for awhile…

More revelations and a "treatment" that works

For over month, I was completely symptom free and full of hope that my problem was solved. I excitedly told the people around me about my dramatic reversal, and laid the blame directly on magnesium. But the truth was, I found it hard to believe that I might have caused the onset of MCS merely by taking a supplement safely swallowed by millions every day. It was just as hard to believe that the mere cessation of swallowing those few pills each day could have reversed the condition all by itself. (I was doing other things at the same time, like practicing brain retraining techniques to address central sensitivity, as well as taking lots of fish oil, cutting back on alcohol, and eating a low salicylate diet, so those other strategies could have been playing a part as well.)

I suspected that the magnesium in itself was not the problem, but rather its amplifying effect on the action of the calcium channel blockers I was taking. I further suspected the medication was the real cause of the problem and determined to wean off it. I began cutting down my dosage, by a quarter for about ten days, by half for another ten days. And then…

My MCS symptoms returned. First, in a minor way that made me wonder if I was imagining it. Then all at once I was waking up swollen-eyed and getting headaches from my bathroom cupboards. I was back to Stage Two. *Again*. Talk about demoralized. I went back to my full dose of Norvasc. After about a week,

my symptoms began to improve again (although not completely reversed). It was difficult to wrap my mind around. After a few weeks, I tried to again to wean off the medication, and again, within about ten days after getting down to half a dose, symptoms dramatically increased in severity. It was not my imagination. While magnesium somehow exacerbated MCS symptoms, the calcium channel blocker improved symptoms.

I went looking for an explanation, and found a research paper on the effect of calcium channel blockers on TRPA1. (20) The introduction confirmed my belief that a problem with TRPA1 is likely responsible for multiple chemical sensitivity. "Many TRP channels are involved in sensory signaling cascades, detecting physiochemical signals in the environment… [But] TRPA1 is phylogenetically separate from the rest, and is a remarkable example of a broad-band chemodetector, responding to many natural and synthetic irritants."

According to the paper, TRPA1 is also "unique in the molecular mechanism of activation." Whereas other channels require an influx of calcium for activation, TRPA1 "does not depend on elevated calcium levels," and neither does elevated calcium "trigger the desensitization" that follows activation. From my reading, the authors of the paper found that calcium channel blockers are able to activate, and therefore desensitize, TRPA1 channels through its own unique action, independent of calcium. While the authors ventured theories about what this action might be, they could not say for sure. Basically, they said more research is required to understand how a drug that should theoretically block activation of the ion channel has the opposite effect.

It was helpful to have some sort of hint of explanation, but the paper raised as many questions for me as it gave answers. In my particular case of MCS, calcium channel blockers clearly help control my symptoms, and I continue to take a full dose every day, and mostly keep myself hovering on the line between Stage One and Stage Two. Some days I don't notice any symptoms at all, other days (especially if alcohol is part of the day) the telltale MCS headache comes back at spicy food or stray blasts of scent, and annoyingly settles in. So I am not cured by any means. But staying on Norvasc helps keep it at bay.

I have wondered if calcium channel blockers might be an effective "treatment" for others with MCS. I have also wondered if perhaps I would have experienced symptoms much sooner in my life if I had not been on calcium channel blockers for the last ten years. I have also wondered the opposite: What if I developed MCS in response to long term use of the medication? What if long term use causes the body to overcompensate for the calcium blockade by multiplying the number of TRP channels on my cells? What if by continuing to take it, I am treating the symptom while exacerbating the underlying cause of the condition?

Ultimately, I still have no idea of the cause of my MCS, or what my essential malfunction might be, other than I have "a TRP problem." TRP channels, and their ability to desensitize themselves, are clearly at the heart of this issue for me, and perhaps the majority of MCS sufferers. One reason I wrote this paper and am now putting it online is in the hope to hear from others about their own unique experiences, which might shed more light on mine. I welcome all opinions and feedback at mcstheory@yahoo.com.

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