

PERSPECTIVE & COMMENTARY

Commentary

The Ising Model Applied on Chronification of Pain

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Abstract

This is a hypothesis-article suggesting an entirely new framework for understanding and treating long-standing pain. Most medical and psychological models are described with boxes and arrows. Such models are of little clinical and explanatory use when describing the phenomenon of chronification of pain due to unknown causes. To date no models that have been provided - and tested in a scientific satisfactory way - lays out a plan for specific assessment due to a specific causal explanation, and in the end serves the clinicians, patients and researcher with tools on how to address the specific pain condition to every individual pain patient's condition. By applying the Ising model (from physics) on the phenomenon of chronification of pain, one is able to detangle all these factors, and thus have a model that both suggests an explanation of the condition and outlines how one might target the treatment of chronic pain patients with the use of network science.

Key Words. Chronic Pain; Persistent Pain; Pain Medicine; Pain Disorder; Measurement

Voltaire claimed that “The art of medicine consists of amusing the patient while nature cures the disease.” That looks more and more true as evidence-based medicine advances. It is hardly controversial to state that longstanding pain for decades has been a challenge to treat. Even today in the era of omics, advanced imaging techniques, sophisticated biostatistics, big data, machine learning and nanotechnology, we still struggle to sort out the underlying principles of an individual's development of longstanding pain. As a logical consequence of this, the medical community does not possess specific and effective treatments to target such unspecified conditions.

In addition, we struggle with another conceptual problem as well, the linear understanding of medical challenges [1]. Linearity in medicine is rare, even in the real world linear systems are rarely found [2]. Fractures might be treated with a cast for some weeks and then the fracture has healed, or simple infections like lower urinary tract infections in fertile women are usually successfully treated with antibiotics; and thus appear to the observer (i.e., both the patient and the doctor) to be of linear nature. But most medical issues may be of a non-linear nature [1–3]. This should not come as a surprise; we have been talking about the biopsychosocial model for decades now, and thus, acknowledged that most medical conditions are multifaceted. Complexity and linearity are not interchangeable entities. For a more detailed elaboration on this, readers are referred to a recent paper by Bruce J. West [4].

Even though medical issues are a complex matter, and chronic and longstanding conditions are even more complex (i.e., more time allows for more interactions to happen), I will argue that it is possible to provide a model for chronification of pain due to unknown causes based on existing knowledge from other or adjacent research fields. For those familiar with complex adaptive systems, much of this will be familiar, but the argument is structured according to the knowledge that most physicians and health care professionals hardly have heard about complex adaptive systems (For readers interested in an introduction to the field of complexity, see Ref. [5]. First, the model is based on four well-known and essential human biological pillars:

- The biopsychosocial model as an idea. One does not have to agree with the model, but the three elements incorporated (i.e., biopsychosocial) are most likely all essential (for a relevant discussion on the biopsychosocial model see Quintner et al. [1]. A word of caution is that many clinicians, and apparently academics as well, forget the importance of verbalized framing of the condition or suffering—or even disease. This ranges from how you frame the problem to yourself in solitude, by yourself in company with others, by others in company with you, to how this is communicated in the media, by official institutions, health care facilities, and even government policies. An aspect in the field of semiotics.)
- Homeostasis or variability as an essential biological principle.
- No central control system responsible for pain detection is identified in the brain (i.e., specific brain networks exclusively associated with pain), indicating (that it is likely that the brain makes use of) a simple interaction as a basic operating system.
- All impulses (i.e., that is sensory stimulations) must be interpreted by the brain, that includes the experience of pain.

Second, let us use low back pain (LBP) as a model for longstanding pain conditions. After all, LBP is the condition with the largest impact on disability on a global scale [6]. Of all the individuals with LBP, approximately 90% have so-called chronic nonspecific LBP. The most effective treatment modality for LBP is cognitive interventions, preferably in a multidisciplinary specialist clinic [7,8]. Even though the interaction between the various factors in complex systems are essential, there will also be components of no or miniscule significance. Despite some knowledge of several significant elements (e.g., yellow flags) [9], we do not know to what extent they are assessed and addressed in the treatments offered to these patients. This is further complicated by these elements being nonexistent in most research protocols. Therefore, these factors are most likely not sufficiently scrutinized in patients with complex conditions. A logical consequence would, therefore, be insufficient treatment outcomes. The concept behind the proposed model is based on the idea that several factors contribute simultaneously to the chronification of pain. These factors can be anything from purely work related perpetuating factors like lack of decision control, empowering leadership, and fair leadership to catastrophizing; or one, or some, or all of them at once. The real challenge is that there is no logic in when different individuals are affected. Many patients one meet in the clinic have been through much worse things without ending up with a longstanding pain condition. But this time it turned out to be different, maybe it was not even perceived as especially troublesome in the beginning. So the crux of the matter is to find out why they succumb to developing a longstanding pain condition right now, because it is likely that neither patients nor clinicians are sure. Another aspect, known from patients with rheumatoid arthritis, is that correct prediction of future

pain can reduce the perceived averseness of a pain episode [10].

There already exists a model that is likely to explain all this, the Ising model [11]. The Ising model was published in 1925 to explain how iron is demagnetized as it is heated, and then not completely remagnetized as the temperature normalizes (i.e., room temperature) again. The Ising model is one of the simplest models of interacting bodies in statistical physics [12]. The Ising model is also an immensely important model in statistical physics, with well above a five-digit number of papers based on it [13,14]. The model assumes binary variables and only local pair wise interactions between neighboring agents (i.e., tiles in the visualization exercise described below) [13]. The Ising model illustrates and explains how and why small changes suddenly lead to large changes, so-called phase transitions. An easily comprehensible example is when water goes from a liquid state to a gaseous state with small changes of temperature around the boiling point; or when water freezes (liquid state to solid state). Other examples from biology are how flocks of birds and schools of fish communicate. When we observe that a flock of birds suddenly changes direction and all the birds follow the same abrupt change of direction, the clue is that every single bird is influenced by their neighboring birds, and thus, the change of direction can change apparently abruptly and in unison. The same is what happens in the heart when electrical signals are transmitted from the SA node; and even when action potentials are transmitted down the axons.

This model, is thus used to illustrate that all applicable factors have an impact (on both the individual itself and all the other factors either directly or indirectly) at any given point in time, of either negative or positive character (for a suggestive list of essential core factors see Table 1). All factors have influence, but the grade of impact will vary. This model also can explain why some people apparently withstands everything negative that might happen to them, while others “break under minimal strain” (i.e., number of negative influences far from or close to the point for initializing a phase transition). The model can explain why you succumbed to chronic pain now, but not earlier; as most factors are in flux, while a few factors stay stable over a lifetime (i.e., your proximity to the point of phase transition at this point in time). These stable factors (even though they can be altered in rare cases), like personality traits, might explain why some people are more vulnerable and some are more resilient in the first place (i.e., magnitude of positive or negative impact). Thus, some factors might shift from positive to negative, or vice versa, in various walks of life. But most importantly—in respect of treatment—it can explain that after a phase transition (in our case, a longstanding pain condition) it is usually not sufficient to change the last few factors to reverse the process and free the patient from pain. That is why it is called a transition in the first place.

Table 1 Suggestive list of candidate factors that might have essential and/or necessary impact on the chronification of pain

Relation to an expanded bio-psycho-social model	Factor	Explanation/comment
Bio	Health status	Incl. duration of pain condition, pain intensity, pain distribution (i.e., number of regions included), level of education, lifestyle, self-reported physical activity level, smoking status, overweight, and comorbidity (especially diseases making individuals more susceptible to certain pain conditions (e.g., diabetic neuropathy))
Bio	Acute illness/disease	Incl. own, family, or others with close relations
Bio	Sleep deprivation	
Bio	Self-perceived health and/or comorbidity	
Bio	Self-perceived level of physical activity	
Psycho	Personality traits	Incl. catastrophizing, rumination and anxiety
Psycho	Self-efficacy	Incl. self-perceived influence on treatment choices (i.e. shared decision-making), and frequency of negative and positive treatment experiences (per modality)]
Psycho	Insufficient coping of stress	Incl. fear of social threat, fear of physical pain, emotional dysregulation, sexual dysfunction, resilience and antifragility, and self-control
Psycho	Negative psychological issues	Incl. anxiety and depression
Psycho	Self-perceived and/or unconscious impairment of function	Incl. fear avoidance behavior
Psycho	Self-perceived stress beyond own influence (partly or totally) and leading a meaningful life	Incl. perceived threat to autonomy i.e. feeling a profound impact on the ability and opportunity to live your life in a way that you find meaningful
Social	Lack of close social (and intimate) relations (usually next of kin)/ Perceived social isolation	Incl. boredom
Social	Negative social issues/context sensitive issues	Incl. work related factors, social and familial factors, and attitudes, actions and verbal responses or uttering from others or one self
Social Semiotics	Socio-economic stability Explanatory model/case conceptualization of own illness	I.e. making meaning, or how the patient's explain their own condition to themselves (or interpret other's explanations, incl. health professionals) incl. expectations and experiences, kinesiphobia, illness perception, experienced injustice and acceptance

It is time for a mental task, a visualization to illustrate the Ising model. Imagine a floor with tiles. Then imagine that these tiles can be turned around like cards. On one side, they are white (i.e., positive impact), and on the other side, they are black (i.e., negative impact). Each tile represents a specific characteristic for all humans (see Table 1 for examples). The number of identical tiles relating to one specific characteristic reflects the impact—or resilience—of that specific trait. Then, we start playing the Ising game. Every tile influences their

neighboring tiles, and only those, due to specific rules (e.g., if a white tile has a black tile to the right and a white tile to the left, then all three of them turn black.). As time goes by these rules play out constantly, and from a bird's eye you will see a constant flux. That is the normal state, the preferred state. Then imagine one more thing; at the center of the floor there is a giant hub. This hub makes it possible to spin the floor like a wheel of fortune. When the floor spins the black and white tiles are getting a bit blurred to the eyes, as it

spins even faster it turns gray. If the shade of gray is darker than the turning point, the entire system (i.e., the individual) undergoes a phase transition. In our case, a chronification of the pain condition in this specific human being. But, in chronification, the spinning itself (e.g., self-perception) may modulate the rules governing the transition probabilities of the tiles.

The beauty of this model, in addition to being a concrete model to facilitate communication and understanding for both health workers and patients, is that it produces an overview of probable factors having significant impact on individuals. This does not infer that we can explain every aspect of the individual's pain condition, but reveals the most likely and appropriate amenable characteristics in every patient. Most factors can probably be assessed with validated questionnaires, and the treatment can be specifically targeted to address these aspects. The impact the various factors have on each individual may vary considerable, and most likely the grade of entropy will determine how comprehensive the treatment ought to be.

From a scientific point of view, this is a satisfying candidate model to explain chronification of pain. The model can easily be falsified. The model can easily be adjusted to closer match the truth as more data are gathered. Thus, also determining the impact of each factor, and a threshold value for when the phase transition will take place. One additional challenge in the Ising model is that the effects are locally constrained, thus knowing which factors are proximate to one another in a complex condition is a demanding task to solve. This is done with network sciences applied on very large data-sets (e.g., big data) from registries (or very large cohorts). Even though the model is fairly simple and easily falsified, it provides a concrete understanding of the complexity of the condition and at the same time reveals how an underlying principle in biology—homeostasis—preserves the temporal fluctuations of each factor. In the beginning—as displayed in the table—the model will include a multitude of parameters. Initially this is important, thus testing of the model in real-life situations can reveal each factors impact on the model, or its redundancy. These factors are included based on the authors subjective experience from clinical work; own research and research collaboration; reading of scientific literature (not only medicine) and fictional literature; life experiences (own and others); informal social experiments and observations; and logical deduction in relation to medicine and complex systems.

Time is often considered an important factor in long-standing pain conditions, for example, unsuccessful return to work. But as is implicit in the model, phase transitions are abrupt and thus time is of less importance. That do not imply that how a condition persists over time is independent of its impact on the surroundings, or vice versa, it is just a consequence of how the other factors override the influence of time passed. Still, as time goes by and nothing changes with a pain

condition, more factors might be activated and apparently making the condition more resistant to treatment interventions. Yet, another aspect related to time, is that the inherent cyclical variation to known elements, such as emotions [16] and coupled dynamics will also influence these variables (i.e., the color of the tiles). The same applies to sleep [16,17], which must also be factored into the model. Thus time is very likely to be considered a paradoxical factor. But one should also remember that occasionally a single event or factor can tweak the system (i.e., individual) out of the said complex condition. This is in line with the Ising model and not a paradoxical function of time.

In the end, the field of medicine need to look to other research fields to solve the issues it has been struggling with for decades without any satisfactory solutions in hand. This article is an attempt to remedy this in long-standing pain conditions. If this model turns out to be applicable to chronification of pain conditions, it might also be applicable to other chronic conditions as well. Bridging the gap between different scientific fields is most likely the future of clinical medicine, other solutions is not in sight at the time being. A likely scenario, if the model is more or less correct, is that algorithms developed from network theories (like those used in chess, poker, and at the stock market) will provide us with clinical algorithms to assess details in vulnerable individuals or relevant factors in longstanding pain patients [18,19]. They will most likely also contribute with treatment algorithms that are more sophisticated, not necessarily more complex, than what human intellect can produce through analog trail and failure research.

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