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# Editorials

## What Does It Mean to Call Chronic Pain a Brain Disease?

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**Abstract: Multiple investigators have recently asked whether neuroimaging has shown that chronic pain is a brain disease. We review the clinical implications of seeing chronic pain as a brain disease. Abnormalities noted on imaging of peripheral structures have previously misled the clinical care of patients with chronic pain. We also cannot assume that the changes associated with chronic pain on neuroimaging are causal. When considering the significance of neuroimaging results, it is important to remember that "disease" is a concept that arises out of clinical medicine, not laboratory science. Following Canguilhem, we believe that disease is best defined as a structural or functional change that causes disvalue to the whole organism. It is important to be cautious in our assertions about chronic pain as a brain disease because these may have negative effects on 1) the therapeutic dialogue between clinicians and patients; 2) the social dialogue about reimbursement for pain treatments and disability due to pain; and 3) the chronic pain research agenda. Considered scientifically, we may be looking for the cause of chronic pain through neuroimaging, but considered clinically, we are in fact often looking to validate pain complaints. We should not yield to the temptation to validate pain with the magnetic resonance imaging scanner (structural or functional). We should not see pain as caused by the brain alone. Pain is not felt by the brain, but by the person.**

***Perspective:** Neuroimaging investigators have argued that brain imaging may demonstrate that chronic pain is a brain disease. We argue that "disease" is a clinical concept and that conceiving of chronic pain as a brain disease can have negative consequences for research and clinical care of patients with chronic pain.*



***Key words:** Pathology, neuroimaging, Canguilhem, Hacker, mereological fallacy.*

*Pathology is literally the study (logos) of suffering (pathos).*

Kumar V, Fausto N, Abbas A: Robbins & Cotran Pathologic Basis of Disease. Philadelphia, PA, Elsevier, 2007

### Why Is It Important That Chronic Pain Be Considered a Disease?

*Yet he didn't seem to have a disease that anybody could take seriously. Only the pain—in his neck, arm and shoulders, pain that made it difficult to walk more than a few city blocks or even to stand very long in one place.*

Roth P: The Anatomy Lesson. Evansville, IN, Vintage Publishing, 1996

Some neuroimaging investigators have recently asked whether the functional, structural, and chemical changes in the brain that are associated with chronic pain ". . . put it into the realm of a disease state."[27] Other investigators have directly asserted that "The major insight that emerged from neuroimaging studies is that chronic pain is a disease of the brain."[6] Others have referred to chronic pain as an "internalized disease state" where ". . . the brain in chronic pain is a distinct state with properties that may not be reversible."[1] In some respects, this is not a new argument. At the 1973 meeting that inaugurated the International Association for the Study of Pain (IASP), John Bonica stated,

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"Chronic pain is the most disabling disease . . ."[5] On its website, the European Federation of IASP Chapters (EFIC) summarizes the current consensus view among professional pain organizations, "Although acute pain may reasonably be considered a symptom of disease or injury, chronic and recurrent pain is a specific healthcare problem, a disease in its own right."[24] One of the summary points from the recently released report from the Institute of Medicine[16] states that "Chronic pain can be a disease in itself." While it is clear that attaining disease status would grant chronic pain greater medical legitimacy and perhaps greater research funding, there may be disadvantages as well.

The effort to define chronic pain as a disease is motivated by an admirable desire to keep chronic pain from being a "mere symptom" of interest to patients, but not fully legitimate as a medical problem. This process of understanding, categorizing, and legitimating symptoms through the diagnosis of causal disease is typical of the clinicopathological method that has reigned in professional medicine for 2 centuries.[22] Neuroimaging investigators extend the search for relevant neuropathology from the spinal cord to the brain and from histopathology to functional neuroimaging. This extension broadens our sense of the anatomical structures and physiological processes involved in chronic pain, but if we assert that chronic pain is a disease on the basis of these findings, we believe it also holds risks of inappropriate or counterproductive medicalization of chronic pain care. Specifically, we believe that defining chronic pain as a brain disease on the basis of neuroimaging studies may have negative effects on 1) the therapeutic dialogue between clinicians and patients; 2) the social dialogue about reimbursement for pain treatments and disability due to pain; and 3) the chronic pain research agenda.

## Structural and Functional Imaging Should Be Interpreted Within a Clinical Context

Structural and functional imaging have greatly assisted the diagnosis of multiple diseases by revealing alterations in structures and processes not otherwise visible. But it is possible to be misled by imaging concerning the causes of chronic pain. Multiple abnormalities noted on spinal structural magnetic resonance images (MRIs) were assumed to cause back pain and often prompted surgical intervention. But we now know these are present in many older adults with no back pain and have no prognostic value at predicting future back pain. For example, herniation of the lumbar disk is found in 25% to 50% of asymptomatic subjects.[9] Similar problems are seen with attributing chronic knee pain to meniscal abnormalities. In 1 study, 61% of the subjects who had meniscal tears in their knees had no pain, aching, or stiffness during the previous month.[12]

Determining which abnormalities are causal and which are incidental requires that imaging results be interpreted as the answers to clinical questions. This is true whether the tissue examined is the intervertebral disk, the dorsal horn cell, or the anterior cingulum. It is true for both structural and functional brain imaging. When interpreting abnormalities found on structural MRIs of lumbar spine or knee, the crucial issue was the prevalence of these abnormalities in patients with no pain. When interpreting the abnormalities on functional neuroimaging, this is not the crucial issue because many studies have compared persons with and without chronic pain. The crucial issue is the role played by these abnormalities in the chronic pain process: are they causes, consequences, or coincidences? Research to date has not given us a clear answer to this question.

### *Neuroimaging Abnormalities Must Cause Dysfunction for the Whole Organism to Qualify as Disease*

Following the French historian of medicine Georges Canguilhem, we argue that disease is a structural or functional change that causes distress and/or dysfunction for the whole organism. It is not enough that structural or functional changes be anomalous or statistically divergent from normal, they must cause a restriction of the ability of the organism to function in its environment to qualify as disease.

In the era of modern pathophysiology, we are accustomed to thinking of pathological and physiological processes as continuous. But Canguilhem reminds us that when focusing on abnormal cellular processes, we should not forget the initial qualitative distinction that led us to designate these processes as pathological. It is ill patients who present themselves to physicians. Only in response to a clinical complaint do physicians begin the search for a pathological lesion. After they define the pathology, only then do they turn to physiology to determine the causes and remedies for that pathology. Not all patient complaints about the functions of his or her body are found to arise from disease (eg, nose shape, breast size). Patient complaint is necessary for a tissue or imaging anomaly to qualify as disease, but it is not sufficient.

Because the patient poses the first question concerning sickness, it is he who defines which tissue changes are pathological. Tissue changes that reduce the patient's ability to function in his environment are pathological while other changes are merely benign variations. "As long as the anomaly has no functional (present or future) repercussions experienced consciously by the individual . . . the anomaly is either ignored or constitutes an indifferent variety . . ."[8] (parenthetical comment added) This means that pathology must be a deviation from the biologically normative, not just the statistically normal.

These clinical roots of pathological discoveries mean that pathology as a science remains dependent on the patient's reports of dysfunction. It also means that only whole organisms can be diseased. Canguilhem summarizes, "the distinction between physiology and pathology has and can only have a clinical significance. This is the reason why, contrary to all present medical custom, we suggest that it is medically incorrect to speak of diseased organs, diseased tissues, diseased cells."[8] We are so accustomed to viewing disordered cells in histological specimens or asymmetrical findings on brain imaging as pathological, we forget that we have no basis on which

to distinguish benign from malign asymmetries unless we consider the whole patient.

This review of the difference between the normal and the pathological helps us understand the significance of the brain imaging findings summarized by neuroimaging investigators. Structural or functional MRI scans of the brain alone cannot distinguish benign from malign variation of function or structure. A congenital defect is a disease only if it produces dysfunction for the organism. If we needed to roll our tongues to access a crucial food, then inability to roll your tongue would be a congenital defect. Since tongue rolling actually has no practical effect on us, it is merely a benign variation.

Chronic pain certainly has significant effects on the lives of patients. But it is not a usual disease either. It is postulated to be a symptom that becomes a disease because its persistence promotes its centralization and expression in functional brain abnormalities. There appears to be both definitional and causal circularity in this argument that undermines the case for chronic pain as a brain disease. Given that the scientific case for chronic pain being a brain disease on the basis of neuroimaging is clouded, we are prompted to ask: what are the effects of defining chronic pain as a brain disease for 1) therapeutic dialogue; 2) social dialogue; and 3) research agenda?

## Does Understanding Chronic Pain as a Disease Get Us Where We Want to Go Clinically?

### *Effects on Therapeutic Dialogue: "Disease" Is a Lens Through Which to Understand and Address Dysfunction and Suffering*

Diseases are not discovered through purely disinterested scientific observation. They are answers to clinical questions posed by suffering or dysfunctional patients. We diagnose diseases in order to help patients.[18] Due to the scientific prestige of objective disease diagnosis, we forget that we would not have the means to define diseases without being set on this mission by suffering patients. Canguilhem addresses the relationship between suffering and science, between the pathos and logos of our epigraph.

"If there were no pathological obstacles there would be no physiology because there would be no physiological problems to solve . . . [W]e can say that in biology it is the pathos which conditions the logos because it gives it its name. It is the abnormal which arouses theoretical interest in the normal."[8]

While diagnosis has always been important in the history of clinical medicine, it has become both more important and more specific in the 20th century when medical textbooks opened with statements such as, "The chief aim towards which all endeavors should be bent in medicine is the prevention and cure of disease."[19] Historian of medicine Charles Rosenberg claims the "modern history of diagnosis is inextricably related to disease specificity, to the notion that diseases can and should be thought of as entities existing outside the unique manifestations of illness in particular men and women . . ."[21] In modern medicine, prince and pauper can be afflicted with the same disease.

As diagnoses became more mechanism based and linked with therapy choice, the process of differential diagnosis became the marker of the scientific physician who systematically considered and ruled out a set of discrete alternatives. Hospital forms now "provided blanks for recording the diagnosis, with little space left for a summary of the patient's own account of his or her sickness."[21] Patients were now located and organized in the hospital by diagnosis, not by who they were outside the hospital. Their disease was not only the reason they were in the hospital; it became their identity. Disease not only justified hospital admission, it justified medical attention in general. Without a disease, a patient had no status and no identity for scientific medicine. "Thus, a poor or homeless person becomes visible to the health-care system when diagnosed with an acute ailment but then returns to invisibility once that episode has been managed. It is almost as though the disease, not its victim, justifies treatment."[21] Patients whose pain cannot be validated by association with disease through imaging or other tests are often sent home with the implicit or explicit message, "we can't find anything wrong with you."

But brain imaging adds neuroanatomical and neurophysiological information, not validity, to pain reports. We verify pain and distress by asking patients, not by showing activation of brain regions associated with distress. How did we discover these were distress regions in the first place? We don't want the validity of pain as a target for clinical care to depend on demonstrating its anatomical substrate. Pain is important and worthy of clinical attention regardless of its source.[10]

### *Effects on Social Dialogue: Should Pain Be Validated Through Association With Disease?*

One still finds disease used as a marker of visibility and legitimacy for patients disabled by pain. This is perhaps even more apparent in medico-legal than clinical processes. In *Pain and Disability*, Osterweis, Kleinman, and Mechanic reviewed the procedures for Social Security Disability Determinations.

"The Social Security Administration uses its concept of impairment as a proxy test for motivation to distinguish those who *cannot* work from those who *will not* work. An impairment is supposed to be a condition beyond a person's control that prevents the person from working. As such, an impairment is considered *prima facie* evidence of a genuine inability to work. Thus, the distinction between objective and subjective evidence of impairments is crucial."[20]

They elaborate further on the definition of impairment. "This concept of a distinct, medically identifiable impairment within the individual anatomical, physiological, or psychological makeup and totally independent of social, economic, or geographic context is at the root of the current problem with cases that turn principally on

the applicant's pain."[20] Here, the distinct mechanism-based notion of disease appears as the concept of impairment, which is used to separate legitimate from illegitimate disability due to pain. At the time this book was written (1987), there was no functional neuroimaging. But a neuroimaging-defined disease would likely play a similar role in disability determinations. If the presence of objective disease (however defined) can legitimate disability due to pain, the absence of objective disease can be used to delegitimate disability due to pain.

When discussing chronic health problems, we often slide unconsciously between calling them diseases, illnesses, disorders, and conditions. We gravitate toward disease when we want to emphasize the legitimacy of pain problems. But epidemiologists, geriatricians, and health policy experts have been gravitating in the opposite direction, because they think the broader terms capture the nature of our looming public health problems better. For example, geriatricians Tinetti and Fried have recently argued that we are at "The end of the disease era" due to the prevalence and importance of "nondisease-specific health conditions such as pain, impaired mobility, and disordered sleep."[25] Chronic conditions are patient defined, as opposed to chronic diseases, which are doctor defined. "Chronic health conditions, a general term that includes both chronic diseases and impairments, have been as a group the leading public health concern since the 1920s."[15] Medicare beneficiaries with 4 or more chronic conditions account for 80% of all Medicare spending. Much of this spending could be avoided if patients with multiple chronic conditions received more appropriate ambulatory care.[31] These conditions are important to patients, to public health, and to the health system, even if they do not qualify as diseases.

At this point, one might ask: is it not possible to define chronic pain as a disease and still advocate a broad biopsychosocial model of pain and a comprehensive approach to care? Ideally, yes, this is possible. However, it is important to remember that the medicalization of problems encountered in society succeeds because it is a simplification of the problem that allows more focused preventive and curative efforts. Thus was tuberculosis transformed from an intractable problem attributed to unavoidable urban poverty and squalor into a treatable disease caused by the tubercle bacillus.[11] In subsequent years, we have learned that environmental factors affecting host resistance are as important as exposure to the pathogen in determining tuberculosis infection and mortality rates.[17] The appeal of a simple model and a focused solution drew us away from a comprehensive biopsychosocial model of tuberculosis until we were forced back into the comprehensive model by further research.

Chronic pain is a similarly complex and socially disruptive problem. Defining it as a disease caused by brain abnormalities may increase our temptation to see it as a medical problem solely caused by disorder within the patient's body rather than complex personal and social challenge originating both within and between the bodies of individual patients.[23] Over the past 2 decades, we have in fact witnessed a widespread turn toward a medical model of chronic pain care and away from a rehabilitative model of chronic pain care.[28] Low back pain chronicity is not only associated with decreased thalamic blood flow and increased medial prefrontal cortex blood flow, as neuroimaging investigators assert. It is also associated with preinjury work satisfaction, local unemployment rates, and marital satisfaction. It is very difficult to determine why one back injury becomes chronic and disabling while another resolves quickly, but it appears that this is due to processes outside the body and brain of the patient as well as those within. Nortin Hadler has often reminded us that disabling backache is far more consistently associated with the psychosocial context of work than with the physical demands of work.[14]

## *Effects on Research Agenda: Are There Risks Associated With Finding the Cause of Chronic Pain in the Brain?*

Functional neuroimaging is an important new tool we can use to learn about the anatomy, physiology, and pathophysiology of brain processes associated with chronic pain. We have no objection to this line of research. Indeed, we believe it would be a serious mistake not to pursue functional neuroimaging in order to better understand the role of the brain in chronic pain. However, we have one serious concern about how this research is interpreted and applied to clinical practice.

We are concerned that psychological processes and concepts are being attributed to the brain and to parts of the brain that are properly attributed only to the person as a whole. This is a problem that is not limited to pain neuroimaging, but is found throughout cognitive neuroscience. This general problem has been termed the "mereological fallacy" by neuroscientist Max Bennett and philosopher Peter Hacker in their 2003 book, *Philosophical Foundations of Neuroscience*.[3] This fallacy is called "mereological" because it involves ascribing properties to parts that should properly be ascribed only to the wholes of which they are parts. This type of error was first noted by Aristotle in 350BC, "to say that the soul is angry is as if one were to say that the soul weaves or builds. For it is surely better not to say that the soul pities, learns, or thinks, but that a man does these with his soul." (*De Anima* 408b 12–15)[4]

Bennett and Hacker describe a modern, neuroscientific cousin of this error that "involves ascribing to the brain (a part of an animal) attributes that can be ascribed literally only to the animal as a whole." They deny that it makes sense "to say that the brain is conscious, feels sensations, perceives, thinks, knows, or wants anything—for these are attributes of animals, not of their brains."[4] Clearly, many human capacities are dependent upon the normal functioning of the brain. But to say that the brain is necessary for these capacities is different than saying that these are capacities of the brain. Bennett and Hacker are inspired by the philosophy of Ludwig Wittgenstein and cite the following quote: "Only of a *human* being and of what resembles (behaves like) a living

human being can one say: it has sensations, it sees, is blind; hears, is deaf; is conscious or unconscious."[30] The brain is part of the human being, but it does not behave like anything and therefore cannot be ascribed these capacities. Unless capacities are somehow manifested in behavior, we have no way of knowing that they are present. Bennett and Hacker explain, "It makes no sense to ascribe consciousness or thought to a chair or an oyster, because there is no such thing as a chair or an oyster falling asleep and later waking up, or losing consciousness and then regaining it; and there is no such thing as a chair or an oyster behaving thoughtfully or thoughtlessly."[4] Brains manifest no behavior, so we have no idea what it means to say a brain feels pain. Feeling pain is a capability of the organism. It enables the animal to act and respond to its environment in certain ways. If this behavior is not apparent, we have no grounds on which to ascribe the ability to the animal or the organ.

As modern scientists and clinicians who have rejected Cartesian dualism, we recoil at the idea that it is the mind that sees, thinks, or feels pain. But many are willing to substitute the brain for the mind and state that the brain sees, thinks, and feels pain. In this way, substance dualism (mental stuff versus physical stuff) is abandoned, but structural dualism (brain as seer, feeler, or knower of representations produced by the body) is retained. One crude version of this postulates a little man or homunculus inside the brain who watches the images produced by the visual system or feels the pain produced by the somatosensory system. We thereby do not solve the hard problems of perception and knowledge, but push them deep inside the brain.

How is this relevant to the discovery of chronic pain as a brain disease through functional neuroimaging? Neuroimaging investigators claim that neuroimaging has given us reason to move from thinking of chronic pain as a syndrome (or a collection of symptoms) to thinking of it as a disease (associated with visible changes in structure and function). As a disease, chronic pain is seen to arise from a localized lesion in the brain. They are not quite saying that brains feel pain, but that brains (when disordered) make us feel chronic pain. Giving pain a home in the brain may provide benefits in the form of new therapeutic targets. It may also pose risks in foreclosing or distracting us from other lines of research.

Attributing chronic pain to localized brain pathology makes chronic pain the product of a defect within the body. It draws our attention toward features of brains (eg, cell density, metabolic rates) and away from features of persons not characteristic of brains (eg, love, fear, morality, action). The attribution of pain to local brain pathology can help us forget that pain arises as a problem for the organism within its physical and social environment. This environment can make pain appear or disappear without any change in internal pathology. Henry Beecher long ago noted that the same pathological lesions could produce overwhelming or minimal pain depending on the environment.[2] This clinical issue echoes current concerns in the neuroimaging literature about whether psychological concepts and functions (like pain) can be associated with discrete localized brain regions independent of the environmental context within which they occur.[29]

Chronic pain depends not only on brain processes, but on personal processes and meanings as well. Perceived threat to the person is as important as nociception for clinical pain conditions. Intense psychosocial distress is often experienced as pain. As Bill Fordyce liked to remind us, pain is "transdermal" with causes both inside and outside our skin.[13] If we pursue chronic pain as a brain disease with our research dollars, we may neglect to pursue all the personal processes relevant to chronic pain with as much vigor. In this, we will have fallen prey to a form of the mereological fallacy.

Neuroimaging is a valuable tool for chronic pain research. But we should not think it implies more than it does. One neuroimaging scientist has stated: "Neuroimaging studies that have defined surrogate measures of pain have firmly brought the problem of pain back into the brain."[26] We believe pain involves the brain, but does not occur within the brain. Tracey provocatively asks, "are we at a stage where we can interpret a brain map or endophenotype reliably without knowing the concomitant behavioral report; that is adopt a 'brain-reading' approach . . .?" Other neuroimaging investigators have also asked whether brain scans can substitute for patient reports of pain.[7] We do not believe we are at this stage and do not believe that brain scans will ever be able to correct or overrule reports of pain by patients.

## Conclusion

Chronic pain challenges us to expand our concepts of disease beyond the bounds of body and brain. Chronic pain has causes inside and outside the body. It is not the brain, or the spinal cord, or any part of the body, but the person who feels pain. We should not yield to the temptation to validate pain with the MRI scanner (structural or functional). We should not see pain as caused by the brain alone. Pain is felt not by the brain, but by the person.

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