

Chronic Pain and Substance Abuse Spectrum Effects and Ethical Considerations

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Chronic pain is frequently accompanied by a constellation of psychological characteristics, that may co-present as frank psychopathology. Several studies have shown the high co-morbidity of chronic pain, depression, anxiety, and/or somatization disorder.¹⁻⁸ Given that: (1) chronic pain and psychological factors are co-morbid and reciprocally-interactive, and (2) unrecognized and/or untreated psychopathology may increase the experience of, and reactivity to (chronic) pain, then it becomes clear that the co-morbidity and putative relationship of these disorders must be considered in any meaningful paradigm for chronic pain management.

Substance Abuse as Bio-psychological Co-morbidity

While considerable research has focused upon particular psychological disorders (e.g., depression, anxiety) that are co-morbid to chronic pain, it is equally important to consider the evident problem of substance abuse (and addiction) in this light, given the noted prevalence of pain, psychologic and substance abuse disorders, and the growing body of evidence to support the putative relationship of these disorders. The abuse of controlled substances among chronic pain patients is common, and is a significant epidemiological problem that exacerbates the impact of chronic pain and psychological conditions, and thus imposes further burdens, if not impediments, upon practical pain management.⁹⁻¹¹

By definition, chronic pain is both a physiologic and psychological event, and we have posited that chronic pain and particular Axis I psychological disorders (e.g., depression, anxiety, somatization and substance abuse) have common underlying substrates.¹² But such substrates are not invariably expressed; we believe that this correlation of chronic pain, emotional reactiv-

ity, and substance abuse demonstrate the interplay of genetic, phenotypic, and environmental-situational factors occurring as a spectrum disorder.¹²⁻¹⁵

On the biological level, several genetic (e.g., serotonin transporter gene) molecular (e.g., variants of the serotonin transporter, 5-HTT(LPR)); neuropharmacologic (e.g., serotonin, norepinephrine, dopamine, glutamate, opiate); and neuroanatomical systems (e.g., orbital cortex, cingulate, and central and medial divisions of the amygdala) are common to these disorders.¹⁶⁻¹⁸ We have raised the possibility that in pain spectrum disorders, the neural and/or glial function, and/or (micro/macro) anatomy of brain networks mediating noxious sensation and perception(s)—as well as those involved in cognitive and emotive dimensions of reinforcement and/or reward—in some way become disrupted or dysfunctional. Genetic variation(s) could predispose the expression of phenotypes for neural and/or glial function to alter the network properties and activity pattern(s) within brain systems to elicit the differential presentation of various features along a pathologic continuum (i.e.- a spectrum of chronic pain, depression, somatization and/or substance abuse).¹⁹ The affective components of chronic pain are similar (if not identical) to those of mood disorder with somatic features.²⁰ We have posited that “...particular individuals have a pre-disposition to...neural sensitization within these pathways, as a consequence of over-reactivity to insult and trauma, inflammation, or aberrant response to environmental input(s)... [this] might induce pathologic patterns of sensory (hyper)reactivity, altered cognitive processing and emotional responses, and loss of impulse control. In this way, persistent pain, psychopathology, and substance abuse may be correlated and reflect related mechanistic processes...”²¹ In this way, psychopathology (including substance abuse) can be seen as an aberrant responsiveness of the peripheral and central nervous system. Koob and LeMoal claim that this could establish

“...addiction [as] a type of chronic pain syndrome characterized by emotional pain, dysphoria...and interpersonal difficulties... [for which certain] ...drugs can be...self-medication.”²²

Evidence for a Genetic Basis?

Chromosomal quantitative trait loci (QTL) have been identified for alleles that affect neural phenotypes that may be involved in the (co-)predisposition to, and co-expression of pain, certain psychopathologies, and substance abuse.²³ The phenotypes for pain, psychopathology, and substance abuse are multi-factorial,^{24,25} and it is probable that phenotypic expression occurs along a continuum that is dependent upon influences within the CNS microenvironment incurred by interactions between internal and external environment(s)—both during critical developmental periods, as well as throughout the lifespan.²⁶ Thus, it may be that genotypic variants might pre-dispose either a somewhat ‘generalized’ pattern of susceptibility in which neural substrates of (internal and external) environmental sensitivity, reinforcement, and reward are altered to affect interpretive/associative aspects of bodily sensations (including discomfort and pain), and emotionality, or a more ‘focal’ diathesis in which particular neural phenotypes directly correlate to certain forms of pain and/or psychopathology and substance abuse. In this model, genetically-influenced expression of neurotransmitters, their receptors and transporters, intracellular signaling molecules and/or ion channels may underlie development of particular types of pain, somatic and cognitive features of depression, somatization, and decreased opioid neuromodulation. This would thus reinforce a need for higher doses of opioids and an enhanced potential for misuse/abuse.^{27,28}

...Or Evidence Biased?

Interpretations of these findings may actually incur bias about the relative importance of genetic influences. Such studies emphasize genetics (and “downstream” biological effects) over environmental factors and, in this way, impart a deterministic perspective. At face value, one could argue that such a bias might be beneficial, in that it grounds chronic pain and substance abuse to a disease-model, and hence establishes this as ‘beyond the patient’s control or discretion,’ and

thereby fortifies the obligation for medical treatment.

However, a problem with such a reductionist viewpoint is that it evaluates only the influence of genes or environment, does not sufficiently account for interaction and synergy among and between variables and, as a result, may foster a “one size fits all” approach to intervention and treatment. This type of over-simplification is implicit to many genetic studies of pain. Without adequate consideration of integrated bio-psychosocial variables, conclusions may err so as to emphasize a genetic determinism or, at the other extreme, the purely psychosocial effects of environment.²⁹

In the former case, ethical problems can arise if and when a particular conclusion is drawn that disproportionately implicates genetics in health disparities, or in the inevitability of developing a particular disorder (e.g., pain, depression,

despite the fact that such lack of response, relapse and recidivism may be caused by robustly biological factors acting within particular psycho-social contexts.

Cause(s), Contexts and Consequences

How causality is regarded can affect ethics. Conclusions drawn from, and within, a particular epistemological set may impact medical treatment, the way the legal system handles pain, psychological suffering, drug use, misuse and abuse, and ultimately how society at large determines responsibility for wellness. Ethical problems arising from reductionism also extend to direct clinical applications of (neuro)genetics. Reducing behavior to genetics infers that it would be appropriate to diagnose or predict the course of chronic pain (and related neuropsychiatric and/or substance abuse disorders) based solely upon molecular variables.³¹ The fact that significant resources are

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substance abuse). Clearly this information and type of thinking can impact insurance coverage, payer premiums, and affect the scope and availability of treatment(s). As well, it becomes tempting to conclude, erroneously, that abnormalities in genes, gene products, and/or neurochemical systems are the direct “cause” of the clinical syndrome. This has led to pain and substance abuse disorders being increasingly and predominantly treated with pharmacological approaches, and may have contributed to the devaluation of more multi-disciplinary strategies.³⁰

In the latter case, the strong effect(s) of biological state(s) may be overlooked or refuted, thereby relegating a particular disorder to solely psychological or social causes, de-emphasizing the need for medical (vs social or legal) intervention, and ascribing to a socially- rather than medically-defined construct of normality or abnormality. In this way, patients often feel stigmatized or castigated as “weak,” socially inapt, or even criminal when they fail to respond or adhere to treatment(s)—

currently devoted to elucidating and testing for genes involved in neuropsychiatric disorders supports the popularity of this belief. However, a number of factors mitigate direct applications of neurogenetic testing. First, we must question whether engaging such resources is justifiable if these findings do not directly enhance treatment. At this time, it is questionable whether genetic information (alone) would be sufficient to categorize pain, and actually ‘personalize’ the treatment of pain patients.

Second, the ethics of pre-symptomatic testing for genetic disorders must be considered. Even when the presence of a gene clearly and reliably predicts the occurrence of a certain disease, the use(s), applications, and limitations of this information can incur profound ethical consequences. As previously mentioned, such testing raises the possibility that persons positively identified with particular genetically “pathological traits” or predispositions might be stigmatized so as to adversely affect their education, career,

and family and social life.³² Thus, ethical considerations of confidentiality and the legal protection of genetic information would be acutely relevant to pain and substance abuse disorders. Knowledge that an individual has a “pain, and/or substance abuse gene” might lead to an over-reaction to, or minimization of their pain experience, in ways such that the distinction between normal and abnormal pain becomes ambiguous, and clinical, occupational and interpersonal relationships could be affected.

Pain medicine, like applied ethics, is an inter-subjective enterprise, and both deal with metaphysical, normative, objective, and knowable entities.^{33,34} Pragmatically, applying any theories of normative ethics in neuroscientific or biomedical contexts requires an incorporation of scientific knowledge to enable decision-making since the ability to make good ethical decision(s) depends upon accurate assessment of facts (as known), the nature and situations of agents involved, and the consequences that follow.^{35,36} A flawed

lished by a relatively confined set of genomic influences, then we may view chronic pain as a spectrum disorder that may co-manifest (other) neuro- and psychopathological effects/conditions.³⁸ Working from the concept that chronic pain and psychological disorders may be correlated along a neuropathologic continuum, it becomes important to recognize that:

- 1) these disorders represent underlying genetic diatheses, and that the expression of various phenotypes depends upon interactions with internal and external environmental factors;
- 2) such genetic-environmental effects makes co-morbidity possible and likely;
- 3) genetic and environmental covariance is probable on several levels of cause and effect; and
- 4) these effects can involve the co-expression of chronic pain and mood, somatization, and substance abuse disorders.

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conceptualization of the relationship of neurogenetics to pain disorders could influence the choice of less-effective treatment approaches, and lead to overestimation of genetic determinism that could be communicated to patients and the public—thereby affecting their constructs, perceptions, and decisional input. To ensure that the ethical assessment of the burdens, risks, benefits, and consequences in pain medicine are valid and accurate, we argue that any epistemological basis for understanding both pain and the person in pain should be grounded upon a scientific model that accounts for the functional integration of genetic, environmental, and experiential variables.³⁷

Toward Practical and Ethical Considerations for Care

If we consider that such co-morbidities may represent environmentally-dependent, differential expression of neural and behavioral phenotypes that are estab-

This bio-psycho-social understanding allows insight to the mechanisms and effects of genetic, phenotypic, and environmental interaction(s) in the expression of chronic pain and substance abuse (as spectrum disorder), but its utility is only evident if we are equally committed to employing a bio-psycho-social approach to treatment of these disorders.

Choosing not to treat, or not to refer a patient, does not constitute viable options, as both are discordant with the pain physician’s stated act of profession, and refute the obligation to use knowledge (of the basis and mechanisms of pathology, and of the manifest effects of such pathology in a given patient) in right ways to guide sound clinical decisions and implement patient-centered care. However, by the same token, the intention and provision of benevolent care does not, and should not, compromise the physician’s moral agency or divert her moral compass. Rather, the alignment of scien-

tific knowledge and moral value must guide therapeutic tenor. What such therapeutics entail may assume a number of viable clinical iterations:

- 1) prudent use of opiates – even in abusing or addicted patients – as consistent with the most stringent therapeutic protocols (of choice of drug, dosing, rotation, etc);
- 2) the assumption of a somewhat more ‘parentalist’ role so as to steward knowledge of the burdens and risks relative to the benefits of using particular opiate vs non-opiate drugs and drug regimens; or
- 3) choosing not to use opiates at all in light of perceived, demonstrable burdens and risks that would affect the particular patient (or population of patients) treated, but offering and providing other therapeutic options and resources toward maximizing pain care. ■

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