



The  
**44<sup>th</sup>**  
JOHN D.  
REGISTER  
LECTURE

# ECHOES OF PAIN IN THE NEUROMATRIX



**ROGER ALLEN, PhD, PT**

**Thursday, Nov. 10, 2016**

7:30 p.m. | Tahoma Room, Thomas Hall

Reception following lecture

## **John D. Regester Faculty Lectureship**

The John D. Regester Faculty Lectureship was established in 1965 to honor the service of John. D. Regester, Ph.D., who joined the Puget Sound faculty in 1924. Regester taught philosophy throughout his career, served as dean of the university, and later was made first dean of the Graduate School.

Under the terms of the lectureship, the address is to be given by a member of the university who exemplifies the qualities of scholarship and intellectual integrity which professors and students have long associated with Regester.

The lecture series is a means of honoring members of the university faculty through an opportunity for them to address the university community on a subject of particular interest to the lecturer. The John D. Regester Lectures are both a recognition of the scholarship and accomplishments of the lecturer and an opportunity for the faculty to develop ideas further and explore them with colleagues and the public. The lectures provide a showcase where students and faculty members can witness their colleagues in the role of productive scholars.

## Echoes of Pain in the Neuromatrix

Pain is a gift. The apparent irony is that the unpleasant suffering aspect of pain actually serves an essential protective biological purpose to command our attention and alert us that the body is being damaged and needs to be protected. Pain provides a powerful incentive for us to escape harm, learn through experience what dangers are to be avoided, and helps us protect already damaged body areas to facilitate healing.

Chronic pain is quite another story. The protective system goes wrong. By definition, chronic pain persists after damage to the body is over, after tissue healing is complete—beyond the time where pain sensations and suffering have purpose. In too many cases, once chronic pain settles in it may last a lifetime. As pain evolves from a beneficial danger signal to an aberrant sensation that won't turn off, the source of its generation moves from the distal body tissue into the nervous system itself. Our emerging understanding of the neuroplastic remodeling that perpetuates pain is forming the basis of a new domain of neuroscience inquiry: "pain pathology."

Traditionally, neuroanatomists have primarily understood pain as a sensory pathway, carrying information about noxious or potentially damaging stimuli from a distal body part to the spine and, ultimately, into the brain. The brain then becomes aware that part of the body is being damaged or put in jeopardy. Our contemporary view of pain is now more far-reaching within our nervous system. As pain messages from peripheral nerves enter the spine and brain, the pain signal diverges and ascends to multiple destinations. We not only "feel" the sensation of pain, but respond to it emotionally, activate motor responses to guard ourselves, perhaps generate fear, imbed the inciting event into memory, and make numerous association connections within the brain. This creates a complex *neuromatrix* within the central nervous system, which links the unpleasant sensation to countless contextual details, body reactions, and feelings. As pain persists over time, the neuromatrix connections are reinforced via repeated activation and expand to adjacent areas in the brain. Both the spine and brain pathologically reorganize themselves based on the strengthening of these connections. In many cases, activation of any component within this neuromatrix (even a smell, thought, or light touch) can then rekindle the sensation of pain itself. The person perceives the pain as coming from a specific part of the body (say, an ankle or shoulder), when it is actually being generated as a function of internal neuromatrix activation. The ultimate expression of this phenomenon is where real and intense pain sensations are essentially an exquisitely detailed memory.

The aspect of any pain experience that challenges our imagination is that while pain is perceived as originating from some part of the physical body, it is actually experienced within our minds. The hardware of the human brain (specifically the “somatosensory cortex” in the post-central gyrus of the parietal lobe) contains a map of the body surface where pain projections from the body come to land as integral experiences in consciousness. Our minds essentially contain a virtual body and it is within this mentally maintained construct that our experience of pain is actually perceived. Whether a toothache or broken finger, it is not the body that feels the pain, it is the mind that perceives and suffers. Realizing that our pain and suffering are perceived in the virtual body of the mind gives us powerful insight to begin understanding the mechanisms of maladaptive chronic pain conditions and how they are modulated.

Chronic neuropathic pain comes in many forms, from the relentless searing limb pain of complex regional pain syndrome (CRPS); to the exhausting overall pain of fibromyalgia syndrome; and the mysterious phantom limb pain, where individuals experience the sensations of cramping, burning, shocking, or squeezing pain in amputated limbs that no longer exist. One of the most maddening aspects of living with chronic pain is that, although it is constant, it unpredictably fluctuates in intensity. On some days it may escalate to an excruciating level very difficult to tolerate. Although many potential triggers have been hypothesized, patients and medical practitioners alike are often at a loss to explain, or predict the occurrence of, these unusually severe flares in pain.

At University of Puget Sound, through a series of collaborative faculty/student research studies, we have uncovered a connection between the experience of psychological stress and severe episodic elevations in chronic neuropathic pain. The remarkable feature of this relationship is that it is delayed. Our studies have demonstrated that painful flares consistently occur 10 days after the experience of particularly stressful events for people with CRPS, fibromyalgia, migraines, and phantom limb pain. We have found this to result from the activity of the hormone thyroxine, which after being released during times of stress is bound by blood proteins and inexplicably held inactive for a period of 10 days. After breaking free from its protein bonds, thyroxine increases excitability of neural pathways, including pain processing within the neuromatrix. This results in significantly increased perception of pain intensity 10 days after the originating stressful event.

Okay, interesting, but is this information beneficial to anyone? We don't yet know enough to be able intervene and prevent this 10th-day hit. However, just knowing that there is a 10-day lag between salient stress and painful flares is of meaningful value to both health care providers and individuals with chronic pain. This can help therapists explain the cause of some painful flares for their patients and allow them to differentiate between stress-related pain increases and those potentially brought on by therapeutic activities designed to help with physical reactivation. Of greatest importance, though, is how this knowledge

may cognitively temper suffering and the emotional impact of pain. Experiencing the sensation of pain is one thing, but how we suffer from it is a more complex matter. The emotional experience associated with pain, or the actual suffering component, is intensified by uncertainty and fear. When we have a plausible explanation for why a flare may have occurred, much of the emotional impact is defused. We still hurt, but knowing why makes it easier to cope with and can help us realize that there is an end in sight to a temporary flare-up. Pain is a mental abstraction of a sensation. To a meaningful extent, knowledge can help us redefine that abstraction and be in a position to exert some control over suffering.

As we work to understand the mechanisms by which thyroid hormones increase pain perception, we are also gaining new insights into how the nervous system processes pain. During this past summer, a Martin Nelson Award for Summer Research afforded the opportunity to study latent stress-related pain flares in people experiencing phantom limb pain. Phantom pain is very different from any other neuropathic pain syndrome we have previously studied. It involves painful sensations following amputation that are perceived to originate from a limb, or limb segment, that no longer exists. Through this work, we are learning that thyroxine upregulates synaptic connections within the neuromatrix. This means that the brain's virtual body becomes highly sensitized to any messages from the network of connections associated with pain. It doesn't matter if a limb no longer exists, it is still part of the brain's virtual body map. Even though the state of the distal body hasn't changed, the experience of pain is heightened. By understanding how stress-related release of thyroid hormones modulates pain intensity, we are better able to conceptualize the importance and workings of the brain's virtual body as the entity within ourselves that actually experiences pain.

This all leads us to many questions that now invite consideration. For example, thyroxine release is a part of our psychophysiological reaction to stress. Basically, it is a long-term hormonal component of the "fight or flight response." Why does it wait 10 days to produce its global physiological effects? What biological purpose, or evolutionary usefulness, is served by this 10-day latent period? Or on a broader scale, if pain is experienced and modulated in our neurologically generated virtual bodies, what does that say about our perception of other dimensions of external reality? Do we ever genuinely perceive what is "out there," or is our experience of everything based on modulated virtual constructs within ourselves?

Regardless of whether pain is an accurate perception of the physical body's condition, a phenomenon of mind, or a complex interaction between the two, the resultant impact on the quality of our lives is quite real. Understanding the comprehensive mechanisms that generate, modulate, and perpetuate pain may ultimately help us more effectively address this ubiquitous dimension of human suffering.

## **Roger Allen, PhD, PT**

For Roger Allen, the topic of this 44th Register Lecture gives focus and meaning to a lifetime of exploring seemingly diverse academic and professional careers. He has been a member of the physical therapy faculty at University of Puget Sound for more than 18 years. His time here represents a return to university teaching following work as a full-time practicing physical therapist, specializing in the treatment of people who experience relentless chronic pain.

Going back to school to pursue physical therapy was also a career shift that was preceded by a 12-year tenure as professor of psychophysiology at a large, research-focused university, which involved in-depth study into the physiological connections linking our thoughts and emotions to physical illness susceptibility. The integration of psychophysiological expertise and hands-on treatment of patients with chronic pain has afforded Allen unique professional perspectives on both pain management and understanding the complex (and often surprising) relationships between our bodies, our minds, and mechanisms within the human brain.

Allen now teaches courses on clinical anatomy, neuroscience, functional neuroanatomy, and psychological aspects of physical therapy practice to our doctor of physical therapy students. He is author of three textbooks and chapters on diverse subjects in the three most recent editions of the encyclopedic benchmark reference Bonica's Management of Pain. He has made more than 100 national and international research presentations at venues including the Nobel Institute for Neurophysiology, World Pain Congress, World Congress of Physical Therapy, World Congress of Neurology, American Pain Society, World Institute of Pain, European Congress of Physical and Rehabilitation Medicine, American Academy of Orthopaedic and Manual Physical Therapists, and regularly at the American Physical Therapy Association's Combined Sections Meetings and Annual Conferences. Allen's published research has appeared in the international Journal of Physical Therapy, Psychophysiology, Journal of Neurological Physical Therapy, European Journal of Pain, Physiotherapy, Physical Medicine and Rehabilitation Clinics of North America, and International Journal of Sport Psychology, and includes an anthologized contribution to the science parody Journal of Irreproducible Results. For his neurovascular innervation research, he received the Brown Sequard Medal, and at University of Puget Sound he has been a John Lantz Senior Research Fellow and recipient of both the Dirk Andrew Pibbs Memorial Research Award and the Teaching Excellence Award (now the Thomas A. Davis Teaching Award).

Over the past two decades, most of Allen's research work has been conducted with the integral involvement of his doctoral physical therapy students and

undergraduate neuroscience interns. These important faculty/student collaborations have ignited and nurtured the sparks of exciting, fresh insights. So far, more than 90 of his Puget Sound students have presented research at national or international conferences, or published their work in professional journals, and four have received international research awards.

### **John D. Regester Faculty Lectures**

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| 2015–Steven Neshyba, chemistry   | 1993–George M. Guilmet,<br>comparative sociology |
| 2014–Leon Grunberg, sociology and<br>anthropology; Sarah Moore, psychology | 1991–Michael Veseth, economics                   |
| 2013–Andy Rex, physics   | 1989–Kenneth Rousslang, chemistry                |
| 2012–George S. Tomlin, occupational therapy                                | 1987–Terry A. Cooney, history                    |
| 2011–Nancy Bristow, history and<br>African American studies                | 1985–Beverly K. Pierson, biology                 |
| 2010–David Lupher, classics  | 1983–Douglas M. Branson, law                     |
| 2009–Suzanne Holland, religion   | 1981–Michael J. Curley, English                  |
| 2008–David Tinsley, German   | 1980–Esperanza Gurza, foreign languages          |
| 2007–D. Wade Hands, economics  | 1979–Francis L. Cousens, English                 |
| 2006–A. Susan Owen,<br>communication studies                               | 1978–Delmar N. Langbauer, religion               |
| 2005–Mott T. Greene, history   | 1977–Jeffrey S. Bland, chemistry                 |
| 2004–Doug Edwards, religion  | 1976–Esther B. Wagner, English                   |
| 2003–Rob Beezer, mathematics   | 1975–Richard E. Hodges, education                |
| 2002–Helen (Ili) Nagy, art   | 1974–Theodore L. Harris, education               |
| 2001–Geoff Proehl, communication<br>and theatre arts                       | 1973–Z. Frank Danes, physics                     |
| 2000–James Evans, physics  | 1972–Frank N. Peterson, sociology                |
| 1999–Geoffrey Block, music   | 1971–Robert G. Albertson, religion               |
| 1998–Denise L. Despres, English  | 1970–John W. Prins, business                     |
| 1997–William Breitenbach, history  | 1969–Leroy Ostransky, music                      |
| 1995–Alan S. Thorndike, physics  | 1968–Gordon D. Alcorn, biology                   |
|  | 1967–John D. Regester, philosophy                |
|  | 1966–Harold P. Simonson, English                 |
|  | 1965–John B. Magee, religion                     |



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