National Vulvodynia Association

NVA News

Volume XIV, Issue II Summer 2009

A Topical Treatment for Provoked Vestibulodynia

Questions & Answers with Paul Nyirjesy, MD

Dr. Nyirjesy is a Professor of obstetrics and gynecology at Drexel University College of Medicine and the Director of the Drexel Vaginitis Center.

NVA: Which treatments are commonly used to manage Provoked Vestibulodynia, also known as vulvar vestibulitis?

Dr. Nyirjesy: Because we don't know what causes Provoked Vestibulodynia (PVD), various treatments may be tried, including topical and intralesional corticosteroids, topical anesthetics (e.g., lidocaine), topical estrogen, oral or topical antidepressants or anticonvulsants, biofeedback, physical therapy, surgical resection of the involved tissue (vestibulectomy) and several complementary or alternative therapies. According to a recent survey, the most commonly prescribed treatment is either an oral antidepressant or anticonvulsant.

NVA: You prescribe topical amitriptyline/baclofen for PVD. How would you describe the effects of these two medications?

Dr. Nyirjesy: Amitriptyline is a tricyclic antidepressant that is often prescribed for the treatment of chronic pain conditions, including vulvodynia. Many women with vulvodynia have experienced relief with oral amitriptyline, which modulates pain by interfering with communication between nerve cells. Baclofen appears to have two functions: (i) it inhibits the release of neurotransmitters, chemicals that relay messages between nerve cells, and (ii) it helps to relax the pelvic floor muscles. Some experts think that abnormally elevated tone and instability of pelvic floor muscles contribute to the pain of PVD.

NVA: Why did you decide to conduct a study on this combination cream?

Dr. Nyirjesy: Up to 60 percent of women using oral amitriptyline to control vulvar pain report significant improvement in symptoms, however,

See TOPICAL TREATMENT, page 2

Chronic Pain and the Brain: Recent Findings

By Katherine Sutton, PhDc, Caroline Pukall, PhD, and Petra Schweinhardt, MD

Ms. Sutton is a PhD candidate and Dr. Pukall is an associate professor in the department of psychology at Queen's University in Kingston, Ontario. Dr. Schweinhardt is an assistant professor in the department of neurology and neurosurgery at McGill University in Montreal, Quebec.

The International Association for the Study of Pain (IASP) defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage." This definition encompasses many types of pain. It is important to note that the pain experience is subjective, i.e., how pain is perceived varies between individuals and even within the same person over time.

See CHRONIC PAIN, page 9

Topical Treatment

(from page 1)

many experience unpleasant side effects that limit its use. Recently, a group of vulvar pain experts proposed the use of a cream containing amitriptyline and baclofen, but we didn't find any published studies on its effectiveness in women with vulvodynia. We did, however, locate several published studies reporting on the pain-relieving effect of topical amitriptyline for other chronic pain conditions in both humans and animals. For example, the combination of amitriptyline and baclofen is used to treat neuropathic pain originating from cancer. We wanted to determine whether or not topical amitriptyline/baclofen could be effective specifically in the treatment of PVD.

NVA: Would you describe your study?
Dr. Nyirjesy: We performed a retrospective evaluation of 38 women with PVD who used amitriptyline/baclofen cream. These women were new patients referred to the Drexel Vaginitis Center between November 2004 and February 2006 for the evaluation of chronic vulvovaginal symptoms.

NVA: What type of questionnaires and tests did you administer?
Dr. Nyirjesy: Women supplied demographic information and completed questionnaires about their vulvovaginal condition, general health, sexual function and psychosocial factors. Using a visual analog scale, they scored the intensity of their vulvovaginal pain with various activities, including sexual intercourse, during the previous four weeks. After completing the questionnaires, they underwent a standard evaluation that included taking a detailed history, physical and vulvovaginal examinations, vaginal pH measurement, saline and 10% potassium hydroxide microscopy and yeast culture. When clinically indicated, we ordered additional studies to determine other vulvovaginal pathogens.

NVA: What was the treatment protocol?
Dr. Nyirjesy: Women used a compounded topical cream containing a combination of 2% amitriptyline and 2% baclofen. We instructed them to clean the vestibular area and then apply a pea-sized amount of the cream to the site of vestibular pain twice daily. They returned for an initial follow-up four to six weeks after initiating therapy, and then as indicated for their clinical care. We performed a physical examination, took cultures and administered questionnaires at each follow-up visit.

NVA: How did you determine whether the cream was effective?
Dr. Nyirjesy: We assessed treatment response in several ways. First, we asked women to give a verbal report of the change in their condition as

See TOPICAL TREATMENT, page 3

NVA News
National Vulvodynia Association
P.O. Box 4491, Silver Spring, Md. 20914-4491
(301) 299-0775; FAX: (301) 299-3999
www.nva.org

NVA News is published three times per year.

Editor:
Phyllis Mate

Contributor: Chris Veasley **Layout:** Andrea Hall

Topical Treatment

(from page 2)

follows: little or no improvement (<30%), moderate improvement (30-60%) or much improvement (>60%). Women with more than 30 percent improvement were considered "responders." Using a visual analog scale, we once again asked them to rate the severity of discomfort experienced with everyday activities, including sex, in the previous four weeks. The scale ranged from 0 to 100, with the worst pain scored as 100. Finally, we utilized a 5-point numerical rating scale to determine any recent change in symptoms. At each visit, women were asked to rate the following factors: extent to which the vestibular pain interfered with social activities, frequency of sexual intercourse, sexual desire, difficulty in becoming lubricated, frequency of discomfort or pain during sex, overall level of discomfort or pain with intercourse and satisfaction with sex life.

NVA: What were your findings?

Dr. Nyirjesy: We identified 38 women for whom we had follow-up data. The median follow-up time was 33 weeks, with a range of eight to 55 weeks. Thirty-seven women were Caucasian and one was Hispanic. Of the 38 patients, four discontinued therapy, either because of localized burning (3), or a lack of improvement (1); these women were considered treatment failures in our analyses. Overall, on verbal report, 29 percent reported *little or no improvement*, 18 percent reported *moderate improvement* and 53 percent reported *much improvement.* When we asked women to describe

Table 1: Quality of Life and Sexual Parameter Mean Scores Pre- and Post-Treatment (n =31)

Parameter	Pre-Treatment	Post-Treatment
# times vulvar pain interfered with social activity 0 (none) to 4 (all the time)	1.3	0.8
Discomfort with daily activities (1 to 100)	42	34
Discomfort with sexual activity (1 to 100)	78.5	46.3
Frequency of sexual intercourse (# times per month)*	1.5	1.5
Sexual desire 1 (very low) to 5 (very high)	1.5	1.5
Difficulty becoming lubricated 1 (never) to 5 (always)	2	1
Frequency of discomfort or pain during sex 1 (never) to 5 (always)*	5	4
Overall level of discomfort/pain with intercourse 1 (very low) to 5 (very high)*	4	2
Satisfaction with overall sexual life 1 (very satisfied) to 5 (very dissatisfied)	5	4

*For questions regarding sexual intercourse, the analysis did not include nine women who reported not having sex.

See TOPICAL TREATMENT, page 4

Topical Treatment

(from page 3)

symptoms in the self-report follow-up questionnaires, 16 percent reported that they felt worse, 22 percent felt the same, 35 percent felt a little better and 26 percent felt a lot better. No one felt 100 percent better. No one experienced systemic side effects attributable to amitriptyline or baclofen. Although 11 women experienced localized burning, only the three women noted earlier terminated treatment because of it.

Follow-up questionnaires were available for 31 (of 38) study participants. This group's average scores are reported in Table 1 (see page 3). Although all of the questionnaire measures showed responses consistent with overall pain improvement, most failed to achieve statistical significance, with a few noteworthy exceptions. In particular, following treatment, women reported (i) an overall decrease in the extent to which their condition interfered with social activities, and (ii) less discomfort or pain with intercourse. Additionally, it was easier for them to become lubricated during sex.

NVA: Other studies have found that, even with successful treatment, women don't necessarily engage in sexual intercourse more often. Was your finding similar?
Dr. Nyirjesy: Yes. Although women in our study reported improvement in daily functioning and less pain with intercourse, their sex lives (e.g., frequency, desire and satisfaction) did not change. Of note, nine women did not attempt sexual intercourse following treatment, compared to five before the initiation of treatment. An analysis of this subgroup showed that six women had responded to treatment, whereas three did not. Eight women reported having a stable male partner and only one did not have a sexual partner.

NVA: To what do you attribute this finding?
Dr. Nyirjesy: When we evaluated the response to therapy using sexual behavior parameters, we noted that women who responded favorably to treatment had reported lower sexual interest and a higher percentage of discomfort with sex at baseline. Thus, the positive response exhibited by some women may have resulted from greater room for improvement in terms of both pain and satisfaction. Additionally, Reed and colleagues found that, when compared to controls, women with vulvodynia expressed different attitudes about sex-related issues. These attitudes included less interest in sex and more negative feelings about themselves as sexual individuals, but the same level of sexual satisfaction, despite inferior quality and quantity of sex. Thus, it is likely that the chronic pain affects sexual factors, including desire; therefore, even when the pain lessens, desire doesn't necessarily return and a woman engages in sex less often. This is an important finding and underscores the need to utilize multidisciplinary treatment to address all facets of the pain disorder, i.e., the physical pain and its sexual, psychological and social consequences.

NVA: Did you find a difference between women who responded to treatment and those who did not?
Dr. Nyirjesy: We compared 27 women who were "moderate and much improved" (responders) to 11 women who reported either no or little improvement (non-responders). Interestingly, at baseline, non-responders were more likely to have rated their sexual interest as moderate to very high and reported a higher rate of diagnosed psychosocial disorders, such as depression and anxiety. When we examined the results of all women who suffered from psychological disorders and/or other chronic pain syndromes (e.g., fibromyalgia, interstitial cystitis, irritable bowel syndrome), we found

See TOPICAL TREATMENT page 5

Topical Treatment

(from page 4)

that non-responders were more likely to suffer from a coexisting pain disorder.

NVA: What conclusions can be drawn from this finding?
Dr. Nyirjesy: These results can be explained in two ways. If you conceptualize vulvodynia as a group of distinct disorders that have been classified together simply because they produce the same clinical syndrome, it is possible that these differences represent multiple etiologic factors or pain mechanisms. Other authors have suggested that, in a subgroup of patients, vulvodynia may actually be the expression of a central nervous system disorder, such as altered central sensory processing or loss of inhibitory control. This could explain the increased number of other chronic pain syndromes among some women with vulvodynia. If the pain is a result of a change in the central nervous system, it would be more difficult to achieve relief by applying a topical medication. Alternatively, perhaps for women with longstanding pain disorders and accompanying depression and anxiety, addressing only the localized pain and ignoring psychological and emotional factors tends to result in treatment failure.

NVA: This study included only women with PVD. Based on your clinical experience, do you think this treatment could be effective for women with Generalized Vulvodynia?
Dr. Nyirjesy: Because it is well-tolerated and easy to try, we have used this treatment in some women with Generalized Vulvodynia. I think it is much more hit-or-miss in this group, i.e., a few women have gotten better, but not as many as in the PVD group. It may be less effective in women with Generalized Vulvodynia because the affected area is more diffuse, making it more difficult to apply the cream to all the symptomatic areas. On the other hand, it may be less effective because the underlying mechanism is different in this vulvodynia subgroup.

NVA: What were the strengths and weaknesses of your study?
Dr. Nyirjesy: This preliminary study was limited by its retrospective nature and by the small

See TOPICAL TREATMENT, page 6

NVA Launches Online Learning Program

Thanks to the generous support of The Patty Brisben Foundation, the NVA is pleased to announce the release of its first online tutorial for women with vulvodynia – *Everything You Need to Know About Vulvodynia*. This comprehensive, self-guided program aims to empower women to make educated decisions about their health care, build strong partnerships with their health care providers and improve their quality of life. The tutorial covers gynecologic and pelvic anatomy/physiology, diagnosis and treatment of vulvodynia, coping with chronic pain, and practical advice on sexual/relationship issues. To view the program, visit: http://learnpatient.nva.org.

Health care providers can obtain flyers about the program for distribution to patients. Please contact Gigi Brecheen at gigi@nva.org or call 301-949-5114.

Topical Treatment

(from page 4)

number of participants, both of which hampered our ability to assess factors associated with response. Our analyses were further impeded by a lack of follow-up surveys for 18 percent of patients. Although our study lacked a control group, this is unfortunately true for the vast majority of PVD treatment studies, including those of systemic amitriptyline. Thus, the improvement that we noted could be due to other factors relating to patient care. Nevertheless, we feel that our study also had unique strengths. These included careful diagnosis, control of conditions possibly associated with symptom exacerbation, and the use of detailed baseline questionnaires, which enabled us to characterize women using clinical, psychological, sexual, demographic and social parameters. The finding that some of these parameters can affect treatment response underscores the position that PVD is more than just a cause of painful intercourse and that accompanying factors should be measured in future treatment studies.

NVA: What do you think are the clinical implications of your study?

Dr. Nyirjesy: We found that most women with PVD who used topical amitriptyline/baclofen cream over an average period of 33 weeks reported improvement in their painful symptoms. Furthermore, the overall improvement rate with this topical treatment is comparable to the 60 percent improvement rate of women using oral amitriptyline. Other studies that have evaluated various therapies for vestibular pain have shown that improvement varies widely, from 35 to 79 percent. Of particular note in our study was that more than 50 percent of the women had experienced symptoms for well over a year and most had failed to respond to other treatments before using this cream. Although local burning, a common adverse event with any topical medication, did occur in 29 percent of women, only eight percent discontinued treatment as a result. None of the women participating in our study reported adverse side effects common with oral amitriptyline, such as drowsiness, oral or vaginal dryness, weight gain and constipation.

In conclusion, this relatively easy and well-tolerated topical treatment may represent a viable alternative to oral medication for some women with PVD, particularly those who do not suffer from a co-existing pain condition or accompanying psychological condition. Additionally, other oral medications used to treat chronic pain, such as anticonvulsants, may also be effective when used topically. Overall, given that topical amitriptyline and baclofen cream is well-tolerated and many women with refractory symptoms responded positively to it, we think that this therapy warrants further investigation in a prospective, randomized, placebo-controlled trial.

(*Editor's Note: To receive a footnoted copy of this article, with a complete set of references, please send an e-mail to gigi@nva.org or call 301-949-5114).*

Selected References

Boardman, L. et al. Topical gabapentin in the treatment of localized and generalized vulvodynia. *Obstet Gynecol* 2008;112:579-85.

Gunter, J. Vulvodynia: new thoughts on a devastating condition. *Obstet Gynecol Surv* 2007; 62: 812-9.

Nyirjesy, P., Halpern, M. Medical management of vulvar vestibulitis: Results of a sequential treatment plan. *Infect Dis Obstet Gynecol* 1996; 3:193-97.

Reed, B. Treatment of vulvodynia with tricyclic antidepressants: efficacy and associated factors. *J Low Genit Tract Dis* 2006;10:245-51.■

NVA Funds First Vulvodynia Treatment Registry

Thanks to the generosity of a longtime donor, we are pleased to announce that NVA has awarded a $50,000 grant to Drs. Georgine Lamvu, Deniz Zolnoun and Lori Boardman to develop and implement the first-ever Vulvodynia Treatment Registry. The purpose of this multi-site registry, launched in September 2009, is to gather data on the efficacy of different treatments for vulvodynia. These treatments include, but are not limited to, topical medications (e.g., lidocaine, gabapentin); oral "pain-blocking" medications (e.g., tricyclic antidepressants, anticonvulsants and muscle relaxants); physical therapy; and surgery for vulvar vestibulitis (aka Provoked Vestibulodynia). Women receiving medical care at the University of North Carolina, University of Central Florida and Florida Hospital will be eligible to participate.

Once enrolled, participants will undergo a thorough medical evaluation and tests to assess vestibular skin and pelvic muscle sensitivity. They will also complete several questionnaires on pain, sexual function and quality of life. All tests and questionnaires will be administered multiple times during a two-year period to assess long-term benefits of treatment. In addition, the investigators hope that data collected through the registry will (i) clarify why only some women benefit from a particular treatment and (ii) identify factors that can predict treatment success. Additionally, the registry's findings will be used to guide the development of controlled studies on treatment efficacy. ■

Viewers React to 20/20 Television Show

On August 7th, millions tuned in to watch 20/20's *Medical Mysteries,* which featured a segment on painful sexual intercourse. Dr. Timothy Johnson, ABC's chief medical editor, discussed the diagnosis and treatment of painful intercourse with Andrew Goldstein, MD, director of the Center for Vulvovaginal Disorders in Washington, DC, and Amy Stein, a New York-based physical therapist, specializing in the treatment of urogynecological pain disorders. He also interviewed three women for the segment: Sara Fontaine and Allison Nugent, two young women who described living with the pain condition, and Christin Veasley, NVA's associate executive director, who was diagnosed with vulvar vestibulitis when she was in college.

During her interview, Sara reported visiting 15 doctors in search of a diagnosis and being treated for several conditions she didn't have. Allison remarked that, "Dealing with a chronic pain condition is difficult no matter what, but handling it when nobody can tell you what it is, or how to treat it, is just beyond the pale." Dr. Johnson noted that many women who suffer from painful sex also experience vulvar pain with activities such as sitting or simply wearing pants.

All the women discussed their pain condition's impact on their relationship with their partners. "All the results were coming back negative and my husband just assumed that it was him – that I wasn't attracted to him anymore," recalled Sara. Allison felt that her pain not only affected her husband, but made her doubt herself, saying, "Part of what makes you a woman is having female sexual organs, and when they're not working properly, it's an assault on your ego as a woman." Allison also disclosed that her pain problem put tremendous stress on her marriage, which ultimately ended in divorce. On a heartening note, Chris and her husband Melvin said that they decided to get married even though they were unable to have sex for the first five years of their relationship. Melvin admitted that he had struggled with the decision to marry, but ultimately concluded that, "Sex is an important part of a relationship, but it's not *the* most important part."

See 20/20, page 8

20/20

(from page 7)

They have been married for nine years and have two lovely daughters.

After the show, hundreds of viewers posted online comments on the 20/20 web site or wrote to NVA. Many expressed disappointment that the show did not identify the women's medical conditions as vulvodynia or vulvar vestibulitis. Some viewers thought that more details on physical therapy and the surgical treatment were needed. For example, the show did not specify that pelvic floor muscle rehabilitation usually requires visiting a physical therapist several times a week for many months, nor did it mention that women who undergo surgery may need up to one year to experience significant relief. Others remarked that featuring three women whose pain was greatly improved or cured did not portray the reality of many women who do not find relief and continue to suffer from this chronic condition.

The show concluded, however, with Allison's helpful advice for women suffering from any condition that causes painful sex. "It's important to seek treatment and talk to your doctor about it, but if he/she doesn't think you have a physical problem, you should find a vulvovaginal expert who does understand," she stated. NVA applauds Sara, Allison, Chris and Melvin for having the courage to share their personal stories on national television. To view the 20/20 segment online, visit: http://abcnews.go.com/2020/ and under "August 7th" click on "Millions of Women Find Sex Unbearable."

Following the show, ABC affiliates in Denver and Memphis covered the topic on their local news and video of the segment was posted on 20/20's website. The producers also posted a 10-minute video of Ms. Stein demonstrating pelvic floor muscle stretches, a questionnaire that differentiates sources of painful sex and a link to the National Vulvodynia Association web site (www.nva.org). NVA issued a press release expressing appreciation of ABC for bringing this rarely-discussed condition out of the shadows, but emphasized that vulvodynia's impact reaches far beyond the bedroom. The release, distributed to thousands of health reporters and editors, stated that millions of vulvar pain sufferers do not find adequate relief and that research on treatments is lacking.

***All Things Gyno* Radio Show**

On August 10th, sex therapist Dr. Laura Berman's satellite radio show covered several gynecological disorders with Elizabeth Gunther Stewart, MD, a Harvard University vulvovaginal specialist and NVA medical advisory board member, Elizabeth A. Stewart, MD, a Mayo Clinic obstetrician/gynecologist, and Judith Florendo, PT, a Chicago-based physical therapist specializing in pelvic floor muscle dysfunction. During the two-hour program, *All Things Gyno*, Mayo Clinic's Dr. Stewart gave an overview of uterine fibroids and Harvard's Dr. Stewart answered listeners' questions about vulvovaginal conditions, clarifying the difference between dermatological disease, vulvodynia, vaginismus and pudendal neuralgia. Ms. Florendo discussed the important role of physical therapy in the treatment of vulvovaginal pain conditions and told women what to expect during their initial evaluation and subsequent treatment sessions. We extend our appreciation to Dr. Berman for covering vulvodynia on her show and to both Dr. Stewarts and Ms. Florendo for their dedication to treating women with gynecological and pelvic pain conditions.

Following these two media events, the NVA's web site traffic doubled and we were contacted by hundreds of women. To keep abreast of future media coverage of vulvodynia, sign up for our bimonthly electronic newsletter by visiting www.nva.org and clicking on "E-Newsletter" in the left column. ■

Chronic Pain

(from page 1)

Types of Pain

Most of the pain we experience, such as the pain of a stubbed toe, is transient. This type of pain dissipates quickly. When pain endures, it is either classified as acute or chronic. Acute pain is a necessary and useful sensation, signaling the brain that an injury has occurred and the body requires time to heal. Acute pain is a mixture of tissue damage, pain sensation and possibly anxiety. This combination of factors leads to pain-related behaviors that protect the injured area, preventing further tissue damage and promoting healing. When pain persists long after it serves any useful function, it is classified as chronic pain. In this situation, tissue damage is no longer apparent and the diagnosis is made in the absence of an identifiable cause. The absence of visible pathology does not mean that the pain is 'all in one's head.' Chronic pain research is still in its infancy and we simply don't understand the mechanisms involved in its initiation or persistence.

In the pain literature, the term 'chronic' refers to both the pain's overall duration and temporal characteristics. To be classified as chronic, the pain syndrome must exist for a minimum of three to six months and be relatively constant, typically on a daily basis. This characterization is applicable to conditions such as chronic back pain and Generalized Vulvodynia, for example. Since a diagnosis of Provoked Vestibulodynia (PVD, aka vulvar vestibulitis) requires that pain is not constant, i.e., that it occurs only upon pressure applied to the vestibule, this condition is classified as *chronic intermittent pain*.

Physiology of Pain

The experience of pain involves a number of factors that can be divided into four general categories: nociceptor activation, sensory-discriminative brain activation, affective (emotional) response, and pain behaviors or evaluations.

Before one consciously perceives a painful sensation, there must be activation of pain receptors known as nociceptors. When a painful stimulus is encountered, nerve signals encoding it travel along fibers to the dorsal horn of the spinal cord, a key area in pain transmission. When these peripheral pain signals arrive at the dorsal horn, they are processed through a gate-control mechanism, which determines whether or not the pain message is sent to the brain. The gate consists of two types of signals that work in combination to determine which messages are transferred to the brain and will be interpreted as pain. Excitatory signals, which are activated by the painful stimulus, open the gate and send the pain message to the brain. Inhibitory signals, which are activated by the brain and various analgesic receptors in the body, close the gate and prevent the pain message from being sent to the brain. The balance between these signals is controlled by multiple factors, including the intensity and duration of the painful stimulus, the body's natural pain inhibitory mechanisms, and when utilized, the effect of pain management methods such as medication.

The second aspect of the pain response is the sensory-discriminative component, or the first conscious perception of pain, i.e., the awareness that one is experiencing a painful sensation. Pain is perceived only when the balance of input to the dorsal horn of the spinal cord tips in favor of the excitatory influences, either because of excessive nociceptive activity or deficient inhibitory influences. The third aspect of the pain response is the suffering, or emotional, component. This aspect is often described in terms of unpleasantness. Fourth are the pain behaviors or evaluations, which result

See CHRONIC PAIN, page 10

Chronic Pain

(from page 9)

from both the sensory perception of pain and the degree of suffering. Pain behaviors can either be thoughts, e.g., "This pain will never end," or observable actions, such as limping, which serve a beneficial function in acute pain situations by promoting healing; in a chronic pain situation, however, pain behaviors or evaluations can substantially interfere with one's normal activities.

Two other aspects of chronic pain are allodynia, a painful sensation experienced in response to a typically non-painful stimulus, and hyperalgesia, a heightened response to a normally painful stimulus. Individuals with chronic pain syndromes, including vulvodynia, tend to experience allodynia and/or hyperalgesia.

How the Brain Processes Chronic Pain

Our understanding of chronic pain is still rudimentary. Chronic pain occurs when pain signals are continuously sent to the brain without being linked to the first step of the pain experience, the presence of a painful stimulus. This process can develop via different routes. One theory is that the balance of excitatory to inhibitory events becomes altered, such that activation of fewer excitatory neurons is needed for a pain signal to be relayed to the brain; for example, in women with vulvodynia, the touch of a Q-tip or pressure from sitting can be abnormally painful. Once a continuous signal of pain is transmitted, its sensory, emotional, and behavioral or evaluative components can intensify one another, resulting in the experience of chronic pain.

Researchers have discovered two distinct, but related, systems within the brain that are associated with pain transmission. The *lateral system* is thought to be associated with the sensory-discriminative component of pain, while the *medial system* is linked to the emotional and behavioral components of the pain experience, e.g., negative thinking and anxiety.

Some variation in which regions are activated is due to the intensity of the pain stimulus, the amount of body surface exposed to the pain, the type of pain stimulus, whether the pain is allodynic or hyperalgesic, and whether the pain is avoidable or can be controlled. Numerous studies have also demonstrated that there are differences in activation among types of pain and individuals, especially those with chronic pain, due in part to the role of psychological context in the modulation of pain intensity.

Brain Processing in Vulvodynia

To date, no brain imaging studies including women with Generalized Vulvodynia have been published, although one such study is underway. Only one published study has investigated PVD using functional magnetic resonance imaging (fMRI) of the brain. This study found that the brain regions activated during painful mechanical stimulation of the vulvar vestibule in women with PVD are generally similar to the areas activated in individuals suffering from other chronic pain syndromes.

Another study using *whole brain voxel-based morphometry* to examine structural changes in the brain found that women with PVD had higher gray matter densities in pain modulation and stress-related areas of the brain. In some of these areas, the gray matter was related to lower pain thresholds and increased negative thinking, as measured by Sullivan and colleagues' Pain Catastrophizing Scale. Older individuals who have long-standing chronic pain typically exhibit a decrease in gray matter density. We propose that there may be bi-directional changes in gray matter, resulting in higher den-

See CHRONIC PAIN, page 11

Chronic Pain

(from page 10)

sities in young individuals with shorter pain duration and lower densities in older individuals with a long course of chronic pain. At this point, we can only speculate about the significance of these gray matter variations. It might mean that women who have suffered from PVD experience changes in their brains as a result of pain or it might mean that they were born that way. Further research is necessary to explore the relevance of these changes; importantly, there are no data available to suggest that they are irreversible. It is also possible that increased gray matter represents an inflammatory response by cells in the brain.

Another fMRI study that we are currently performing was designed to assess the neural correlates of attention and catastrophizing during painful genital stimulation in women with PVD. In addition, our research team will use spinal imaging to assess possible neuropathic pain processes in PVD. Although many of the current treatments for PVD are the same as those recommended for neuropathic pain, for example, antidepressants, topical medications and Botox, confirmation of a neuropathic process in these and other studies would justify, and perhaps expand, the treatment options available.

Brain Processing in Chronic Pain Conditions

Compared to healthy controls, individuals with PVD or other chronic pain conditions consistently show differences in brain activation. The above-mentioned fMRI study of women with PVD showed similar patterns of neural changes as fMRI studies of other chronic pain conditions, including fibromyalgia, irritable bowel syndrome, and idiopathic back pain. Many studies suggest that there is overlap between other chronic pain disorders and vulvodynia, with interstitial cystitis/painful bladder syndrome being the most frequent co-morbid disorder. As with other chronic pain syndromes, such as chronic pelvic pain, it is likely that physical factors, peripheral and central sensitization, and psychological factors interact to produce the chronic pain. Perhaps similar underlying mechanisms can lead to various forms of chronic pain, although this hypothesis has yet to be proven. Because pain is a subjective experience based on the interaction of multiple factors, there is not one single pattern of findings that has been exactly replicated. Further research is needed to determine whether patterns of brain activation are similar among various chronic pain syndromes.

Brain Research and Improving Patient Care

An understanding of the various components involved in the processing and experience of chronic pain will aid in developing better assessment and treatment options for individuals suffering from chronic pain syndromes such as vulvodynia. It is clear from the findings presented in the empirical literature thus far that pain is not simply a consequence of changes in sensory-motor areas; in fact, the emotional circuitry may be just as important as the sensory component. Because all of the systems in pain processing are interrelated, targeting each of them would likely be most beneficial to outcome. For example, focusing on changing the emotional circuitry using Cognitive Behavioral Therapy (CBT), a treatment that has been successfully used in some women with vulvodynia, may also have a beneficial effect on the level of pain experienced. Understanding the changes that occur in the central nervous system also has the potential to shed light on why some individuals with chronic pain suffer from one or more co-existing conditions. By examining neural correlates of chronic pain, and emotional disorders such as anxiety and depression, one can determine potential overlap and develop treatment interventions that

See CHRONIC PAIN, page 12

Chronic Pain

(from page 11)

target a wider array of symptoms. These findings are extremely relevant in the development of treatment targets for individuals with chronic pain.

Results from the two studies completed to date indicate that both structural and functional brain changes exist in women with PVD. Further research will assist in our understanding of the complex relationship between the physical sensations and psychological aspects of pain. Future research using fMRI and related technology can then be used to create a model of chronic vulvar pain. This model would facilitate an understanding of pain mechanisms at the spinal level and throughout the brain.

There are many ways to improve treatment once a chronic vulvar pain model is developed. Brain imaging scans pre- and post-treatment, in conjunction with self-report and physical measures, can help determine treatment efficacy, i.e., whether various therapies have reversed or minimized some of the initial changes found in women with vulvodynia. Longitudinal studies utilizing brain imaging will facilitate a deeper understanding of the way in which women with vulvodynia are affected over time and provide more information regarding the overlap between vulvodynia and other chronic pain conditions.

(Editor's Note: To receive a footnoted copy of this article, with a complete set of references, please send an e-mail to gigi@nva.org or call 301-949-5114.)

Selected References

Borsook, D. et al. (2007) Neuroimaging revolutionizes therapeutic approaches to chronic pain. *Molecular Pain*, 3:25.

Edwards, R.R. (2005) Individual differences in endogenous pain modulation as a risk factor for chronic pain. *Neurology,* 65: 437-443.

Fenton, B.W. (2007) Limbic associated pelvic pain: a hypothesis to explain the diagnostic relationships and features of patients with chronic pelvic pain. *Medical Hypotheses,* 69: 282-286.

Keefe, F.J. et al. (2004) Psychological aspects of persistent pain: current state of the science. *The Journal of Pain,* 5: 195-211.

Maihöfner, C. & Handwerker, H.O. (2005) Differential coding of hyperalgesia in the human brain: A functional MRI study. *NeuroImage,* 28: 996-1006.

Pukall, C.F. et al. (2005) Neural correlates of painful genital touch in women with vulvar vestibulitis syndrome. *Pain,* 115: 118-127.

Schweinhardt, P. et al. (2008) Investigation into the neural correlates of emotional augmentation of clinical pain. *NeuroImage,* 40: 759-766.

Schweinhardt, P. et al. (2008) Increased gray matter density in young women with chronic vulvar pain. *Pain*, 140: 411-419. ■

Visit NVA's New Web Site and Raise Funds for Research

When you visit www.nva.org, you will see an Amazon logo at the bottom of our home page. If you click on it before shopping at Amazon, NVA will receive 5% of the purchase price at no cost to you. Over the past five years, we have raised more than $10,000 this way. Thank you for your past and future participation!