

The Neuromatrix Theory of Pain: Implications for Selected Nonpharmacologic Methods of Pain Relief for Labor

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Women experience the pain of labor differently, with many factors contributing to their overall perception of pain. The neuromatrix theory of pain provides a framework that may explain why selected nonpharmacologic methods of pain relief can be quite effective for the relief of pain for the laboring woman. The concept of a pain "neuromatrix" suggests that perception of pain is simultaneously modulated by multiple influences. The theory was developed by Ronald Melzack and represents an expansion beyond his original "gate theory" of pain, first proposed in 1965 with P. D. Wall. This article reviews several nonpharmacologic methods of pain relief with implications for the practicing clinician. Providing adequate pain relief during labor and birth is an important component of caring for women during labor and birth. *J Midwifery Womens Health* 2004;49:482-488 © 2004 by the American College of Nurse-Midwives.

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INTRODUCTION

The experience of pain is a subjective sensation that is modulated by multiple factors. The neuromatrix theory of pain provides an effective organizing framework to explain this phenomenon.¹ This theory of pain perception was conceived by Ronald Melzack, one of the original co-creators of the "gate theory" of pain. The neuromatrix pain theory retains some key aspects of the gate theory of pain, but it offers a more comprehensive framework for understanding the subjectivity of pain. It recognizes the importance of both ascending and descending inputs to the conscious experience of pain and includes additional inputs that were not part of the gate theory, such as the important contributions of memory and past experiences.² This article reviews the neuromatrix conceptualization of pain and describes possible mechanisms of selected nonpharmacologic methods of pain relief frequently used by women in labor.

DEFINITION OF PAIN

The International Association for the Study of Pain (1996) defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or, described in terms of such damage."³ Labor is a normal physiologic phenomenon. Labor may be the only normal physiologic process that is usually described as painful. Why? One proposed reason is that the pain of labor alerts a woman to the labor process, so that she can get to a safe place in which to birth her infant.⁴ On the other hand, some women do not experience the sensations of labor as "painful," but rather, as pleasurable sensations, even orgas-

mic.⁵ Why does this huge variation in women's perceptions of their sensory and emotional experiences exist, when, presumably, the sensory stimuli of the basic physiologic process is the same for all laboring women?

MODELS THAT DESCRIBE THE EXPERIENCE OF PAIN

Prior to 1965, a simple neurophysiologic model of pain predominated. All physical pain was thought to emanate from activation of specific pain receptors in the periphery (called nociceptors), which initiated pain impulses that traveled through a spinal pathway to the brain.⁶ This model was a simple sensory stimulus-response model. The brain's contribution in this model was its perceptive response to the ascending afferent sensory inputs. The contributions of psychological or affective components to pain were not recognized.

Gate Control Theory

In 1965, Ronald Melzack and P. D. Wall revolutionized the understanding of pain with the introduction of the gate control theory, which recognized that the perception of pain is inherently more complex than simple receiving and recording. The gate control theory "forced the medical and biological sciences to accept the brain as an active system that filters, selects and modulates inputs."⁷ This was a major advance in recognizing the contribution of the brain not only to the ultimate perception of pain, but also to the nature of pain itself.

Implicit in Melzack and Wall's original gate control concept was the idea that a gate was either opened or closed at the level of the spinal cord (i.e., impulse transmission was either facilitated or inhibited at that level). If impulse transmission is sufficiently inhibited at the level of the spinal cord, then perception of pain (which occurs in the brain) is blocked. Melzack later noted that this theory fails

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to account for the perception of pain in the absence of sensory stimuli (such as occurs with phantom limb pain), and it fails to account for the perception of the body “as a unity.”²

THE NEUROMATRIX OF LABOR PAIN

Melzack has since moved beyond his initial gate control theory to a reconceptualization known as the “neuromatrix.”⁷ Neuromatrix refers to parallel and cyclic processing loops in the brain whose outputs converge to affect the ultimate perception of pain that is experienced by the conscious mind. Melzack describes the neuromatrix as a “. . . network, whose spatial distribution and synaptic links are initially determined genetically and are later sculpted by sensory inputs. . . . Thalamocortical and limbic loops that comprise the neuromatrix diverge to permit parallel processing in different components of the neuromatrix and converge to permit interactions between the output products of processing.”⁷ Melzack notes that repeated “cyclical processing and synthesis” of nerve impulses results in a characteristic “neurosignature” for a particular individual that is determined by a combination of genetic and sensory influences. There is increasing evidence that the concept of neural plasticity, long recognized as an important component of neural development, may also have an important role in pain pathways. Experimental evidence demonstrates that both synaptic architecture and neuropeptide expression are modified by sensory input and noxious events.^{7,8} For example, representation of a specific area of the body in the somatosensory cortex will become more detailed in response to repeated synaptic transmission originating from that particular area.⁹

How does this relate to the woman in labor, and how is this different from the gate control theory that is so familiar to clinicians? The neuromatrix theory incorporates many of the same elements of the gate control theory. Both theories view the brain as the ultimate arbitrator of the multiple dimensions of pain. However, the gate control theory emphasizes the opening or closing of a gate at the level of the spinal cord as the preeminent mechanism controlling the ultimate perception of pain. The neuromatrix theory of pain recognizes the simultaneous convergence of a panoply of influences, including one’s past experiences, cultural factors, emotional state, cognitive input, stress regulation, and immune systems, as well as immediate sensory input (Figure 1).¹ The multiple influences that create pain perception are generated from 3 parallel processing networks: sensory-discriminative (somatosensory components), affective-motivational (limbic system components), and evaluative-cognitive (thalamocortical components).⁷ Additional

contributions of the autonomic nervous system, the stress response system, and immune system modulation are also recognized in this model.

Synaptic inputs to the 3 networks can be either phasic or tonic. “Phasic” inputs refer to brief, short inputs such as cutaneous sensory input or focused attention; “tonic” refers to longer-lasting modulatory inputs such as cultural learning and past experiences. As evident in Figure 1, the contributions of all 3 parallel processing networks converge to create individual pain perception and “action systems,” or what the person does in response to their pain. Action systems (also referred to by Melzack as “action programs”)² include both involuntary and voluntary pain-coping strategies that the individual uses.

INFLUENCES ON THE PERCEPTION OF PAIN DURING LABOR

Past Experiences

Past experiences of pain can affect subsequent pregnancies in either positive or negative ways.¹⁰ Prior experience with very intense pain can be a positive influence if it was managed in a way that elicited a feeling of accomplishment, or this past experience can be a source of increased anxiety when anticipated a second time. Similarly, women who had very little pain in a prior pregnancy may be more confident because the prior experience with pain was manageable or they may feel more anxious, secondary to concern that they will not be able to solicit help in a timely manner.¹⁰ Prior experiences with labor and birth can have an especially significant impact on subsequent pregnancies.¹¹ Women bring the memory of all past experiences with them when they are in labor, even if these memories are not at the level of consciousness. This may be advantageous to women who have had prior positive birthing experiences, especially if they experienced lower levels of pain or a sense of accomplishment that they look forward to repeating. Alternatively, past labor experiences that were negative may contribute to increased anxiety and pain in subsequent births. In addition, some women who report experiencing intense pain during labor have described how the experience of labor pain helped them cope with other painful or stressful experiences in their lives and enhanced their subsequent ability to cope. This may imply that past recognition of labor as painful does not necessarily mean that this pain had a negative affective component.^{10–12} Primiparas more frequently report the pain of labor as more “intense” or “very painful” than multiparas do. However, Melzack found a wide variability in laboring women’s pain scores on the McGill pain questionnaire, a pain assessment tool that takes into account not only the severity of pain, but also the quality of pain (with different description choices such as sharp, gnawing, or cramping). Melzack noted “striking individual differences” in laboring women’s pain scores, with

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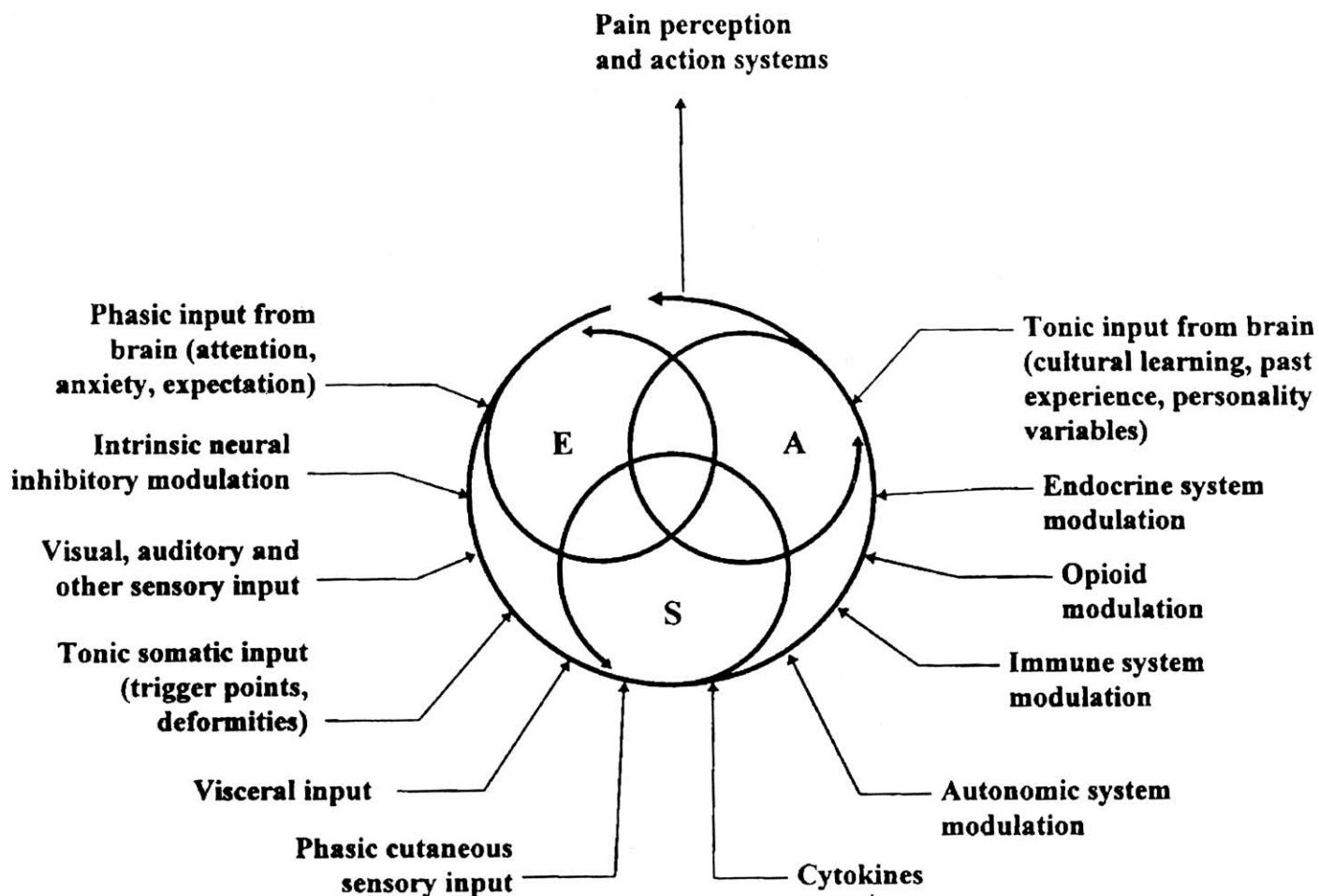


Figure 1. The body-self neuromatrix: Three parallel processing networks: (S) Sensory discriminative; (A) Affective-motivational; (E) Evaluative-cognitive. Reprinted with permission from Melzack R, 1999.⁷

some women reporting severe pain, and some women reporting almost no pain at all.¹³

Cultural Factors

“Did you ever notice that it’s hard to tell how far along in labor the Amish women are by looking at their faces?” This observation was from a labor and delivery nurse at a small rural hospital in Pennsylvania. What is culturally acceptable in terms of pain expression will vary in different cultures. In addition, cultural expectations of labor and specifically labor pain have a strong influence on pain perception.¹⁴ Cultural norms will influence what are considered acceptable movements or noises. Thus, a health care provider who cares for women during labor should be aware of the norms in the communities in which she or he practices to correctly interpret non-verbal signals. Concomitantly, providers must be aware of cultural preferences and acceptability of different methods of pain relief to provide culturally sensitive care.

PHYSIOLOGIC PATHWAYS OF PAIN

Sensory Input

Although the neuromatrix model does place a new emphasis on past experiences and cultural factors, sensory input will always be an important component of any theory of pain. Sources of nociceptive input emanate from several areas during labor and birth. Nociceptors are “receptor cells that respond selectively to noxious stimulation.”⁶ Nociceptive impulses are transmitted from 1 nerve cell (neuron) to another across synapses. The usual pathway in the transmission of sensory pain impulses to the brain is from nociceptive afferent fibers in the periphery to dorsal horn neurons in the spinal cord, where impulses can often be inhibited by various mechanisms. If neurons are sufficiently excited (as opposed to inhibited), neural transmission continues up the spinal cord to the thalamus and on to the somatosensory cortex and cingulate gyrus, where pain is perceived.^{6,15}

Nociceptive impulses during the first stage of labor are thought to result from ischemia in contracted myometrial

cells. This ischemia stimulates A-delta and C nociceptive fibers in the uterus, which, in turn, conduct the impulse via afferent nerve fibers to the spinal cord at the level of T10 to L1.¹⁶ The hypothesis that ischemia is the source of nociceptive input derives in part from observations that labor pains are stronger when there is not enough time for the uterus to relax in between contractions. Compression of the ganglia near the cervix and lower uterine segment is also thought to cause nociceptive input during late first stage and the second stage of labor. Stretching of the cervix during dilation, and stretching of the perineum during birth, constitute additional somatic sensory stimuli. These afferent impulses from the cervix and perineum are transmitted via the pudendal nerves to enter the level of the spinal cord at S2 through S4.¹⁶

One way to diminish the sensation of pain is to inhibit the afferent messages at the level of the dorsal horn. Thinly myelinated A-delta fibers and small visceral nonmyelinated C afferent nerve impulses travel relatively slowly to the spinal cord because of a lack of or minimal myelin sheath material. In contrast, large myelinated A-beta fibers that travel from the skin and muscles conduct impulses much more quickly. All 3 types converge in the dorsal horn of the spinal cord. In the dorsal horn, nociceptive-specific neurons are only activated by high-threshold nociceptive input, and they have a small range of receptivity. Wide dynamic range neurons respond to multiple types of afferent input and have a wide range of receptivity.¹⁷⁻¹⁹ Thus, when the stimulus from these neurons is assigned spatial and temporal characteristics in the thalamus and cortex, the pain is perceived as generalized and originating in an area larger than the anatomical position of the uterus. Wide dynamic range neurons respond not only to nociceptive input but also mechanical and thermal afferent input.

The receptive fields of dorsal horn neurons are not static, but dynamic, and will change the frequency of pain impulse transmission to the brain in response to varying stimuli and neurotransmitters and neuromodulators.^{17,19} Nociceptive stimulation of C fibers causes the release of several neurotransmitters and neuropeptides, such as glutamate and Substance P, from synaptic vesicles in the dorsal horn. These substances stimulate the dorsal horn neurons in the spinal cord, which results in increased frequency of pain impulse transmission. However, incoming impulses also stimulate the release of endogenous opioids that decrease the area of the neuronal receptive field, thereby decreasing the rate of firing.^{15,19} Enkephalins, dynorphins, and endorphins are endogenous opioid-peptide compounds that are found in several areas of the brain and spinal cord, as well as peripherally. The release of these peptides by interneurons in the dorsal horn of the spinal cord diminishes the sensation of pain via presynaptic inhibition of the afferent neurons projecting to the brain. The net effect is to inhibit the number of action potentials carrying messages up to the brain.^{15,20}

HOW DO NONPHARMACOLOGIC PAIN INTERVENTIONS WORK?

Interventions That Interfere With Afferent Transmission of Pain Impulses: Effects of Touch/Cutaneous Stimulation

Sensory A-beta fibers transmit impulses more quickly than C fibers; therefore, if one stimulates A-beta fibers through touch (such as rubbing a stubbed toe), one can significantly reduce the transmission of the C pain fibers, the pain fibers responsible for longer-lasting, aching types of pain.^{6,16} This phenomenon forms the basis of several pain relief modalities that are based on touch therapy, such as massage. Sterile water injections are another pain relief modality that are hypothesized to work on this principle, where small amounts of sterile water (0.1 mL) are injected intracutaneously at specific points over the sacrum for the relief of severe back pain in labor.²¹ For an excellent review of the effects of massage, sterile water injections, and other selected nonpharmacologic pain relief modalities, refer to the article by Simkin in this issue.²²

Interventions That Affect Pain Perception Directly Via Cortical Influences: Aromatherapy

The sense of smell is quite powerful. For example, certain strong odors, such as garlic, can be detected by the human olfactory system in a concentration as small as 0.000032 mg per cubic meter of air.²³ Odor can be a very powerful stimulus for memory associations.²⁴ Olfactory nerve transmission proceeds from the olfactory receptor cell and the olfactory nerve to the olfactory bulb, which is located at the anterior end of the brain. Projections from the olfactory bulb extend to the prepyriform cortex, the amygdala, and the hypothalamus.⁶ The amygdala is part of the limbic system, the emotional center of the brain, originally known as the “rhinencephalon” or “nose brain.” Afferent neural projections to the amygdala may explain why certain odors often have strong emotional or affective connotations for individuals. Due to the strong links between odor and memory, odors have a very personal significance, and therein may lie their usefulness as an adjunctive therapy in labor. A scent of the woman’s choosing may evoke feelings of security, love, or other emotional associations.²⁴ The sense of smell is the only 1 of the 5 senses in vertebrates that does not require impulse transmission to synapse in the thalamus on its way to the cortex.⁶ Thus, direct communication with the cortex allows rapid transmission and recognition of signals that are not subject to inhibition via synaptic influences.⁹

Neural connections from the olfactory bulb to the hypothalamus might explain how odors affect the experience of pain via a second physiologic pathway (i.e., direct impact on the hypothalamic-pituitary-adrenocortical [HPA] axis). This axis controls the well-characterized “fight or flight” response, and is another important modulatory input of the neuromatrix theory. There are many therapeutic modalities known to mitigate the stress response (e.g., relaxation

breathing and guided imagery). Direct neural connections from the olfactory bulb to the hypothalamus could explain the effects that have been attributed to aromatherapy.

Recently, a large prospective British study evaluated the use of essential oil aromatherapy for laboring women in a large teaching hospital.²⁵ Women who entered the maternity unit between the years 1990 and 1998 were offered aromatherapy for labor to relieve pain or anxiety, relieve nausea or vomiting, enhance a sense of well-being, or augment uterine contractions. Reports of women who accepted aromatherapy ($n = 8058$) were compared with the reports of a comparison group ($n = 15,799$) of women who did not choose aromatherapy when offered. Ten essential oils were used based on the recommendations of an aromatherapist. Administration included putting drops on a pillow, in a bath, or on the woman's brow or palm, with massage, or in a perineal lavage or spray. The researchers reported that more than 50% of the mothers rated the aromatherapy as helpful, with only 14% rating it as unhelpful. Only 7% of the women in the study used the aromatherapy specifically for pain relief, and the oils used for this purpose were primarily lavender and frankincense. Of this group ($n = 537$), 54% of those women who used lavender rated it as helpful, and 64% of the women who used frankincense rated it as helpful. The rate of epidural use was lower in women who chose aromatherapy for pain relief compared with the rates of epidural use in the women who did not choose aromatherapy (29% vs 44% in primigravidae and 14% vs 17% in multigravid women).²⁵ Limitations of the study included lack of randomization. Nonetheless, this large-scale investigation offers some evidence that olfactory elements could influence the perception of pain in labor.

Interventions That Affect Afferent Messages From the Brain

Neurotransmitters (opioid peptides commonly called endorphins, serotonin, and norepinephrine) release in the dorsal horn from descending tracts that originate in the hypothalamus and brainstem inhibit the sensation of pain.⁶ The endogenous opioid peptides bind to opioid receptors on dorsal horn neurons, thus diminishing propagation of pain transmission. Serotonin and norepinephrine are activated by opioids and appear to have a synergistic effect with endogenous opioids. Studies have shown reduced analgesic effects of opioids when serotonin and norepinephrine antagonists are administered.¹⁹ These descending signals from the brain may explain the mechanism of action of many comfort measures commonly used by midwives, such as music therapy, imagery, and the comforting presence of a significant other or doula. These modalities reflect significant cognitive, affective, and stress-regulation system input. Research has demonstrated that music can reduce pain and anxiety.²⁶ A randomized, controlled trial from Thailand examined the utility of music in reducing the sensation of labor pain.²⁷ One hundred ten women were enrolled in the study and were randomly assigned to either the

experimental or the control group. Primiparous women ($n = 55$) were able to choose from among 5 different types of "soft" music and were compared with a matched control group ($n = 55$) who did not listen to music. Matching criteria included age, education, amount of time in the latent phase of labor, reported history of painful menstruation, and presence or absence of ruptured membranes. Women entered the study when they were at 3- to 4-cm dilatation and continued in the study for 3 hours; hourly pain measurements were collected with use of the Visual Analog Sensation of Pain Scale. The women in the music group reported less pain and distress than the women who were in the control group ($P < .001$). The study was based on the gate control theory of pain; the authors explained that "the action people take to reduce pain affects brain centers serving attention, cognition, and emotion that activate descending nerve impulses to close the 'gate' located in the dorsal horn of the spinal cord."²⁷ The neuromatrix theory of pain could enrich the explanation of the music's efficacy in reducing pain perception by placing particular emphasis on how cultural and past personal experiences with the music selection choices might be more relevant than the specific rhythms and tones used, underscoring the "parallel processing" of the multiple inputs contributing to pain perception.

Other Factors and Interventions That May Influence Release of Endogenous Opioids

Women who are in good physical condition are known to have enhanced secretion of endorphins during acute exercise.²⁸ In addition, women in good physical condition seem to tolerate labor better than women who are not in good condition.^{29,30} Although not directly measuring physical condition or percentage of body fat, Melzack found women with higher weight-to-height ratios had significantly higher average pain scores for labor than women with lower weight to height ratios.¹³

Earlier studies demonstrated that epidural anesthesia significantly reduces plasma β -endorphin levels.^{31,32} Without epidural anesthesia, plasma β -endorphin levels progressively increase throughout labor.³³ β -endorphins (as with any opioid) are associated with feelings of euphoria; thus, these findings might explain why women receiving epidural anesthesia may not experience the same type of "natural high" that has been reported by some unmedicated women. Further research is needed to explore this phenomenon and the potential effects epidurals may have on infant outcomes and maternal-infant attachment.^{34,35} In addition, the significance of peripheral measurements of hormones and neurotransmitters should be interpreted with caution because plasma levels do not necessarily correlate with central nervous system levels (or effects) of these compounds.

Acupuncture/Acupressure

Several recently published studies have shown the effectiveness of both acupuncture and acupressure in reducing

both labor pain and the use of pharmacologic anesthesia.^{36–38} Traditional Chinese medicine recognizes acupuncture as a means to correct imbalances in “qi” or vital energy.³⁹ Needling, electrical stimulation, or pressure at specific points along meridian pathways can stimulate the flow of qi, thus correcting imbalances.^{39,40} Specific acupuncture points successfully used for pain reduction in labor include large intestine 4 (also known as the Hoku point),^{36,38} as well as bladder 25–36, bladder 54,³⁷ and bladder 67.³⁸ A significant challenge is explaining the mechanism of how acupuncture works within a Western scientific paradigm. One hypothesis is that the efficacy of acupuncture is mediated by endogenous opioids because evidence exists that administration of opioid antagonists (e.g., naloxone) have blocked the effects of acupuncture analgesia.³⁹ There is also neuronal imaging evidence that acupuncture affects the pain neuromatrix in some way. Functional magnetic resonance imaging by Wu and others demonstrated that specific areas of the brain were activated with “real” electroacupuncture compared with sham electroacupuncture.⁴¹ Wu’s functional magnetic resonance imaging studies found brain activation in the hypothalamus, somatosensory-motor cortices, the medial occipital cortex, and the prefrontal cortices when real electroacupuncture was used (electrical stimulation of actual acupuncture points). Wu states that, “The pattern of activation . . . by real electroacupuncture, compared to sham electroacupuncture, confirmed our previous proposition that acupuncture at analgesic acupoints activates the pain neuromatrix. . . .”⁴¹

IMPLICATIONS FOR PRACTICE

Given that the neuromatrix framework includes input from past emotional and cognitive experiences, it is important for the clinician to explore with each woman in labor what comfort measures have worked for her for any type of previous pain or discomfort. It is also important to explore what measures have not worked and even what measures are damaging or repulsive. For example, negative associations may exist with simply being touched for a woman who has been sexually abused. Touch therapies, such as massage, may not be experienced as comforting, and vaginal examinations may be traumatic for a woman who has a history of sexual abuse.

Ideally, labor preparation for all pregnant women should occur in the prenatal period, allowing the woman to identify her own personal repertoire of coping resources. For example, on one prenatal assessment form,⁴² there is a question that asks a woman to identify specifically what methods she uses to deal with stress (with some options suggested such as exercising, talking to a friend, or praying). A woman’s responses may help to identify comfort strategies that will uniquely work for her in decreasing stress, anxiety, and pain. Early prenatal preparation also

encourages the woman to identify resources (e.g., meditation exercises or therapy), essentially allowing her the opportunity to remodel her neurosignature (i.e., with repetitive positive inputs) when past experiences have been negative.⁴³

CONCLUSION

The neuromatrix theory of pain is an updated framework that recognizes pain as a whole body-mind-spirit experience. Melzack states that “the neuromatrix theory guides us away from the Cartesian concept of pain as a sensation produced by injury, inflammation, or other tissue pathology and toward the concept of pain as a multidimensional experience produced by multiple influences.”² Midwives have traditionally recognized labor and birth to be a multidimensional, whole body-mind-spirit experience. Thus, as a theory of pain, the neuromatrix theory interfaces particularly well with the midwifery model. This theory may also explain why some of the time-honored non-pharmacologic modalities for labor pain relief commonly used by midwives can be effective.

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