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Editorial

Orgasm utilizes the pain pathway: is orgasm "nonaversive pain"?

There are limited resources available when attempting to understand orgasm and orgasmic dysfunction in *Sexual Medicine Reviews* (*SMR*), *The Journal of Sexual Medicine*, *Sexual Medicine*, or other publications. Responding to the need to better understand this crucial sexual health function, the International Society for the Study of Women's Sexual Health assembled a multidisciplinary expert panel to investigate and publish a consensus document on orgasm. The society's process has generated much communication, development of new hypotheses, and further discussion. In the spirit of advancing contemporary concepts of orgasm, this editorial reviews evidence that, neurologically, the orgasm system is inextricably linked to the pain system; thus, the feeling of orgasm can be considered, paradoxically, a form of "nonaversive pain." For example, the intense facial grimace expressed during pleasurable orgasm can be surprisingly similar to that of persons in extreme pain[1] (Figure 1).

Consider the following points that address the link between orgasm and pain. Orgasm attenuates pain without affecting tactile thresholds[2]; conversely, pain (eg, vestibulodynia) is well known to block orgasm. Orgasm occurs with concurrent activation of the sympathetic and parasympathetic systems, a striking exception to the general rule of their reciprocal activation. Of note, in the event of trauma within the spinal cord, selective interruption of the pain pathway (ventral) but not the tactile pathway (dorsal) blocks orgasm and pain but not tactile genital sensation.[3] Finally, the brain regions that classically respond to pain[4] are also selectively activated during orgasm,[5,6] and those regions contain inhibitory interneurons that could provide a reciprocal inhibitory link between the systems.[7]

The following represents our current understanding of the link between orgasm and pain. It is likely that activation of the reticular activating system (RAS) is a crucial link between orgasm and pain. Characteristic of pain and orgasm is the activation of intense sympathetic arousal. This is manifested as the increased heart rate, blood pressure, and respiratory rate associated with pain and the hypogastric nerve efferent activity necessary for ejaculation. The paleospinothalamic system, which conveys agonizing pain (eg, severe burn), activates the RAS and other brainstem/limbic systems and likely activates orgasm and pain. The adjacent neospinothalamic system, which conveys localizable pain (eg, touching hot stove), is less likely to involve the RAS and projects more exclusively via the thalamus to the sensory cortex[8] (Figure 2).[9] Berić and Light[3] reported that traumatic injury restricted to the ventral spinal cord, through which the paleo- and neospinothalamic systems ascend to the brain, blocked pain and orgasm. In addition, those patients could perceive genital stimulation via their still-intact dorsal column system, but even when their genital stimulation was intense, orgasm could not be elicited. Thus, to experience orgasm, it seems necessary to have the intense stimulation (ie, nonaversive pain) that activates the RAS.

The brain regions classically activated by painful stimulation—including the medial prefrontal cortex, insula, amygdala, periaqueductal gray,[4] and nucleus accumbens[10]—are also activated by orgasm, at least in women[5,6] (Figure 3). Each of those regions was reported to contain high levels of the inhibitory neurotransmitters, GABA (γ-aminobutyric acid), and/or opioids.[7] This neuroanatomic configuration could provide the neurotransmitter basis for the inhibition of pain by orgasm and, reciprocally, the inhibition of orgasm by pain.

The intensities experienced in orgasm and pain may be accounted for by the relative neural intensities of excitation and inhibition.[11] There is extensive evidence, even in the simplest spinal cord reflexes, that neural inhibition and excitation function cooperatively in the coordination of antagonistic muscle activity. This occurs at the wide range of intensities from precision finger movement to vigorous limb exertion. To enable graceful, nonspastic movement at all intensities, an increase in the intensity of inhibition accompanies an increase in the intensity of excitation.[11]

To characterize the process of concurrent increases in excitation and inhibition, we developed the metaphor of a faucet with hot water (excitation) and cold (inhibition; Figure 4).[12] In this model, the temperature of the water represents the firing speed of action potentials in sensory neurons. For example, neurons fire faster with forceful touch (hot) than with gentle touch (warm). In this model, the flow rate of the water represents the number of activated neurons. For instance, more neurons are activated by burning a large area of skin (higher flow rate) than by touching a hot stove (lower flow rate). Thus, flow rate and temperature can vary jointly or independently.[12] In this model, neural excitation can include concurrent activation of the parasympathetic system (penile erection) and the sympathetic system (increased heart rate, blood pressure, respiratory rate, and ejaculation). Orgasm, in which the sympathetic and parasympathetic systems are activated concurrently, is evidently an exception to the general rule in which these 2 systems are activated reciprocally, classically described in textbooks as "fight or flight = sympathetic" vs "rest and recovery = parasympathetic."

In the faucet model with hot and cold water (Figure 4), the inhibition intensity can enable the relative excitation intensity to increase without becoming aversive. If the hot water flow significantly exceeds the cold water flow at low or high flow rates, it would be perceived as minimally painful (touching a hot stove) or agonizingly painful (burning a large area of

Figure 1. The facial grimaces of 6 individuals. At first glance, one could assume that some or all are experiencing pain. However, all are experiencing orgasm, thus supporting the linkage between orgasm and pain.

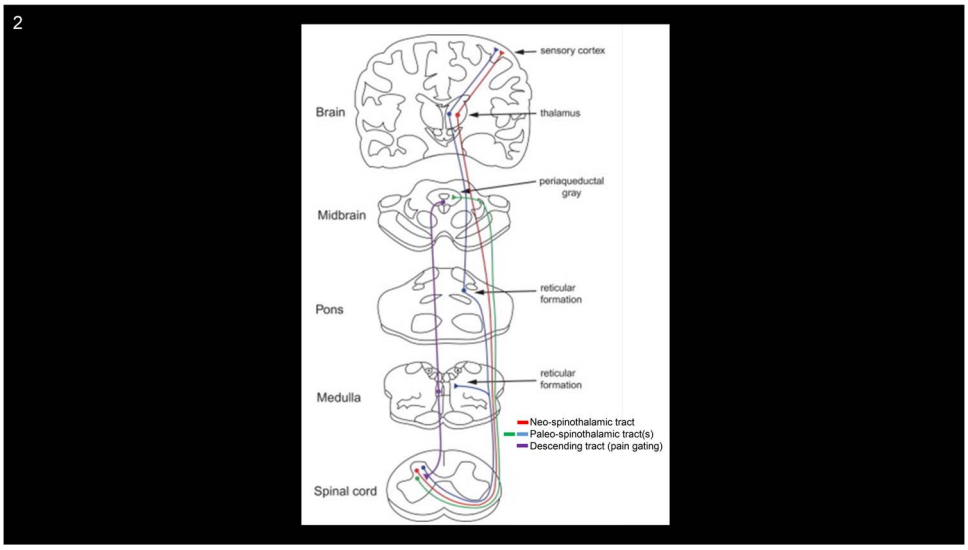

Figure 2. Two pain pathways are represented: the paleospinothalamic and neospinothalamic systems. The paleospinothalamic conveys agonizing pain (eg, severe burn); it activates the reticular activating system (RAS) and other brainstem/limbic systems and likely activates orgasm and pain. The adjacent neospinothalamic system, which conveys localizable pain (eg, touching a hot stove), is less likely to involve the RAS and projects more exclusively via the thalamus to the sensory cortex.[8] The figure further represents the descending brainstem–spinal cord pathways that inhibit pain input (ie, pain gate system). Modified from RPA & Serie.[9]

skin), respectively. But if the cold water flow was similar to that of the hot water flow, the combination of excitatory and inhibitory neuron firing could be perceived as mildly pleasant at a joint low flow (caressing) or intensely pleasurable at a joint high flow (exhilarating). If the excitation intensity markedly exceeds the inhibition intensity, the combination is perceived as painful at different intensities. If, however, the inhibition matches the excitation at all intensities, the combination is perceived as pleasurable at these different intensities. Thus, the inhibition can enable the excitation to increase in intensity without becoming aversive or painful.[11]

It is self-evident that to exist, pleasure and pain must have an evolutionarily adaptive function in relation to the organism's (including the human's) response to environmental events. It is likely that pain is the cognitive component of a behavioral response that is maladaptive: "stop or withdraw from, and do not repeat" (ie, detrimental to the well-being of the organism). Conversely, pleasure is the cognitive component of a behavioral response that is adaptive: "keep doing that and/or do that again" (ie, beneficial to the well-being of the organism). Perhaps an extreme example of "do that again, what you just did" is repetitive copulatory thrusting stimulation that provides the recruitment of increasing numbers of neural elements, enabling neural excitation to reach the high intensity necessary to overcome the high threshold of ejaculation. Dopamine is a neurotransmitter produced by neurons of the ventral tegmentum that project into the nucleus accumbens.[13] This mesolimbic pathway plays a key role in reinforcement (ie, "do again what you just did").[14] This is consistent with the critical role of dopamine

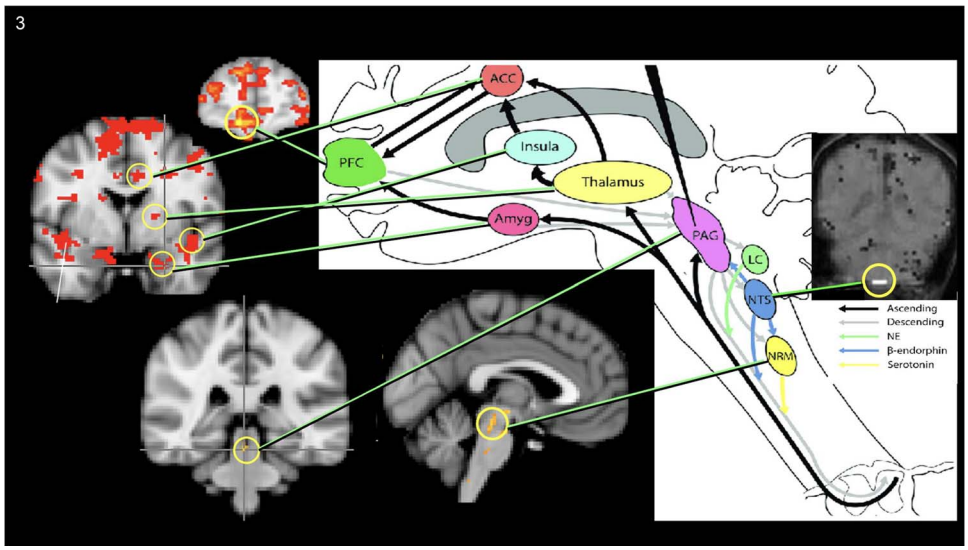

Figure 3. The right side represents the brain regions classically activated by painful stimulation. The left side represents the brain regions activated by orgasm as determined by functional magnetic resonance imaging, at least in women. The brain regions shared between orgasm and pain include the medial prefrontal cortex, insula, amygdala, periaqueductal gray, and nucleus accumbens. Of note, each of those regions contains inhibitory neurotransmitters, which could provide the neurotransmitter basis for the inhibition of pain by orgasm and, reciprocally, inhibition of orgasm by pain.

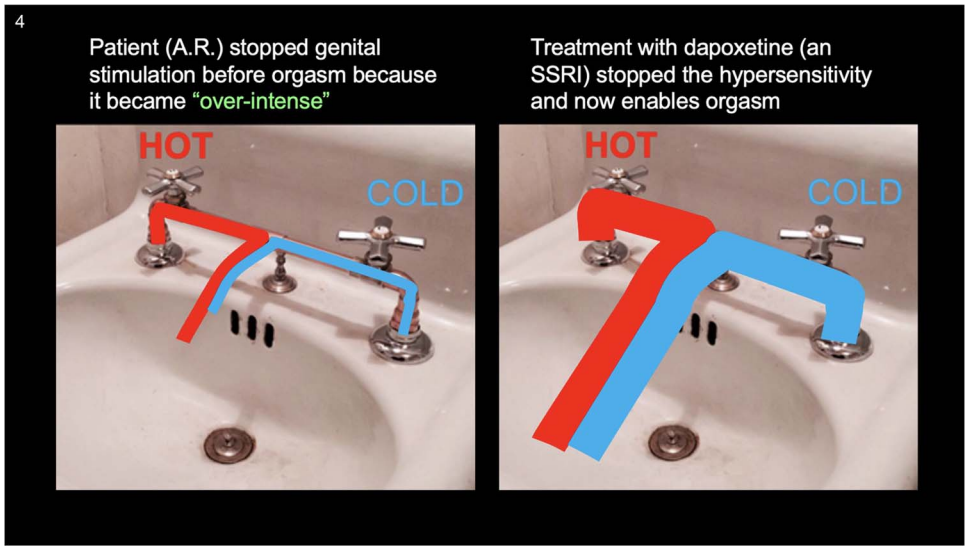

Figure 4. In this faucet model of orgasm and pain, hot water represents neural excitation and cold water represents inhibition. The water temperature (distance from faucet) represents the firing rate, and the water flow rate (volume of flow) represents the number of neurons firing. In this example, a patient stopped genital stimulation before orgasm because it became "overintense." The left side shows excitation exceeding inhibition at low flow rates, representing aversive low-level stimulation. After administration of a selective serotonin reuptake inhibitor, inhibition was increased, enabling the excitation to increase to nonaversive intensities, resulting in normal orgasms.

in facilitating sexual response and orgasm.[15] An example of the role of dopamine in orgasm is the experience with bremelanotide, a centrally acting Food and Drug Administration–approved medication for hypoactive sexual desire disorder in premenopausal women. Bremelanotide, which enhances dopaminergic activity, has been shown to increase the orgasm domain score of the Female Sexual Function Index.[16]

In spinal cord protective reflexes, when the tension on a contracted muscle reaches an intensity that risks tearing the muscle from its tendon, the high-threshold Golgi tendon organ system triggers a new set of inhibitory neurons that immediately turn off the active motor nerve, suddenly relaxing that muscle.[17] It seems likely that these protective reflexes have been maintained as the central nervous system has evolved in complexity. In the brain, the protective reflex mechanism may be represented by orgasm. For example, the intense excitation at orgasm is essential for triggering the high-threshold ejaculatory system, at least in men; this could trigger the intense inhibition characteristic of the refractory period. Perhaps when ejaculation does not occur in women, the inhibition is not as intense, which, upon continued genital stimulation, could enable further orgasms.

Scratching an itch and sneezing represent a form of pain (ie, irritation) and its inhibition, possibly similar to orgasm. Perhaps the pleasurable feeling of scratching an itch[18] represents a low-intensity orgasm. Similarly, a sneeze might represent a higher-intensity orgasm in the respiratory system.[19] Some women who have fits of repetitive sneezing have claimed

regularly experiencing multiple orgasms. Thus, intense sensory stimulation can be perceived as intensely pleasurable, as long as concurrent inhibition prevents it from exceeding the inhibitory capacity. However, if that capacity is markedly superseded, the stimulation is perceived as painful. In this view, orgasm occurs at the point at which the excitation minimally exceeds the inhibitory capacity. Following orgasm, as in the case of protective reflexes, a higher-intensity inhibition is triggered, thus reducing the excitation intensity and resolving the feeling of orgasm.

The following findings provide supportive evidence. A study demonstrated that vaginal stimulation significantly increased the threshold to detect and tolerate painful finger compression without significantly affecting the threshold to detect innocuous tactile stimulation.[2] As the perceived intensity of vaginal self-stimulation increased from (1) mild pressure to (2) moderate pressure feeling pleasurable to (3) orgasm, the pain threshold increased concurrently from baseline to about 45%, >70%, and >100%, respectively.[2] The concurrent finding in this study that tactile thresholds remained unchanged is evidence that vaginal stimulation inhibits pain specifically, producing analgesia but not anesthesia. It has been shown in the laboratory rat that vaginal stimulation activates the descending pain-inhibitory system from the periaqueductal gray (Figure 2), which can account, at least in part, for its pain-attenuating action.

We know that pain-inhibitory opiate medications inhibit sexual response and orgasm, whereas withdrawal from opiate addiction induces hypersexual response and intense orgasms.[20] A patient complaining of "overintense" genital response preventing her from continuing stimulation to orgasm reported that taking dapoxetine, a short-acting SSRI (selective serotonin reuptake inhibitor), enabled her to experience intense genital stimulation generating intense orgasms (I. Goldstein, personal communication, September 22, 2022; Figure 4). SSRIs are used clinically to treat premature ejaculation by delaying orgasm. In women and men, the recreational drug ecstasy, or MDMA (3,4-methyl enedioxy methamphetamine), increases synaptic levels of serotonin and norepinephrine by blocking their reuptake, thus inhibiting and delaying orgasms; however, with continued genital stimulation, those eventual orgasms are experienced more intensely than without the drug.[21]

The experience with MDMA provides additional support for our hypothesis that orgasm and pain share the same intense arousal-producing neural pathways and systems in the spinal cord and brain. Neural excitation and inhibition play a crucial cooperative role, with the inhibition enabling the excitation to intensify to the level of orgasm, even enabling abnormally intense orgasm when excessive inhibition is applied pharmacologically. When the intensity of the inhibition is sufficiently exceeded by the intensity of the excitation, the result is experienced as pain. The presence of inhibitory neural systems in the brain regions congruent with the regions that respond to pain and orgasm provide a neural mechanism for this interaction. Considering the principle of the combined role of excitation and inhibition (hot and cold) can provide a helpful model for the medical practitioner to explain the mechanism of orgasm to the patient and to formulate pharmacologic strategies focused on sexual response and orgasm, whether to augment (eg, adrenergic/dopaminergic), attenuate (eg, serotonergic/GABAergic), or both.

SMR readers research and manage a variety of sexual health concerns. This principle may be applicable to the treatment of a variety of pathologic problems involving orgasm, including premature or delayed orgasm, anhedonia, anorgasmia, and persistent genital arousal disorder/genitopelvic dysesthesia. Continue to read your journal to learn the newest theories in sexual function and dysfunction; volunteer to review for your journal; and now that *SMR* no longer requires you to be invited to write a review, please consider submitting your systematic, scoping, and narrative sexual medicine reviews.

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Barry R. Komisaruk, PhD, Associate Editor

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