

# Similarities between Severe Tinnitus and Chronic Pain

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## Abstract

The symptoms and signs of severe tinnitus and chronic pain have many similarities and similar hypotheses have been presented regarding how the symptoms are generated. Pain and tinnitus have many different forms. The severity of the symptoms of both varies within wide limits, and it is not likely that all forms have the same pathology. Some individuals with severe tinnitus perceive sounds to be unpleasant or painful. This may be similar to what is known as allodynia, which is a painful sensation of normally innocuous stimulation of the skin. Many individuals with chronic pain experience a worsening of their pain from repeated stimulation (the "wind-up" phenomenon). This is similar to the increasingly unpleasant feeling from sounds that are repeated that many individuals with severe tinnitus experience. There are also similarities in the hypotheses about the generation of pain and tinnitus. Although less severe tinnitus may be generated in the ear, it is believed that severe tinnitus in many cases is caused by changes in the nervous system that occur as a result of neural plasticity. Acute pain caused by tissue injury is generated at the site of injury but chronic pain is often generated in the central nervous system, yet another similarity between chronic pain and severe tinnitus. The changes in the nervous system consist of altered synaptic efficacy including opening of dormant synapses. For pain, this is believed to occur in the wide dynamic range neurons of the spinal cord and brain stem. Less is known about the anatomic location of the changes that cause severe tinnitus but there are indications that it may be the inferior colliculus. It is also possible that other auditory systems than the classical ascending pathways may be involved in severe tinnitus.

**Key Words:** Chronic pain, neural plasticity, tinnitus

**Abbreviations:** DRG = dorsal root ganglion, GABA = gamma amino butyric acid, HFS = hemifacial spasm, HTM = high threshold mechanoreceptors, IC = inferior colliculus, LTM = low threshold mechanoreceptor, TGN = trigeminal neuralgia, WDR = wide dynamic range neurons

**T**here are many forms of tinnitus and pain, and the pathologies of these different forms most likely differ (McFadden, 1982; Jastreboff, 1990, 1995). Tinnitus can be a nuisance or a severe debilitating disorder that can totally ruin a person's life. Severe tinnitus may lead to suicide. Similarly, pain can be a nuisance that is treatable with common analgesics, or chronic pain can be debilitating and totally ruin a person's life, and may lead to sui-

cide. The neural mechanisms of chronic pain are different from that of acute pain (Price et al, 1992; Coderre et al, 1993), and the neural abnormality that causes severe tinnitus may be different from that causing mild to moderate tinnitus. Many symptoms and signs of chronic pain and severe tinnitus are similar. Both severe tinnitus and chronic pain are hyperactive disorders, and similar hypotheses about their neural mechanisms have been presented. These hypotheses have been of two main kinds: a peripheral and a central hypothesis. The peripheral hypothesis assumes that the cause of pain and tinnitus is found at the anatomic location of the symptoms, thus the location where the pain is felt and, for tinnitus, the ear. The central hypothesis, conversely, assumes that changes in the function of specific parts of the

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central nervous system are the causes of chronic pain and severe tinnitus and that the anatomic location of the pathology that causes the symptoms is different from that from where the symptoms are perceived to be originating. The central hypothesis for pain has gained support during recent years (Woolf, 1983; Devor, 1988; Coderre et al, 1993) but that does not exclude a peripheral involvement in chronic pain (Ochoa, 1986) and severe tinnitus (Lenarz et al, 1995) in addition to the central pathology.

Tinnitus and chronic pain both represent formidable challenges to the physicians to whom such patients turn because of the diversity of the disorders and the lack of objective signs of pathology. Tinnitus is not covered to any great extent in textbooks on medicine, and chronic pain is seldom given the attention it deserves.

### Signs of Tinnitus and Chronic Pain

Tinnitus and chronic pain have few objective signs, but a number of characteristic symptoms have been identified. Individuals with chronic pain typically perceive normal stimulation of the skin to be painful (allodynia<sup>1</sup>), and pain sensation to painful stimulation may be exaggerated (hyperpathia<sup>2</sup>). Another phenomenon, the "wind-up" phenomenon (Mendell, 1984; Woolf and Thompson, 1991), that often occurs in severe pain describes the worsening of pain sensations from repeated stimulation with the stimulus. The painful or unpleasant sensation of sound that many individuals with severe tinnitus experience resembles allodynia. The experience reported by many individuals with severe tinnitus where repeating the same sound causes an increasing unpleasant sensation may be analogous to the wind-up phenomenon.

Chronic pain and severe tinnitus are often associated with emotional reactions such as anxiety, and both tinnitus and pain can arouse such bodily reactions as nausea and sickening feelings. These reactions can evoke general stress responses such as elevation of blood pressure, increase of blood cortisol levels, and increased muscle tonus.

That pain can be modulated by somatic stimulation was suggested by Melzack and Wall

(1965) and is known as the "gating" hypothesis. Tonndorf (1987) has alluded to that hypothesis as also being valid for tinnitus and suggested that the beneficial effect of electrical stimulation of the ear may be explained by such "gating" effects. Some individuals with severe tinnitus feel a relief of their tinnitus from sound exposure (Feldman, 1971; Aran and Cazals, 1981), which may be similar to the pain relief from electrical stimulation (transdermal electrical nerve stimulation) (Willer, 1988). In fact, one treatment of tinnitus, the tinnitus retraining therapy, described by Jastreboff et al (1996), makes use of that method to relieve tinnitus.

### Where Are Severe Tinnitus and Chronic Pain Generated?

Both tinnitus and pain may be associated with many different disorders and can be caused by trauma. However, most individuals with severe tinnitus and chronic pain have no other known pathology. Tinnitus and pain may resolve spontaneously or can become chronic diseases that are difficult to treat.

Tinnitus may be generated in the ear but severe tinnitus is often generated in the nervous system. Independent of where and how tinnitus is generated, it will be perceived as a sound and thus often referred to the ear. Chronic pain is also believed to be generated in the central nervous system, thus at an anatomically different location from where the sensation is felt. Neural plasticity is believed to be involved in both severe tinnitus and chronic pain. The common denominator for severe pain and chronic pain is sensitization of specific neural structures through neural plasticity that can be caused by altered balance between inhibition and excitation and by establishment of new neural pathways through opening of synapses that are normally ineffective (dormant) (Wall, 1977). Such changes in the nervous system may be more or less permanent.

One strong indication that the anatomic location of the generation of tinnitus is not always the ear but often the central nervous system stems from the fact that individuals with severed VIII cranial nerve can experience tinnitus. This is similar to phantom pain (Melzack, 1990, 1992), where a person feels pain that is located to an amputated body part, such as a leg.

It has been difficult conceptually to accept the possibility that pain that is felt at a specific location is, in fact, not a result of neural activity

<sup>1</sup>"Allodynia" is usually defined to mean the pain that is elicited by stimuli that ordinarily are innocuous.

<sup>2</sup>"Hyperpathia" is used to describe an explosive increase in reaction to pain when a painful stimulus exceeds a certain threshold, with a continuing sensation of pain after the stimulation has ceased.

generated at that location but rather a result of neural activity that is generated somewhere in the central nervous system. That it is possible to perceive pain located to an amputated limb is a strong indication that pain can be generated in central neural structures without input from the location where the pain is felt.

### NEURAL MECHANISMS OF SEVERE TINNITUS AND CHRONIC PAIN

The current hypotheses about how tinnitus and chronic pain are generated are similar in many respects. It is generally believed that tinnitus and chronic pain can be a result of reorganization of the central nervous system. These hypotheses are supported by increasing evidence that even the adult nervous system has a large ability to reorganize itself through neural plasticity. Such reorganization may be initiated by novel input from the periphery or by absence of input. The reorganization may persist after the abnormal input has ceased or when the normal input has been reestablished after being interrupted.

The hypotheses about the neural mechanisms of chronic pain are more detailed and better supported than those of tinnitus. We will therefore first consider the hypothesis about the neural mechanisms of chronic pain.

#### Pain

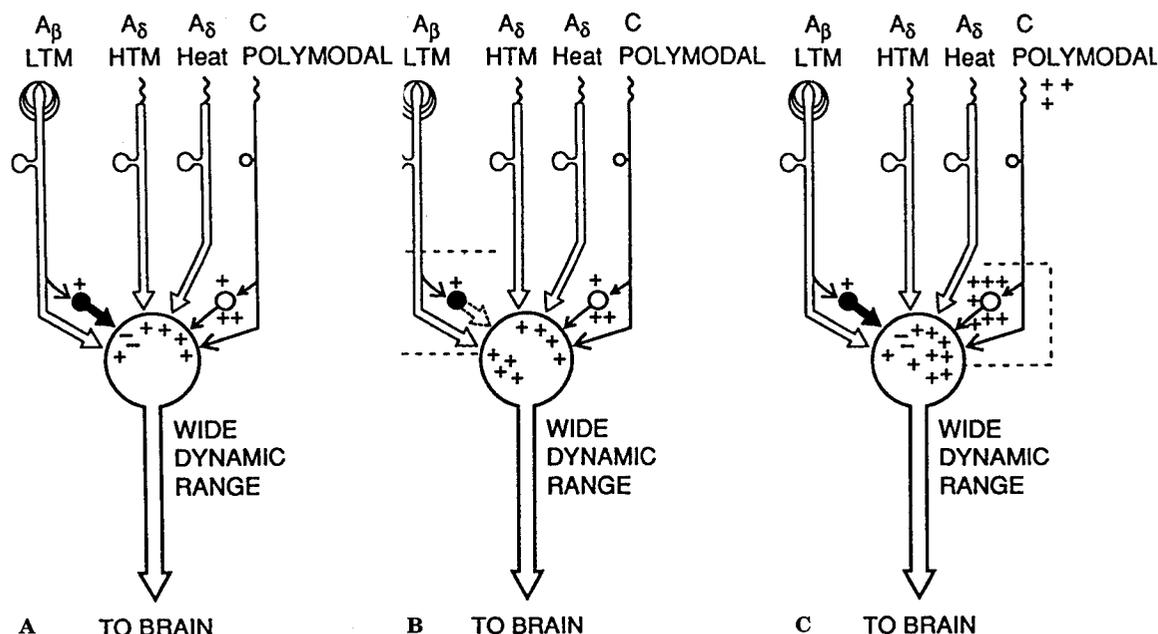
Pain is normally elicited by stimulation of specific receptors (nociceptors) that are different from those mediating sensory information. Acute pain may be caused by injuries of various kinds and inflammatory processes may cause pain that lasts a long time. This kind of pain information is mediated by specific pain receptors and carried in neural pathways that are separate from those carrying somatosensory information. Normally, only very strong stimulation of sensory receptors can elicit pain sensation. Acute pain such as that caused by cuts and bruises has two components: a fast response that is a result of activation of the mechanoreceptors (touch receptors) and a slow, delayed component that is a result of stimulation of specific pain receptors where the information travels in specific pathways to the brain. This acute pain sensation may abate over time or persist, depending on the kind of injury.

Chronic pain is in many aspects different from acute pain. Chronic pain is often associated with altered perception of sensory stimulation

in such a way that innocuous stimuli produce pain (allodynia). This means that somatosensory receptors in patients with chronic pain can mediate pain via neural pathways that normally only mediate innocuous sensation (Price et al, 1992; Coderre et al, 1993), which means that new connections in the central nervous system have been established in such individuals. The fact that stimulation that normally causes acute pain often gives rise to an exaggerated response (hyperpathia) to painful stimuli, with a continuing sensation of pain after the stimulation has ceased, means that the neural circuits that mediate pain are altered in individuals with chronic pain. Thus, when acute pain has turned into chronic pain, it is no longer the neural activity from the periphery that causes the pain sensation but rather chronic pain is believed to be caused by self-sustained neural activity in central nervous structures.

Reorganization of the central nervous system can be caused by overstimulation or by deprivation of normal input, or it may be a result of novel input to certain nuclei. Evidence has been presented that injury may induce a sustained increase in excitability at the spinal segmental level that is maintained after local anesthesia of the injured area (Woolf, 1983). This means that after some time, the neural activity that gives rise to sensation of pain becomes independent of the peripheral injury that caused the changes in the nervous system to develop. Phantom pain from amputations that are performed under general anesthesia is an example of such sustained changes in the central nervous system that may be the result of overstimulation of neural structures that are not subject to general anesthesia. It can be avoided by local anesthesia of the peripheral nerve that carries the neural activity from the limb to be amputated (Bach et al, 1988; Coderre et al, 1993).

The current hypotheses about the reorganization of the central nervous system that causes chronic pain have focused on specific neurons known as the wide dynamic range (WDR) neurons (Fromm, 1991; Wilcox, 1991; Price et al, 1992; Coderre et al, 1993; Dubner and Basbaum, 1994). These neurons normally mediate touch and vibrations, but they may change their responses to such stimuli. The WDR neurons have inputs from several different kinds of receptors (Fig. 1), and it is believed that chronic pain may arise if these neurons' excitability increase. This may occur if the excitatory input (from polymodal C-fiber receptors) increases or if the inhibitory input (from low-threshold



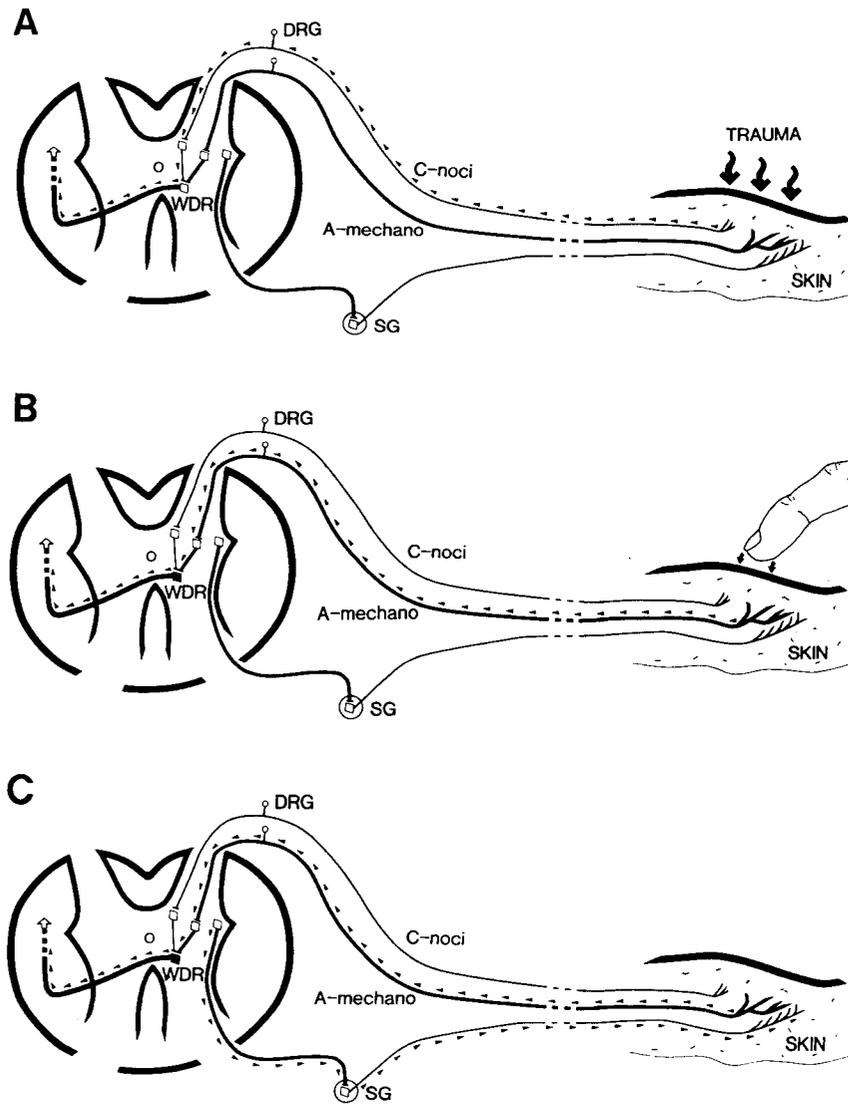
**Figure 1** Hypotheses of how changes in the wide dynamic range (WDR) neurons in the spinal horn can lead to chronic pain. *A*, Normal innervation of WDR neurons. Large circles: sensory transmission, small open circles with + signs: facilitatory interneurons, filled circles and - signs: inhibitory interneurons. *B*, Loss of inhibitory controls from low-threshold mechanoreceptors (LTMs) ( $A\beta$  afferents). *C*, Exaggeration of facilitatory mechanisms activated by C polymodal afferents. The large circles illustrate the WDR neurons and the signs indicate the postsynaptic inhibitory (-) of excitatory (+) transmission to the WDR neurons. The small open circles with + signs indicate facilitatory interneurons that receive input from small polymodal fibers. The filled circles indicate inhibitory interneurons. The dashed-line boxes in *B* and *C* show the changes in synaptic activity that occurred. HTM: High-threshold mechanoreceptor afferents (from Price et al, 1992).

mechanoreceptors [LTM]) decreases. The excitatory input may increase as a result of tissue injury that stimulates pain receptors, and the loss or decrease of inhibitory input to the WDR neurons may occur as a result of injury to peripheral nerves (see Fig. 1C). Both such changes have the effect of increasing excitability of the WDR neurons. Changes in the input to the WDR neurons may change their function in other ways in addition to increasing their excitability. Thus, the maximally obtainable firing rate may increase, and new routes for the output of the WDR neurons may be established by opening of dormant synapses. Normally, these neurons connect only to the somatosensory system, but when their function changes, they also serve as input to pain circuits. This means that normally dormant synapses that connect the output of the WDR neurons to pain circuits may be opened. It explains why stimulation of touch receptors that normally produce innocuous sensations can become painful (allodynia).

These hypotheses of chronic pain from changes in the function of the WDR neurons

assume that the changes are caused by injuries to peripheral nerves such as those of the arm. Similar models and hypotheses have been presented to explain face pain (trigeminal neuralgia) (Fromm, 1991) that is associated with irritation of the trigeminal nerve root by a blood vessel.

The sympathetic nervous system may be involved in severe pain and that may intensify the pain and stimulate skin receptors. This condition is known as reflex sympathetic dystrophy (Loh and Nathan, 1978; Price et al, 1992). The involvement of the sympathetic nervous system may develop because pain increases sympathetic nervous activity (Fig. 2). Sympathetic nervous activity causes liberation of norepinephrine at the terminals of the sympathetic nerve fibers that innervate mechanoreceptors and this increases the sensitivity of these receptors. If enough norepinephrine is secreted, it can activate the mechanoreceptor without any mechanical stimuli. Since mechanoreceptors mediate pain in the condition of chronic pain (allodynia), such sympathetically mediated



**Figure 2** Physiologic model of pain involving the sympathetic nervous system. *A*, Acute response to cutaneous trauma. Action potentials in C-nociceptors (C-noci) propagate through the dorsal root ganglion (DRG) to the spinal cord where they activate and sensitize the wide dynamic range (WDR) neurons whose axons ascend to higher centers. Sympathetic activity modulates the sensitivity of the mechanoreceptors (SG: sympathetic ganglion). *B*, WDR neurons remain sensitized and now respond to activity in large diameter A-mechanoreceptors, which are activated by light touch (allodynia). *C*, The same sensitized WDR neurons respond again to A-mechanoreceptor activity, but this activity is initiated by sympathetic efferent actions on the sensory receptor, in the absence of cutaneous injury or chronic stimulation (from Roberts, 1986).

stimulation increases the pain and thus further increases the sympathetic activation. Involvement of the sympathetic nervous system may thus establish a vicious circle (Roberts, 1986; Campbell et al, 1988; Price et al, 1992) that may persist if not broken by, for example, temporary blockage of the sympathetic system or permanent blockage by sympathectomy.

### Tinnitus

Less is known about the neural mechanisms of tinnitus than that of chronic pain. However, evidence has been presented that some forms of severe tinnitus are the result of changes in the function of the nervous system that are similar to those assumed to cause chronic pain (Moller, 1997a). The fact that tinnitus occurs in individuals in whom the auditory nerve has been

severed is a strong indication that tinnitus is not always generated in the ear but in some cases is generated in the central nervous system. As was hypothesized regarding chronic pain, the changes in the central nervous system result in hyperactivity and opening of pathways that are normally closed (opening of dormant synapses). These changes may be brought about by overstimulation or by deprivation of input to the auditory nervous system.

It is known that overstimulation from exposure to loud noise can cause damage to the cochlea but overstimulation can also cause changes in the function of the central auditory nervous system. Animal experiments have shown that noise exposure can cause development of hyperexcitability of neurons in the IC by decreasing GABAergic inhibition (Szczepaniak and Moller, 1996a), which may occur by a reduction

in inhibitory input from the cochlea. These changes may be similar to those shown in Figure 2C regarding chronic pain, where reduction in the inhibitory input from LTMs to the WDR neurons results in increased excitability. The high-frequency region of the basilar membrane is known to supply a large amount of inhibition to the auditory nervous system (Sachs and Kiang, 1968).

High-frequency hearing loss may therefore reduce the inhibitory input to the auditory nervous system, similar to the reduction of inhibition to WDR neurons from LTM receptors in chronic pain (see Fig. 2B). A decrease of GABAergic inhibition may also occur as a result of inhibitory interneurons becoming dormant because of disconnection of excitatory input or because of reduction of excitatory input to such inhibitory interneurons, as has been hypothesized as the mechanism for temporal lobe epilepsy (Bekenstein and Lothman, 1993). The fact that the incidence of tinnitus increases by age may to some degree be a result of a reduction of GABA in the brain with age (Caspary et al, 1995).

Overstimulation may also increase the excitability of neurons in the auditory nervous system in a similar way as hypothesized for chronic pain (see Fig. 2C). Although tinnitus that is associated with noise-induced hearing loss may be generated in the cochlea because of injury to hair cells, overexposure may also cause changes in the function of parts of the central auditory nervous system, and the latter is likely to be what causes severe tinnitus.

It is possible that the inferior colliculus (IC) of the auditory system has a role in chronic tinnitus that is similar to the role of WDR neurons in chronic pain. IC neurons are under very strong (GABAergic) inhibitory influence (Pollak and Park, 1993), and if that influence is reduced, their firing can increase five- to tenfold. Overstimulation can reduce that inhibitory control (Szczeplaniak and Moller, 1995, 1996a), and inhibition can be reestablished by drugs that are GABA<sub>A</sub> or GABA<sub>B</sub> agonists (benzodiazepines and baclofen, respectively; Szczeplaniak and Moller, 1996b). The beneficial effect of benzodiazepines on tinnitus supports the hypothesis that reduced inhibition in the auditory nervous system is involved in certain forms of tinnitus. However, no clinical evidence has been presented regarding the beneficial effect of baclofen.

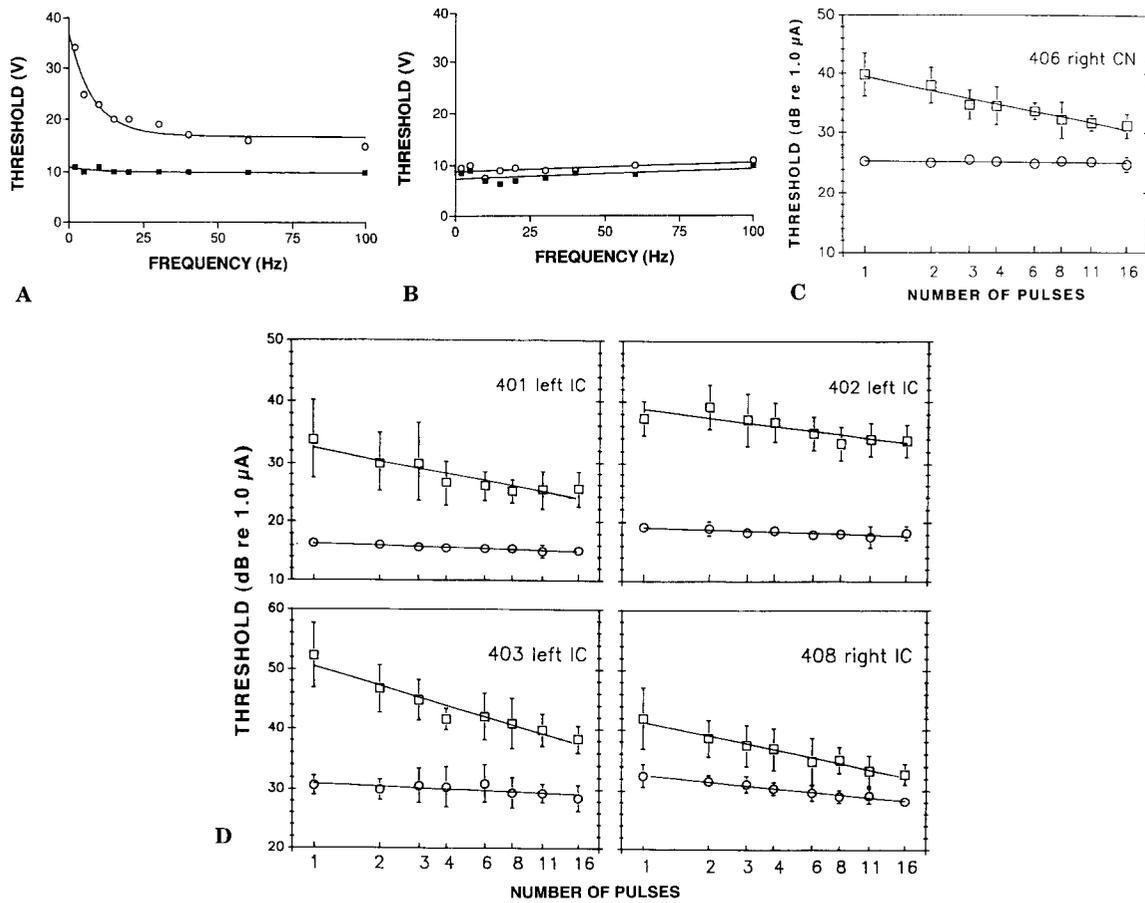
As is presumed to occur in WDR neurons, an abnormally high firing rate of IC neurons may open dormant synapses to neural circuits other

than those normally involved in hearing. The observation that the nonclassic ascending auditory nervous system is involved in some forms of severe tinnitus (Moller et al, 1992) supports that hypothesis.

Similar to what may occur in connection with chronic pain, the sympathetic nervous system may be involved in severe tinnitus (Adams and Wilmot, 1982). The hair cells of the cochlea have abundant sympathetic innervation (Densert, 1974; Densert and Flock, 1974). It is, therefore, conceivable that increased sympathetic activation can increase the sensitivity of cochlear hair cells and, in absence of sound, elicit neural activity that resembles that generated by sounds. The observation that stress can aggravate tinnitus supports the hypothesis that the sympathetic nervous system can be involved in severe tinnitus because stress activates the sympathetic nervous system. The involvement of the sympathetic nervous system in tinnitus is further supported by the finding that sympathectomy or blockage of a sympathetic ganglion (the stellate ganglion) can alleviate tinnitus in some patients (Garnet Passe, 1951). It has, however, been claimed that the effect of a sympathetic block on tinnitus is instead related to restoration of blood supply to the ear.

### **Signs of Reorganization of the Central Nervous System**

Change in temporal integration is one sign of reorganization of the central nervous system that can be determined. Temporal integration, which means that the response to a stimulus is affected by previous stimulation, is a common feature of the central nervous system. Temporal integration of somatosensory input can be studied by stimulating the skin with electrical impulses presented at different frequencies. In individuals who do not have chronic pain, temporal integration of painful electrical stimulation is different from temporal integration of sensation at threshold (Moller and Pinkerton, 1997). In individuals without chronic pain, the electrical current applied to the skin that is needed to elicit a just noticeable sensation is little affected by previous stimulation while the threshold for pain stimulation decreases exponentially as a function of the repetition rate of the stimulation (Figure 3A). Although the threshold of sensation is little altered in individuals with chronic pain, the pain threshold is much lower and nearly



**Figure 3** Temporal integration. *A*, Threshold for sensation (filled squares) and pain (open circles) from electrical stimulation of the skin on the forearm shown as a function of stimulus repetition rate in an individual without pain. The solid line is an exponential function fitted to the experimental data points. *B*, Similar graph as in *A*, showing results from an individual with chronic pain. *C*, Behavioral threshold for electrical stimulation of the cochlear nucleus (CN) in a cat as a function of the number of electrical impulses (horizontal scale) before (open squares) and after noise exposure (open circles) that caused a hearing loss of approximately 50 dB. The stimuli were presented at an interval of 15.75 msec. The horizontal scale showing the number of impulses presented is logarithmic and the straight solid lines fitted to the data points therefore indicate exponential relationships between the number of pulses presented and the threshold. *D*, Similar graph as in *3C* showing temporal integration of electrical stimulation of the inferior colliculus (IC) (from Gerken et al, 1991).

independent of the stimulus rate (see Fig. 3B), indicating that both threshold and temporal integration of painful stimuli are altered in individuals with chronic pain.

Animal studies have shown that the temporal integration in the auditory nervous system is altered after deprivation of input to the auditory nervous system (Gerken et al, 1991) in a way similar to temporal integration of pain stimuli in individuals with chronic pain. When the input from the periphery was eliminated by destruction of the cochlea (Gerken, 1979) or reduced by noise exposure (about 50 dB; Gerken et al, 1991), the behavioral threshold to electrical stimulation

of the cochlear nucleus (see Fig. 3C) and the IC (see Fig. 3D) changed in a way similar to that of stimulation of the skin in individuals with chronic pain. The threshold normally decreases exponentially with the number of impulses presented because of temporal integration. After impairment of hearing, the threshold became lower both for stimulation of the cochlear nucleus and the IC, and did not decrease with increasing number of impulses, indicating increased excitability and a change in temporal integration. Thus, these experiments showed that sound deprivation caused a decrease in the threshold of hearing that was larger for sounds of short

duration than for sounds of long duration. If these results are applicable to severe tinnitus, they may explain why some individuals with tinnitus experience greater hypersensitivity to impulsive sounds as well as a sensation of unpleasantness.

### **Is Tinnitus Generated in the Classic Auditory Nervous System?**

Since severe tinnitus is perceived as sound, it has been assumed that tinnitus is generated in the same parts of the nervous system as those normally involved in processing sound and are associated with the classic ascending auditory pathway. However, severe tinnitus often evokes reactions that do not commonly occur in response to sound. The various emotional reactions that often are associated with severe tinnitus indicate that tinnitus may activate neural circuitry other than that normally activated by sound (Moller et al, 1992; Lockwood et al, 1998). It has been suggested that the nonclassic (or polysensory) ascending auditory pathway is involved in tinnitus (Moller et al, 1992). Little is known about the role of the nonclassic ascending auditory pathway, but its abundant connections to parts of the brain other than strictly sensory regions, such as the limbic system (Rouiller, 1997), may explain the emotional reactions to sound that many patients with severe tinnitus experience.

Neurons of the polysensory auditory pathway receive input from the somatosensory system. This makes it possible to test the hypothesis that the polysensory auditory pathway is involved in severe tinnitus. The input from the somatosensory system is excitatory in some neurons and inhibitory in other neurons. If the polysensory system is involved in tinnitus, stimulating the median nerve electrically would be expected to alter the perception of the tinnitus. In a study of 26 patients with tinnitus, 4 perceived their tinnitus to be stronger and 6 weaker, and 16 did not notice any change in their tinnitus during stimulation of the median nerve (Moller et al, 1992). Some patients reported that their tinnitus changed its character to become less unpleasant by electrical stimulation of the median nerve. These results were taken as support of the hypothesis that tinnitus is not always caused by neural activity in the classic auditory nervous system. That some of the patients experienced a decrease in their tinnitus and some experienced an increase is in agreement with the fact that some of the neurons of the nonclassic

auditory system receive inhibitory input from the somatosensory system, whereas other neurons receive excitatory input (Aitkin et al, 1978). Similar stimulation of the median nerve in non-tinnitus individuals had no or a very small effect on their perception of sound, which was taken as an indication that tinnitus may originate from activity in neural circuitry that is not normally involved in hearing. Imaging studies of patients who can voluntarily alter their tinnitus have lent further support to the hypothesis that something other than the classic auditory system is activated in some patients with tinnitus (Lockwood et al, 1998).

The activation of the nonclassic (polysensory) auditory nervous system in tinnitus patients may be similar to the activation of pain circuits from the somatosensory system in patients with chronic pain (allodynia). That parts of the brain involved in emotions (limbic system) are activated in some forms of tinnitus is similar to what is assumed to explain the strong emotional components often seen in connection with chronic pain. The change in the neural pathways that are associated with severe tinnitus and chronic pain may be explained by opening of dormant synapses, a hypothesis presented by Wall (1977) to explain symptoms of chronic pain. This hypothesis was met with skepticism when presented because it is only relatively recently that it has become evident that even the adult nervous system has a large capability of changing itself.

Thus, there is considerable evidence that at least some forms of chronic pain and severe tinnitus are caused by reorganization of specific parts of the central nervous system. This reorganization may be brought about by deprivation of input or novel input but other unknown factors are most likely involved.

### **Other Hyperactive Disorders**

In this article, evidence was reviewed regarding neural plasticity as being a cause of chronic pain and severe tinnitus. Other hyperactive conditions have been linked to similar neural plasticity. Thus, many years ago, it was shown that novel stimulation of the amygdala over time can result in seizure activity elicited by the same stimulation. This phenomenon is known as the kindling phenomenon (Goddard, 1964), and it is probably a special form of neural plasticity where novel stimulation over time results in increased excitability in specific nuclei. When the excitability reaches a certain level,

sustained neural activity occurs. Such self-sustained activity is similar to epileptic seizures. Recently, evidence has been presented that similar principles are involved in other disorders. One example is hemifacial spasm (HFS), where evidence has been presented that the spasm and synkinesis that are typical of HFS are caused by hyperactivity of the facial motor nucleus brought about by novel antidromic activation (Moller and Jannetta, 1984; Moller, 1987, 1997b). Studies in humans undergoing microvascular decompression operations for HFS (Moller, 1987) and animal models of HFS (Sen and Moller, 1987) have shown evidence that hyperactivity of the facial motonucleus causes the spasm and opening of dormant synapses causes the synkinesis (Moller, 1993, 1997a).

### CONCLUSIONS

Chronic pain and severe tinnitus belong to a category of severe disorders that have no detectable structural changes nor are any other objective signs of these disorders known. Thus, the symptoms of these disorders are not caused by any injury as such but rather functional changes caused by altered synaptic efficacy. Diseases have traditionally been associated with anatomic changes such as those that can be detected by various kinds of imaging techniques. Severe tinnitus and chronic pain that are associated with altered synaptic efficacy have no anatomic abnormalities that can be observed by known imaging techniques. Aside from the patients' description of their symptoms, electrophysiologic tests are the only way to objectively demonstrate the pathologies underlying these disorders. This means that diagnosis and monitoring the success of treatment must be based mainly on the patients' description of their symptoms. This is an obstacle in studies of these diseases, and it means that patients with these disorders may be met with some skepticism from the health care individuals from which they seek help. As a result, treatment is likely to be delayed or not used sufficiently.

The fact that it is difficult to determine which factors give rise to chronic pain and severe tinnitus further complicates research and treatment of these disorders. Although it is known that chronic pain can develop from injuries to peripheral nerves, far from all individuals with peripheral nerve injuries acquire chronic pain. The same is the case for tinnitus, where cochlear injuries sometimes precipitate severe tinnitus,

but extensive cochlear injuries may not cause severe tinnitus in other individuals. This means that other and unknown factors are necessary for the development of these disorders.

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