Study into the sensory system in human body

Pain is complex phenomenon that can be defined as a feeling, an experience, a perception or a sensation. There is no human that is without the experience of pain. Our forebears had considerable difficulty in defining pain in scientific terms. Modern investigations of pain have made easier and better to understand and describe the structure of pain. This essay commences with some definitions of pain and continues with the mechanisms and neural pathways. Also the effects that allow pain sensation are mentioned.

Sensory system is a part of the nervous system including sensory receptors that receive stimuli from environment, neural pathways that convey this information to brain and some specific parts of brain that processes this information. There are many different subsensory processes. The human sensory system consists of the following parts: visual, auditory, gustatory, olfactory, and somatosensory. The somatic sensory system is arguably the most diverse of the sensory systems, mediating a range of sensations-touch, pressure, vibration, limb position, heat, cold, and pain-that are transduced by receptors within the skin or muscles and conveyed to a variety of central nervous system targets (Purves et al., 2007). These following paragraphs focus the subsystem is related the mechanisms responsible for sensations of pain.

Sensory impulses from nearly all parts of the body are transmitted to the central nervous system, bringing information about conditions in the various tissues and organs and in our surroundings (Brodal, 2004). Pain is the one of important stimuli and experience in somatic sensory system. There are some explanations to understand the pain. According to the classical view in 16th

century, pain was considered to be a hard-wired system in which noxious input was passively transmitted along sensory channels to the brain (Figure 1) (Bingel and Tracey, 2008). Bear et al., (2001) mentioned that the somatic sensory system is different from other sensory systems in two interesting way. First, its receptors are distributed throughout the body rather than being concentrated at small and specialized locations; second, because it responds to many different kinds of stimuli (Bear et al., 2001).

Pain has been defined by the International Association for the Study of Pain as follow “ pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” (Merskey and Bogduk, 1994). The pain we feel is caused by nociceptor activation by noxious stimuli, and when we feel we more or less automatically ascribe it to something that harms our body (Brodal, 2004). The relatively unspecialized nerve cell endings that initiate the sensation of pain are called nociceptors (Purves et al., 2007). They are a kind of sensory receptors that respond potentially damaging stimulus by sending signals to spinal cord and brain. Pain is transmitted from the periphery to spinal cord by two types of nerve fibres: slow conducting and fast conducting (Sengupta and Kumar, 2005). These are AÉ¤ which conduct at 5-30 meters/second, and C fibres which conduct less than 2 meters/second toward to CNS. Nociceptors with fibers C is unmyelinic with low conduction and nociceptor with fibers AÉ¤ is large myelinic with rapid conduction (Pace et al, 2006). According to these types of axons, there are two pain pathways that one of them is slow and another is fast. In general, the faster conducting AÉ¤

nociceptors respond Figure 1. Pain perception: ancient and curent concepts. Adapted from Bingel and Tracey (2008)

either to dangerously intense mechanical or to both intense mechanical and thermal stimuli; the majority of unmyelinated C fiber nociceptors tend to respond to thermal, mechanical and chemical stimuli, and are therefore said to be polymodal (Purves et al., 2007). These two different nociceptors are related with two categories of pain perception. The first pain brief and well-localised, the second is more diffuse, delayed and protracted. Ploner et al. (2002), studied cortical representation of first and second pain sensation in humans (Ploner et al., 2002). This study shows that brief painful stimuli evoke sustained cortical activity corresponding to sustained pain perception comprising early first pain-related and late second pain-related components. Cortical activity was located in primary (S1) and secondary (S2) somatosensory cortices and anterior cingulate cortex. Time courses of activations disclosed that first pain was particularly related to activation of S1 whereas second pain was closely related to anterior cingulate cortex activation. Both sensations were associated with S2 activation. These results correspond to the different perceptual characteristics of both sensations and probably reflect different biological functions of first and second pain. First pain signals threat and provides precise sensory information for an immediate withdrawal, whereas second pain attracts longer-lasting attention and motivates behavioral responses to limit further injury and optimize recovery (Ploner et al, 2002). Forss et al (2005) mentioned that following a tissue injury, the AÉ¤-fiber mediated first pain is often described as sharp and pin-prick-like, in contrast to the dull, long-lasting, and burning C-fiber

mediated second pain. AÉ¤ mediated acute pain elicits immediate avoidance reactions to harmful stimuli whereas the C-fiber system has been suggested to be involved in longer-lasting processes, such as tissue inflammation (Forss et al., 2004).

From the periphery to the spinal cord, nociceptive messages are primarily conveyed by AÉ¤ and C fibres (Gauriau and Bernard, 2001); these nociceptive primary afferents enter the spinal cord via the dorsal roots of the spinal nerves (Figure 2). They entry collectively form the dorsolateral fasciculus (tract of Lissauer), which is present at all spinal cord levels (Patestas and Dartner, 2009) when they reach the dorsal horn of the spinal cord. Axons in Lissauer’s tract typically run up and down for one or two spinal cord segments before they penetrate the grey matter of the dorsal horn (Purves et al., 2007). After reaching the specific lamina within the spinal cord, the first order nociceptive contact to second order neurons in lamina 1 and lamina 5 of the spinal cord gray matter and then cross the midline. The second order neurons send their information via two pathways to the brainstem and thalamus. They are the dorsal column medial-lemniscal system that mediates tactile discrimination, vibration, form recognition, joint and muscle sensation, conscious proprioception and the anterolateral system that conveys pain and temperature information. First order neurons contributing to the anterolateral system terminate in the dorsal horn, and second order neurons in the dorsal horn send their axons across the midline and ascend on the contralateral side of the cord in the anterolateral column to their targets in the thalamus and brainstem (Purves et al., 2007). The anterolateral system mediates different ways of pain. One of them is the

sensory discriminative aspects. It is important in the localization, intensity and quality of painful or thermal stimuli. It contains the ventral posterior nucleus (VPL), and the primary and secondary somatosensory cortex (S1 and S2). The ventral posterior nucleus receives sensory information from anterolateral system and it projects to the somatosensory cortex. According to Patestas and Dartner's summary (2009), nociceptive signals relayed from the spinal cord directly to the ventral posterior lateral, the ventral posterior inferior, and the intralaminar nuclei of the thalamus via the spinothalamic tract (neospinothalamic, direct pathway of the ALS) are transmitted to the somatosensory cortex (both to S-I and S-II). The postcentral gyrus is the site where processing of pain localization, intensity, quality, and sensory integration takes place at the conscious level. The primary somatosensory cortex sends projections to the secondary somatosensory cortex, which is believed to have an important function in the memory of sensory input (Patestas and Dartner, 2009).

Other parts of the system convey information about the affective-motivational aspects of pain-the unpleasant feeling, the fear and anxiety, and the autonomic activation that accompany exposure to a noxious stimulus (Purves, 2007). Sensory information is trasmitted from spinal cord to the reticular formation, superior colliculus, periaquiductal grey, hypothalamus and amygdala. Also nociceptive inputs reach anterior cingulate cortex (AAC) and insular cortex via midline thalamic nuclei. The anterior cingulate and anterior insular cortices are connected with the limbic cortex, which plays a role in the emotional aspect of pain (Patestas and Dartner, 2009). Rainville et al., (1997) mentioned that a modulation of pain-

related activity in AAC that closely parallels a selective change in the perceived unpleasantness of painful stimuli (Rainville et al., 1997). According to Neugebauer et al., (2004) dependt on environmental conditions and affective states, amygdala appears to play a dual facilitatory and inhibitory role in the modulation of pain behavior and nociceptive processing at different levels of the pain neuraxis (Neugebauer et al., 2004). There are various research and evidences about the relationship between amygdala and pain. Bornhovd et al., (2002) found that bilateral activation of the amygdala correlate with perceived pain intensity (Bornhovd et al., 2002). The response functions for stimulus show a positive correlation with the perceived pain intensity of heat stimuli compared to non-painful when the painful signal is changed (Figure 3).

Figure 2. The descending pain modulatory system. Adapted from Bingel and Tracey (2008)

Figure 3 Bilateral activation of the amygdala by painful stimuli. According to this experiment, there are some scales that are related with perceived stimulus or non-stimulus: P0 is pain but can’t be noticed; P1 is sensation that felt warm but not painful; P2 is lowest painful stimulus; P3 is intermediate and P4 is maximum pain. Adapted from Bornhovd et al. (2002).

PAIN MODULATION

Pain sensation can be modulated by drugs, prior injury or some effects of circumstances like emotion. Firstly, I’d like to mention the effects of injury. Following a painful stimulus associated with tissue damage, stimuli in the area of the injury and the surrounding region that would ordinarily be

perceived as slightly painful are perceived as significantly more so, a phenomenon referred to as hyperalgesia (Purves et al,. 2007) which results from a combination of sensitization of peripheral nociceptive nerve terminals and facilitation of central pain pathways (Ritter, 2010). Allodynia is different from hyperalgesia. This phenomenon typically occurs immediately after the painful event and can outlast the pain of the original stimulus by several hours (Purves et al., 2007). Two processes contribute to hyperalgesia and allodynia: peripheral sensitization of nociceptors where events around the damaged site combine to allow a lower intensity stimulus to evoke an action potential in the fibre, and central sensitization where changes occur in the spinal processing of primary (1°) afferent inputs, continuing hyperalgesia and enlarging the area of hyperalgesia and allodynia (Holdcroft and Jaggar, 2005). However, when the afferent fibers or central pathways themselves are damaged – a frequent complication in pathological conditions including diabetes, shingles, AIDS, multiple sclerosis and stroke (Purves et al., 2007)- this damage triggers some changes to the structure and function of nervous system. This change may be result of a neuropathic pain that has been defined by the International Association for the Study of Pain “ initiated or caused by a primary lesion or dysfunction in the nervous system.” (Merskey and Bogduk, 1994). Neuropathic pain can be characterized as a pain is in an area with sensory loss corresponding to the damaged nerve or central lesion. It can arise spontaneously (i. e., without any stimulus), or it can be produced by mild stimuli that are common to everyday experience, such as that the gentle touch and pressure of clothing, or warm and cool temperatures (Purves et al., 2007). It can be described as burning, electric, tingling, and shooting. A simple focal peripheral nerve injury unleashes a range of

peripheral and central nervous system processes that can all contribute to persistent pan and abnormal sensation (Dworkin et al., 2003).

Also pain can be modulated by emotion such that fear or anxiety. Early evidence came from the World War II, the research of H. K. Beecher who mentioned pain modularity mechanisms for emotion in his article that is called Pain in Men Wounded in Battle. He noted an important attenuation of pain experienced by soldiers in combat situations. He observed that as many as three quarters of badly wounded soldiers reported no to moderate pain and did not want to pain relief medication (Beecher, 1946). He indicated that soldiers often experienced little or no pain. He noted that strong emotion can block pain and the circumstances which have led to the wound can have been associated with anxiety, emotional stress, and fear (Beecher, 1946). We can conclude through this study that the perception of pain depends on its context. Bingel and Tracey (2008) said that pain is a complex, subjective experience comprising sensory, cognitive and emotional components, a large distributed network is accessed during nociceptive processing (Bingel and Tracey, 2008). According to functional and anatomical studies in animals and humans, the descending pain modulating pathway in the brain stem is connected with a number of higher level brain areas including cingulo-frontal regions, the amygdalae and the hypothalamus (Hadjipavlou et al., 2006). The amygdala is believed to be involved in coding the uncertainty associated with pain and fear (Bornhovd et al., 2002; Misslin, 2003) and

believed to be relevant for planning anti-nociceptive strategies (Bingel et al., 2002). Neugebauer et al, (2009) said that a multidimensional experience pain not only includes nociceptive and nocifensive but also emotional-

affective and cognitive components (Figure 4) (Neugebauer et al., 2009). Also he mentioned that pain can lead to anxiety and depression and patients suffering from anxiety and depression experience pain are more strongly and more likely to develop chronic pain. Amygdala plays important roles in emotional responses, stress and anxiety and is believed to be a critical component of the pain matrix (Ossipov, 2010). The amygdala is almond-shaped groups of nuclei in the medial temporal lobe (Figure 5). The lateral (LA), basolateral (BLA) and central (CeA) nuclei are specific and important for sensory processing. Sensory inputs from the LA and BLA to the CeA are part of the fear and anxiety related circuitry (LeDoux, 2000). Rhudy and Meagher (1999) made an experiment about the effects of induced fear and anxiety on radiant heat pain threshold. They indicated that fear and anxiety have divergent effect on pain reactivity in humans: fear reduces pain, whereas anxiety has a sensitizing effect (Rhudy and Meagher, 1999). They concluded that emotional states modulate human pain reactivity.

Figure 4 Pain as a multidimensional experience. Different components interact to form the complex nature of pain. Their reciprocal relationships are indicated by arrows. Adapted from Neugebauer (2009).

Figure 5 Amygdala function in pain. Adapted from Neugebauer (2009).

Pain is a complex phenomenon which is constantly modulated by inhibitory and facilitatory mechanisms. Drugs such as analgesics and anesthetics affect the modulation of pain. Analgesics, especially morphine are used for pain control within the medical field. Some studies indicate that morphine profoundly reduces the emotional reaction of pain perception (Rossi et al.,

1994; Jacquet and Lajtha, 1973). Morphine is one of opiate analgesics that can activate opioid receptors and produce a strong analgesic effect (Wang et al., 2009). Opioid receptors in the brain are a group of receptors that include endorphins, dynorphins and enkephalins which are released by neurons. By acting at opioid receptors, opiates such as morphine or heroin are extremely potent pain-killers, but are also highly addictive drugs. Positron emission tomography (PET) studies indicated that the presence of endogenous opioid release and the changes of opioid receptor occupancy in cortex and sustained clinical pain (Zubieta et al., 2001; Petrovic et al., 2005). Systemic administration of opiate receptor agonists morphine or fentanyl is able to attenuate the pain-evoked responses in many supraspinal areas such as thalamus, primary and secondary somatosensory cortex (Casey et al., 2000; Kurata et al., 1999). Wang et al (2009) studied the morphine modulation of nociceptive processing in the rat medial and lateral pain pathways and they mentioned that morphine suppressed the pain-evoked changes in the information flow from medial to lateral pathway and from cortex to thalamus (Wang et al., 2009).

Pain which important for warning an animal and human about potential dangerous circumstances, dues to several effects. It’s related with its structure, several damages, drugs, emotion etc. I mentioned some effects but there are also several other factors like attention, memory that can be objects of more researches in the future. Present studies open up many new questions that can be addressed by future working.