PAIN IN FISH

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Introduction

The welfare of the mammals and birds that are our pet, farm or laboratory animals has become an important and commonly accepted concept. Much research has been conducted on the recognition and assessment of pain in these animals. However, pain perception in non-mammalian vertebrates such as fish has just started being studied adequately.

Traditionally, a difference is made between the simple detection of pain, called nociception, and the psychological experience of pain, with emotional (distress, fear, etc) and cognitive (knowing that one hurts, description of pain, anticipation, etc) aspects.
Nociception has a more mechanistic and physiological aspect, and refers to the detection of painful (noxious), or potentially harmful, stimuli by the nervous system. Nociception is a vital information from the body, and all animals are able of a more or less refined nociception.

In the popular view, the neuro-anatomical and physiological features of fish do not allow nociception or the experience of pain and stress. This fuels the idea that pain in non-mammalian species is unimportant or intrinsically different than in mammals.

In the following, we will study various aspects of the biology of fish in relation with pain. We will first consider the simplest reaction to pain and stress, the physiological response of the body. The physiological response occurs independently of whatever the animal might be feeling or even "thinking", and is a general and undifferentiated reaction.

We will go further, and make observations about the most obvious behavioral responses of fish subjected to pain. Again, these will be observations without consideration of the inner world of the fish. However, behavioral responses are more specific than physiology, and more characteristic of fish (a cat or a man subjected to pain would also display specific behaviors, but these behaviors would be characteristic of cats or of humans, respectively).

In a next step, we will study the anatomy of the fish nervous system and its relevant features in relation with the detection and the perception of pain. We will see that the brain of all vertebrates, from fish to mammals, including batrachians, reptiles, birds, and even humans, is constructed on the same basal pattern. Each species then developed its own characteristic features throughout evolution, starting from this same basal pattern.

Finally, we will catch a glimpse of more elaborate behaviors of fish. We will see that emotionality is no foreign word to fish, and this alone has implications on the way fish have to handle pain and stress. We will see that maybe some species of fish do have an inner world, a "fish inner world" in which the experience of pain and stress can appear distressing.

Physiological responses of fish to pain and stress

The basic functioning of the muscles, liver, hormonal control mechanisms and nervous systems of fish are similar to those in birds and mammals. Of significant importance, the adrenal system producing stress hormones functions in very similar ways in fish and mammals (Gallo & Civinini, 2003).

Stress reactions in fish are seen when a maximal emergency response is induced, for example when fish are removed from water. These include:

- Increased production of adrenaline, noradrenaline and cortisol
- Changes in cardiovascular and respiratory responses
- Rapid escape motor responses (fast-start responses)
- Cessation of normal behaviors like feeding, swimming

In teleost fish, as in other vertebrates including mammals, stress reactions release the hormones adrenaline, noradrenaline and cortisol into the blood plasma.
In scientific terms, stress reactions involve the activation of the sympathochromaffin (adrenal) system and of the hypothalamo-pituitary-interrenal (HPI) axis, with the consequent increase of plasma catecholamines (adrenalin, noradrenalin) and corticosteroids (cortisol), respectively.
Generally, adrenaline and noradrenaline stimulate immediate, short-lived changes (increase of cardiac load and dilatation of respiratory tracts), while cortisol induces changes which may last hours or days and can also have a negative influence on reproduction and growth of the animal subjected to permanent stress.

Prolonged exposition to stress, especially stress due to crowding in farmed fish, can result in states of immunodepression, hence increasing susceptibility to disease (Ortuno et al., 2001).

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Basic behavioral responses of fish to pain and stress

A number of behaviors that are not simple reflexes can be affected in a way that indicates a response to a potentially painful event. Furthermore, these behaviors can be affected for a long time after the occurrence of the noxious stimuli, suggesting discomfort in the fish.

- Feeding activity can be disturbed as a basic reaction to pain or stress (Gregory & Wood, 1999; Sneddon et al., 2003, Sneddon, 2003). The initial reaction of the fish is often a sudden drop in food ingestion, eventually resulting in complete cessation of feeding.

- Swimming, the most general behavior pattern of fish, appears different under painful conditions as compared to fish not subjected to pain. Examination of swimming ability or swimming pattern can provide a sensitive index to general stress and pain in fish (Xu et al., 2005). Various patterns of swimming, like swimming into shallow water, swimming lethargically at the surface, lying listlessly on the pond or tank bottom, floating downstream or swimming erratically can be indicators of suffering. Critical swimming speed and the length of time a certain swimming velocity can be maintained all may be used as an indicator of pain.

- Respiration is also thought to be a useful means to gauge pain in fish. A difference between resting and active metabolism can be quantified simply by counting breaths (opercular beats) per minute or more precisely, by measuring respiratory gases. Ventilation rate was observed to increase in fish subjected to pain (Sneddon, 2003), similar to observations in mammals and humans.

- Motor responses to painful stimuli include:

  1. Fast-start reactions, which are even suspected, under certain conditions, to have a motivational basis (Chandroo et al., 2004)
  2. Avoidance behavior, like escape or non-approach, including associative learning (between a painful stimulus and a neutral event, that will in turn be avoided in the future), and development of avoidance strategies (Chandroo et al., 2004; Yue et al., 2004)
  3. In some species, affective responses such as vocalization
  4. Coordinated reaction, such as biting the source of pain, rocking from side to side or rubbing the affected area (Sneddon et al., 2003; Sneddon, 2003)

- Fish can react to chronic painful or stressful stimuli with unfamiliar responses such as color changes or subtle alterations in posture and water column utilization.

Fish avoid noxious stimuli, show a reluctance to resubmit themselves to noxious stimuli, and learn to associate neutral stimuli with painful stimuli. They are able of developing strategies to avoid painful or stressful situations and can remember bad experiences for a long time. Fish show that they are indeed capable of perceiving pain by displaying specific or altered behaviors.

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Neuroanatomy of fish

The nervous system is made of two parts:

- The peripheral nervous system (PNS), which is composed of peripheral receptors and peripheral nerves.
- The central nervous system (CNS), which is composed of the brain, cerebellum and brainstem as well as the spinal cord.

The peripheral and central nervous systems are continuous. The peripheral nervous system contains the sensory nerves that connect the peripheral receptors with the central nervous system.
Sensory information from the periphery is detected by peripheral receptors (on the skin, for example), then runs along peripheral nerves to enter the spinal cord and brainstem. From there, it is processed into the brain.

<u>The peripheral nervous system (PNS)</u>

The PNS is made of peripheral receptors and nerves that convey sensory information towards the spinal cord (also called medulla) and brain.
The receptors, nerve fibers and transmitter molecules that convey information about pain in vertebrates are called the nociceptive system. Nociceptors are receptors sensitive to potentially damaging stimuli. They are the free nerve endings of nociceptor nerve fibers of two types:

- A-delta fibers are myelinated nerve fibers that display fast conduction velocities. A-delta fibers are responsible for eliciting the "first pain" sensation, of short duration and well localized, and initiate withdrawal behavior. They participate in acute short-term responses.

- C fibers are unmyelinated nerve fibers that display relatively slow conduction velocities. C fibers are responsible for eliciting the "second pain", which is slow, poorly localized and long-lasting. These fibers are implicated in prolonged nociceptive stimulation or dull pain.

The existence of nociceptors was demonstrated in fish (Sneddon, 2003; Sneddon et al., 2003). Besides, both types of nociceptor fibers exist in fish, in spite of differences between species (Chandroo et al., 2004).

<u>The central nervous system (CNS)</u>

1. *Spinal pathways:*

Peripheral sensory and nociceptive signals are first integrated and processed at the level of the spinal cord and brainstem. In general, both fish and higher vertebrates show similar organization of major spinal pathways, which contain several nerve fiber tracts involved in the transmission of nociceptive information. Depending on the species, one or more of these spinal tracts have been identified in fish (Chandroo et al., 2004). Sensory and nociceptive information from the head and mouth is conveyed through a separate nerve, called the trigeminal nerve, which also contains nociceptive nerve fibers in the fish (Sneddon, 2003).

2. *Biochemistry:*

Biochemical transmission of pain in vertebrates implies a peptide called substance P, a neurotransmitter and neuromodulator that has also been found in the hypothalamus and forebrain of fish.

Endogenous opioids (morphine-like substances produced in the brain), like enkephalins and endorphins, can suppress the intensity of pain. These substances and their receptors are found in the brain and spinal cord of higher vertebrates.
A comparable distribution of opiate receptors and substances is found in both elasmobranches (rays and sharks) and teleosts (bony fish). Analgesia can be achieved by using morphine in fish similar to other vertebrates. Morphine-induced analgesia can also be blocked by opiate antagonists (e.g. naloxone).

3. *Brain structures:*

Fish have the necessary primitive brain areas for sensitive and nociceptive processing to occur (e.g. the medulla and brainstem). Furthermore, all vertebrates develop a forebrain (e.g. the diencephalon with the thalamus and hypothalamus, and the telencephalon with the cerebral hemispheres). The grey matter covering the telencephalon is called the pallium.
In mammals, the pallium has evolved to form the laminated cerebral cortex, an integrating structure called neocortex. Fish also have a pallium, in most cases unlaminated, that is involved in the processing of sensory information, among others.

In all vertebrates, the sensory (and nociceptive) information proceeds from the periphery, through relay nuclei in the medulla and brainstem, to the thalamus. In turn, the thalamus sends extensive neural projections onto the pallial and sub-pallial structures of the telencephalon.

In fish, sensory and nociceptive responses were elicited in all those brain areas including the telencephalon, suggesting the existence of a nociceptive pathway from the periphery to the higher brain structures (Dunlop & Laming, 2005).
Similar to higher vertebrates, the telencephalon of fish may mediate sensory integrative and executive functions like the regulation of avoidance learning, habituation, general arousal and social behavior, motivation and emotional learning (see a review by Chandroo et al., 2004 for references).

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The experience of pain and stress in fish

We have seen so far that fish confronted to painful stimuli do indeed show specific physiological and behavioral reactions. They possess the necessary brain structures and molecules to process the neural information elicited by painful events. We can now reasonably assume that fish do sense pain. Is it possible to go further and examine the question of whether and how they experience pain?

Fish display a number of higher functions which point to the fact that these animals are able of elaborate behaviors similar to higher vertebrates. Emotionality is involved in these cases and can be modulated by the administration of drugs as in higher vertebrates. Here are some examples.

- Some species have social networks that can prove complex and highly structured, which implies that they are at least able to recognize specific individuals and remember the nature of their relationship (for example in a hierarchy). It has been shown that the brain circuits that regulate social behavior in non-mammalian vertebrates (and fish) are largely similar to those in mammals (Goodson, 2005).

- Fish are able to learn and memorize. The fish brain contains structures homologous to the mammalian amygdala (involved in emotional behaviors and memory) and hippocampus (involved in spatial and temporal memory). The corresponding structures in fish have been located in the telencephalic pallium (Portavella et al., 2004; Portavella & Vargas, 2005).

- In humans, pain interferes with competing tasks such as learning and memory tests, whereas administration of opioids increases performance. This is due to the fact that nociception captures attention. This has been proven to occur in fish as well (Sneddon et al., 2003b), which means that fish are cognitively disturbed when they sense painful stimuli.

- Alertness and fear responses can be modulated in fish by the administration of anti-anxiety drugs like barbiturates or benzodiazepine (Rehnberg et al., 1989; Aparecida et al., 1999; Ide & Hoffmann, 2002).

Emotions are thought to involve relatively primitive brain circuits (LeDoux, 2000). A group of cerebral structures of vertebrates, called limbic system, as well as specific dopaminergic neural systems, are involved in aspects of emotional behavior (including fear), memory, learning, affective and motivational processes, among other functions.
Limbic and dopaminergic structures are present in fish as in other vertebrates (see Chandroo et al., 2004, for a review). The physiology, behavior and neuroanatomy of fish all point to the existence of a homologous system in fish, involving structures partly different than in mammals. This and all observations that have been made with fish suggest that these animals are to some extent at least able to experience fear, pain and stress as emotionally negative events.

There is a vivid debate concerning the question of whether fish can experience pain and stress psychologically. Rose (2002) stresses the fact that the brain structures of fish and humans did not develop to the same extent. He concludes that fish are not conscious because they do not have the brain structures involved in conscious and other superior functions in humans (frontal lobe of the neocortex, among others), and hence they can have no awareness of pain and stress.

However a comparison of fish and man can be very misleading, since fish do not necessarily experience the world as humans do, and there is no reason why they should. A form of "consciousness" might exist in fish and might have nothing in common with our own. Furthermore, nobody knows how much prefrontal cortex is necessary in order to perceive emotional aspects of pain. Maybe the pallium of fishes is not so developed than the neocortex of man, but maybe it is sufficient to make the psychologically negative experience of pain.

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