

Brain processes for “good” and “bad” feelings: How far back in evolution?

Commentary on [Key](#) on Fish Pain

Jaak Panksepp

Department of Integrative Physiology and Neuroscience
Washington State University

Abstract: The question of whether fish can experience pain or any other feelings can only be resolved by neurobiologically targeted experiments. This commentary summarizes why this is essential for resolving scientific debates about consciousness in other animals, and offers specific experiments that need to be done: (i) those that evaluate the rewarding and punishing effects of specific brain regions and systems (for instance, with deep-brain stimulation); (ii) those that evaluate the capacity of animals to regulate their affective states; and (iii) those that have direct implications for human affective feelings, with specific predictions — for instance, the development of new treatments for human affective disorders.

Keywords: emotional feelings, deep brain stimulation, brain reward, brain punishment, scientific inference.

Jaak Panksepp jpanksepp@vetmed.wsu.edu is Professor of Integrative Physiology and Neuroscience in College of Veterinary Medicine at Washington State University. His research is devoted to the analysis of the neuroanatomical and neurochemical mechanisms of emotional behaviors (in the emerging fields of affective and social neurosciences), with a focus on understanding how various affective processes are evolutionarily organized in the brain, and looking for linkages to psychiatric disorders and drug addiction. <http://ipn.vetmed.wsu.edu/people/faculty-ipn/panksepp-j>



Key’s (2016) key proposition is that “it is impossible to ever know what a fish feels.” This is reminiscent of LeDoux’s (2012, p. 666) nonscientific assertion that “we will never know what an animal feels.” Empirical predictions or lack thereof, not absolute declarations of what exists or does not exist in the world, are where this discussion needs to be situated. Key argues against the seemingly soft-minded belief that fish feel pain, at least based just on the simple studies of behavioral nociceptive (pain) reflexes which, in his estimation (and mine), do not constitute adequate scientific evidence for experiential states. In any event, discussions of how the spinal cord disconnected from the brain can still manifest nociceptive reflexes, automatically taking the body away from harmful stimuli, do not constitute compelling evidence one way or the other. Unfelt spinal reflexes can probably remove the body from harm’s way without the need for feelings, but such evidence is inadequate for determining what may be happening elsewhere in the brain.

Affective (valenced) feelings are clearly elaborated by higher subcortical and paleocortical networks to sustain affectively guided learned behavioral patterns rather than simple reflexes. The evidence is quite substantial that subcortical limbic and upper brainstem circuits are sufficient for affectively experienced mental life, at least in mammals, where the necessary brain research has been done (Panksepp, 1998).

Key denies that “fish should be given the ‘benefit of the doubt’ and unconditionally bestowed with the ability to feel pain.” He is scientifically correct: Neither behavioral evidence, nor empathy alone, is sufficient to resolve this issue. In rigorous science, general conclusions — for example, that animals feel their emotional arousals — have to be based on abundant predictions that lead to convergent evidence for any novel conclusion that is put forward. That criterion has, I believe, been satisfied for emotional feelings in all mammals that have been extensively studied with relevant brain manipulation approaches (e.g., deep brain stimulation, both electrical and chemical: Panksepp, 1981, 1982) — although, as noted earlier, many behavioral neuroscientists still believe that we can never know what non-speaking animals feel.

My own research has been devoted to studying emotional affective (feeling) states in animals, rather than sensory or homeostatic affects (which are less empirically tractable). My criteria have been simple:

- (i) If one can evoke coherent emotional action patterns by stimulating specific regions of animal brains, across species (quite easy to do), and those evoked states serve as rewards and punishments in simple learning tasks (which has been abundantly affirmed), then the data support the probable existence of affective experiences (Panksepp, 1998). Why? Because we humans do not have any rewards or punishments that we do not experience as either “desirable/“good” or undesirable/“bad” (Panksepp, 1982, 1998), and the evidence that one needs an expansive anthropoid neocortex for emotional feelings is nil.
- (ii) Those same brain manipulations should produce corresponding types of feelings in humans, and there is abundant evidence that they do (for an early summary, see Panksepp, 1985, and see Damasio et al., 2000, for comparable neural correlates for human emotional feeling in homologous human brain regions with PET imaging [fMRI is less adequate for monitoring feelings]).
- (iii) This knowledge should be sufficient to guide the development of new psychiatric treatments, and that project is achieving successes (Panksepp et al., 2015; Panksepp & Yovell, 2015; Panksepp, 2015; Yovell et al., 2015). In addition, it has long been known that other animals get addicted to the same drugs as humans; to our surprise, crayfish also “choose” to go back to places where they received amphetamines/cocaine or morphine (Huber et al., 2011). That should clearly be tried in fish too (for precedents, see Collier et al., 2014; Lau et al., 2006). Direct brain stimulation would be harder.

Surely there will never be “proof” that other mammals experience affective states in exactly the ways that we do, rather than in their own homologous ways, and there is enough data to make

the latter a credible provisional conclusion. Science does not deal with “proof” but only with “the weight of the evidence,” comparing different novel differential predictions following from competing hypotheses. All we will ever have is the weight of evidence for one interpretation of the world or another. The one that makes the best predictions should “win.” I am not sure what Key’s upper brain predictions might be. Spinal cord analyses will not suffice, nor will claims that painful feelings are simply generated by the cortex. The cortex participates in many feelings, especially sensory ones, but there is too much evidence for subcortical loci of control for various other feelings in animals — for all basic emotions and some for homeostatic imbalances like hunger and thirst, which are likewise felt states — to dismiss them. The subcortical locus of control is supported by many radical decortication studies (e.g., Panksepp et al., 1994; Valenstein, 1966). The issue of feelings in anencephalic children remains completely open (see Merker, 2007, and discussants), despite Key’s deconstruction.

I was a bit chagrined that Key spent so much time denying that any form of consciousness can exist below the cortex. Obviously it can: Moruzzi and Magoun’s (1949) classic demonstrations showed that massive damage of the reticular formation eliminates all indices of sentience in animals. This was preceded by the finding that massive damage of the Periaqueductal Gray (PAG) can pretty much erase all behavioral indices of consciousness in several species of mammals (Baily & Davis, 1942, 1943) as well as the few humans that have had such unfortunate brain damage (Schiff, 2007). In any case, the issue of anencephalic children with clear waking states also remains completely open, since often the remaining cortical fragments are highly gliotic and probably dysfunctional (Shewmon et al., 1999).

Surely Key would acknowledge that there is abundant inferential behavioral evidence that fish might be feeling pain. From this perspective, I was disappointed that Key did not cover the most compelling behavioral studies suggestive of pain in fish (e.g., Jones et al., 2012; Sneddon, 2009; Sneddon et al., 2003a, 2003b). In any event, the possibility of pain in fish has yet to be tested with the most robust strategies — namely neurobiological ones.¹ Those are the most compelling approaches — and in fish research, there has been little research at that level.

If one takes the more humble approach to this topic, the strictly empirical one, then the issue of pain in fish remains as open a question as before Key’s well-argued denial of affective processes

¹Some of my statements in this commentary could be interpreted as implying that I believe pain in animal research is justified. I did believe that as a young scientist (at the lowest possible intensity levels, to answer important scientific questions, for instance, involving standard injections of drugs), and I still feel that such sacrifices for solid scientific knowledge are justifiable though open to debate. During my academic career, I chose mostly to pursue animal research that involved no pain, with heavy emphasis on positive emotions. For personal reasons, from 1998 onward, I have only participated in animal experiments involving no pain, except for standard injections of drugs: Perhaps the last experiments that involved more than injection and standard surgical stress were conducted in Panksepp (1980), in which I used tail-shock to identify the threshold for squeaking in infant rats — at levels that I could barely detect on my fingertips. The finding was that simply holding the rats would eliminate the squeaking, which highlights how social touch is analgesic. I did study the primal emotions of fear (FEAR) and separation distress (PANIC), but I have restricted practically all of my research to positive emotions since then, especially PLAY, which included the tickling of perhaps a thousand juvenile rats. One of our favorite findings is that tickling rats makes them better experimental subjects (Cloutier et al., 2012).

in fish-brained creatures. Although the data stream for painful qualia in fish is more modest than for mammals, there is abundant evidence for a diversity of emotional feeling in common laboratory mammals (Panksepp, 1982, 1998, 2011a, 2011b), and the most compelling data have arisen from relevant brain manipulations. Similar strategies deserve to be implemented in fish research. Thus, the issue addressed by Key remains wide open for future empirical resolution.

It is noteworthy that it is easier scientifically to conclude that something exists than that it does not. Thus, closure on such important questions remains premature. The weight-of-evidence for experiences of aversive and rewarding emotional feelings in animals remains substantial, and with abundant clinical implications (Panksepp, 2015; Panksepp & Biven, 2012). If comparable studies were conducted in fish, I anticipate that credible neuroscientific evidence for some kind of aversive pain-type feelings could be demonstrated, especially since the experience of pain probably evolved to protect the body in anticipatory ways and thereby automatically predict survival trajectories when there are still opportunities to escape/avoid destruction.

The key issue is: Can extreme points of view on this topic be differentiated with neurobiological approaches? I think they can. Would Key be willing to interpret rewarding and punishing subcortical brain circuits in mammalian brains as evidence for certain feelings? If they remain intact after radical decortication, would that not be consistent with a subcortical locus of control? Further, since fish nociceptive responses are modulated by opioids (Sneddon, 2009), consider the following critical experiment: Rodent studies have shown that when sustained putative pain is inflicted on rats, if given the chance, they will self-administer (consume) more opioids than rats not undergoing nociceptive stimuli/states (Martin et al., 2007). I assume that Key might predict that fish will not self-administer opioids under such presumptive states of pain. If such experiments were conducted in fish (much harder in aquatic organisms), and the fish learned to self-administer more opioids, would Key be willing to agree that the weight of evidence was swinging toward the existence of aversion/pain-related central states in fish brains? If not, why not? In any event, differential predictions provide compelling scientific differentiation of views that could help resolve the affective problem at hand. The fact that cortical systems process such feelings into complex decision-making and other higher brain regulatory processes does not mean the neural fonts of consciousness are cortically situated.

References

- Bailey, P., & Davis, E.W. (1942). Effects of lesions of the periaqueductal gray matter in the cat. *Proceedings of the Society for Experimental Biology and Medicine*, 351, 305–306.
- Bailey, P., & Davis, E.W. (1943) Effects of lesions of the periaqueductal gray matter on the *Macaca mulatta*. *Journal of Neuropathology and Experimental Neurology*, 3, 69–72.
- Barrett, J.E. (2015) The pain of pain: challenges of animal behaviour models. *European Journal of Pharmacology*, 753, 183-190. doi: 10.1016/j.ejphar.2014.11.046

Cloutier, S., Panksepp, J., & Newberry, R.C. (2012). Playful handling by caretakers reduces fear of humans in the laboratory rat. *Applied Animal Behaviour Science*, 140, 161–171. doi: 10.1016/j.applanim.2012.06.001.

Collier, A.D., Khan, K.M., Caramillo, E.M., Mohn, R., & Echevarria, D.J. (2014). Zebrafish and conditioned place preference: a translational model of drug reward. *Progress in Neuropsychopharmacology and Biological Psychiatry*, 55, 16-25. doi: 10.1016/j.pnpbp.2014.05.014

Damasio, A.R., Grabowski, T.J., Bechara, A., Damasio, H., Ponto, L.L.B., Parvizi, J., & Hichwa, R.D. (2000) Subcortical and cortical activity during the feeling of self-generated emotions. *Nature Neuroscience*, 3, 1049-1056.

Huber, R., Panksepp, J. B., Nathaniel, T., Alcaro, A., & Panksepp, J. (2011). Drug-sensitive reward in crayfish: An invertebrate model system for the study of SEEKING, reward, addiction, and withdrawal. *Neuroscience & Biobehavioral Reviews*, 35, 1847-1853. doi: 10.1016/j.neubiorev.2010.12.008

Jones, S.G., Kamunde, C., Lemke, K., & Stevens, E.D. (2012). The dose-response relation for the antinociceptive effect of morphine in a fish, rainbow trout. *Journal of Veterinary Pharmacology and Therapeutics*, 35, 563-70.

[Key, B. \(2016\)](#). Why fish do not feel pain. *Animal Sentience* 2016.003.

Lau, B., Bretaud, S., Huang, Y., Lin, E., & Guo, S. (2006). Dissociation of food and opiate preference by a genetic mutation in zebrafish. *Genes, Brain and Behavior*, 5, 497-5050.

LeDoux, J. (2012). Rethinking the emotional brain. *Neuron*, 73, 653-676. doi: 10.1016/j.neuron.2012.02.004

Martin, T.J., Kim, S.A., Buechler, B.S., Porecca, F., & Eisenach, J.C. (2007) Opioid self-administration in the nerve-injured rat. *Anesthesiology*, 106, 312-322.

Merker, B. (2007). Consciousness without a cerebral cortex: A challenge for neuroscience and medicine. *Behavioral and Brain Sciences*, 30, 63–134. doi: 10.1017/S0140525X07000891

Moruzzi, G., & Magoun, H. W. (1949). Brain stem reticular formation and activation of the EEG. *Electroencephalography & Clinical Neurophysiology*, 1, 455–473. doi: 10.1016/0013-4694(49)90219-9

Panksepp, J. (1980) Brief social isolation, pain responsivity, and morphine analgesia in young rats. *Psychopharmacology*, 72, 111-112.

Panksepp, J. (1981). Hypothalamic integration of behavior: Rewards, punishments, and related

- psychobiological process. In P.J. Morgane & J. Panksepp (Eds.), *Handbook of the Hypothalamus* (Vol. 3, Part A): *Behavioral Studies of the Hypothalamus* (pp. 289-487). Marcel Dekker, New York.
- Panksepp, J. (1982). Toward a general psychobiological theory of emotions. *Behavioral and Brain Sciences*, 5, 407-467. doi: 10.1017/S0140525X00012759
- Panksepp, J. (1985) Mood changes. In P.J. Vinken, G.W. Bruyn, & H.L. Klawans (Eds.), *Handbook of Clinical Neurology* (Revised Series, Vol. 1, 45): *Clinical Neuropsychology* (pp. 271-285). Amsterdam: Elsevier Science Publishers.
- Panksepp, J. (1998). *Affective Neuroscience: The Foundations of Human and Animal Emotions*. New York: Oxford University Press.
- Panksepp, J. (2011a). Cross-species affective neuroscience decoding of the primal affective experiences of humans and related animals. *PLoS One*, 6, e21236. doi: 10.1371/journal.pone.0021236
- Panksepp, J. (2011b). The basic emotional circuits of mammalian brains: Do animals have affective lives? *Neuroscience & Biobehavioral Reviews*, 35, 1791–1804. doi: 10.1016/j.neubiorev.2011.08.003
- Panksepp, J. (2015). Affective preclinical modeling of psychiatric disorders: Taking imbalanced primal emotional feelings of animals seriously in our search for novel Antidepressants. *Dialogues in Clinical Neurosciences*, 17, 249-265.
- Panksepp, J., & Biven, L. (2012). *Archaeology of Mind: The Neuroevolutionary Origins of Human Emotions*. New York: Norton.
- Panksepp, J., Normansell, L.A., Cox, J.F., & Siviy, S. (1994). Effects of neonatal decortication on the social play of juvenile rats. *Physiology & Behavior*, 56, 429-443.
- Panksepp, J., Wright, J.S., Döbrössy, M.D., Schlaepfer, T.E., & Coenen, V.A. (2015) Affective neuroscience strategies for understanding and treating depressions: from preclinical models to novel therapeutics. *Clinical Psychological Science*, 2, 472-494. doi: 10.1177/2167702614535913
- Panksepp, J., & Yovell, Y. (2014). Preclinical modeling of primal emotional affects (SEEKING, PANIC and PLAY): Gateways to the development of new treatments for depression. *Psychopathology*, 47, 383-93. doi: 10.1159/000366208
- Schiff, N. D. (2007). Global disorders of consciousness. In M. Velmans & S. Schneider (Eds.), *The Blackwell Companion to Consciousness* (pp. 589–604). Oxford, UK: Blackwell.

- Shewmon, D., Holmes, G., & Byrne, P. (1999). Consciousness in congenitally decorticate children: developmental vegetative state as self-fulfilling prophecy. *Developmental Medicine and Child Neurology*, 41, 364-374. doi: 10.1017/S0012162299000821
- Sneddon, L.U. (2009) Pain perception in fish: indicators and endpoints. *ILAR Journal*, 50, 338-342. doi: 10.1093/ilar.50.4.338
- Sneddon, L.U., Braithwaite, V.A., & Gentle, M.J. (2003a). Do fishes have nociceptors? Evidence for the evolution of a vertebrate sensory system. *Proceedings of the Royal Society of London B: Biological Sciences*, 270, 1115-1121.
- Sneddon, L.U., Braithwaite, V.A., Gentle, M.J. (2003b). Novel object test: examining nociception and fear in the rainbow trout. *Journal of Pain*, 4, 431-440. doi: 10.1067/S1526-5900(03)00717-X
- Valenstein, E.S. (1966). The anatomical locus of reinforcement. In E. Stellar and J. M. Sprague (Eds.), *Progress in physiological psychology*, Vol. 1 (pp. 149–190). New York: Academic Press.
- Yovell, Y., Bar, G., Mashiah, M., Baruch, Y., Briskman, I., Asherov, J., Lotan, A., Rigbi, A., & Panksepp, J. (2015) Ultra-low-dose buprenorphine as a time-limited treatment for severe suicidal ideation: A randomized, controlled trial. *American Journal of Psychiatry*. (in press).