COGS 001 Term Paper – Brian Tomasik

The International Association for the Study of Pain (IASP) defines *pain* as "unpleasant sensory and emotional experience associated with actual or potential tissue damage" [LT08]. A key part of what constitutes pain is, thus, a subjective feeling of discomfort. This is to be distinguished from mere *nociception*, or the "the neural processes of encoding and processing noxious stimuli" [LT08], which can occur without conscious awareness. Determining whether another organism feels pain is fundamentally a philosophical question, with the solipsists taking the extreme position that no conscious experience apart from one's own can be concluded to exist. A more reasonable view, I think, is to recognize that the hypothesis of pain in other organisms can help us explain certain behaviors and may therefore be justifiably inferred.

The important question, then, is which behaviors to look for when identifying pain. According to [Zim86], a painful experience "should elicit protective motor and vegetative reactions, having an adverse effect on the animal's general behavior." [SBG03] applied this criterion in the case of rainbow trout, finding that injection of acetic acid or bee venom induced anomalous rocking behavior and increased the time taken to resume feeding. A follow-up study [Sne03] showed, moreover, that fish injected with the analgesic morphine exhibited fewer of these reactions. Inspired by this work on fish, Barr et al. [BLDE08] carried out a similar experiment with prawn crustaceans, demonstrating both prolonged behavioral reactions to adverse stimuli and diminished reaction with an analgesic.

The first stage of the experiment served as a control. To the antennae of half of the animals the experimenters applied benzocaine, while to the other half they applied only seawater; after an observation period, they applied seawater again to a fraction of each type of prawn. The researchers found that the analgesic acted as an aversive stimulus, causing increased grooming of the affected body part; however, the impact was short-lived, disappearing after the subsequent application of seawater. Thus, the researchers suggest, the benzocaine was not itself responsible for later adverse reactions to noxious stimulants. Moreover, the benzocaine certainly did not decrease prawn activity, demonstrating that it was not acting as a general anesthetic in a way that would inhibit all types of behavior.

In the second part of the experiment, the researchers divided the prawn from the first part into four groups, receiving either seawater, sodium hydroxide, acetic acid, or a mechanical pinch, the latter three being negative stimuli. The treatments were applied to only one of the antennae of each prawn, with the other antenna left alone. The researchers found that prawn given a noxious stimulus showed significantly higher rates of rubbing the afflicted antenna against the side of the tank compared to the untreated antenna, indicating that the prawn correctly understood the location of the damage. In addition, the chemical treatments (though not the mechanical pinch) caused significantly more grooming of the treated antenna. The authors viewed this as demonstrating "prolonged location-specific change in behavior that was not merely a reflex" (p. 5). If the prawn were capable of only nociception, they would presumably exhibit just an immediate reaction against the noxious treatments (such as a violent tail flick, which was also observed), not an extended period of behavior change.

In isolation, this result might not be completely satisfying. For instance, Lynne Sneddon of Liverpool University was quoted in a a news article follow-up to the study[1] as saying, "You could argue the shrimp is simply trying to clean the antenna rather than showing

[1] http://www.guardian.co.uk/science/2007/nov/08/animalrights.sciencenews

a pain response." Richard Chapman at the University of Utah added, "Even a single-cell organism can detect a threatening chemical gradient and retreat from it." The suggestion, I take it, is that prawns might have some sort of "clean me off" signals triggered by the chemical-covered antenna, and these signals could be unconscious (just as, say, human immune responses are unconscious).

This criticism is weakened, however, by the second piece of evidence that Barr et al. present: The rubbing and grooming actions were significantly reduced in the prawn group receiving benzocaine relative to the group receiving seawater. Importantly, the control from the first part of the experiment showed that this was not because the analgesic caused a general decline in activity—indeed, prawn receiving the analgesic showed significantly more activity in the first observation period. Rather, whatever mechanism caused the rubbing and grooming, it could be turned off by an analgesic. It would seem a coincidence, then, if the same substance, benzocaine, that inhibits the pain pathway in higher species was also the substance that happened to inhibit the (presumably unrelated) "clean me off" pathway in prawns, especially since the authors demonstrated that benzocaine did not have a general inhibitory effect at the doses given.

Still, maybe it was a coincidence. Benzocaine acts by binding to sodium channels and thereby inhibiting nerve firing for pain signals [Ben]. But maybe the same mechanism was acting to inhibit transmission of the signals telling the prawn that its antenna was dirty? One way to do disprove that possibility would be to find a chemical substance X which induces cleaning behavior that doesn't shut off when benzocaine is applied. Assuming the "clean me off" signals are always transmitted by the same mechanism regardless of the chemical applied, this would falsify the hypothesis that benzocaine merely inhibited the cleaning impulse. Moreover, if X was known not to cause pain in other organisms, this result would be completely consistent with the hypothesis that benzocaine is inhibiting the pain pathway. Unfortunately, such a substance X might not exist.

The cleaning-response hypothesis does have one piece of evidence in its favor: It predicts that the prawns will decrease their rubbing in response to benzocaine only in the cases where chemical irritants were applied; since benzocaine is hypothesized to shut down the "clean me off" signals, it would not inhibit rubbing that had been caused by mechanical pinching.[2] Indeed, this turned out to be the case: Benzocaine did not appear to significantly reduce post-pinching rubbing.[3] The authors explain this finding by suggesting that benzocaine may only turn off chemical receptors, not mechanical receptors. This suggests a follow-up study: See if there are analgesics that are known to target the types of mechanical receptors found in prawn, and test whether they inhibit rubbing. This would basically amount to repeating the study that Barr et al. already did but with a proper choice of analgesic. Of course, I don't know if analgesics of the desired type actually exist.

Neither of the follow-up studies mentioned in the previous two paragraphs is particularly satisfying, because both rely on finding some chemical that may or may not exist. There's no single variable that we can tune and get an interesting finding regardless of how things turn out. Designing a good experiment is challenging, because as the IASP definition of pain emphasizes, unpleasant experience is fundamentally a subjective phenomenon. For every apparent pain response, we can—at the end of the day—always hypothesize that the response is unconscious. This reflects David Chalmers's "hard problem": Why is any-

[2] Though what does cause the pinching-induced rubbing would remain unexplained.

[3] Of course, failure to find a significant difference doesn't mean there wasn't one, though we hope that the authors took a sample size sufficient to guarantee good power. The number of prawns pinched was 36, half with analgesic and half without.

thing conscious, anyway? Why aren't we philosophical zombies? Still, we do know that we are conscious. So maybe the more lines of evidence we have that an organism behaves similarly to the way we would in a situation, the more confidence we can have that it's conscious as well.

In this spirit, Robert Elwood, the fourth author of the Barr et al. study, undertook a follow-up investigation with Mirjam Appel [EA09] of crustacean pain. They took a new angle, this time focused on learning and motivation. As the introduction to the study notes, there is a wide body of literature investigating shell choice in hermit crabs. These crabs show sophisticated ability to evaluate the quality of different shells, and are willing to incur costs, such as fighting other members of their species [BE04], to obtain better shells. If hermit crabs are capable of feeling pain, then unpleasant experience should be one factor that affects their motivational tradeoffs among shells, and it was on this basis that Elwood and Appel designed their investigation.

The authors collected a sample of 104 wild hermit crabs with varying shell sizes and types. 49 of them were placed into a control group receiving no treatment. With the rest, the authors drilled two small holes into their shells and inserted wires bent against the sides of the shell. The wires were then electrified[4] at a level known to be low enough that most crabs would not evacuate their shells during the process. 20 s after shock in the treatment group, or after just 240 s of waiting by the control group, the authors introduced a second shell into each crab's tank. After an initial period of hesitation, some of the crabs left their shells to investigate the new one, and some of those moved in.

On the hypothesis that hermit crabs felt pain during the shocking process, their assess-

[4] I suppose this gives new meaning to the phrase "shell shock."

ment of the quality of their current shell should have decreased. Indeed, this appeared to be the case, as reflected by the fact that significantly more of the shocked crabs left their shells to investigate the new one, and those that did showed significantly less hesitation before deciding to move in (as measured by lower approach and investigation times, as well as less probing of the new shell with their chelipeds). Importantly, the authors note, the new shell was not introduced until after the shocking had ended, so the change in motivation on the part of the treated crabs must have been due to memory of the shock event. This delay in response to the aversive stimulus makes "the findings [...] difficult to interpret as a nociceptive reflex" (p. 4), the authors claim.

I find this point relatively convincing. Still, I can imagine a skeptical objection: Maybe 20 s of waiting after the shock wasn't enough; perhaps the treated crabs still had unconscious nociceptive signals floating around in their bodies impelling them to leave when they got the chance. This could be tested by varying the waiting period between the end of shock and the introduction of the new shell. As long as the period wasn't longer than the crabs's ability to remember events, we would expect the same type of response. In fact, if hermit crabs have a known maximum memory length,[5] then we can examine a further question: Do the crabs stop favoring abandonment of their old shells after roughly that length of delay, as the pain-memory hypothesis predicts?

A second criticism I can imagine is aimed at the notion that the shock is a painful stimulus. Maybe the crabs were just reacting to the fact that small holes had been drilled in their shells and wires inserted. Or maybe the electricity wasn't painful but just noticable—like the feeling (or unconscious detection) that a small organism was crawling around the

[5] For instance, [JE89] suggests that crabs can remember specific shells for up to 40 min.

crab's abdomen. In other words, maybe the treated crabs merely felt their shells as being physically abnormal, in the same (non-painful) way that a smooth shell might feel different from a rough one. Elwood and Appel observed some circumstantial evidence against this alternate hypothesis: Namely, one of the shocked crabs rubbed its abdomen against the new shell and another groomed its abdomen, suggesting an agitating stimulus. Still, to more soundly distinguish between the hypothesis of pain and the hypothesis of merely a different shell feel, we could try to induce the motivational tradeoff in a way that didn't involve the shell directly. For instance, perhaps the crabs could be trained to prefer one side of the tank to the other, by shocking them or applying radiation exactly when they visit one side. If this sort of classical Pavlovian conditioning could be done successfully (which itself would be an interesting finding), then we could place crabs alternately on one side of the tank or the other and observe whether they escape more readily from shells on the negatively associated side. If so, their escape would not be due to the feel of their shell at all but rather to a higher-level understanding that their shell is associated with being on the bad side of the tank. The motivational tradeoff would in this case not be one shell against another but "good current shell" vs. "bad side of tank," a more complicated cost-benefit calculation. Another approach, inspired by the Barr et al. prawn study, would be to apply an analgesic to some of the crabs before shocking them and see if those individuals showed less desire to leave their old shells. Unfortunately, this approach could run into the same objection as in the prawn study: What if the analgesic just happens to be shutting off the non-conscious touch sensors that allow the shocked crabs to detect in a non-painful way that their shells are abnormal? On the other hand, this approach has the virtue that it doesn't require full conditioning of the crabs and so might be more feasible in practice.

References

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