Reply to Arandia and Di Paolo

We thank Arandia and Di Paolo for their thoughtful comments. Since we agree with many of the comments, we think the contention mostly comes down to a matter of different emphasis. The point of our review was to show that predictive processing (PP) turns the biomedical model on its head because of the primacy of generative top-down processes. Its value does not lie so much in challenging the biomedical model starting from its anomalies – e.g. medically unexplained symptoms – but by starting from the cases it accommodates most easily – e.g. acute pain. It shows that even here, where there is a tight coupling between lesion and symptoms, perception is still determined by top-down predictions quickly updated upon meeting bottom-up signals. And once this is understood, anomalies like chronic pain and placebo effects emerge as phenomena that lie on a continuum with acute pain and treatment effects, but where top-down predictions play a dominant role compared to signal. An obvious implication of this framework is that physiological disorders cannot be treated in isolation, but always within the psychosocial context that affect top-down predictions of bodily states (a conclusion that, at least in its clinical implications, is really not far away from that of enactive psychiatry [6]). We thought that the framework leads to an important reconceptualization of pain. If valid, it shatters the artificial but pervasive dichotomy between acute pain and chronic pain, and the dichotomy between treatment effect and placebo effect, dichotomies that ensued from the biomedical model in the first place.

Whilst we deemed this to be the main thrust of the paper, Arandia and Di Paolo [1] focus most of their critique on our brief account of open-label placebo (OLP), arguing that it is paradoxical. They also maintain that predictive processing invites neurocentric explanations that downplay embodied and environmental factors.

We would like to make one concession for each point.

With regard to OLP, we admit that our presentation was mistaken, precisely because thoughts such as ‘placebos are inert’ and ‘placebo may still help’ can only be considered as conscious, person-level information, while PP operates unconsciously. When this is acknowledged, OLP needn’t be paradoxical. Like in the case of the Muller-Lyer visual illusion, where we perceive lines of different length despite being told that they are equal [10](pp.88-89), we respond to placebo treatment despite being honestly told that it is a placebo. This is because the information that the treatment is a placebo is received at a particular level of the hierarchy in which it is given low precision relative to the prediction of higher-level priors. These priors embody general predictions about the patient’s bodily and pre-reflective engagement with the therapeutic ritual and about its positive outcome. And these predictions are precise enough to suppress conscious information about whether treatment should be effective or is a placebo (indeed, OLP differs from double-blind placebo by appearing paradoxical to the patient on a reflective level [8][9], but the difference between the two may be more formal than actual in the experiential context of therapy [7]). This need not be an ad hoc explanation. Insofar as concepts like ‘prior’ or ‘prediction error’ describe actual neurophysiological processes and not abstract entities [4], the implementation of PP in concrete cases such as OLP can be tested and inspected scientifically. If studies then find that PP is not instantiated in the brain, we should abandon PP and perhaps look elsewhere for other generative processes frameworks. Moreover, we agree with Arandia and Di Paolo that the uncertainty regarding the evolution of illness cannot be reduced to changing weights between prediction and sensory signals. But here we are dealing with two conceptions of ‘uncertainty’ – one experiential (the feeling of uncertainty), one theoretic (probabilistic uncertainty; i.e. the sub-consciousley processed degree of precision of predictions). These two conceptions should not be conflated, in the same way that experiential surprise (the conscious feeling of surprise)
should not be conflated with ‘surprisal’ (the sub-consciously processed implausibility of a certain sensory state given a certain prior) in PP theory.

With regard to the neurocentrism critique, we agree that we did not stress the significance of social context enough. With more space, we would have clarified that the brain is simply a mediating organ [5], that perception can only arise in active interaction with body and environment, and that embodied and enactive perspectives are fundamental in the understanding of pain (like Arandia and Di Paolo [2][1], we are theoretical pluralists). We disagree with the claim that PP is necessarily internalist, however. Some researchers [3][10] have recently suggested that prediction error minimisation extends beyond the brain to include the individual’s social environment. Cultural practices can play a central role in tuning the precision mechanism that balances the relative influence of bottom-up and top-down streams of information in the brain and can thus be constitutive of perception. The same goes for the body. With specific reference to pain, it has been argued [11] that pain perception is physically realised across the homeostatic processes that makes up the body as a whole. Under this interpretation, what travels up the neural axis is not nociceptive signal but is itself prediction error already been processed at the level of the peripheral nervous system, autonomic, neuroendocrine, and immune systems. The body is not just another source of sensory input for the brain but is part of the overall PP system.

In sum, Arandia and Di Paolo’s critique has allowed us to add significant clarifications to our paper, but we do not find it undermines our key message.

Acknowledgements
Research related to this work has been funded by an Economic and Social Research Council (ESRC) grant (ES/V005731/1) (GO).

Conflicts of interest
No conflicts of interest to declare.

Reference list
