Journal Club

Editor's Note: These short reviews of recent *JNeurosci* articles, written exclusively by students or postdoctoral fellows, summarize the important findings of the paper and provide additional insight and commentary. If the authors of the highlighted article have written a response to the Journal Club, the response can be found by viewing the Journal Club at www.jneurosci.org. For more information on the format, review process, and purpose of Journal Club articles, please see http://www.jneurosci.org/content/jneurosci-journal-club.

A Multisensory Perspective on the Role of the Amygdala in Body Ownership

Arran T. Reader* and Laura Crucianelli*

Department of Neuroscience, Karolinska Institutet, 171 77, Stockholm, Sweden

Review of Spengler et al.

A sense of ownership over one's own body is essential for effective interaction with the world: acting upon objects or communicating with others relies on distinguishing between the parts of the world that constitute our self, and the parts of the world that do not. The sense of body ownership is frequently associated with activity in the ventral premotor cortex, intraparietal sulcus, and insula (Grivaz et al., 2017), and is believed to stem from multisensory integration (Ehrsson, 2012): congruent sensory signals are combined to provide a feeling of bodily self that is distinct from the surrounding environment. This is emphasized by the rubber hand illusion (RHI), in which synchronous, but not asynchronous, stroking of a rubber hand and the real hand (which is hidden from view) can induce a sense of ownership over the false limb (Botvinick and Cohen, 1998).

In an article in *The Journal of Neuroscience*, Spengler et al. (2019) proposed a role for the amygdala in mediating the sense of body ownership. In line with the oft-reported role of this area in threat-related processing, they hypothesized that the amygdala may be involved in protecting against distorted body perception and that susceptibility to body illusions, such as the RHI, might therefore be determined in part by amygdala activity. To test this hypothesis, they performed three experiments. In the first, they recruited twin women with bilateral amygdala lesions (resulting from Urbach–Wiethe disease) and compared their subjective experience in the RHI (agreement with statements about the illusory experience and illusion onset time) with that of 13 healthy controls. In the second experiment, they examined whether illusion onset correlated with amygdala volume in healthy participants. In a third study, they assessed responses to the RHI after the administration of intranasal oxytocin, which has been found to have an inhibitory effect on the amygdala (e.g., Martins et al., 2019).

The response of the patients to the RHI was striking. Both immediately reported the strongest possible feeling of ownership over the rubber hand. Their onset time for the illusion was 1 s, whereas the average onset for control participants was >2 min. In the second experiment, the authors found a positive correlation between amygdala volume and illusion onset: people with a larger amygdala took longer to experience the illusion. Finally, Spengler et al. (2019) found that the administration of intranasal oxytocin increased the strength of the illusion and reduced onset time compared with placebo, in keeping with other research on the RHI (Crucianelli et al., 2019). From these consistent results the authors concluded that amygdala activation and structural integrity influences susceptibility to the RHI, and that the amygdala helps protect the body from potentially damaging illusory perceptions.

The study by Spengler et al. (2019) provides insight into potential subcortical mechanisms underlying the experience of body ownership. We agree with the authors that the amygdala may help to maintain a coherent perception of the bodily self, but we do not necessarily agree with a threat-related role for the amygdala in body ownership. Instead, we believe that the results are adequately explained by deferring to the classic conceptualization of body ownership as deriving from multisensory integration.

As previous work has established, the RHI relies on the manipulation of multisensory signals (vision, touch, proprioception) that contribute to the sense of bodily self. In addition to these bottom-up sensory signals, a feeling of body ownership may be influenced by top-down processes, such as our expectations of reality (e.g., that a hand seen extending from the body in a first-person perspective is very likely to be one's own) (Apps and Tsakiris, 2014) or internal models of our own body appearance (Tsakiris, 2010). We propose that the amygdala may help mediate between these

Received April 26, 2019; revised July 25, 2019; accepted Aug. 3, 2019.

We thank Professor Henrik Ehrsson and Catriona Scrivener for helpful comments on a draft of this work.

The authors declare no competing financial interests.

*A.T.R. and L.C. contributed equally to this work as joint first authors.

Correspondence should be addressed to Arran T. Reader at arran.reader@ki.se.

https://doi.org/10.1523/JNEUROSCI.0971-19.2019

bottom-up and top-down processes to support the conscious sense of bodily self.

The amygdala has an established role in multisensory integration (Ghazanfar and Schroeder, 2006; Van der Stoep et al., 2019), a process that is essential to ascertain whether different sensory inputs share a common source (e.g., a touch seen on a rubber hand and a touch felt on the real hand). Multisensory integration occurs in the amygdala even in contexts devoid of affective content (Morrow et al., 2019), and this integration is supported by reciprocal projections to primary sensory cortical areas (Janak and Tye, 2015), by a large proportion of neurons responsive to two or more sensory inputs (Morrow et al., 2019), and by intrinsic connectivity between different unimodal subregions (Benarroch, 2015). Importantly, the amygdala is sensitive to novel multisensory input (Ghazanfar and Schroeder, 2006), which means it must also have access to information about previously experienced or expected sensory input. Notably, the amygdala is functionally connected to the posterior parietal cortex, where the established perception of the body, built up with experience, is putatively stored (Longo et al., 2010). It is also functionally connected to the insula (Roy et al., 2009), which is involved in bodily awareness (Grivaz et al., 2017), and it projects onto the ventral premotor cortex (Ishida et al., 2018; Rizzo et al., 2018), a region that has been associated with the experience of ownership over the false hand during the RHI (Guterstam et al., 2019). Together, the functional and anatomical connectivity of the amygdala suggests that it is well situated for supporting these cortical areas that are commonly associated with the sense of body ownership. This may involve comparing established knowledge about the own body with ongoing sensory feedback about the body. If online sensory feedback conflicts with the stored representation of the body, as at the start of the RHI, it is plausible that one maintains a feeling of ownership over their real (hidden) hand since this is the source of established bodily experience. However, as the synchronous seen and felt touches continue, it becomes evident that they must share a common source: one's own body (Apps and Tsakiris, 2014). If this occurs, then the feeling that the false limb is one's own can arise. According to this view, the amygdala may be part of a system that "gates" conscious bodily self-perception, limiting the influence of online sensory information about the body until it is strong enough to override experience.

Behavioral support for this hypothesis is found in the incredible speed with which the amygdala-lesioned patients reported the RHI (Spengler et al., 2019). This might occur if their conscious perception immediately resolves to the most likely conclusion given everyday experience (that a hand viewed from the first-person perspective is one's own), or if their internal body model is immediately disregarded in favor of the false hand. This is a plausible outcome if damage to the amygdala interferes with the ability to balance top-down information and bottom-up sensory signals. Indeed, damage to the amygdala or amygdala connectivity can also result in disorders of bodily self-awareness (e.g., Jenkinson et al., 2013; Pacella et al., 2019). In healthy participants, increased amygdala activation was observed when incongruent multisensory information was presented during a RHI paradigm (Tsakiris et al., 2007), further suggesting that the amygdala is sensitive to discrepancies between incoming sensory feedback and established sensory expectations regarding what constitutes the real body. Effects on the conscious experience of body ownership in healthy individuals can also be observed when amygdala activity is reduced with intranasal oxytocin, or when comparing RHI onset with amygdala volume, as reported by Spengler et al. (2019). The greater the activity (or size) of the amygdala, the longer it takes to resolve conflict between top-down information and congruent multisensory information arising from the real and false hands because inconsistency between different sources of online sensory information can be more readily detected (e.g., the asynchronicity of seen and felt touches). This delays the establishment of a coherent percept of an owned limb.

Another possible interpretation of the results is that the amygdala is simply involved in multisensory integration during the RHI, rather than mediating between multisensory information and top-down processes. Indeed, the speed of illusion onset in the Urbach–Wiethe patients reported by Spengler et al. (2019) could reflect an overriding influence of visual feedback on hand ownership (e.g., Martinaud et al., 2017) in the absence of multisensory integration that normally occurs in the amygdala. Similarly, downregulation of the amygdala in healthy participants could speed the onset of the RHI by limiting the sensitivity of the amygdala to online multisensory conflict, placing greater weight on the more salient visual information rather than the conflicting proprioceptive feedback. If this is the case, we might expect that decreased amygdala activity would result in the experience of ownership over the rubber hand, even if it was stroked asynchronously with the real one. Unfortunately, Spengler et al. (2019) did not perform this classic control test for the RHI. However, other research suggests that intranasal oxytocin increases the strength of the RHI only when synchronous stroking is applied to the real and fake hands, not with asynchronous stroking or purely visual feedback (Crucianelli et al., 2019). As such, this interpretation seems less tenable.

In conclusion, we propose that the findings reported by Spengler et al. (2019) may reflect a role for the amygdala in mediating top-down and bottom-up information for the purpose of maintaining a sense of body ownership. As emphasized by Spengler et al. (2019), the amygdala is infrequently reported in neuroimaging studies of body ownership, which may be due to its small size. However, it is possible that cortical areas associated with body ownership are supported by subcortical areas, such as the amygdala, and we hope that further research will investigate the alternative hypotheses of amygdala function discussed here.

References

Apps MA, Tsakiris M (2014) The free-energy self: a predictive coding account of self-recognition. Neurosci Biobehav Rev 41:85–97.

Benarroch EE (2015) The amygdala: functional organization and involvement in neurologic disorders. Neurology 84:313–324.

Botvinick M, Cohen J (1998) Rubber hands 'feel' touch that eyes see. Nature 391:756.

Crucianelli L, Paloyelis Y, Ricciardi L, Jenkinson PM, Fotopoulou A (2019) Embodied precision: intranasal oxytocin modulates multisensory integration. J Cogn Neurosci 31:592–606.

Ehrsson HH (2012) The concept of body ownership and its relation to multisensory integration. In: The new handbook of multisensory processes (Stein BE, ed), pp 775–792. Cambridge, MA: MIT.

Ghazanfar AA, Schroeder CE (2006) Is neocortex essentially multisensory? Trends Cogn Sci 10:278–285.

Grivaz P, Blanke O, Serino A (2017) Common and distinct brain regions processing multisensory bodily signals for peripersonal space and body ownership. Neuroimage 147:602–618.

Guterstam A, Collins KL, Cronin JA, Zeberg H, Darvas F, Weaver KE, Ojemann JG, Ehrsson HH (2019) Direct electrophysiological correlates of body ownership in human cerebral cortex. Cereb Cortex 29:1328–1341.

Ishida H, Inoue KI, Takada M (2018) Multisynaptic projections from the amygdala to the ventral premotor cortex in macaque monkeys:

anatomical substrate for feeding behavior. Front Neuroanat 12:3.

Janak PH, Tye KM (2015) From circuits to behaviour in the amygdala. Nature 517:284–292.

Jenkinson PM, Haggard P, Ferreira NC, Fotopoulou A (2013) Body ownership and attention in the mirror: insights from somatoparaphrenia and the rubber hand illusion. Neuropsychologia 51:1453–1462.

Longo MR, Azañón E, Haggard P (2010) More than skin deep: body representation beyond primary somatosensory cortex. Neuropsychologia 48:655–668.

Martinaud O, Besharati S, Jenkinson PM, Fotopoulou A (2017) Ownership illusions in patients with body delusions: different neural profiles of visual capture and disownership. Cortex 87:174–185.

Martins D, Mazibuko N, Zelaya F, Vasilakopoulou S, Loveridge J, Oates A, Maltezos S, Mehta M, Howard M, McAlonan G, Murphy D, Williams S, Fotopoulou A, Schuschnig U, Paloyelis Y (2019) Do direct nose-to-brain pathways underlie intranasal oxytocin-induced changes in regional cerebral blood flow in humans? bioRxiv. Advance online publication. Retrieved February 28, 2019. doi:10.1101/563056.

Morrow J, Mosher C, Gothard K (2019) Multisensory neurons in the primate amygdala. J Neurosci 39:3663–3675.

Pacella V, Foulon C, Jenkinson PM, Scandola M, Bertagnoli S, Avesani R, Fotopoulou A, Moro V, Thiebaut de Schotten M (2019) Anosognosia for hemiplegia as a tripartite disconnection syndrome. Elife 8:e46075.

Rizzo G, Milardi D, Bertino S, Basile GA, Di Mauro D, Calamuneri A, Chillemi G, Silvestri G, Anastasi G, Bramanti A, Cacciola A (2018) The limbic and sensorimotor pathways of the human amygdala: a structural connectivity study. Neuroscience 385:166–180.

Roy AK, Shehzad Z, Margulies DS, Kelly AM, Uddin LQ, Gotimer K, Biswal BB, Castellanos FX, Milham MP (2009) Functional connectivity of the human amygdala using resting state fMRI. Neuroimage 45:614–626.

Spengler FB, Scheele D, Kaiser S, Heinrichs M, Hurlemann R (2019) A protective mechanism against illusory perceptions is amygdala-dependent. J Neurosci 39:3301–3308.

Tsakiris M (2010) My body in the brain: a neurocognitive model of body-ownership. Neuropsychologia 48:703–712.

Tsakiris M, Hesse MD, Boy C, Haggard P, Fink GR (2007) Neural signatures of body ownership: a sensory network for bodily self-consciousness. Cereb Cortex 17:2235-2244.

Van der Stoep N, Van der Stigchel S, Van Engelen RC, Biesbroek JM, Nijboer TC (2019) Impairments in multisensory integration after stroke. J Cogn Neurosci 31:885–899.