The Amygdala in Autism: Not Adapting to Faces?

Functional magnetic resonance imaging (fMRI) adaptation has become increasingly popular in cognitive neuroscience and has the power to provide insight into how subpopulations of neurons within a small area selectively respond to similar or different types of stimuli or experimental manipulations. The assumption at the core of fMRI adaptation is that if a subpopulation of neurons selectively responds to one kind of stimulus/manipulation, then repeated exposure to the same stimulus/manipulation in quick succession (“short-lag,” usually within seconds to minutes) or over longer periods of time (“long-lag,” ranging from several minutes, hours, or days) will reduce neuronal activity in that neuronal subpopulation (1). Thus, the brain adapts or “habituates” to repeated exposure to the same stimulus/manipulation over time. However, it should be noted that the neural mechanisms underlying short-lag adaption are more understood than the underlying mechanisms for long-lag adaptation (2).

In this issue of the Journal, Kleinhans et al. (3) demonstrate that a normative long-lag fMRI-adaptation effect in the amygdala due to repeated exposure to faces is reduced in individuals with autism spectrum conditions. This is yet another piece of evidence of atypical amygdala function in autism spectrum conditions (4), which—together with structural abnormalities (5)—is broadly consistent with the amygdala theory of autism (6). Additionally, the authors demonstrate that normative “face-adaptation” effects in the amygdala are important yet absent features of face processing in individuals with autism.

To understand the key points of the Kleinhans et al. study, it is important to walk through their results. The participants (adults with autism spectrum conditions and healthy comparison subjects) were shown two sets of neutral faces in two fMRI scanning runs, separated by 5 to 6 minutes. During the first scanning run, the authors observed no group differences in amygdala response to neutral faces. Both groups recruited the amygdala to an equal degree when processing a neutral face. However, in the second imaging run (5 to 6 minutes later, when participants viewed a different set of neutral faces), the authors observed an increased amygdala response in autism. On the face of it (no pun intended), this increased activation appears to be evidence of amygdala hyperactivity in autism.

Past studies have also found hyperactivity in the autistic amygdala during face processing, and one provocative psychological interpretation of this result suggested that this was an anxiety or arousal response to attending to the eyes (4). Behavioral studies show that individuals with autism avoid looking at the eyes (7) and have difficulty understanding them (8). However, Kleinhans et al. provide a more parsimonious biological explanation of previously observed hyperactivity in the autistic amygdala.

First, Kleinhans et al. point out that the amygdala response in the autism group never exceeded the average activation that comparison subjects showed during imaging run 1. How can the amygdala in the autism be “hyperactive” if the amygdala response never exceeded that of the comparison group at the beginning of scanning? The answer lies within observing amygdala response over time. Kleinhans et al. found that increased amygdala response in the autism group during imaging run 2 was an epiphenomenon of their failure to show the simple face-adaptation effects that occurred in the amygdala of comparison subjects. Whereas the amygdala of comparison subjects adapts and

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shows less activation to repeated exposure to faces over time, the amygdala in autism does not adapt to faces over time. It is this parsimonious biological explanation that provides a more feasible account for the apparent amygdala hyperactivity during face processing in autism.

Second, the current study essentially targets a neural mechanism underlying reduced face-adaptation effects in autism spectrum conditions. In 2007, Pellicano et al. (9) first demonstrated that children with autism show disruption of a robust face-adaptation effect in the typical population called the “face-identity aftereffect.” Linking face-adaptation to the social impairments in autism, Pellicano et al. also found that the reduction of face-identity-adaptation effects was associated with greater social impairment in autism. Kleinhans et al. provide support for this observation by also showing that reduction of face-adaptation effects in the amygdala is also associated with greater social impairment.

One important caveat to the Kleinhans et al. study is the reported absence of differences in face-adaptation effects in the fusiform face area. While it is interesting that only the amygdala but not fusiform showed differences in face adaptation, we must withhold judgment about the lack of group differences. The lack of a face-adaptation effect in the fusiform may have been the result of the more general role the fusiform plays in processing invariant aspects of faces and the fact that the current study used different facial identities across the two imaging runs. The prediction based on the Pellicano et al. study would be that reduced face-adaptation effects would have been observed in the fusiform if the same identities of faces were used across the two runs. Alternatively, the abnormalities in amygdala but not fusiform response to neutral faces may have been driven by differential functional connectivity with these areas. Related to the idea of differential connectivity, the amygdala but not fusiform might also be subject to modulatory effects of top-down processing from areas further downstream in face processing, such as the prefrontal cortex.

Another important caveat of the Kleinhans et al. study is that the only comparisons reported were in two a priori-selected regions of interest: the amygdala and fusiform gyrus. If an exploration across the whole brain were performed, would there have been any other areas showing reduced face-adaptation effects? Nor do we know whether the observed reduction in adaptation was specific to faces or more widespread across other types of stimuli. This important point was raised at the end of the Pellicano et al. article, and it needs to be reiterated. One interesting yet unexplored comparison would have been to test whether similar types of reduced adaptation effects occur for other complex visual stimuli, such as houses, or for other functions subserved by the amygdala, such as emotion. If reduced adaptation effects are specific to faces, this would provide a key insight into the nature of face processing deficits and social impairments in autism. However, if reduced face-adaptation effects are simply the first of many types of altered adaptation effects, this would implicate more domain-general neural mechanisms as atypical in autism spectrum conditions.

Finally, another way to reinterpret face processing in light of reduced face-adaptation effects is to think about the role of expertise-/experience-dependent factors in face processing in autism. Klin et al. (7) documented that individuals with autism spend less time looking at the eye region of faces. Perhaps individuals with autism show reduced face-adaptation effects simply because they are not matched with the comparison group on face expertise or experience with faces? Exploring how expertise/experience modulates the reduction of face-adaptation effects would be a fruitful avenue of exploration. If reduced adaptation effects are a more general phenomena in autism, might this be reflected in the strong drive to “systemize” (10) or engage in “intense restricted interests”? Kleinhans et al. raise many stimulating questions for future research.
References


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