New Primate Model Linked to Neural Pathogenesis of Autism

Derek Dziobek1,2, James Ashe1,3 and Xiaofeng Lu2,4*

1Department of Neuroscience, University of Minnesota, Minneapolis, Minnesota 55455, USA
2Brain Science Center, Veterans Administration Medical Center, Minneapolis, Minnesota 55417, USA
3Department of Neurology, Veterans Affairs Medical Center, Minneapolis, Minnesota 55417, USA
4Department of Neurology, University of Minnesota, Minneapolis, Minnesota 55414, USA

*Corresponding author: Xiaofeng Lu, Central Brain Science Center, Veterans Administration Medical Center, Minneapolis, Minnesota, USA, Tel: 612-467-4583; E-mail: luxxx049@umn.edu

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Abstract

We know remarkably little about the pathogenesis of autism, and the neural behavior in this process at the level of single neurons has been ignored completely. Here we discuss an effective animal model in the non-human primates providing the essential information for fundamental solution in understanding of neural system problem of autism.

Editorial

Autism is a devastating neurological disorder of unknown cause, unclear pathogenesis and without an effective treatment that appears to be increasing in prevalence. Approximately 1 in 68 American children are on the autism spectrum, a figure which has been growing 10-17% annually. The monetary cost of autism exceeds $11.5 billion dollars a year in the US [1], and the strain on families whose members struggle with this disorder is immeasurable. Thus, it is desirable and obligatory to create an efficient animal model that can exhibit levels of social and cognitive interaction as close as possible to humans, so that there will be more opportunities to start neurophysiological examinations in the animal models. Here we discuss a possibility to create a non-human primate model linking a solution to this problem.

One of the defining features of autism is an impairment of social cognition [2]; this deficit may be reflected in the abnormal pattern of eye movements that has been documented in autistic individuals [3,4] and an autistic pattern of diminished eye contact can be detected in infants from a very early age [5]. The link between social cognition, visual perception and eye movements is also supported by the finding of low levels of activation in the cerebellum in autism subjects who have reduced eye contact [6]. The putative involvement of the cerebellum in social cognition is intriguing because this structure has the most consistent neuroanatomical and structural abnormalities in autistic individuals [7], and its strong projections to eye control regions in the cerebral cortex via the thalamus [8-10] provide functional connections that can link the abnormal cerebellar anatomy to higher order cognitive control of eye movements.

In an effort to characterize natural social behaviors in the non-human primate that might be targeted in developing a primate model of the disorder in our laboratory, we examined preferences for different classes of visual images [11]: (i) neutral non-animate objects, (ii) images of familiar foods, and (iii) images of human faces. We trained non-human primates on a task in which they were presented two visual images simultaneously, and are asked to choose between them. The main finding of this study is that, when given a choice of two pictures to look at, where one is a picture of a human face and the other is a picture of an inanimate object, a monkey will prefer to look at the picture of the human face more than 90% of the time. This is regardless of whether the human face is familiar or unfamiliar or if the competing image is of something with high value to the monkey, such as food.

Our data suggest that the preference of non-human primates for human faces, even when the competing object was a familiar food, is driven by considerations of social cognition that are so prominent in humans. We believe that this natural tendency of non-human primates to prefer images of other primates could be used to probe autistic behavior in monkey models of autism.

This progress provides opportunities for further research to carry out more efficient physiological studies during behavioral task to see neural correlation to the behavioral output and to analyze behavioral changes after inactivation or over-activating of local regions of brain. Eliciting changes in the subjects’ behavioral output by inactivating or over-activating relevant brain regions via pharmacological or electrical stimulation would provide much needed insights into which neural circuits and processes could be perturbed in human cases of autism. Coupled with the aforementioned connections between the cerebellum and cerebral cognitive and eye control regions, a functional circuit may underlie the social deficits seen in autistic individuals. As a first step toward understanding neural pathogenesis of autism, such pathways need to be investigated in our new generated primate model soon.

References

4. Jones W, Carr K, Klin A (2008) Absence of preferential looking to the eyes of approaching adults predicts level of social disability in 2-year-old children from a very early age [5]. The link between social cognition, visual perception and eye movements is also supported by the finding of low levels of activation in the cerebellum in autism subjects who have reduced eye contact [6]. The putative involvement of the cerebellum in social cognition is intriguing because this structure has the most consistent neuroanatomical and structural abnormalities in autistic individuals [7], and its strong projections to eye control regions in the cerebral cortex via the thalamus [8-10] provide functional connections that can link the abnormal cerebellar anatomy to higher order cognitive control of eye movements.

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