Predictors of effects of propranolol on language & connectivity in autism

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Our purpose is to examine how markers of sympathetic reactivity predict response to propranolol in autism. Drugs that address the core features of autism are lacking. Agents that decrease NE activity in the brain have shown some benefits in language and social communication, as well as behaviors in autism. Our preliminary work has suggested that agents which decrease NE activity in the brain, such as propranolol, benefit individuals with autism in tasks that require semantic network flexibility. Furthermore, propranolol, unlike other agents under exploration for treatment of core features of autism, is available in a genereic form and is inexpensive, increasing its availablity for underserved patients. Therefore, our first specific aim is to examine the effect of propranolol in autism on a range of language tasks, and to determine who is most likely to respond, examine whether this response is predicted by sympathetic reactivity as indicated by Galvanic skin response and heart rate variability. We will accomplish this by performing cognitive testing on an off propranolol in patients with autism, and determine whether sympathetic reactivity predicts the response to drug. Also, since recent research has demonstrated that the interaction between activated brain regions is decreased in autism, as measured by functional connectivity MRI (fcMRI), we will begin to explore the effect of propranolol on fcMRI. We will accomplish this by examining fcMRI during task performance on and off propranolol in patients wih autism, and determine whether sypmathetic reactivity predicts connectivity response to drug. In our first experiment, funded by NAAR, we showed an increase in connectivity on a word categorization task with propranolol. Therefore, our second sepcific aim is to compare the effect of propranolol on functional connectivity in autism patients with high and low sypathetic reactivity as assessed by Galvanic skin response and heart rate variability. Our hypothesis is that functional connectivity and language will improve more with propranolol in patients with the highest degree of sympathetic reactivity. Our long term goal is to utilize these studies to help to develop future cost-effective, rational pharmacotherapy to help in the treatment of individuals with autism, which can be optimized on an individual basis.

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