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Representation of internal models of action in the autistic brain

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Abstract

Children with autism spectrum disorder (ASD) exhibit deficits in motor control, imitation, and social function. Does a dysfunction in the neural basis of representing internal models of action contribute to these problems? We measured patterns of generalization as children learned to control a novel tool and found that the autistic brain built a stronger than normal association between self generated motor commands and proprioceptive feedback; furthermore, the greater the reliance on proprioception, the greater the child's impairments in social function and imitation.

Theory suggests that in learning to perform a movement, the brain builds an association between motor commands and sensory feedback. These internal models allow the brain to predict the sensory consequences of self-generated motor commands, and produce motor commands that maximize expected rewards at a minimum effort 1. Children with autism exhibit impairments in motor control 2 and imitation 3. Is there a fundamental difference in how these children build associations between their motor commands and sensory feedback?

Generalization is a signature of the activation fields of neurons with which the brain forms an internal model 4. To quantify the representation of internal models in the autistic brain, we measured patterns of generalization as autistic children learned to control a novel tool. 14 children with ASD (age 10.5±1.7) and 13 typically developing (TD) children (age 10.4±1.8) played a game in which they held a robotic arm in hand and reached in order to capture animals that had escaped from a zoo (see supplementary information). The robot perturbed the children's arm movements by producing a force field, and the children learned to control the tool so to capture the animals. In this task, the TD brain builds an association between self-generated motor commands and the sensory consequences (visual and proprioceptive). The strength of each association can be inferred by how the brain generalizes the learning from the trained movements to novel movements. The training took place in the left workspace (Fig. 1a, target 1) while a velocity dependent field pushed their hand perpendicular to the direction of motion. We quantified generalization in the right workspace in the intrinsic coordinates of the arm (target 3, identical joint rotations as compared to target 1), and in the extrinsic coordinates of the task (target 2, identical hand motion as compared to target 1). Movements to targets 2 and 3 were always in 'error-clamp' trials, trials in which the robot produced a channel that artificially eliminated movement errors but allowed us to measure force output at the hand.

In the baseline period in which no perturbations were present, both ASD and TD groups produced straight reaching movements (Fig. 1b). Upon presentation of the field, hand trajectory was perturbed (Fig. 1b) and with training the lateral deviations declined (Fig 1c), indicating comparable learning rates ($F(1,979)=1.8$, $p=0.20$). In randomly selected trials, an error-clamp was presented. We quantified the amount of adaptation/generalization on each error-clamp trial by computing the ratio of the peak lateral force produced by the child and the ideal force required for compensation on that trial (Fig. 1d). The three targets were presented randomly. Whereas for target 1, six out of 96 trials were error-clamp, for other targets all trials were error-clamp. Therefore, for targets 2 and 3 the children were never trained in a force field and never experienced error. This design allowed us to simultaneously assay learning and generalization.

Fig. 1d plots the adaptation index for each target direction during the error-clamp trials. The average of the first five trials in the test block was used as a measure of generalization (Fig. 1e). Superficially, the learning appeared normal in autism: performance for target 1 was indistinguishable from TD both at the last trial of learning ($p=0.18$) and the test trials ($p=0.94$). However, the generalization patterns were strikingly different ($F(1,25)= 15$, $p<0.001$, interaction between group and target direction): TD generalized to the right workspace both in intrinsic ($p<0.001$) and extrinsic ($p=0.003$) coordinates, whereas ASD generalized only in intrinsic coordinates ($p<0.0001$) and not in extrinsic coordinates ($p=0.30$). Furthermore, ASD generalized about twice as strong as TD in intrinsic coordinates (Bonferroni post hoc t-test, $p=0.0017$), reflecting a much stronger than normal association between motor commands and proprioceptive feedback 5.

In this task, the neurons that participate in representing the internal model include cells in the primary motor cortex (M1) 6, as well as the premotor cortex 7. These cells have distinct activation fields and axonal connectivity. Activation fields of M1 cells tends to be in the intrinsic coordinates of joints and muscles 8, and these cells are strongly connected to the adjacent somatosensory cortex. In contrast, activation fields of premotor cells tend to be in the extrinsic coordinates of the task 9, and the cells have dense long-range connections to the posterior parietal cortex. In the TD brain, reach adaptation produced generalization in both coordinate systems, consistent with a representation that engaged both the short-range connections of the primary motor/somatosensory regions, and the long-range connections of the premotor/posterior parietal regions. However, in the ASD brain there is an overgrowth of localized cortical connections 10 with increased white matter volume in M1 that predicts motor impairment 11. Our results here suggest that one consequence of this anatomical mis-wiring in the ASD brain is a representation of internal models that place an unusually strong reliance on proprioception.

When we observe another person performing a movement, the internal models to execute the same movement may also be activated in our brain 12. A strong prediction of this idea is that if the person that we are watching makes errors, those errors should help teach our own internal model. Indeed, after volunteers observe another person reach while holding a robot that is producing a force field, they perform better than naive if they are tested on the same field 13. This is consistent with the hypothesis that observation of an action instantiates the same internal models that are required for production of that action. However, because this instantiation relies on visual cues, internal models that place a greater than normal reliance on proprioception while discounting visual consequences might place the observer at a significant disadvantage in understanding other people's actions and imitating their movements. To test our hypothesis, we looked for correlations between how the children represented our simple reaching task and clinical measures of motor, imitation, and social function.

We found that the greater the proprioceptive-driven generalization in our task, the greater the impairments in general motor function, social interaction, and imitation/praxis.For example, on the Autism Diagnostic Observation Schedule G (ADOS-G) Module 3, a standardized observational assessment of social, communicative, and stereotyped behaviors in children with ASD, we found that greater Reciprocal Social Interaction scores (indicative of greater social impairment) were associated with greater proprioceptive generalization (R=0.572, p=0.032, Fig. 2a). The Total T Score from the Social Responsiveness survey, a questionnaire that is administered to the parents and inquires about the child's social interactions in naturalistic settings, was similarly correlated with proprioceptive generalization (R =0.586, p=0.003, Fig. 2b). We also found that the greater the proprioceptive-driven generalization, the greater the impairment in clinical measures of basic motor skill function (R=0.577, p=0.004), as measured using the total score from the Revised Physical and Neurological Examination of Subtle Signs.

We next asked whether the patterns of generalization were related to the ability of the children to imitate movements. Imitation was quantified by asking the children to reproduce movements of an examiner 14 –some meaningful gestures (pretending to use a key in a lock), and others non-meaningful (tapping of right hand on the left forearm three times). The exam was videotaped and analyzed to score each trial as correct or incorrect. As expected, children with ASD were impaired in imitation as compared to the TD group (p<0.01). However, the greater the internal model's relative reliance on the intrinsic coordinates of movements (generalization to target 3 minus target 2), the greater the impairment in imitation (R=−0.57, p=0.006, Fig. 2c).

Finally, we asked whether the patterns of generalization were also related to the ability of the children to perform skilled movements in response to verbal commands and with common tools (i.e., praxis) 14. Gestures to command were assessed by verbally asking the child to perform transitive ("Show me how you brush your teeth") and intransitive ("Show me how you salute") actions. Tool use was assessed by giving the child a tool (e.g., a comb) and asking her/him to show how to use it. Consistent with previous findings 14, 15, children with ASD were impaired in performance of gestures to command (p<0.01) and tool use (p<0.01). Furthermore, the greater the internal model's relative reliance on the intrinsic coordinates of movements (generalization to target 3 minus target 2), the greater the impairment in the ability to perform gestures to command (R=−0.544, p=0.009) and to use common tools (R=−0.551, p=0.008).

Our findings demonstrate that when ASD children learn a motor task, the internal models that they form place a stronger than normal association between the self-generated motor commands with proprioception. This suggests a greater than normal dependence on cortical regions where movements are represented in intrinsic coordinates of motion (M1, somatosensory cortex), and less dependence on regions where movements are represented in extrinsic coordinates (premotor, posterior parietal). A stronger than normal association between motor commands and proprioceptive feedback may be a consequence of the fact that M1 and somatosensory cortex are nearby cortical regions, and in ASD the short-range cortical connections are over-expressed 10.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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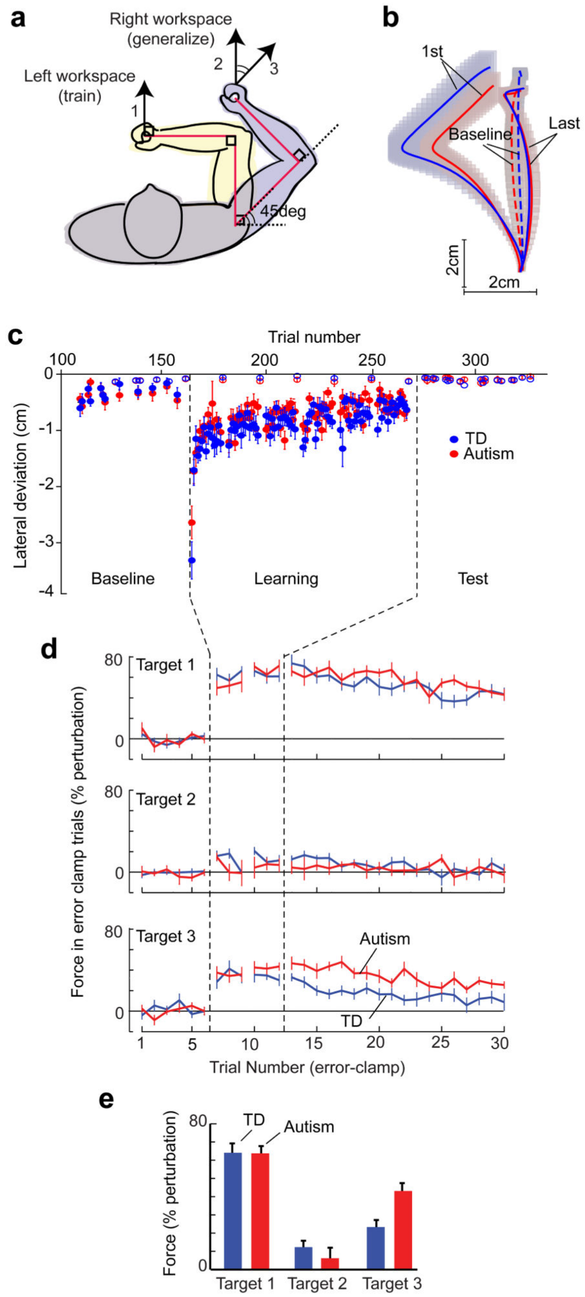

Figure 1.

(a) Children held the handle of a robotic arm and played a game in which the objective was to capture animals that had escaped from a zoo. At the start of the trial, the robot moved the child's arm to a starting posture. Next, an animal would appear at the target location (8 cm). If the child could reach the target in time (0.5 ± 0.05s), the animal would be captured and the child was given points which later could be traded in for a prize. The robot produced a velocity dependent curl force field. Learning took place in the left posture (T1) and generalization was quantified in the right posture (T2, identical joint motion as T1; T3, identical hand motion as T1). The target sequence was random. Study was approved by the local IRB. Written consent was obtained from a parent/guardian and written assent was obtained from the children. **(b)** Across subject mean ± SEM hand paths during the last trial of the baseline block and the first and last trials of the learning block. Red lines are for autistic children. **(c)** Movement error mean ± SEM for T1, as quantified through maximum lateral hand deviation; negative value indicates hand deviation to the left. The filled circles indicate trials in which the robot perturbed the hand and the unfilled circles indicate error-clamp trials. **(d)** In error-clamp trials, the robot produced a channel from the start position to the target, essentially eliminating movement errors. We measured the force that the child produced against the channel walls. **(e)** The average of force in the first five error-clamp trials in the test block.

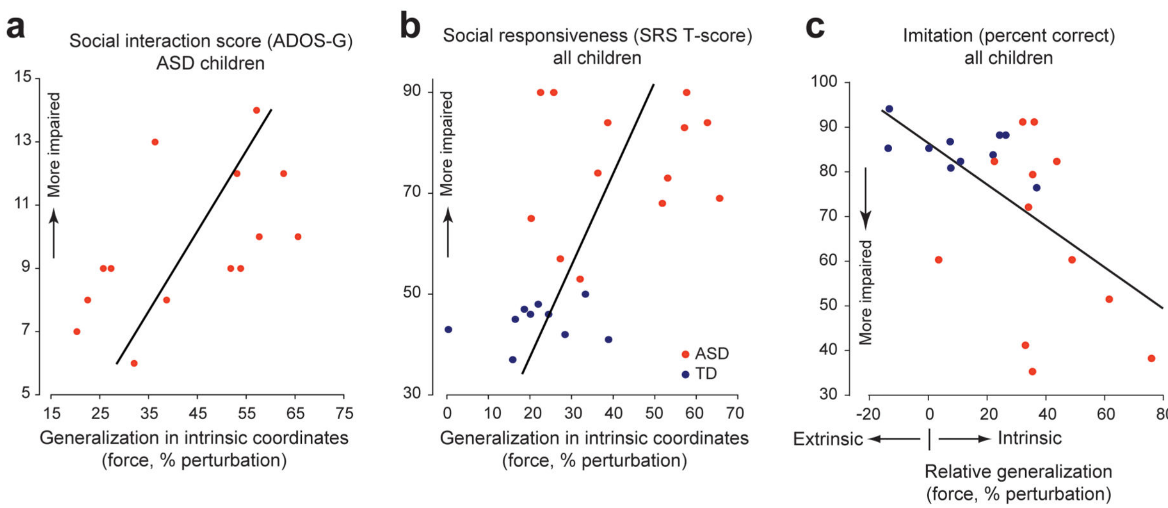

Figure 2.

(a) Autism Diagnostic Observation Schedule is a standardized interview and observational assessment of social, communicative, and stereotyped behaviors used for diagnosis of autism. The x-axis represents the force produced for T3. **(b)** The Social Responsiveness Scale, a measure of social anxiety/avoidance in naturalistic settings, was scored for most of the TD (10/13) and ASD (13/14) children. **(c)** Imitation was measured by asking the child to reproduce a sequence of 36 actions (performed one at a time), some meaningful and others meaningless 14. The x-axis represents the force produced during the test of generalization (T3 minus T2).