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Atypical Learning in Autism Spectrum Disorders: A Functional Magnetic Resonance Imaging Study of Transitive Inference

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Abstract

Objective—To investigate the neural mechanisms underlying impairments in generalizing learning shown by adolescents with autism spectrum disorder (ASD).

Method—Twenty-one high-functioning individuals with ASD aged 12–18 years, and 23 gender, IQ, and age-matched adolescents with typical development (TYP) completed a transitive inference (TI) task implemented using rapid event-related functional magnetic resonance imaging (fMRI). They were trained on overlapping pairs in a stimulus hierarchy of colored ovals where A>B>C>D>E>F and then tested on generalizing this training to new stimulus pairings (AF, BD, BE) in a "Big Game." Whole-brain univariate, region of interest, and functional connectivity analyses were used.

Results—During training, TYP exhibited increased recruitment of the prefrontal cortex (PFC), while the group with ASD showed greater functional connectivity between the PFC and the anterior cingulate cortex (ACC). Both groups recruited the hippocampus and caudate comparably; however, functional connectivity between these regions was positively associated with TI performance for only the group with ASD. During the Big Game, TYP showed greater recruitment

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Authors' contributions: Dr. Solomon designed the study, oversaw all aspects of data collection and analysis, and wrote the manuscript. Drs. Carter, Ragland, Frank, Niendam, and Lesh, and Mr. Beck and Mr. Matter made substantial contributions to study design, data analysis, and interpretation. All co-authors read all drafts of the manuscript, and approved the final version.

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of the PFC, parietal cortex, and the ACC. Recruitment of these regions increased with age in the group with ASD.

Conclusion—During TI, TYP recruited cognitive control-related brain regions implicated in mature problem solving/reasoning including the PFC, parietal cortex, and ACC, while the group with ASD showed functional connectivity of the hippocampus and the caudate that was associated with task performance. Failure to reliably engage cognitive control-related brain regions may produce less integrated flexible learning in those with ASD unless they are provided with task support that in essence provides them with cognitive control, but this pattern may normalize with age.

Keywords

learning; fMRI; adolescents; reasoning; problem solving

INTRODUCTION

Individuals with autism spectrum disorders (ASD) learn facts, details, and routines [1–6] relatively well but exhibit impairments in generalizing learning from one context to another [7,8]. This situation-focused learning profile may help explain their characteristic behavioral inflexibility [9], which has a profound impact on their academic, social, and adaptive functioning.

Transitive inference (TI) is a form of relational reasoning where training on adjacent pairs in a hierarchy in which A>B>C>D>E>F produces generalization in the form of associations between untrained novel pairs (e.g. B>D, B>E, and A>F). Extensive rodent [10,11], non-human primate [12], computational modeling, and human neuroimaging literature about the hippocampus [13–16], the striatum [17], and the PFC [18–21] have advanced understanding of the neural substrates of this form of generalization, leading to the development of several mechanistic models that can be used to derive testable hypotheses[22].

One of these mechanistic models suggests that TI is the result of conjunctive encoding by the hippocampus, which is thought to store memories of elements of different experiences and to flexibly compare and recombine them to permit generalization of learning [22,23]. A second one of these models suggests that TI emerges due to the development of associative strength-based reinforcement histories of stimuli, meaning that stimuli that are more frequently reinforced develop stronger memory traces that support inferences based on their relative values [24–26]. Such reward-based working memories are thought to be produced by the act of interworking of the striatum [27,28] and the prefrontal cortex (PFC)[20,29–34]. The formation of a U-shaped serial position curve, whereby the outer end-item pairs, which have higher relative values, show greater accuracy, has been taken as evidence for this view. [35,36] The more explicit and hippocampally-mediated learning suggested by the first model and the more striatally-mediated learning suggested by the second one are thought to be competitive[35,37] in that they cannot occur simultaneously.

Findings of a recent behavioral study of TI suggest that young adults with ASD are poorer at the generalization of learning assessed by TI, and may rely on a strategy involving

conjunctive representations by the hippocampus with less evidence of the beneficial influences of striatally mediated associative strengths governing typical behavior [38]. The goal of the current study was to test this hypothesis using functional magnetic resonance imaging (fMRI) in adolescents with ASD and TYP. We predicted that the group with ASD would perform more poorly than TYP and use a conjunctive strategy evidenced by greater hippocampal involvement, whereas the TYP group would use a more associative strategy as evidenced by greater prefrontal, parietal, and striatal recruitment and functional connectivity. Finally, we predicted that both groups would show a lack of simultaneous hippocampal and striatal recruitment with no functional connectivity between these regions, given that the neural substrates of conjunctive versus associative learning are thought to operate competitively [35,37].

METHOD

Participants

Thirty individuals with ASD and 27 typically developing individuals were recruited through psychiatrists, psychologists, speech and language pathologists, advocacy groups, state-funded centers for persons with developmental disabilities, and MIND Institute's Subject Tracking System database and were enrolled in the study. The groups were matched for age, gender, and IQ. One individual with ASD was removed due to less than chance performance during training. Four individuals with ASD and 2 with TYP were excluded because they showed root mean square motion (RMS) greater than 1mm. None were outliers based on percent signal change (as calculated by the art_groupoutlier function from the ArtRepair toolbox [http://cibsr.stanford.edu/tools/human-brain-project/artrepair-software.html] for SPM8). Two additional individuals with TYP were excluded because their IQs were greater than 2 standard deviations above the mean. Four with ASD were excluded because their IQ scores were at the very low end of the borderline range and produced a sample unmatched on IQ. The final sample included 21 adolescents with ASD (mean age = 15 years; SD = 1.9; range = 12.2–17.9) and 23 with typical development (mean age = 14.8 years; SD = 1.9; range = 12.3–17.8), who were matched on age, gender, RMS motion, and IQ. Four to five women were enrolled in each group [39]. See Table 1.

All participants had a Full Scale IQ > 70 on the Wechsler Abbreviated Scales of Intelligence [40]. Participants with ASD had scores in the autism spectrum range on the Autism Diagnostic Observation Schedule-2 [41] (ADOS-2), the Social Communication Questionnaire[42] (SCQ), and met diagnostic criteria based on a checklist of items from the *DSM-5* [43]. Exclusion criteria for participants with ASD included diagnoses with known genetic etiologies, and current parent-reported diagnoses of depression, anxiety disorders, or psychosis. Participants taking antipsychotic medications were excluded. The 1 participant taking psychostimulants (from the group with ASD) was asked to stop for 48 hours prior to the study. All other participants were psychotrophic medication free. After receiving a complete description, parents of all participants gave written consent, and their minor children gave assent to participate in the study, which was approved by the University of California, Davis Institutional Review Board.

Measures

Descriptions of standard measures used to diagnose ASD are included in Supplement 1, available online.

Ovals TI Task [44] was adapted from Townsend, Richmond, Vogel-Farley, and Thomas (2010) [45]. Participants were trained on a hierarchy of six colored ovals where (A>B>C>D>E>F) through presentations of 5 "premise" or trained pairs (AB, BC, CD, DE, EF; see Figure 1[a]). After two training sessions, TI was tested through the presentation of 3 novel inference pairs (BD, BE, AF) without feedback during a "Big Game". See Figure 1(b). Timing for the task is shown in Figure 1(c). Jittering schedules were devised using Optseq [46] and ranged between 2–4 s for the inter-stimulus interval (ISI) and 2–8.5 seconds for the inter-trial interval (ITI). See Figure 2. As more thoroughly described in Supplement 1, available online, the task was designed to optimize participant performance. We used the social stories technique that provided participants with simple scripts about events they would encounter during testing; a graphic representation of the entire task with an indication of where the participant was in the task at that point; frequent positive performance updates; and prizes for good performance. Upon task completion, participants we assessed for awareness of the hierarchy (the percentage of stimuli for which the correct position in the hierarchy was reported) as awareness can be an important contributor to performance [24,47,48]. A chi-square test of independence was conducted and revealed no significant difference in awareness between the ASD and TYP group ($X^2 = 7.27$, $p = .201$). Only participants with better than chance performance after training session 2 were retained (1 participant with ASD was excluded).

Behavioral Data Analysis

To account for the repeated nature of the behavioral data in training sessions as well as for the heterogeneity of variances across block, pairs, and diagnoses, between group differences in stimulus pair accuracy was examined using linear mixed models implemented in SAS. Data was transformed using a square root transformation to better approximate a normal distribution.

fMRI Analyses

Information about imaging data acquisition and preprocessing can be found in Supplement 1, available online.

Imaging Data Analysis—We first report whole brain analyses followed by region of interest (ROI) and functional connectivity analyses. In the whole brain analysis, at the first level, regressors were included for each run and each pair type for both training sessions 1 and 2. Two sets of 2-way analyses of variance (ANOVAs) were performed at the second level, which included contrast images of the stimulus or feedback phase as dependent variables, both versus implicit baseline. For both ANOVAs, the between-subject factor was diagnosis, and the within-subjects factor was block. Since the structure of the task during training and test was not parallel (i.e. there was no feedback in the Big Game), we separately examined group inference pair performance during the Big Game using the same approach. Although the groups were matched, given the significant cognitive development occurring

during adolescence, we used age as a covariate. We report all positive effects. Analyses of both the stimulus and feedback epochs included only correct trials to ensure that group comparisons include only trials where participants are engaged in the task as recommended by best practice parameters [49,50]. There were no between group differences in numbers of trials included in analyses ($t(42) = 0.91$, $p = .37$). We thresholded random effects analyses at a voxel-wise height threshold of $t = 3.19$ for a $p < .001$ and report clusters that are Family-wise error-corrected (FWE) at $p < .05$ across the whole brain based on recent recommendations for cluster-extent – based thresholding [51]. Given that our task did not utilize an implicit baseline, to give us greater confidence that our task was assessing TI learning, versus lower level cognitive processes, we constructed Bayesian state-space learning curves for each phase of the task for each individual participant, which were used as parametric modulators in the general linear model (GLM). See Supplement 1, available online, for within-group analyses, which demonstrate that our task captured higher level learning processes in both groups.

To test hypotheses about the hippocampus and the caudate, we employed ROI and functional connectivity analyses. We produced unbiased bilateral ROIs using the AAL Atlas [52] for both the hippocampus (546 voxels) and the caudate (546 voxels). Parameter estimates extracted from these regions during the feedback phases of the task were subjected to t-tests and correlations with Bonferroni correction.

To test hypotheses about functional connectivity with other brain regions, we used cognitive control related seed regions in the PFC, ACC, and parietal cortex, and the putamen, for which there were group differences in whole-brain analyses during training sessions 1 and 2, and/or the Big Game. These functional seeds were prepared by using a 5mm sphere around the peak of each seed (Brodmann area [BA]40 [−48 −37 31], BA9 [−30 20 40] BA24 [−6 −19 46]). Functional connectivity analyses were conducted using the beta series correlation method [53] with custom-written Matlab [54] scripts. See Supplement 1, available online, for a more extensive discussion of this method and motion scrubbing [55,56].

RESULTS

Behavioral Results

There were significant fixed effects of session ($F(1,42) = 19.07$, $p < .001$); individual pair type ($F(1,284) = 71.35$, $p < .001$); and a session by individual pair type interaction ($F(1,284) = 67.90$, $p < .001$). However, there were no significant interactions with diagnosis. Mean accuracy rates for both groups were lower in the second, more challenging, session where trials were presented in a mixed versus sequential order. Overall, performance on end item pairs was better. The session by pair type interaction was driven by the fact that accuracy rates for inner pairs during the second session were significantly different from those in the first session ($t(81.5) = 8.21$, $p < .001$), whereas this was not the case for the outer pairs ($(t) = 1.52$, $p=.13$), suggesting that both groups showed a more characteristic U-shaped serial position curve whereby outer pair (AB, EF) accuracy was higher than inner pair accuracy (BC, CD, DE) by the second training session. This pattern is characteristic of associative learning.[35,37] During the Big Game, Student's t-tests showed there were no group differences in premise or inference pair performance (all p's > .3). However, for the group

with ASD, there was a significant negative correlation between inference performance and SCQ scores that remained after co-varying age (r = −.60, p = .004).

Whole-Brain Analyses

A 2×2 ANOVA was conducted using age in months as a covariate to investigate neural recruitment during the stimulus phase of training sessions 1 and 2, which revealed a positive effect of the task in both groups involving recruitment of regions involved in relational reasoning[19] including bilateral cerebellum ([−24, −64, −17], [−36, −49, −32], and [27, −70, -17]); right occipito-temporal cortex (RBA 37 [42, −67, −2]; left ACC (BA 32 [−3, 5, 43]); and left premotor regions (BA 4 [−39, −25, 64] and [−30 −28 70]). Consistent with our hypothesis, there was a main effect of diagnosis such that the TYP group showed greater recruitment of the left dorsolateral PFC (BA 9 [−30, 20, 40]. They also showed greater recruitment in left sensory cortex (BA 2 [−54,-31,37]). See Figure 3 and Table S1, available online.

A second 2×2 ANOVA using age as a covariate was conducted to investigate neural recruitment in the feedback phase of training sessions 1 and 2, which revealed a positive effect of task, with both groups showing elevated activity in the body of the caudate bilaterally ([−18, −10, 31], [18, 17, 19]), and in the right tail of the caudate ([24, −43, 16]). There were no significant group differences or interactions in the feedback phase.

During the Big Game, there was greater recruitment of the left inferior lateral parietal lobe (BA40 [−48 −37 31]), the left anterior cingulate (BA24 [−6 −19 46]), and the left putamen ([−27 −13 1]) in the TYP group with no other significant main effects or interactions. There was also an effect of age in the group with ASD revealing greater recruitment of the right dorsolateral PFC (RBA9 [24 32 28]), the bilateral posterior cingulate (RBA31 [15 −64 16], LBA31[−6 −28 40], [0 −37 40], [0 −19 46], RBA23[6 −61 16]), the bilateral extrastriate cortex (RBA19[36 −79 22], [36 −79 13], LBA19[−36 −82 19]), the left anterior cingulate (LBA32[−3 44 16], [0 35 22], LBA24[−6 11 31]), the left superior temporal sulcus (LBA39[−45 −52 7]), the left superior temporal gyrus(LBA22[−51 −61 16]), and the anterior portion of the right premotor cortex (RBA8[24 35 43], [18 38 52]).

ROI Analyses

Counter to hypotheses, ANOVAs using parameter estimates averaged over the hippocampal ROI showed there were no significant group differences in the recruitment of the hippocampus throughout training (all p's > .14). There also were strong positive associations between recruitment of the hippocampus and the caudate for both groups (ASD: r =.651, p=. 001; TYP: r =.455, p=.003) during training. See Figure 4.

Functional Connectivity Analyses

There were no group differences in the whole-brain functional connectivity analyses conducted with the bilateral Atlas-derived seeds in the hippocampus and caudate. During the feedback phase of Training Block 2, there was greater functional connectivity in the ASD versus the TYP group between the left dorsolateral PFC seed (BA9 [−30, 20, 40], BA 8 [24, 14, 40]), and the dorsal ACC (BA 32 [18, 8, 49]). There were no significant differences for

the PFC, parietal cortex, and ACC, derived from areas of group difference in whole-brain analyses for training sessions 1 and 2 and the Big Game.

Brain Function and Big Game Performance

An ANOVA was conducted to examine the effects of hippocampus and caudate functional connectivity on task performance in individuals with ASD and TYP. While there were no main effects of functional connectivity strength or group, there was a significant interaction of functional connectivity strength and group ($F(1,40)=12.06$, $p=.001$). Functional connectivity between the hippocampus and the caudate during training was positively associated with Big Game performance for the group with ASD, and negatively associated with performance for TYP at a trend level (ASD: $r = .645$ $p = .001$; TYP: $r = -.347$, $p = .105$). See Figure 4.

DISCUSSION

We used fMRI and a newly adapted child and ASD-friendly TI paradigm to investigate whether the neural substrates of learning in adolescents with ASD and TYP was more consistent with a conjunctive or an associative learning strategy. Contrary to hypotheses, the group with ASD showed comparable task performance to TYP, and incorporated elements of both conjunctive and associative learning strategies when completing the task. Supportive of the contention that they used associative learning, the group with ASD showed a U-shaped serial position curve by the end of training and recruitment of the striatum during feedback processing that was comparable to TYP. Furthermore, they exhibited functional connectivity between the hippocampus and the caudate that was positively associated with Big Game performance. The TYP group also evidenced associative learning in their recruitment of the caudate during feedback processing. However, compared to individuals with ASD, they showed greater recruitment of cognitive control-related brain regions in the PFC, parietal cortex, and ACC during learning and the Big Game. The group with ASD appeared to “catch up” to TYP in their recruitment of these brain regions during the BIG Game. Unexpectedly, there also was strong functional connectivity between the hippocampus and caudate during learning in both groups, although it was positively associated with task performance in those with ASD and negatively associated with performance in those with TYP.

As is commonly found in studies of individuals with ASD [57], affected adolescents used alternative task strategies. Recently, it has been suggested that when the PFC cannot be brought online “proactively” to sustain task-based working memories due to patients’ cognitive control deficits [58,59], they may engage in a less efficient strategy where rules and task memories are retrieved from the hippocampus “reactively” on a trial-by-trial basis engendering greater response conflict involving the ACC [60]. Findings of the current study for the group with ASD (reductions in PFC recruitment during training; greater PFC/ACC functional connectivity; and the relationship between hippocampal connectivity and Big Game performance) are reminiscent of this pattern. Interestingly, the lack of group differences in the training session feedback phase suggests that those with ASD are able to process feedback comparably to TYP, and that it is the inability to represent, versus process

this feedback, that is impaired in ASD. Perhaps because the participants with ASD relied more on hippocampal conjunctive encoding during learning, the extent to which they made successful inferences depended on additional connectivity of the hippocampus with the caudate, allowing their associative learning abilities to contribute to TI performance. In fact, the prevailing view is that implicit learning, which is reliant on the striatum, is relatively intact in ASD [38,61,62] (but see [63–65] for examples showing impairments in learning related to motor tasks and to [6] for a study showing slower implicit learning). Recently, it also has been suggested that the hippocampus and the caudate interact cooperatively during spatial information processing such as that involved in conceptualizing a stimulus hierarchy [66,67], especially in cases where environments share elements like the hierarchy we employed [68]. This raises the possibility that such spatial information processing mechanisms may be used by those with ASD to compensate for PFC impairments.

While hypotheses about the TYP group were not entirely confirmed, the brain regions used by this group were consistent with reasoning/problem solving research that views TI as a form of deductive reasoning subserved by a network that also includes occipital, parietal, temporal, and anterior prefrontal regions, in addition to the striatum [69]. According to this view, occipito-temporal cortex and visual cortical brain regions permit premise pair processing, with information integration recruiting the PFC and the ACC [19].

Previously our group found interesting group differences in performance on end-item pairs[38] that were not replicated in the current study. This may have been a consequence of the highly ASD- and child-friendly task design, which included frequent instructions and progress reports presented visually as is recommended by ASD clinical experts [70]. Few were unable to learn the task, suggesting we successfully ameliorated the generalized deficits observed in patients[71]. Another possible explanation for the failure in replication is that current study participants were adolescents versus the adults from the prior one. TYP adults may show continued cognitive development into adulthood[72], which produces performance on end item pairs that is superior to same-aged adults with ASD. While our findings of increased recruitment of the brain regions associated with mature problem solving in the group with ASD with age would argue against this interpretation, the prevalence and extent of this catch up and its relationship to behavior remain unclear.

The current study is limited in several respects. Although it met benchmarks for adequate fMRI sample size [49], recent criticisms about relatively small n's in such studies (e.g. [73]) are well-taken. Given the heterogeneity present in ASD and the variable cognitive strategies affected individuals are known to utilize, a larger study including a wider cognitive ability range would permit better exploration of potential ASD learning phenotypes. Finally, although the use of Bayesian state space learning curves in both groups provided confidence that our task assessed learning versus lower level perceptual and motor processes, it was designed without an explicit baseline condition. Future studies should include a clearer baseline and/or more trials to increase the power of learning curve-based analyses to detect group differences.

In conclusion, the current study suggests interesting directions for future research with implications for educational and psychosocial intervention. For example, studies that

manipulate the task supports provided during learning -- such as we did somewhat inadvertently with our ASD- and child-friendly new paradigm – can be used to investigate the mechanisms by which learning and problem solving in those with ASD can be made more flexible and integrative of contextual information, and the degree to which such supports attenuate group performance differences. This is consistent with both the social stories approach mentioned above, which provides students with clear and explicit scripting about what to expect and with an extensive body of work suggesting that learning and memory can be enhanced when task support is provided at the time of testing [74]. The study of the relationship between such experimental studies and real world behavior at school and other environments holds the potential to motivate new interventions that optimize learning, promote more flexible attention allocation, and improve daily adaptive functioning. Furthermore, the study was conducted as follow-up to our prior behavioral study of transitive inference, which was provocative in demonstrating that young adults with ASD showed an AE pair versus a BD pair deficit as in common in groups with psychopathology including persons with schizophrenia (e.g.[75]). Although the current study was not longitudinal, and did not include a second comparison group, it was designed as a necessary first step towards understanding the neural mechanisms underlying our provocative findings about TI in young adults with ASD, and a precursor to a larger developmental study of adolescents and young adults with ASD and schizophrenia that would investigate dissociations between the development of prefrontal and hippocampal neural mechanisms of learning and memory in these two patient groups. Such a study also could help us further investigate whether individuals with ASD increasingly recruit brain regions involved in mature problem solving as they become young adults, and whether this maturation influences the cognitive strategies they employ during daily living.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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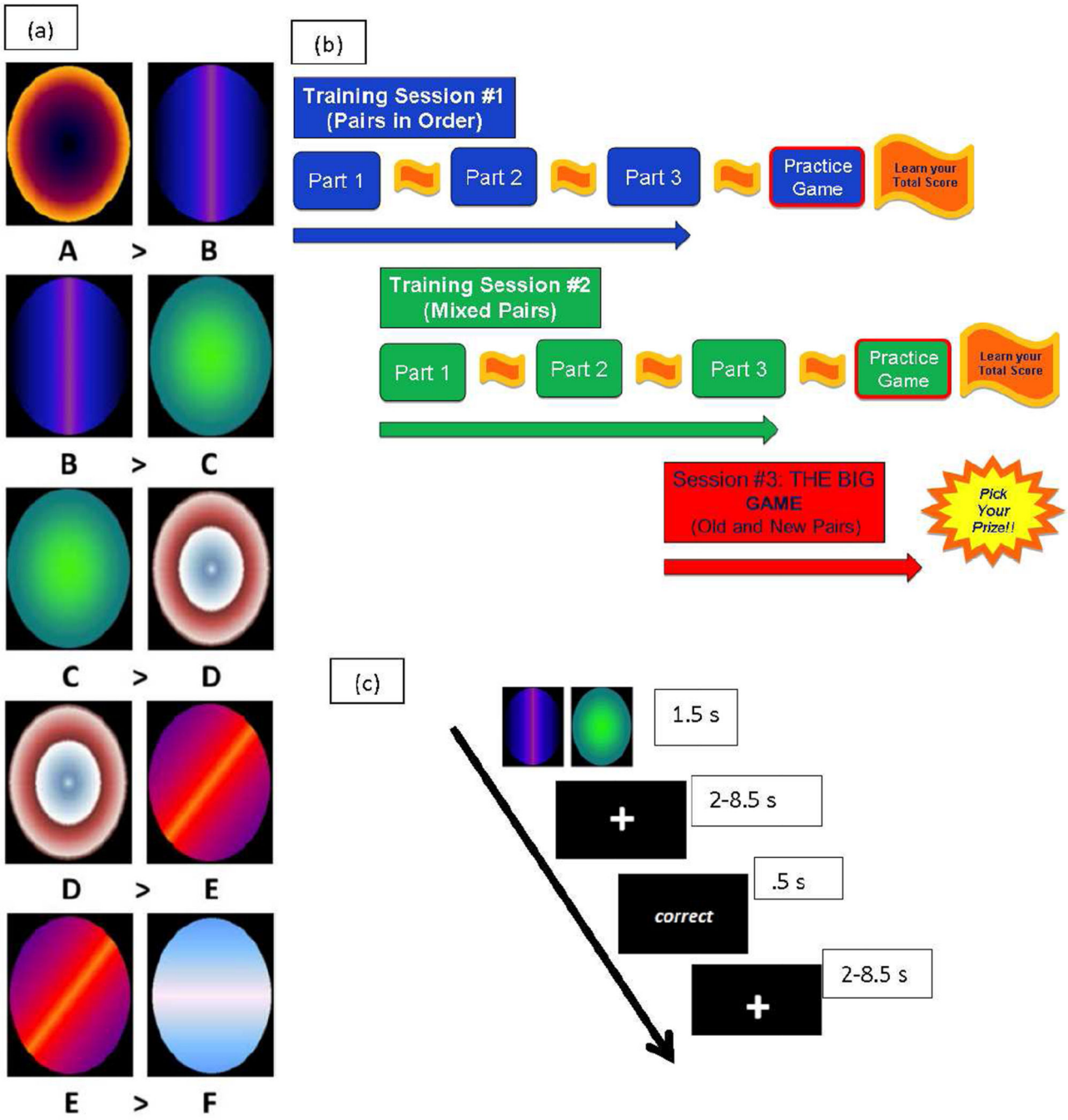

Figure 1.

Transitive inference task. (A) A 5-pair hierarchy of colored ovals is presented in the task. There were 6 different oval orders administered to reduce the potential for confounding by individual stimuli. Ovals constitute a stimulus hierarchy in which A>B>C>D>E>F. (B) Schedule shown to participants at the beginning of the task and at the beginning of training sessions 1 and 2 and the Big Game. It shows that training occurs in brief sessions after which participants are shown their performance, and that training sessions conclude with

several practice trials. It also shows that after the Big Game, participants can pick a prize based on their earnings from the task. (C) Timing of the task.

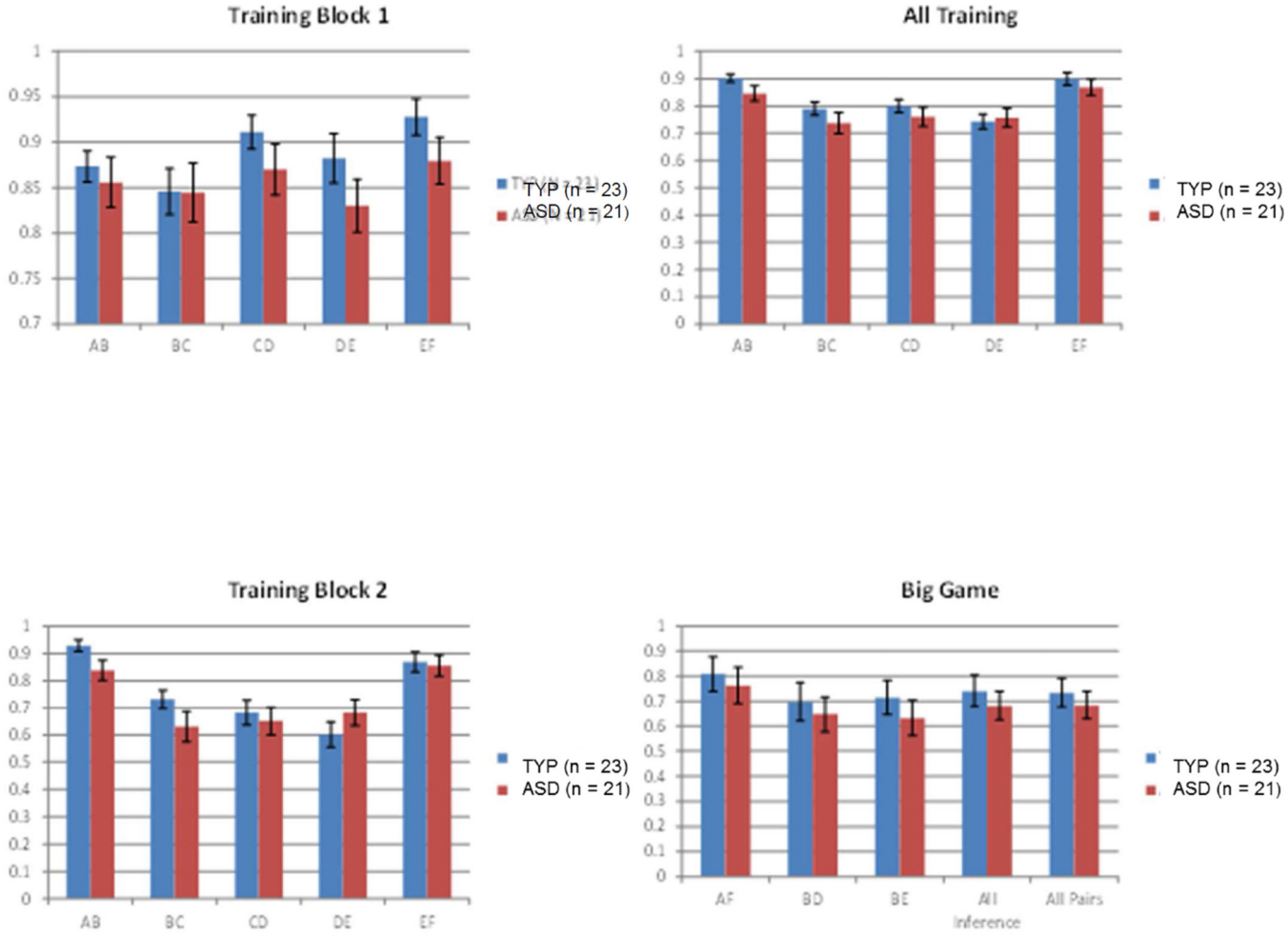

Figure 2.

Accuracy rates on the Ovals Transitive Inference Task during training and the Big Game. Note: Both groups show the formation of a serial position curve by the end of Training Block 2, suggesting they both use associative learning. There are no group differences in inference performance. ASD = autism spectrum disorder; TYP = typically developing.

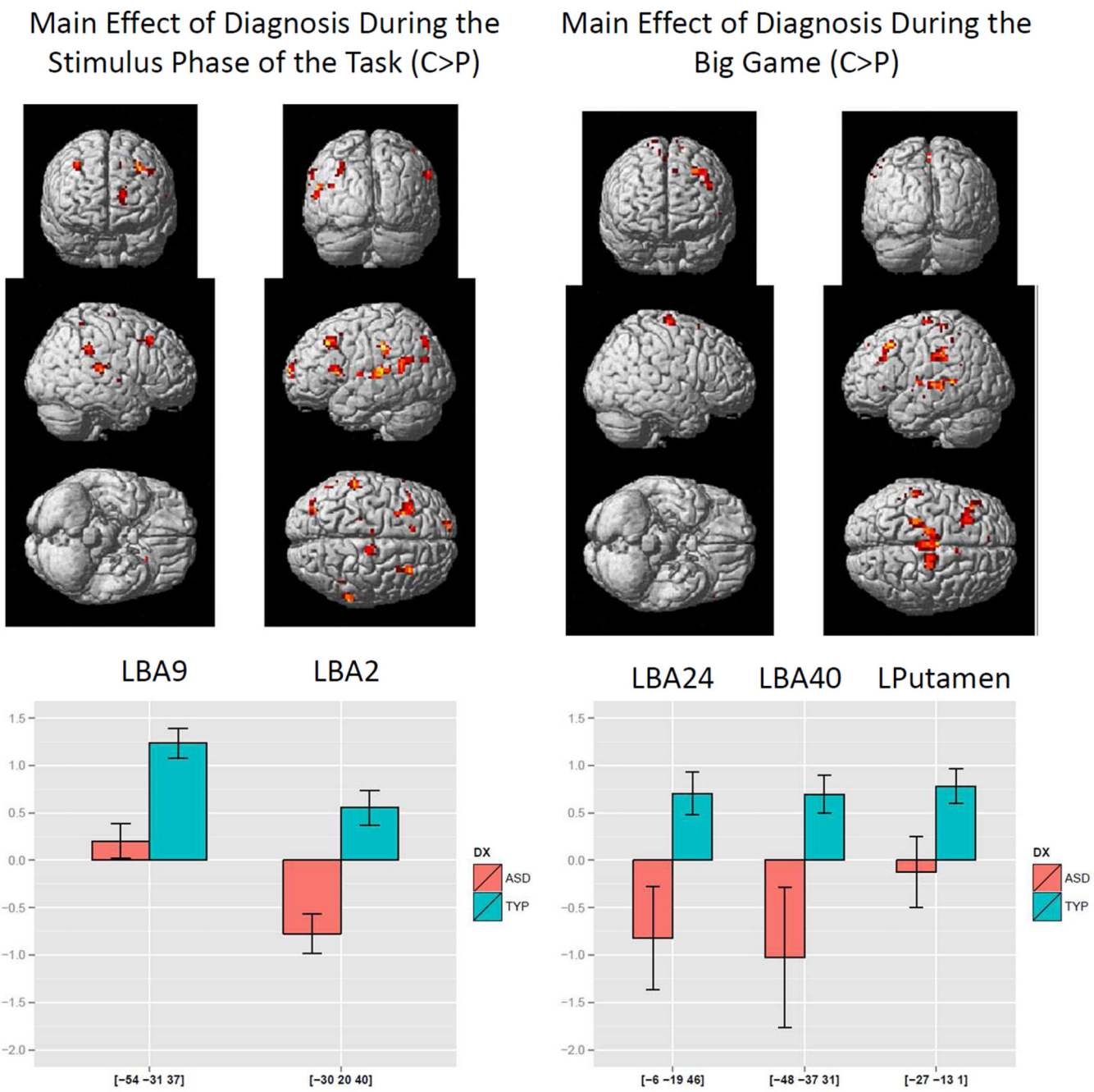

Figure 3.

Significant group differences in neural recruitment during training and the Big Game. Note: The typically developing (TYP) group shows greater activation in brain regions including the left prefrontal cortex and the left superior temporal sulcus during the stimulus phase of training than the group with autism spectrum disorder (ASD). During the Big Game, the TYP group shows greater recruitment of the posterior cingulate and pre-motor areas than the group with ASD. Both groups show activation in the caudate bilaterally during the feedback phase of training. These are not shown since there were no group differences. LBA = left Brodmann area.

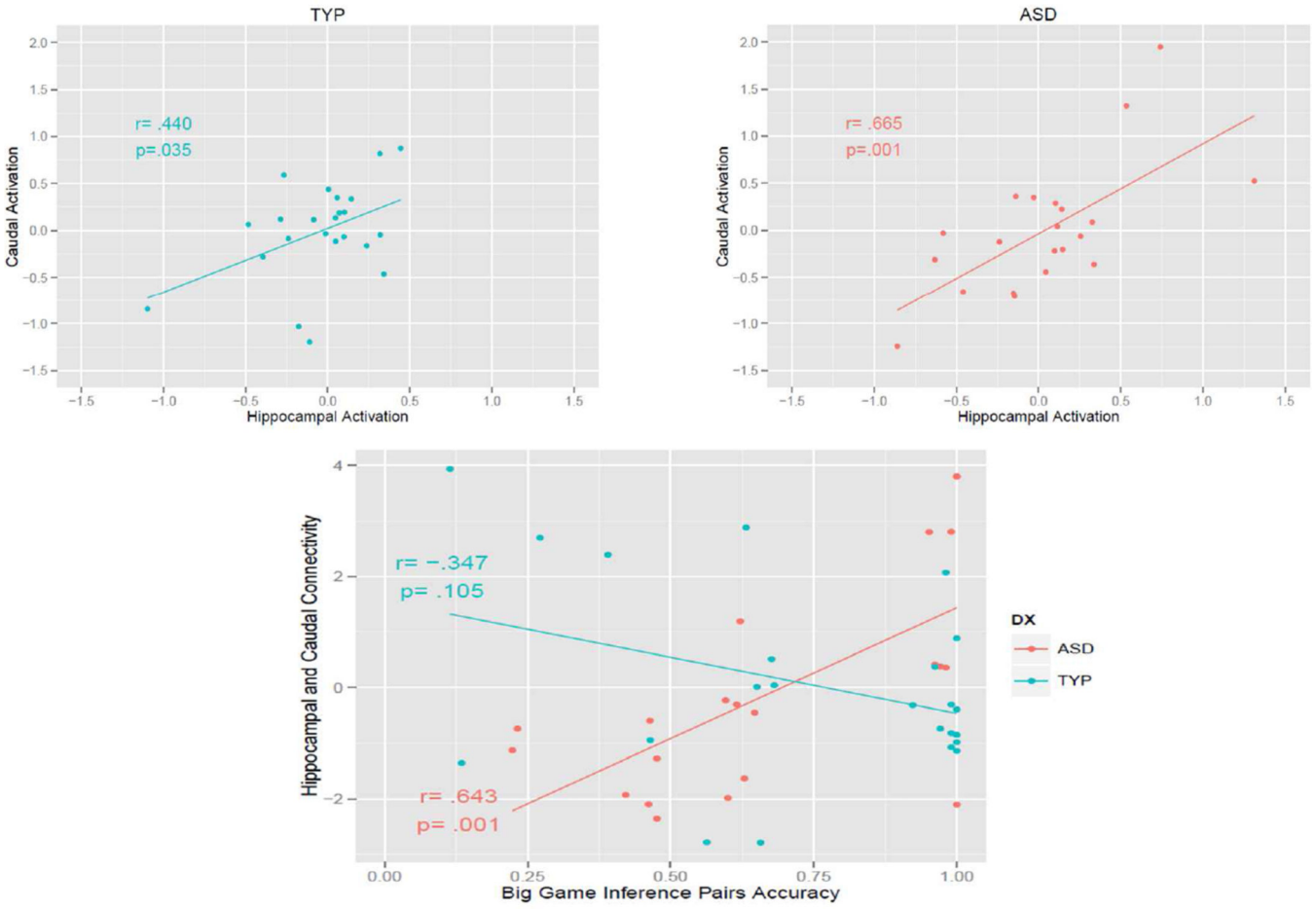

Figure 4.

Competition or cooperation between the hippocampus and the caudate. (A) Top two graphs show that neural activity in the hippocampus as operationalized by parameter estimates is positively correlated in both the autism spectrum disorder (ASD) and typically developing (TYP) groups. (B) The bottom graph shows that functional connectivity between the hippocampus and the caudate is positively related to Big Game inference performance in the group with ASD.

Table 1

Participant Characteristics

	ASD	TYP
N	21	23
Gender (M:F)	17:4	18:5
	M(SD)	M(SD)
Age (years)	15(1.9)	14.8(1.9)
FSIQ-4	100.9(14.3)	104.5(7.5)
VCI	99.9(14.5)	105.3(8.2)
PRI	103(15.9)	102.7(10.4)
ADOS	6.8(1.5)	--
ADOS: Severity	6.3(1.8)	--
SCQ	23.6(4.4)	3.3(2)
SRS	73.1(9.7)	43.4(8.2)
RMS Motion	0.36(0.23)	0.26(0.18)
Training 1	0.86(0.09)	0.89(0.06)
Training 2	0.73(0.17)	0.76(0.11)
All Pairs	0.68(0.25)	0.73(0.28)
Training 1 RT	788.35(134.63)	765.92(93.48)
Training 2 RT	848.29(155.14)	887.30(116.07)
Big Game RT	773.88(134.30)	828.19(135.75)
Awareness	0.48%(0.41%)	0.38%(0.35%)

Note: ADOS = Autism Diagnostic Observation Schedule; ASD = autism spectrum disorder; FSIQ-4 = Full Scale IQ on the Wechsler Abbreviated Scale of Intelligence (which consists of 4 subscales); PRI = Perceptual Reasoning Index; RMS = root mean square motion; RT = reaction time; SCQ = Social Communication Questionnaire; SRS = Social Responsiveness Scale; TYP = typically developing; VCI = Verbal Comprehension Index.