

Brief Reports

## Brief Report: Recognition Memory and Stimulus–Reward Associations: Indirect Support for the Role of Ventromedial Prefrontal Dysfunction in Autism

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### INTRODUCTION

Both the medial temporal lobe and ventromedial prefrontal cortex have been implicated in autism. Evidence for involvement of the medial temporal lobe is based on behavioral/neuropsychological, animal lesion, and autopsy studies (Bachevalier, 1994; Barth, Waterhouse, & Fein, 1995; Bauman & Kemper, 1994; Dawson, Meltzoff, Osterling, & Rinaldi, 1998). In previous papers (Dawson, 1996; Dawson *et al.*, 1998), we have proposed, along with other investigators, that autism involves dysfunction of parts of the medial temporal lobe (amygdala, hippocampus) and the ventromedial cortex. These brain regions, taken together, form the limbic system, which is critical for processing social and emotional information (Barbas, 1995; Brothers, 1990; Damasio, 1994; LeDoux, 1994). The purpose of this report is to provide additional data on brain function in autism and to introduce a new hypothesis regarding the role of the ventromedial prefrontal dysfunction in core impairments in autism.

In a recently published study (Dawson *et al.*, 1998), we examined the performance of young children with autism, Down syndrome, and typical development on two neuropsychological tasks: one tapping the medial temporal lobe and ventromedial prefrontal cortex (delayed nonmatching to sample; DNMS) and another tapping the dorsolateral prefrontal cortex (delayed response). Compared with Down syndrome and typically developing children, children with autism performed

significantly worse on both tasks. However, the severity of autistic symptoms was strongly and consistently correlated with performance on the DNMS task, but not the delayed response task.

Although the clinical and experimental literatures indicate that performance on the DNMS is severely affected by damage to the amygdala and hippocampus, data in monkeys have also demonstrated that performance on this task is significantly affected by damage to other brain regions, most importantly, the ventromedial prefrontal cortex (Bachevalier and Mishkin, 1986; Kowalska, Bachevalier, & Mishkin, 1991; Meunier, Bachevalier, & Mishkin, 1997). In the DNMS task, a sample object is presented and the child is encouraged to reach for the object and retrieve the reward that is under it. A delay follows, after which the familiar object is presented alongside a novel object. The correct choice is to select the novel object, that is, only the novel object is associated with a reward. Several trials involving unique objects are administered. This task requires two kinds of skills thought to be mediated by different brain regions: (1) visual object recognition memory, mediated by the medial temporal lobe (Meunier, Hadfield, Bachevalier, & Murray, 1996; Mishkin, 1978; Squire, Zola-Morgan, & Chen, 1988; Zola-Morgan, Squire, & Amaral, 1989) and (2) the ability to form rules regarding the relation between a stimulus (novel object) and a reward, mediated by the ventromedial prefrontal cortex (Bachevalier and Mishkin, 1986; Diamond, Towle, & Boyer, 1994; Kowalska, Bachevalier, & Mishkin, 1991; Meunier *et al.*, 1997). The DNMS also taps a novel preference in that the child must reach for the novel object to receive credit for a correct response.

In the present study, we addressed the question of which of these skills accounts for the poor performance

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on the DNMS by young children with autism. We did this by conducting two additional neuropsychological tests with the sample of children who were previously tested in the Dawson *et al.* (1998) study. First, for only that subgroup of children who were able to reach criterion performance on the DNMS at very short delays (indicating that they were able to acquire the rule regarding stimulus-reward associations), we evaluated whether increasing the memory demands of the task by imposing longer delays affected performance. We reasoned that, if impairments in visual recognition memory were present, the children should show increasingly impaired performance as the memory demands are increased on the DNMS. Second, using the entire sample of children who participated in the previous study, we examined whether children with autism have difficulty on a task that selectively tests object recognition memory and novelty preference, the Paired Comparison Task, which does not require establishing a rule regarding stimulus-reward associations (Diamond, 1995).

## METHOD

### Participants

Three groups of children participated in the study, all of whom participated in the Dawson *et al.* (1998) study: 20 children with Autistic Disorder ( $N = 13$ ) or Pervasive Developmental Disorder - Not Otherwise Specified (PDD.NOS) ( $N = 7$ ) (hereafter referred to as the autism group); 19 children with Down syndrome;

and 20 children with typical development. Descriptive statistics on the participants are shown in Table I. Only the subgroup of children who reached criterion on stage one of the DNMS were administered the DNMS with delay. The descriptive statistics on this subgroup of participants are shown in Table II.

Diagnosis of Autistic Disorder or PDD.NOS was based on parent interview and a structured play session specifically designed to assess autistic symptoms listed in the Diagnostic and Statistical Manual Third Edition—Revised (American Psychiatric Association, 1987). Diagnosis of each child was made independently by the first and third authors to ensure reliability. In addition, each child was administered the Childhood Autism Rating Scale (CARS; Schopler, Rechler, & Renner, 1986) and all children in the autism group, as described in Table I, scored above the clinical cutoff (30) on the CARS.

The three groups of children were matched in terms of their receptive language mental age as assessed by the Preschool Language Scale—3 (PLS; Zimmerman *et al.*, 1991) and the communication subscale of the Vineland Adaptive Behavior Scales (Sparrow, Balla, & Cichetti 1984). In addition, children with autism were matched to children with Down syndrome in terms of chronological age and verbal IQ. Children with autism had significantly higher nonverbal ability as compared to the children with Down syndrome and typically developing children. Nonverbal ability was assessed by administration of a battery of developmentally graded visual-spatial tasks derived by the authors

Table I. Participant Characteristics—Full Sample<sup>a</sup>

Group	N (male/ female)	Ethnicity	CA (months)	Vineland <sup>b</sup> MA (months)	Vineland Scale <sup>b</sup> IQ	PLS <sup>c</sup> MA (months)	PLS IQ	Nonverbal MA (months)
Autism	20 (19:1)	18 Caucasian 2 Biracial	64.6 (15.1)	30.4 (13.4)	62.0 (16.4)	28.1 (14.9)	58.9 (14.3)	51.0 (26.2)
Down	19 (16:3)	17 Caucasian 1 African American 1 Native American	65.3 (16.5)	27.3 (10.2)	57.2 (8.2)	29.9 (12.3)	56.7 (9.4)	34.1 (11.8)
Typical	20 (19:1)	17 Caucasian 3 Biracial	30.9 (14.4)	32.4 (14.6)	103.4 (4.4)	31.8 (14.8)	105.9 (12.6)	33.2 (13.4)
<i>F</i>			.00	.78	.70	.35	.31	5.89
<i>p</i>			ns <sup>d</sup>	ns	ns <sup>d</sup>	ns	ns <sup>d</sup>	.005

<sup>a</sup> Numbers represent means and standard deviations (in parentheses).

<sup>b</sup> Vineland Scale refers to Communication Subscale.

<sup>c</sup> Preschool Language Scale.

<sup>d</sup> Comparison is between autism and Down syndrome groups only.

**Table II.** Participant Characteristics—Subsample Administered DNMS with Delay<sup>a</sup>

Group	N	Vineland <sup>b</sup> MA (months)	PLS <sup>c</sup> MA (months)	Nonverbal MA (months)
Autism	14	32.7 (14.0)	31.1 (13.7)	58.3 (24.5)
Down	13	29.3 (11.1)	32.1 (12.1)	36.5 (12.8)
Typical	19	33.0 (14.8)	32.4 (15.0)	34.1 (13.1)

<sup>a</sup> Numbers represent means and standard deviations (in parentheses).

<sup>b</sup> Vineland Scale refers to Communication Subscale.

<sup>c</sup> Preschool Language Scale.

from the Bayley Scales of Infant Development—Second Edition and the Stanford Binet IV. Tasks increased in difficulty based on normative data for each task provided by the Bayley and Stanford Binet manuals. Children were assigned the mental age of the highest task passed. Nonverbal mental age (MA) was used as a covariate in analyses.

### Neuropsychological Tasks

#### *Visual Paired Comparison*

All children were administered the paired comparison task which assesses visual recognition memory and novelty preference (Nelson, 1995). The child was shown a "junk" object at the outset of each visual paired comparison trial and allowed to play with the object until he or she lost interest. After a delay, the child was given a choice of that object or a new one. Six trials were administered, three with a 30-second delay and three with a 5-min delay. The dependent variable was percentage of trials correct (chose the novel rather than familiar object).

#### *Delayed Nonmatching to Sample with Delay*

The child was shown a novel object (the sample) and encouraged to reach for it. The child then reached for and displaced it to retrieve a reward (dry food snack, such as cheerios) underneath. The sample was then removed and a delay of 5 seconds was imposed. Following the delay, the child was shown the sample again paired with something new (the nonmatching object), and rewarded for reaching toward the nonmatching (novel) object. New stimuli were used on each trial. In stage one of this task, trials were administered until the child had reached criterion performance (defined as

reaching for the novel object on five consecutive trials), or a maximum of 15 trials had been administered. If the child reached criterion performance, stage two of the task was administered, and it is the results of stage two that we are reporting the present paper. In stage two, the task was repeated, but with a delay of 30 seconds imposed between the times the sample was removed and the novel object and sample were shown. The numbers of children who reached criterion and thus were administered the delay condition were 14 (autism), 13 (Down syndrome), and 19 (typical). The subgroups of children did not significantly differ in terms of their verbal abilities on the Vineland Scale and Preschool Language Scale. The dependent variable was percentage of trials correct (i.e., chose novel rather than previously rewarded item).

## RESULTS

### Visual Paired Comparison

Analysis of variance with nonverbal MA entered as a covariate and percentage correct as the dependent variable indicated that there was no group difference in performance on this task either at the 30-second or 5-minute delay. Means and standard deviations for the 30-second delay condition for the autism, Down syndrome, and typical groups were .87 (.24), .86 (.20), and .84 (.21), respectively [ $F(2, 55) = .35$ , NS]. Means and standard deviations for the 5-minute delay condition were .72 (.31), .71 (.30), and .80 (.27), respectively [ $F(2, 55) = 1.22$ , NS].

### DNMS with Delay

Analysis of variance with nonverbal MA entered as a covariate and percentage correct as the dependent variable indicated that there was no group difference in performance on the DNMS with delay task. Means and standard deviations for the autism, Down syndrome, and typical groups were .82 (.20), .82 (.18), and .77 (.22) [ $F(2, 55) = 1.62$ , NS].

## DISCUSSION

Results indicated that developmentally matched children with autism, Down syndrome, and typical development do not differ in their performance on the visual paired comparison task, a simple task that assesses novelty preference and visual object recognition. Children with autism had no difficulty recalling objects for







delays longer than that used previously with the DNMS. Furthermore, the subgroup of children with autism *who were able to reach criterion on the DNMS task* were able to perform the DNMS task with a delay equally well as children with mental retardation and typical development. These results suggest it is unlikely that an impairment in visual object recognition accounted for the poorer performance on the DNMS in children with autism when the full sample was tested, as reported in Dawson *et al.* (1998). Instead, it appears more likely that the poor performance on the DNMS task by children with autism, which we reported for a larger sample of children, reflected a difficulty in forming an abstract rule regarding stimulus–reward associations (i.e., rule that novel object is associated with a reward). In other words, in the earlier report (Dawson *et al.*, 1998), it appears that those children who were not able to reach criterion on the DNMS at brief delays accounted for the lower performance on the DNMS relative to controls. Once these children were eliminated from the sample, the groups no longer differed on the DNMS either at short or long delays.

Although future research needs to replicate these findings, we believe that these findings offer indirect support for the hypothesis that autism involves dysfunction of the ventromedial prefrontal cortex, a region that is critical for generalizing and inhibiting stimulus reward associations. We presently are examining performance on a task (object discrimination reversal) that selectively taps these skills and which has been shown to be affected by lesions to the ventromedial prefrontal region in monkeys (Jones & Mishkin, 1972; Meunier, Bachevalier, & Mishkin, 1997).

We hypothesize that an impairment in generalizing and inhibiting stimulus–reward associations may contribute to the early impairments found in joint attention in autism (Dawson, Meltzoff, Osterling, and Brown, 1998). Expectations regarding the anticipated reward value of a stimulus serve to motivate attention beginning in the second half of the first year of life. Establishing such expectations for social stimuli may be especially challenging because of the relatively unpredictable, variable nature of social reward feedback. Joint attention taxes this system even further by requiring the coordination between the child's own expectations regarding the reward value of a stimulus and those of others. For example, when showing an object to his or her parent, the child must coordinate his own interest in the object with his expectations that the mother will likely respond in a rewarding way by likewise showing interest in the object. We further hypothesize that, once a child with autism has established

an association with a specific stimulus and an anticipated reward, he or she will have difficulty flexibly modifying this association in response to varying social reward feedback. For example, in the standard social referencing situation, the child must inhibit his or her own expectations regarding the reward value of an object and must instead incorporate the feedback provided by the adult to form a new expectation that serves to guide motivation and behavior. In this and other ways, the ability to generalize and inhibit expectations regarding the association between stimuli and their reward value—a skill believed to be mediated by the ventromedial prefrontal cortex—may play an important role in the development of early joint attention skills (Dawson, Carver, and McPartland, 2000).

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