Original Article

autism

Autism
1–16

DOI: 10.1177/13623613231223354
journals.sagepub.com/home/aut
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Atypical pattern separation memory and its association with restricted interests and repetitive behaviors in autistic children

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Abstract

Emerging research suggests that episodic memory challenges are commonly encountered by autistic individuals; however, the specific nature of these memory challenges remains elusive. Here, we address critical gaps in the literature by examining pattern separation memory, the ability to store distinct memories of similar stimuli, and its links to the core autistic trait of repetitive, restricted interests and behaviors. Utilizing a large sample of over 120 autistic children and well-matched non-autistic peers, we found that autistic children showed significantly reduced performance on pattern separation memory. A clustering analysis identified three distinct pattern separation memory profiles in autism, each characterized by reduced or increased generalization abilities. Importantly, pattern separation memory was negatively correlated with the severity of repetitive, restricted interest and behavior symptoms in autism. These findings offer new evidence for challenges in pattern separation memory in autism and emphasize the need to consider these challenges when assessing and supporting autistic individuals in educational and clinical settings.

Lay abstract

Memory challenges remain understudied in childhood autism. Our study investigates one specific aspect of memory function, known as pattern separation memory, in autistic children. Pattern separation memory refers to the critical ability to store unique memories of similar stimuli; however, its role in childhood autism remains largely uncharted. Our study first uncovered that the pattern separation memory was significantly reduced in autistic children, and then showed that reduced memory performance was linked to their symptoms of repetitive, restricted interest and behavior. We also identified distinct subgroups with profiles of reduced and increased generalization for pattern separation memory. More than 72% of autistic children showed a tendency to reduce memory generalization, focusing heavily on unique details of objects for memorization. This focus made it challenging for them to identify commonalities across similar entities. Interestingly, a smaller proportion of autistic children displayed an opposite pattern of increased generalization, marked by challenges in differentiating between similar yet distinct objects. Our findings advance the understanding of memory function in autism and have practical implications for devising personalized learning strategies that align with the unique memory patterns exhibited by autistic children. This study will be of broad interest to researchers in psychology, psychiatry, and brain development as well as teachers, parents, clinicians, and the wider public.

Keywords

ASD, heterogeneity, pattern separation, recognition memory, RRIB

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Introduction

Cognitive challenges are prevalent in autism (Desaunay et al., 2020; Griffin et al., 2021; Velikonja et al., 2019) and significantly affect their prospects for independent living, job stability, and long-term well-being (Buitelaar et al., 1999; Chang et al., 2018; Hrabok et al., 2013; Kulp et al., 2002). Typical memory function plays a vital role in cognitive learning and academic success; however, memory function remains one of the least characterized aspects of cognitive functions in autistic children (Chen et al., 2019; Desaunay et al., 2020; Griffin et al., 2021; Kerns et al., 2017; Velikonja et al., 2019; Williams et al., 2006a). Understanding the memory abilities and challenges faced by autistic children remains an important and open research question. Here, we address critical gaps in the literature on episodic memory in autism and investigate whether the capacity to form memories for distinct but similar stimuli is atypical in autistic children and whether this capacity is associated with their phenotypic clinical features.

Episodic memory function refers to the ability to encode stimuli and subsequently retrieve this information to help guide future behaviors (Sugar & Moser, 2019). As a multifaceted cognitive function, episodic memory can be investigated and assessed using various approaches. One common method is the recognition paradigm. This paradigm consists of an "encoding phase," in which participants view a series of stimuli, followed by a "test phase" in which the participant is asked to distinguish items seen during the encoding phase from new images. This approach examines the ability to distinguish between memories of previously experienced stimuli and those that have not been encountered (Velikonja et al., 2019). Previous studies of memory in autistic children have primarily focused on conventional recognition memory paradigms and results from these studies have been equivocal, with some studies showing reduced recognition memory (Anns et al., 2020; Li et al., 2021; Loveland et al., 2008; Mogensen et al., 2020; Narzisi et al., 2013; Williams et al., 2006b) and others showing preserved memory performance (Hashimoto et al., 2021; Jiang et al., 2015; Lind & Bowler, 2009). While recognition memory paradigms capture a critical component of episodic memory function, little is known regarding other key elements of memory function, and their relation to clinical symptoms, in autistic individuals.

A significant gap in the existing autism literature concerns the lack of understanding of pattern separation memory (PSM), the ability to maintain distinct memories of similar, but not identical, stimuli (Stark et al., 2013; Yassa & Stark, 2011). PSM is typically assessed using a Behavioral Pattern Separation for Objects (BPSO) task. This task consists of an encoding phase comparable with conventional recognition paradigms in which participants view a series of images. During the subsequent test phase, participants are asked to distinguish between "targets" (old items encountered during the encoding phase), "lures" (items that are similar to targets but are actually new items), and "foils" (new items that are unrelated to the target) (Figure 1(a)) (Stark et al., 2013). Unlike conventional recognition memory tasks, BPSO systematically examines the strength of memory representations and their differentiation from parametrically dissimilar items. Therefore, the BPSO paradigm complements conventional recognition memory paradigms by probing the ability to differentiate the similarity of items stored in memory to new and unrelated items.

Despite the critical role of pattern separation in episodic memory, this approach has received little attention in the context of autism with the exception of one study in adults. South et al. (2015) reported atypical PSM in autistic adults, who were more likely to incorrectly identify lures as foils compared with controls. This specific pattern of errors suggests that autistic adults incorrectly identified items that were similar to the targets as completely new items, indicating a reduced generalization ability (i.e. *under-generalization*; Figure 1(b)). Considering emerging evidence of episodic memory challenges and age-related memory changes in autism (Desaunay et al., 2020; Griffin et al., 2021; Solomon et al., 2016), a significant and unaddressed question is whether and how PSM may be affected in autistic children.

Here, we aimed to characterize memory profiles, including PSM and recognition memory, in autistic children and matched neurotypical (NT) peers and examine relations between memory function and clinical symptomatology. We had three goals for this study. Our first goal was to investigate PSM and overall recognition memory using a BPSO task in autistic children. Based on previous findings (Desaunay et al., 2020; Griffin et al., 2021; Qian & Lipkin, 2011; Sahay et al., 2011; South et al., 2015), we predicted that autistic children would show atypical PSM and challenges in recognition memory. We hypothesized that autistic children would exhibit *under-generalization* of pattern separation, characterized by isolated memory representations that result in a tendency to incorrectly label similar items as entirely new ones.

The second goal of our study was to investigate the relationship between PSM and repetitive and restricted interest and behavior (RRIB), a core phenotypic symptom of autism. Based on the hypothesized link between excessive attention to details and PSM (Sahay et al., 2011; South et al., 2015), we predicted that the severity of RRIB would be associated with one of two possible patterns of PSM in autistic children. The first possibility is that individuals with more severe RRIB would show an excessive focus on core features of the target items which would result in *under-generalization* of pattern separation (Figure 1(b)) (Stark et al., 2013). However, an alternative hypothesis is that children with more severe RRIB would place an excessive focus on non-core features of the target items

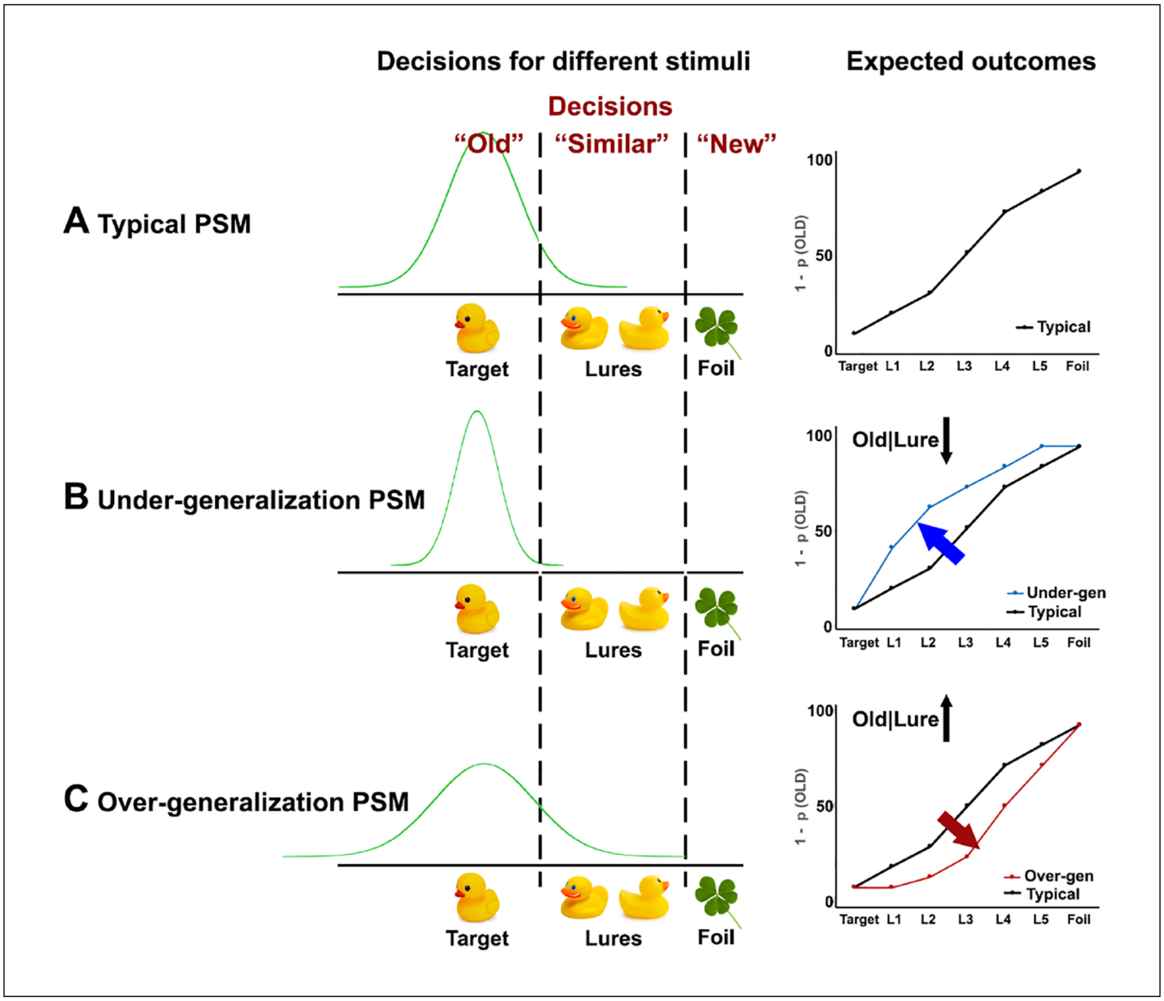

Figure 1. Schematic illustration of three potential PSM subtypes in autistic children. (a) Typical PSM. (b) Under-generalization subtype of PSM. (c) Over-generalization subtype of PSM.

In the test phase of the Behavioral Pattern Separation for Objects (BPSO) task, individuals were presented with three types of stimuli: targets (items they have seen in the encoding phase), lures (new items similar to the target), and foils (items that are completely new and unrelated to the target). The green curves represent the likelihood of memory representations for target items as a function of decreasing similarity. The typical memory representation centers on the target item with a reasonable distribution, but the *under-generalization* type has a circumscribed memory representation with a tighter distribution while the *over-generalization* type has a diffuse memory representation with a flatter distribution. Therefore, the probability of calling target, lure, and foil items as "Old" differs across three potential patterns of PSM. The PSM metric measures the likelihood of rejecting items in the recognition phase as "Old" (1 – p(Old)) across all types of items, including target, different levels of lures (L1 to L5 with decreasing similarity to target items), and then the completely new item type, foils. Compared with the typical PSM, the *under-generalization* PSM (b) is associated with less diffuse memory representations, leading to a higher likelihood of rejecting Lures as "Old." Thus, a steeper/convex curve is expected as a function of decreasing similarity. The opposite should hold for the *over-generalization* PSM (c) which is associated with more diffuse memory representations, resulting in a lower likelihood of judging Lures as "Old," and a shallower/concave tuning curve as a function of decreasing similarity. PSM: pattern separation memory.

that are not useful in distinguishing between items. In this case, children with more severe RRIB would exhibit an *over-generalization* of pattern (i.e. an increased generalization) separation (Figure 1(c)) (Stark et al., 2013), characterized by broad and fuzzy memory representations that exaggerate the connection between old and similar experiences.

The third goal of our study was to characterize the heterogeneity of PSM in autistic children using an unbiased data-driven approach. We conducted a cluster analysis using multiple PSM measures which index memory as a function of similarity of stimuli. In light of the extensive literature highlighting heterogeneity in autism (Chen et al., 2019; Fountain et al., 2012; Gotham et al., 2009, 2012; Jones et al., 2009; Kjelgaard & Tager-Flusberg, 2001; Norbury & Nation, 2011; Wei et al., 2015), we hypothesized that our analysis would reveal multiple subgroups of autistic children characterized by distinct and atypical profiles of PSM.

Table 1. Demographic, neuropsychological, and clinical measures in ASD and NT groups.

Measures	ASD (*N* = 69)	NT (*N* = 57)	t/χ^2	*df*	*p*
Gender (M/F)	59/10	48/9	0.04	1	0.840
Age	10.08 ± 1.25	10.04 ± 1.21	0.19	124	0.846
WASI scale[a]					
Full-scale IQ	115.83 ± 16.03	119.61 ± 14.20	−1.37	120	0.173
Verbal IQ	110.95 ± 15.16	120.37 ± 15.37	−3.40	120	0.001
Performance IQ	117.63 ± 18.19	114.53 ± 14.82	1.02	120	0.308
ADI-R[b]					
Social skill	19.76 ± 5.63				
Verbal communication	16.48 ± 4.47				
RRIB	5.76 ± 2.61				
ADOS[c]					
Social interaction	11.05 ± 3.07				
RRIB	2.19 ± 1.44				
Creativity	0.42 ± 0.56				

ASD: autism spectrum disorder; NT: neurotypical; WASI: Wechsler Abbreviated Scale of Intelligence; IQ: intelligence quotient; ADI-R: Autism Diagnostic Interview–Revised; ADOS: Autism Diagnostic Observation Schedule; RRIB: repetitive and restricted interest and behavior.
[a]Data from four ASD are missing.
[b]Data from 11 ASD are missing.
[c]Data from 10 ASD are missing.

Materials and methods

Participants

One hundred twenty-six children (69 with autism spectrum disorder (ASD); 57 NT) aged 7 to 13 years were recruited locally from schools and clinics in the Great San Francisco Bay Area. Inclusion criteria for all children included normal full-scale intelligence quotient (FSIQ > 80) as measured by the Wechsler Abbreviated Scale of Intelligence (WASI) (Wechsler, 1999) and no previous head injury. The ASD and NT groups were matched on full-scale IQ, performance IQ, age, and sex (Table 1). The diagnosis of ASD was confirmed by an experienced clinical psychologist based on the standard criteria of the Autism Diagnostic Interview–Revised (ADI-R) (Lord et al., 1994) and/or the Autism Diagnostic Observation Schedule (ADOS) (Luyster et al., 2009). Three autistic children were reported to have comorbid attention deficit hyperactivity disorder (ADHD), and separate analyses of memory function were performed with and without these three children (see Supplementary Results for more details). For NT children, additional inclusion criteria included no history of genetic, neurological, psychiatric, or learning disorders; no personal and family history (first degree) of developmental cognitive disorders; and no significant difficulty during pregnancy, labor, delivery, or immediate neonatal period or abnormal developmental milestones, based self-reported questionnaires completed by parents or caregivers. All study protocols were approved by the Stanford University Review Board, and informed written consent was obtained from the legal guardian of each child. Please see Table 1 for participant demographic, neuropsychological, and clinical information and Supplemental Table S1 for more information about handedness, race, ethnicity, socioeconomic status, and parent education level.

BPSO task

We used a BPSO task, also known as a Mnemonic Similarity Task (Stark et al., 2013, 2019). Briefly, the task consisted of an encoding phase followed by a test phase. In the encoding phase, children were presented with a series of color images of everyday objects, with 2 s for each image and inter-stimulus intervals of 0.5 s (a total of 128 items). They were required to make an indoor/outdoor judgment for each object. During the test phase that immediately followed the encoding phase, children were instructed to perform a surprise recognition memory test. They were asked to respond "Old," "Similar," or "New" for each item in a new series of images (a total of 192 items). One-third of the items were exact repetitions of items presented in the encoding phase (i.e. targets); one-third of the items were perceptually similar to target items but not identical (i.e. lures); and one-third of the items were new items unrelated to target items (i.e. foils). To measure behavioral judgments for varying degrees of item similarity (Yassa et al., 2011), lure items in this task were divided into five bins based on their relative similarity to targets, with lures that are most similar to targets in bin L1 and items that were least similar to targets in bin L5. Each trial of the recognition task was timed for 3 s, so that if the participant failed to provide a response within 3 s, a "NA" response was recorded. More details of this task can be found in the Supplementary Methods.

Overall recognition memory

To examine the recognition memory performance in autistic children compared with the NT group, we calculated accuracy scores for all items and for each stimulus type (i.e. target, lure, and foil) for each group. The accuracy was calculated by dividing the number of correctly recognized items (i.e. participants correctly identifying target items as "Old," lures as "Similar" to target items, and foils as "New" items) by the total number of items for all items for each stimulus type and then multiplying this number by 100%. We also calculated a conventional recognition memory score as follows:

$$\text{Recognition memory score} = \frac{N_{\text{Old}|targets}}{N_{targets}} - \frac{N_{\text{Old}|\text{foils}}}{N_{foils}},$$

where N represents the number of items of each stimulus type (i.e. target or foil). Only the valid responded items were considered for the number of relevant items. This score measures the differences between the hit rate (i.e. correctly labeling targets as "Old") and the false alarm rate (i.e. incorrectly labeling foils as "Old") and represents an overall recognition memory performance for target items while controlling for response bias for indicating an "old" response (Stark et al., 2013). To determine performance differences between the two groups, we used planned two-sample t tests for accuracies of each stimulus type and the recognition memory score. Cohen's d was calculated to evaluate the effect size for significant group differences.

Pattern separation memory

To estimate children's PSM, we calculated an overall PSM score and continuous fine-grained PSM metrics of 1 – p(Old) arranged by the similarity of stimuli to the target, as developed by Stark et al. (2013). The overall PSM score was calculated as follows:

$$\text{PSM score} = \frac{N_{\text{Similar}|lures}}{N_{lures}} - \frac{N_{\text{Similar}|foils}}{N_{foils}},$$

where N represents the number of items of each stimulus type (i.e. lure or foil). Only the valid responded items were considered for the number of relevant items. This score measures the difference between the hit rate for lure items (i.e. correctly labeling lures as "Similar") and the false alarm rate of foil items identified as "Similar," which corrects for response biases in using "Similar" response.

To characterize children's performance as a function of recognition difficulty, we also calculated the PSM metric as the rejection rate of the "Old" (1 – p(Old)) for the lure items with continuous similarity from the most similar to the least similar lures (namely, L1–L5), to the targets, as follows:

$$PSM_{L_i} = 1 - \frac{N_{Old|L_i}}{N_{L_i}}.$$

We also calculated PSM metric for targets

$$PSM_{targets} = 1 - \frac{N_{\text{Old}|targets}}{N_{targets}},$$

and for the foil items

$$PSM_{foils} = 1 - \frac{N_{Old|foils}}{N_{foils}},$$

where N represents the number of items and i represents the level of similarity from 1 to 5. This metric is the percentage of rejecting "Old" responses and represents the ability to differentiate lure from target items with a lower value indicating reduced ability. The benefit of this approach is that it characterizes the PSM across individuals along the similarity/difficulty dimension and integrates the information from all three stimulus types. In addition, the original response rates of "Old," "Similar," and "New" for all three types of stimuli (i.e. target, lure, and foil) were also calculated for both ASD and NT to understand the sources of error in PSM for each stimulus type.

Autism symptom measures

To examine whether RRIB is related to individual differences in PSM in autistic children, the subscale score of RRIB on the ADI-R was used. Data on ADI-R from 11 autistic children were missing; separate analyses of memory function were performed both with and without these 11 children (see Supplementary Results). Correlation coefficients between RRIB and PSM measures, including overall PSM score and PSM metric (1 – p(Old)) for L1, L2, L3, L4, and L5, were calculated using Spearman's correlations. Multiple comparison was corrected based on false discovery rate (FDR). As control analyses, we also calculated additional correlation coefficients of PSM measures with social subscale scores on the ADI-R and full-scale IQ as well as the correlation coefficient of recognition memory score with RRIB.

Heterogeneity of PSM: clustering and cross-validation

To investigate the heterogeneity of pattern similarity memory in autistic children, we conducted hierarchical clustering analysis using continuous fine-grained PSM metrics. The input to this analysis included seven measures of the PSM metric (i.e. 1 – p(Old)) for targets, L1, L2, L3, L4, and L5 of lures, and foils. We used hierarchical clustering with Euclidean distance and Ward-linkage criterion

(Murtagh & Legendre, 2014) because of their robustness and wide use in the behavioral literature (Murtagh & Contreras, 2012). To determine the optimal number of clusters, we varied the number of clusters from two to eight and used 30 indices of internal validity measures (*NbClust* package in *R*) (Charrad et al., 2014). The final optimal number of clusters was determined based on the majority vote of these 30 indices. Two-sample t tests were used to compare each subgroup of ASD with NT children on fine-grained PSM metrics and error rate for each stimulus type. FDR was used to correct multiple comparison for L1–L5 and Cohen's d was calculated to evaluate the effect size.

Community involvement statement

Our study was inspired by parents asking about memory functioning in autistic children, but community members were not involved in the design, data analysis, and interpretation of this study.

Data and code availability statement

The de-identified aggregated data and corresponding scripts for the analysis can be downloaded from here: https://github.com/scsnl/Chen_Autism_2023

Results

Reduced recognition and PSM in autistic children

We first examined overall accuracy of recognition memory across all items and observed significantly lower recognition accuracy in autistic children compared with NT, $t(124) = -3.85$, $p < 0.001$, Cohen's $d = -0.69$. The ASD group also showed reduced performance on each of the three stimulus types, including target, $t(124) = -4.24$, $p < 0.001$, Cohen's $d = -0.76$; lures, $t(124) = -2.90$, $p = 0.005$, Cohen's $d = -0.52$; and foil items, $t(124) = -2.84$, $p = 0.005$, Cohen's $d = -0.51$ (Figure 2(a) and Table 2). Moreover, we found that conventional recognition memory scores were lower in ASD compared with NT children, $t(124) = -4.42$, $p < 0.001$, Cohen's $d = -0.79$ (Figure 2(b)). Similarly, overall PSM scores were lower in the ASD compared with the NT group, $t(124) = -2.49$, $p = 0.014$, Cohen's $d = -0.45$ (Figure 2(c)). These findings suggest that both conventional recognition and PSM were affected in autistic children, and autistic children had low discriminability between different stimulus types.

Sources of error in PSM in autistic children

The next step in the analysis was to identify the sources of error associated with diminished performance on the PSM

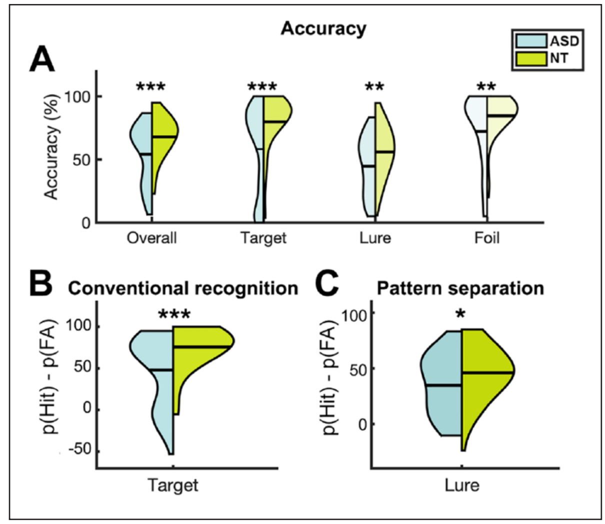

Figure 2. Overall recognition memory and pattern separation memory (PSM) on the Behavioral Pattern Separation for Object task. (a) Overall accuracy and accuracy for targets, lures, and foils. Autistic children showed significantly lower accuracy compared with NT peers across all types of stimuli. Violin plots show mean values and full distributions separately in each group. (b) Conventional recognition memory score calculated as p(Hit) –p(FA) for target items, in which the p(Hit) is the hit rate of incorrectly judging target items as "Old" and the p(FA) is the false alarm rate of correctly judging foil items as "Old." Autistic children showed significantly lower performance on recognition memory relative to NT peers. (c) PSM score calculated by p(Hit) – p(FA) for lure items, in which the p(Hit) is the hit rate of correctly judging lure items as "Similar" and the p(FA) is the false alarm rate of incorrectly judging foil items as "Similar." Autistic children showed significantly lower performance on PSM than NT.
ASD: autism spectrum disorder; NT: neurotypical.
$^{*}p < 0.05$. $^{**}p < 0.01$. $^{***}p < 0.001$.

task in autistic children. We examined the types of responses ("Old," "Similar," and "New") made by autistic children for the three stimulus types (target, lure, and foil) in comparison with NT children. Results revealed that, compared with NT, autistic children showed a general tendency to identify targets as "Similar," $t(124) = 3.17$, $p = 0.002$, Cohen's $d = 0.57$, or "New," $t(124) = 2.63$, $p = 0.010$, Cohen's $d = 0.47$, as well as identify lures as "New," $t(124) = 4.61$, $p < 0.001$, Cohen's $d = 0.83$ (Figure 3(a) and Table 2). These results were consistent with the *under-generalization* pattern associated with excessive separation of memory representations (see Figure 1(b)). In addition, a second pattern of results shown by autistic children was that they had a greater tendency to accept novel foils as "Old," $t(124) = 2.88$, $p = 0.005$, Cohen's $d = 0.52$ (Figure 3(a)). This result suggests that autistic children had memory difficulties which impacted their ability to distinguish the Target and Foil items (see Figure 1(c)). Together, these results identify multiple sources of errors underlying PSM difficulties and implicate both

Table 2. PSM and overall recognition memory in ASD relative to NT.

	ASD *M* (*SD*)	NT *M* (*SD*)	*t*	*df*	*p*	Cohen's *d*
Accuracy (%)						
Overall	54 (23)	68 (16)	–3.85	124	<0.001	–0.69
Target	58 (34)	80 (22)	–4.24	124	<0.001	–0.76
Lure	45 (23)	56 (20)	–2.90	124	0.005	–0.52
Foil	72 (29)	85 (18)	–2.84	124	0.005	–0.51
Recognition (target vs. foil)	0.48 (0.41)	0.76 (0.24)	–4.42	124	<0.001	–0.79
Pattern separation (lure vs. foil)	0.35 (0.27)	0.46 (0.24)	–2.49	124	0.014	–0.45
Error types (%)						
Similar—Target	27 (27)	14 (16)	3.17	124	**0.002**	**0.57**
New—Target	14 (22)	6 (10)	2.63	124	**0.010**	**0.47**
Old—Lure	30 (19)	35 (18)	–1.48	124	0.141	0.27
New—Lure	25 (23)	9 (13)	4.61	124	<**0.001**	**0.83**
Old—Foil	10 (13)	4 (6)	2.88	124	**0.005**	**0.52**
Similar—Foil	10 (9)	10 (13)	–0.04	124	0.970	–0.01
Lure bins (%)						
Target	32 (27)	19 (19)	3.10	124	**0.002**	**0.56**
L1	41 (30)	36 (29)	0.96	124	0.341	0.17
L2	66 (29)	60 (31)	1.22	124	0.226	0.22
L3	75 (27)	67 (29)	1.67	124	0.098	0.30
L4	77 (26)	76 (26)	0.31	124	0.755	0.05
L5	81 (23)	85 (19)	–1.15	124	0.252	–0.21
Foil	90 (13)	96 (6)	–2.89	124	**0.005**	**–0.52**

ASD: autism spectrum disorder; NT: neurotypical; PSM: pattern separation memory; FDR: false discovery rate.
In error type analysis and PSM metric/lure bins analysis with multiple comparisons along various levels of similarity, *p* values that passed FDR correction at $q < 0.05$ are shown in bold.

reduced generalization ability and failure to remember items in autistic children. Analyses were also performed in which children with comorbid ADHD ($n = 3$) were removed from the ASD sample and results revealed the same effects as those from the full ASD sample (Supplemental Table S2). An additional analysis was performed to examine whether autistic children were negatively affected by the length of the memory session, and results showed that performance in both ASD and NT groups was comparable in the first and second half of the memory sessions (Supplemental Table S3). Together, these results showed that differences between the two groups were unlikely due to attention challenges in ASD.

Fine-grained analysis of PSM in autistic children

To investigate children's ability to separate similar from identical experiences in a more fine-grained manner, we examined the proportion of responses that were identified as "Old" as a function of similarity level to the target items in two groups (i.e. targets, L1–L5, then foils; Figure 3(b) and Table 2). Interestingly, results did not reveal significant group differences on Lure items between ASD and NT groups, but did show significantly reduced labeling of target items as "Old," $t(124) = 3.10$, $p = 0.002$, Cohen's $d = 0.56$, as well as increased labeling of novel foil items as "Old," $t(124) = –2.89$, $p = 0.005$, Cohen's $d = –0.52$, in ASD compared with NT. These results are consistent with previous analysis indicating reduced memory ability in autistic children; however, the *under-* or *over-generalization* patterns of PSM on lure items were not shown here.

Relationship between PSM and RRIB in autistic children

The next goal was to examine whether RRIB, a core autism symptom, is associated with PSM in autistic children. Although no significant correlation was found between RRIB and overall PSM score (Supplemental Figure S1), we observed a significant negative correlation between RRIB and the fine-grained PSM metric for the lure L1 items that are most similar to targets, which measures the likelihood of not identifying lure L1 as "Old," $r(56) = –0.42$, FDR $q = 0.001$ (Figure 4(a)). Specifically, children with more severe RRIBs were more likely to incorrectly identify L1 lures as "Old." Further analysis revealed that the correlation between PSM at L1 was correlated with circumscribed interests, $r(45) = –0.30$, $p = 0.038$, and repetitive motor behavior subtypes, $r(45) = –0.39$, $p = 0.007$, but not with insistence on sameness, $r(45) = –0.17$, $p = 0.243$. By contrast, the correlations between RRIB with the fine-grained PSM metric at other

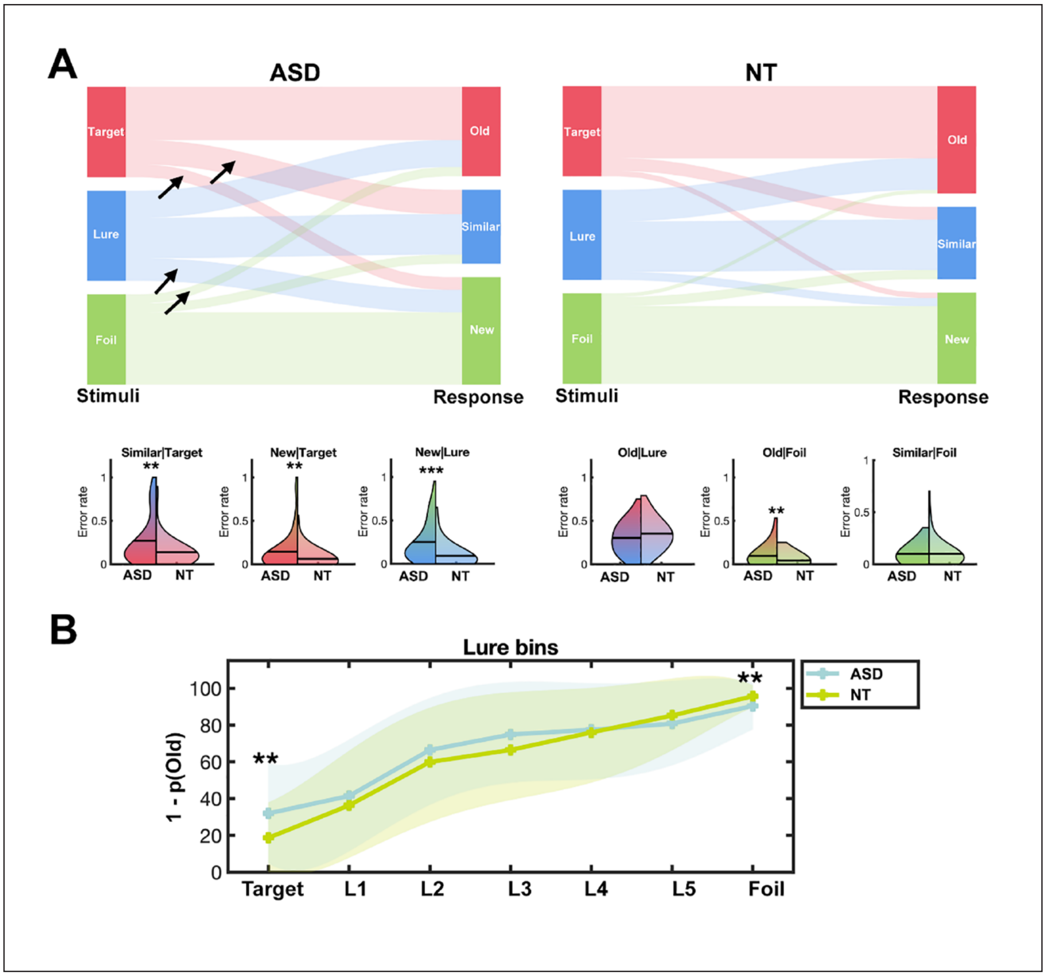

Figure 3. Sources of error in pattern separation memory (PSM) in autistic children compared with NT children. (a) Flow charts showing three responses ("Old," "Similar," and "New") to three types of stimuli (target, lure, and foil) in autistic children compared with NT. The colors represent different types of stimuli and corresponding correct responses, and the thickness of the triaged lines represents the proportions of different responses given each stimuli type. Arrows indicate the types of errors made significantly differently between two groups. The violin plots show error rates for each type of error for the three stimulus types in autistic children compared with NT children. Surprisingly, autistic children showed the *under-generalization* pattern of PSM reflecting a tendency to incorrectly label target or similar items as "Old" (i.e. excessive separation of memory representations), and a failure to remember by incorrectly labeling completely novel foil items as "Old" (i.e. less separation of memory representation). (b) Fine-grained PSM metrics for ASD compared with NT. PSM metrics characterize the rejection rate of "Old" responses (1 – p(old)) along the dimension of similarity to targets, including targets, lures (L1, the most similar, to L5, the least similar), and foils. The shadows show the standard deviation of the data. As the similarity level decreases, autistic children revealed a shallow tuning curve of 1 – p(old) metric, with higher rejection rate of "Old" for target items but also a lower rejection rate of "Old" for foil items.
ASD: autism spectrum disorder; NT: neurotypical.
$^{**}p < 0.01$. $^{***}p < 0.001$.

levels of lure items (L2–L5) were not significant ($ps > 0.5$), and they were significantly different from that of L1 (all $ps < 0.006$ based on Fisher's Z test; see Supplemental Figure S1). In addition, this effect was specific to RRIB as no significant correlations were identified between PSM metric for L1 and either the social subscale scores of ADI-R or full-scale IQ in children with ASD ($ps > 0.05$; Supplemental Table S4). Moreover, we found no significant correlation between RRIB and recognition memory score (Figure 4(b)). Additional analyses were also performed in which children with comorbid ADHD ($n = 3$) were removed from the ASD sample and the results remained reliable (Supplemental Figure S2). Additional results on the relationships between PSM and IQ scores are reported in Supplementary Results.

Together, these results suggest that greater difficulty in differentiating highly similar lures from targets is specifically associated with more severe RRIB symptoms and highlight the importance of examining PSM for understanding memory function in autistic children.

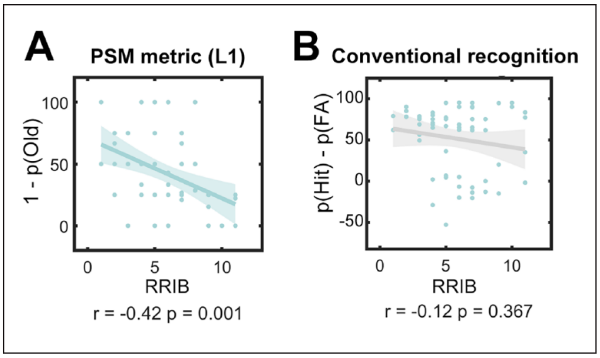

Figure 4. Relation between PSM and RRIB in autistic children. (a) A significant relationship between RRIB and the rejection rate of labeling lures (L1; the lure items most similar to Targets) as "Old" (1 – p(Old)). Fitted line is colored as blue if it is significant after FDR correction. Correlations of RRIB and with other similarity levels of lure items are presented in Supplemental Figure S1. (b) No significant relationship between overall recognition memory and RRIB.
PSM: pattern separation memory; RRIB: repetitive and restricted interest and behavior; Hit: hit rate; FA: false alarm rate.

Distinct cognitive profiles of heterogeneous PSM in autistic children

Results from previous analyses showed that autistic children demonstrate reduced generalization ability of PSM in the error type analysis; however, neither *under-* nor *over-generalization* patterns emerged in the PSM metric across various item types (e.g. Targets, different levels of Lures, and Foils). To examine the heterogeneity of cognitive profiles in ASD, we used a hierarchical clustering analysis to examine whether autistic children cluster into distinct subgroups based on PSM performance. Results from the hierarchical clustering analysis revealed three subgroups in autistic children: "moderate under-generalization," "high under-generalization," and "over-generalization" (Figure 5(a) and Supplemental Figure S3).

The *moderate under-generalization* subgroup had the largest proportion of autistic children, including 55% of the children in the ASD sample ($n=38$; Figure 5(b)), and this subgroup was characterized by a higher rate of not identifying lure items as "Old," especially for lure items with a mid-level similarity to the targets (i.e. L3), $t(93)=3.45$, $p=0.001$, FDR $q<0.05$, Cohen's $d=0.77$; Table 3). Additional analysis revealed that the *moderate under-generalization* subgroup had reduced conventional recognition memory score, $t(93)=–3.55$, $p<0.001$, Cohen's $d=–0.74$, but no difference in overall PSM score, $t(93)=–0.93$, $p=0.356$, compared with the NT group. Analysis of error types showed that the *moderate under-generalization* subgroup's reduced recognition memory stemmed from a greater tendency to identify target items as "Similar" (i.e. lower hit rate for target items; $p<0.001$, FDR $q<0.05$). Although this subgroup's overall PSM score was not different from the NT group, they still showed the hypothesized reduced generalization ability, that is, less likely identifying lure items as "Old" but accepting them as "New" compared with NT ($ps<0.004$, FDR $qs<0.05$; Supplemental Figure S3 and Table S5).

The *high under-generalization* subgroup included 17% of the children in the ASD sample ($n=12$), and children in this subgroup showed an even more extreme reduced generalization ability compared with the *moderate under-generalization* subgroup. Specifically, children in this subgroup showed an overall trend not to identify targets or lures as "Old" compared with NT (Figure 5(c)), especially for items that were highly similar (target, lure L1–L3, $ps<0.013$, FDR $qs<0.05$; Table 3). Consequently, this subgroup showed reduced conventional recognition memory due to a lower hit rate for target items compared with NT children, $t(67)=–4.16$, $p<0.001$, Cohen's $d=1.32$. Error type analysis confirmed that children in the *high under-generalization* subgroup were less likely to identify target items as "Old" and accept them as "New" ($ps<0.05$, FDR $qs<0.05$), and less likely to identify lures as "Old" and accept them as "New" ($ps<0.004$, FDR $qs<0.05$, Supplemental Figure S3 and Table S5).

The *over-generalization* subgroup consisted of 28% of the ASD sample ($n=19$) who showed a trend for embracing experiences as "Old." Specifically, this subgroup was characterized by a shallow tuning curve and a significantly reduced tendency for not labeling lures or foils as "Old" compared with NT ($ts<–2.28$, $ps<0.025$, FDR $qs<0.05$ for all except L1 and L4; Figure 5(d) and Table 3). Further analysis revealed that this subgroup was characterized by difficulties differentiating between target and foil items (i.e. recognition memory score), $t(74)=–3.67$, $p<0.001$, Cohen's $d=0.97$, and differentiating lures and foil items (i.e. overall PSM score), $t(74)=–5.26$, $p<0.001$, Cohen's $d=–1.39$ compared with the NT peers. Moreover, the error analysis revealed that the *over-generalization* subgroup had a higher tendency to identify lures as either "Old" or "New," and to confuse "Old" and "New" responses for target and foil items (all $ps<0.005$, FDR $qs<0.05$; Supplemental Figure S3 and Table S5).

An additional analysis revealed no significant subgroup differences in RRIB scores, $F(2,55)=0.05$, $p=0.95$. This was probably because the RRIB only correlated with the 1 – p(old) metric on L1 item, but the clustering with three subgroups were identified with the 1 – p(old) metric over all item types (i.e. target, lure, and foil). Together, results suggest that children with ASD show heterogeneous patterns of PSM characterized by differences in how they focus on individual stimulus features and how they generalize memory representations.

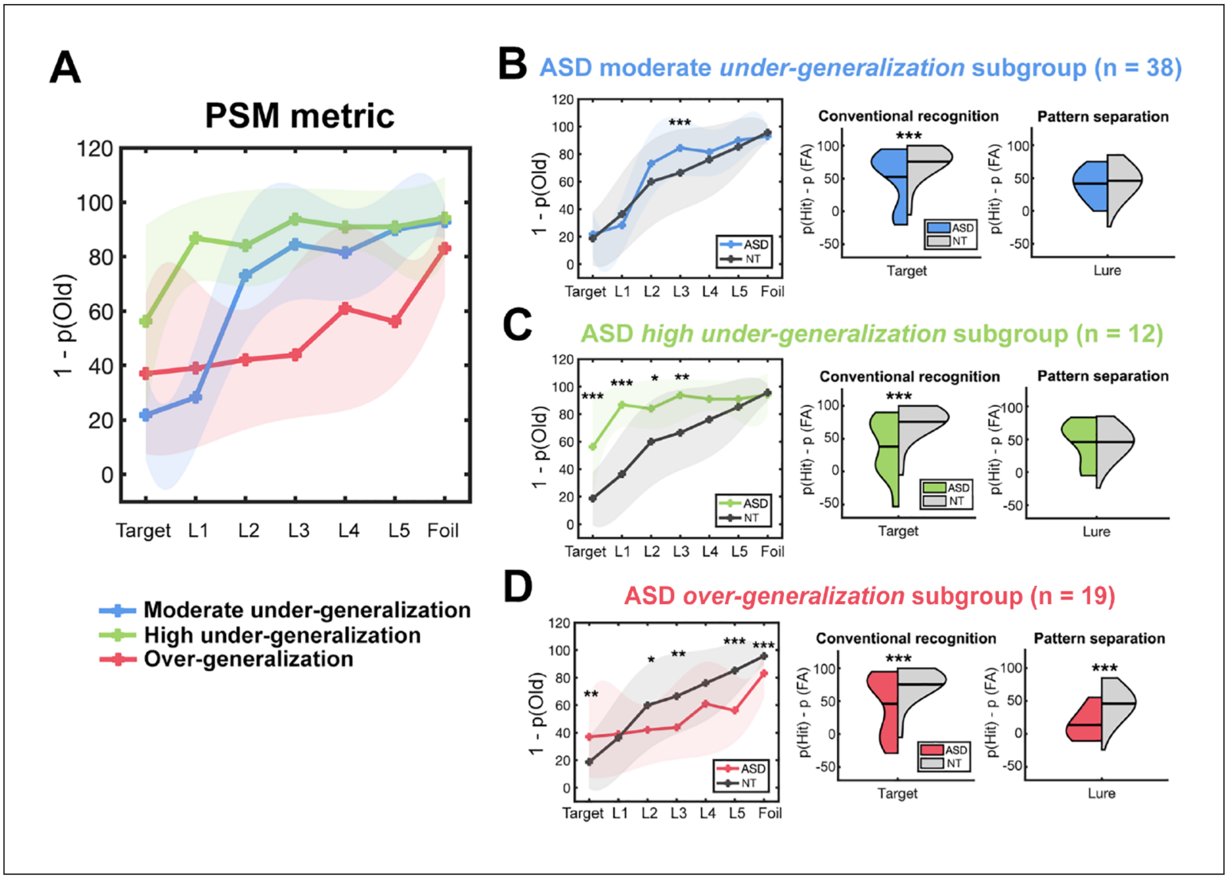

Figure 5. Subgroups with distinct profiles of atypical PSM in autistic children. (a) Hierarchical clustering (Supplemental Figure S3) revealed three subgroups of autistic children with distinct PSM profiles: *moderate under-generalization* ($n = 38$), *high under-generalization* ($n = 12$), and *over-generalization* ($n = 19$). PSM was assessed using the rejection rate of "Old" responses (1 – p(old)) as a function of similarity to targets, lures (L1, the most similar, to L5, the least similar), and foils. The shaded area represents one standard deviation. (b–d) The PSM metric, traditional recognition and PSM scores are shown for *moderate under-generalization*, and *high under-generalization* and *over-generalization* subgroups of autistic children relative to NT children. Significant differences with FDR $q < 0.05$ are marked for the comparison between ASD and NT on the PSM metric at different levels of similarity.
PSM: pattern separation memory; ASD: autism spectrum disorder; NT: neurotypical.
$^*p < 0.05$. $^{**}p < 0.01$. $^{***}p < 0.001$.

Discussion

PSM represents the ability to form distinct memories for similar stimuli and is an essential feature of episodic memory. Here, for the first time, we extend our understanding of memory function in autistic children by demonstrating weak PSM in autistic children. Our analysis of PSM and core autism diagnostic features further revealed that children with more severe RRIB scores showed increased generalization, characterized by difficulties in differentiating lures from targets. Our clustering analysis identified three distinct subgroups of autistic children based on PSM abilities, revealing heterogeneity of PSM across affected individuals. Our findings expand our understanding of the memory function in autistic children to include pattern separation and their connections to core autism symptomatology. Our findings are relevant to cognitive theories of ASD and have important implications for developing effective interventions for children with memory difficulties in clinical and educational settings.

PSM difficulties in autistic children

Previous memory studies in autistic children have primarily focused on conventional recognition memory paradigms, which do not include tasks with differing pattern separation requirements (Anns et al., 2020; Hashimoto et al., 2021; Jiang et al., 2015; Li et al., 2021; Lind & Bowler, 2009; Loveland et al., 2008; Mogensen et al., 2020; Narzisi et al., 2013; Williams et al., 2006b). Consequently, prior task designs used to investigate episodic memory in autistic children have failed to adequately address the strength of memory representations for similar stimuli or their relationship with previously encountered stimuli.

Table 3. PSM and overall recognition memory in the three subgroups of autistic children.

	ASD *M* (*SD*)	NT *M* (*SD*)	*t*	*df*	*p*	Cohen's *d*
Recognition (target vs. foil)						
Moderate under-generalization	0.52 (0.40)	0.76 (0.24)	–3.55	93	<0.001	–0.74
High under-generalization	0.38 (0.44)		–4.16	67	<0.001	–1.32
Over-generalization	0.46 (0.44)		–3.67	74	<0.001	–0.97
Pattern separation (lure vs. foil)						
Moderate under-generalization	0.42 (0.21)	0.46 (0.24)	–0.93	93	0.356	–0.19
High under-generalization	0.46 (0.32)		0.01	67	0.992	0.01
Over-generalization	0.14 (0.22)		–5.26	74	<0.001	–1.39
Lure bins (%)						
Target						
Moderate under-generalization	22 (16)	19 (19)	0.82	93	0.417	0.17
High under-generalization	56 (35)		5.21	67	<**0.001**	**1.66**
Over-generalization	37 (29)		3.13	74	**0.003**	**0.83**
L1						
Moderate under-generalization	28 (18)	36 (29)	–1.5	93	0.132	–0.32
High under-generalization	87 (14)		5.86	67	<**0.001**	**1.86**
Over-generalization	39 (30)		0.34	74	0.731	.09
L2						
Moderate under-generalization	73 (27)		2.13	93	0.036	0.45
High under-generalization	84 (20)		2.54	67	**0.013**	**0.81**
Over-generalization	42 (23)	60 (31)	–2.28	74	**0.025**	**–0.60**
L3						
Moderate under-generalization	84 (17)		3.45	93	**0.001**	**0.77**
High under-generalization	94 (11)		3.19	67	**0.002**	**1.01**
Over-generalization	44 (27)	67 (29)	–3.01	74	**0.004**	**–0.80**
L4						
Moderate under-generalization	81 (20)		1.09	93	0.277	0.23
High under-generalization	91 (14)		1.92	67	0.059	0.61
Over-generalization	61 (35)	76 (26)	–2.00	74	0.049	–0.53
L5						
Moderate under-generalization	90 (14)		1.29	93	0.200	0.27
High under-generalization	91 (14)		.97	67	0.334	0.31
Over-generalization	56 (24)	85 (19)	–5.32	74	<**0.001**	**–1.41**
Foil						
Moderate under-generalization	93 (6)		–2.16	93	0.034	–0.45
High under-generalization	94 (15)		–0.58	67	0.567	–0.18
Over-generalization	83 (17)	96 (6)	–4.76	74	<**0.001**	**–1.26**

ASD: autism spectrum disorder; NT: neurotypical; PSM: pattern separation memory; FDR: false discovery rate.
In error type analysis and PSM metric/lure bins analysis with multiple comparisons along various levels of similarity, *p* values that passed FDR correction at $q < 0.05$ are showed in bold.

The BPSO task was specifically designed to systematically assess an individual's ability to establish and maintain separate memory representations for similar items, offering a more nuanced and complementary examination of memory representation integrity compared with conventional recognition memory paradigms. Our study revealed that autistic children exhibited significant challenges in both PSM and overall recognition memory, when compared with a well-matched NT group. The presence of PSM difficulties may offer a plausible explanation for the inconsistent findings reported in previous studies of recognition memory autistic children (Anns et al., 2020; Hashimoto et al., 2021; Jiang et al., 2015; Li et al., 2021; Lind & Bowler, 2009; Loveland et al., 2008; Mogensen et al., 2020; Narzisi et al., 2013; Williams et al., 2006b). Specifically, we propose that the limitations of conventional recognition memory task designs, which inadequately assess the strength of memory representations and their differentiation from parametrically dissimilar items, may contribute to the inconsistencies of previous findings. PSM, on the contrary, provides a more sensitive design for capturing the unique challenges that autistic children face when asked to differentiate similar items in memory.

Our finding of a significant difference in overall PSM scores between ASD and NT groups is not consistent with results from a prior report that showed comparable PSM performance between autistic adults and their comparison group (South et al., 2015). Our findings suggest that autistic children may have more severe difficulties in their PSM (Cohen's $d=0.327$) compared with autistic adults (Cohen's $d=0.051$) (South et al., 2015). This finding is consistent with previous reports of improvements in memory performances as a function of age in ASD (Solomon et al., 2016). Further studies with longitudinal designs are required to systematically investigate how PSM changes with development in this population.

Heterogeneous patterns of atypical PSM in autistic children

Heterogeneity of behavioral abilities and clinical symptomatology is a defining characteristic of ASD. Previous studies have consistently shown that autistic children exhibit a wide range of cognitive strengths and challenges (Chen et al., 2019; Fountain et al., 2012; Gotham et al., 2009, 2012; Jones et al., 2009; Kjelgaard & Tager-Flusberg, 2001; Norbury & Nation, 2011; Wei et al., 2015). Therefore, the second goal of our study was to investigate the heterogeneity of PSM profiles in autistic children compared with NTs using an unbiased, data-driven approach. Hierarchical clustering analysis uncovered three subgroups of autistic children with distinct patterns of PSM.

The first two subgroups constituted the majority of our ASD sample (72%) and they displayed varying levels of reduced generalization ability characterized by *moderate under-generalization* (effect size $=0.77$ for L3) or *high under-generalization* (effect size >0.81 from L1 to L3) subgroups. The two subgroups also showed reduced overall performance on recognition memory tasks (effect sizes $=-0.74$ and -1.32). The error patterns in the two subgroups included a tendency to classify targets as "Similar" or "New" and lures as "New." The results from these two subgroups suggest that even subtle differences in sensory inputs could lead to the formation of distinct memory patterns, resulting in a low threshold for considering an item as "New." This PSM pattern indicates narrow and circumscribed memory representations that are excessively separated from representations for items with shared features. This PSM pattern suggests that memory representations are narrow and highly specific, with an excessive degree of separation between memories of items that share similar features. The discovery of *moderate and high under-generalization* subgroups is consistent with results from a previous study of PSM in autistic adults (South et al., 2015), which reported that autistic individuals were more likely to reject target or lure items (Figure 1(b)). This pattern of *under-generalization* is consistent with a look-up-table learning style (Qian & Lipkin, 2011) and the weak central coherence account of ASD (Frith, 2003; Happe & Frith, 2006). According to these theories, which emphasize a unique detail-focused cognitive processing style, autistic individuals may store each item precisely in memory. However, these memory representations are not easily connected to other items, even when they share common features.

The third subgroup, which comprised 28% of the ASD sample, displayed an *over-generalization* pattern of PSM (effect size <-0.60 for L2, L3, and L5). This pattern was characterized by a general difficulty in differentiating between various types of items, even when items had only a few overlapping features. Specifically, this subgroup made errors by misidentifying new foil items as targets or vice versa and by categorizing lure items as either "Old" or "New." Previous studies have identified these error types as "failure to remember" errors, but their increased generalization on lure items may provide an underlying mechanism for their memory failure: The *over-generalization* subgroup exhibited broad and "fuzzy" memory representations, as illustrated in Figure 1(c), possibly due to less separation between memory representations and a lack of well-defined boundaries between items. As a result, this subgroup demonstrated unique and atypical pattern separation not previously reported in autistic adults (South et al., 2015) and showed reduced performance on recognition memory tasks.

The *over-generalization* pattern in PSM has been reported in the elderly, patients with mild cognitive impairment (Stark et al., 2013), and patients with anxiety and depression (Balderston et al., 2017; Leal & Yassa, 2018). Although no prior PSM studies have been conducted in autistic children, a similar pattern of results has been reported in studies of similarity-based category learning and generalization in ASD (Alderson-Day & McGonigle-Chalmers, 2011; Church et al., 2015; Gastgeb et al., 2009). For example, Church et al. (2010) found that autistic children were less likely to correctly recognize the mean category representation, analogous to the target item in our study, and more likely to label a random pattern as belonging to the same category, suggesting a difficulty to establish effective boundaries of object categories in ASD. In line with their findings, one possible explanation for the *over-generalization* pattern of PSM in autistic children could be related to a difficulty to group-related items and form similarity-based representations of their relationships. This could lead to the observed response pattern in which affected children are less likely to make a "similar" judgment for stimuli.

Atypical PSM in autistic children is related to RRIB clinical symptoms

The final goal of our study was to investigate the relationship between PSM and RRIB, a core phenotypic symptom of ASD. We found that more severe RRIB was linked to greater challenges in PSM in autistic children. Specifically, increased severity of RRIB was associated with a heightened *over-generalization* pattern of PSM, in which children were more likely to incorrectly identify similar (i.e. lures) or new items (i.e. foils) as items they had previously seen (i.e. targets). Further analysis showed that this relationship was likely to be driven by circumscribed interests and repetitive motor behavior subtypes, but not insistence on sameness. These correlations were observed only when the lures were highly similar to the target items (Condition L1) but not for other degrees of item similarity, suggesting RRIB contributes to reduced PSM under conditions where attention to detail is most critical. The results may appear surprising since one might expect that excessive attention to detail (Sahay et al., 2011), a key behavioral feature captured by RRIB in autistic individuals (Mottron et al., 2006), would be linked to excessive separation of similar items (i.e. *under-generalization*) rather than the *over-generalization* pattern of PSM observed in our findings.

One possible explanation for our results is that autistic children with more severe RRIB may excessively focus on detailed non-core features that are insufficient for distinguishing between similar items. Narrowed-focus on non-core features makes similar items appear more alike for affected children, resulting in an *over-generalization* pattern of PSM. Alternatively, it is also possible that the weak PSM in ASD compromises these children's ability to differentiate seemingly similar experiences, so they are more likely to fixate on non-core and idiosyncratic features when interacting with objects (i.e. circumscribed interests). While a previous study of PSM in autistic adults did not report a significant relationship between PSM and RRIB (South et al., 2015), another study reported a positive correlation between RRIB and recognition memory performance for social scenes in autistic children (Solomon et al., 2019). The inconsistency of findings linking RRIB and memory function in ASD further highlights the heterogeneous nature of the ASD population and stresses the need for additional research on this topic. Finally, we failed to identify a significant relationship between RRIB and conventional recognition memory measures in autistic children, suggesting that PSM is more sensitive to core clinical features of ASD than conventional recognition memory measures.

Implications for learning and education in children with autism

Our findings of *over- and under-generalization* subgroups of autistic children based on PSM may offer valuable and novel insights for clinical and educational practices in ASD. For example, when teachers, clinicians, and parents are aware that a particular child tends to show increased or reduced generalization ability in learning, they might find it beneficial to adapt learning strategies for that child accordingly. For children who tend to show reduced generalization and have difficulty in recognizing similarities between items, it may be beneficial to emphasize the shared features between items during learning. Conversely, for children who tend to show increased generalization and struggle with establishing well-defined boundaries between similar object items, it may be helpful to focus the child's attention on the distinct and core features that differentiate similar items during the learning process.

It is important to note that it remains unclear whether the visual memory patterns identified by the BPSO task extend to memory representations for other types of stimuli encountered in a child's life, such as auditory, social, orthographic, and numerical stimuli. This question could be explored in future studies. Nevertheless, our findings generally suggest that considering children's specific memory patterns is an essential step in supporting autistic children during their various social and academic learning opportunities.

Conclusions

In conclusion, our study is the first to identify challenges in PSM in autistic children. Our findings further reveal significant heterogeneity of PSM in ASD, characterized by three subgroups with *moderate under-generalization, high under-generalization*, and *over-generalization* patterns of PSM. This suggests a high degree of variability in the ways in which items are represented in memory across autistic children. Furthermore, challenges in PSM were associated with more severe RRIB, underscoring the influence of clinical phenotypic features on fine-grained aspects of memory function and representation in ASD. More broadly, our study emphasizes the need for a comprehensive and systematic investigation of memory function in autistic children to better understand learning patterns that may impact their social, educational, and professional opportunities.

Author contributions

Conceptualization: L.C., M.R.-L., and V.M.; Data collection: L.C., M.R.-L., and J.B.K.; Data analysis: L.C. and J.L.; Writing—Original Draft Preparation: L.C. and J.L.; Writing—Review & Editing: all authors.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This research was supported by the United States National

Institutes of Health to V.M. (HD059205, MH084164, HD094623, and MH121069), and by the Stanford Maternal & Child Health Research Institute Postdoctoral Support Awards to J.L.

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Supplemental material

Supplemental material for this article is available online.

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