ABSTRACT

Much research about memory in autism concerns the hypothesis that autism is similar to adult-onset amnesia. Initial support for the hypothesis came from post-mortem studies of individuals with autism showing abnormalities in the hippocampus and related brain structures, as well as behavioral studies finding contrasts between intact cued recall and impaired free recall and recognition in autism. The hypothesis was later brought into question by the finding of intact performance in individuals with autism on explicit memory tasks typically impaired in adult-onset amnesia. The present paper proposes a possible reconciliation of these contradictory findings, suggesting that there is selective damage to the limbic-prefrontal episodic memory system, sparing the limbic-only perceptual representation system, and the semantic memory system. This view is consistent with other evidence for early selective damage to other systems involving cooperation between the limbic system and the medial prefrontal cortex in autism.

Key words: autism, memory, limbic system, prefrontal cortex, episodic memory, semantic memory, perceptual representation system

INTRODUCTION

Autism is characterized by impairments in communication and social interaction, and by restricted interests and activities (American Psychiatric Association, 1994). Two current hypotheses about cognitive functioning in autism are the theory of mind hypothesis (Frith, 1989; Baron-Cohen, 1995) which claims that people with autism have a deficit in attributing mental states to themselves and to others; and the weak coherence hypothesis (Frith and Happe, 1994) which suggests that people with autism have a deficit in the integration of information. A third line of research shows executive function deficits in autism, providing indirect evidence for frontal lobe dysfunctions (Ozonoff et al., 1991).

The study of memory in autism goes back at least to Hermelin and O’Connor (1970), and similarities between autism and adult-onset amnesia have been pointed out as early as Boucher and Warrington (1976). One influential paper (DeLong, 1992) went as far as equating autism with the ‘developmental syndrome of hippocampal dysfunction’. This view has since been challenged by research in both memory and autism. Vargha-Khadem et al. (1997) showed that early hippocampal dysfunction results in episodic memory impairment but not autism; and a number of papers (such as Minshew and Goldstein, 1993; Bennetto et al., 1997, Renner et al., 2000) showed normal or close-to-normal recognition and free recall in high-functioning autism, a pattern that differs from that in adult-onset amnesia.
The main claim of the present paper is that most of these findings can nevertheless be reconciled in a way that preserves DeLong’s (1992) core insight, although not his view that hippocampal dysfunction accounts for other aspects of autism apart from memory. It is argued that the memory profile in autism involves selective damage to episodic memory, which is subserved by both the hippocampus and the prefrontal cortex.

Five Types of Memory

In his (1995) review, Tulving distinguishes five types of memory systems: the procedural memory system, working memory, the perceptual representation system, semantic memory, and episodic memory. Procedural memory includes nondeclarative motor and cognitive skills, as well as simple conditioning. This type of memory is not dealt with in the present paper. Likewise, the present paper does not deal with working memory, whose subsystems hold ‘on-line’ information during the execution of cognitive tasks. The paper discusses the last three memory systems on Tulving’s list: the perceptual representation system, semantic memory, and episodic memory.

Of these three memory systems, the perceptual representation system is clearly the most basic – a limbic (probably rhinal cortex) representation of ‘raw’, nondeclarative, perceptual and cognitive information. Declarative information is derived from the perceptual representation system through at least two different pathways (Tulving and Markowitsch, 1998; Aggleton and Brown, 1999). One, from the rhinal cortex to the parahippocampal cortex, derives fact information (semantic memory); the other, from the rhinal cortex to the hippocampus and then the medial prefrontal cortex, derives event information (episodic memory).

The perceptual representation system is probably unimodal, and is sensitive to transformations that semantic and episodic memory are not sensitive to (such as the orientation of three-dimensional objects). Items in the perceptual representation system are rich in context, as are items in episodic memory. However, whereas context and item are bound together in the perceptual memory system, contextual information is factored out of individual items in episodic memory and can be used to create organization between different items. Items in semantic memory are, by contrast, relatively context free. Semantic and episodic memory differ in that episodic memory has to do with conscious recollection of previous experiences of events, whereas semantic memory is concerned with the acquisition and use of the knowledge of what is, or could be, in the world (Tulving and Markowitsch, 1998). The present paper makes the claim that the perceptual representation system and semantic memory are relatively intact in autism, whereas episodic memory is selectively impaired.

Three Types of Emotion

The relationships between the perceptual representation system, episodic memory, and semantic memory are in many ways similar to the relationships between three emotion-processing systems. LeDoux (1996) suggests a distinction between physiological ‘emotions’ and more cognitive ‘feelings’ (emotions with
cognitive content and meaning). In addition there is a semantic (fact-based) aspect to the processing of emotions. LeDoux associates emotions with a basic limbic (amygdaloid-complex) system and feelings with a prefrontal system that converts limbic input into prefrontal outputs. Factual knowledge about emotions can be associated with either Broca’s area or the parietal cortex depending on whether facts about emotions are represented as words or as pictures.

One example of the distinction between the outputs of the limbic and prefrontal emotion-processing systems is the contrast between the emotion ‘being in a state of fear’ (heart pounding, hands cold, etc.) and the feeling of ‘feeling afraid’. This type of distinction has been argued to be useful in the study of autism (e.g. Buitelaar and van der Wees, 1997; Ben Shalom, 2000), with autism argued to involve an intact emotions system and an impaired prefrontal feelings system. In other words, the suggestion is that people with autism may be incapable of converting limbic emotions into medial prefrontal feelings. In addition it may be argued that in high-functioning autism the system mediating factual knowledge of emotions is relatively intact, and that this explains the partly preserved ability for ‘cognitive empathy’ – that is, the ability to reason about other people’s emotions.

To summarize, the study of emotion in autism suggests a distinction among three types of emotion systems: a limbic-only, a limbic-prefrontal, and another system. Of these three, the limbic-prefrontal system has been argued to be selectively impaired. I will claim that a somewhat parallel situation may hold between three memory systems in autism: a limbic-only (perceptual representation) system, a limbic-prefrontal (episodic memory) system, and another (semantic memory) system. Specifically, I hypothesize that the limbic-only memory system and the other memory systems are relatively intact in autism, while the limbic-prefrontal memory system is selectively impaired.

Predictions Derived from the Hypothesis

The more general hypothesis that the perceptual representation system and semantic memory system are relatively intact in autism, whereas the episodic memory system is selectively impaired, gives rise to the following predictions.

1. Memory tasks that do not depend on episodic memory but on the perceptual representation system or semantic memory, such as rote memory and memory for facts, will show intact performance in autism.

2. Memory tasks that depend on episodic memory and that cannot be compensated for using compensatory strategies involving either the perceptual representation system or semantic memory, will show impaired performance in autism. Such tasks would include tests of source memory, temporal order memory, and memory for personally experienced events.

3. Memory tasks that depend partly or wholly on episodic memory but which can be compensated for by the perceptual representation system or semantic memory, such as free recall and recognition, will show a mixed performance in subjects with autism. The level of performance may depend on many factors, including the cognitive level of the subjects tested. Qualitatively, there should be
signs of the use of atypical strategies. The successful use of compensatory strategies, at least by more able individuals with autism, may derive from the fact that autism is a developmental disorder. These types of compensations may be harder to acquire when a memory disorder is acquired in adulthood.

Evidence relating to the above predictions will be presented within the next three sections of the paper. The first of these sections considers evidence relating to the early hypothesis of similarities between memory profiles in autism and in adult-onset amnesia. The next section considers evidence relating to the more recent hypothesis that the memory profiles in autism reflect impaired organization of information in memory. The third section considers evidence relating to episodic memory in autism. The evidence reviewed is then related to the three specific predictions presented above.

**Autism and Adult-Onset Amnesia**

In the past, most of the research into memory in autism has focused on the question of whether the memory profiles of autism and adult-onset, e.g. temporal lobe amnesia are similar. Such amnesia is characterized by severe deficits in recognition and recall, especially after filled intervals between study and testing (Squire, 1987).

Evidence that the two memory profiles are similar comes from both neuroanatomical and behavioral studies. Anatomically, several post-mortem studies of individuals with autism reported findings of abnormalities in the hippocampus and related brain structures (Bauman and Kemper, 1985; Kemper and Bauman, 1993). Gross medial temporal lobe pathology has been linked in particular to low-functioning autism (DeLong and Heintz, 1997). Animal models of autism implicate the medial temporal lobes as possible sites of impairment (Bachevalier 1991, 1994). Neuroimaging studies are not yet conclusive, but a recent review (Rumsey and Ernst, 2000) states that “limbic-based memory and emotional systems” are a top priority in neuroimaging studies of autism. Behaviorally, a seminal study by Boucher and Warrington (1976) revealed impaired recognition and free recall after filled delays in people with low-functioning autism.

Evidence from other studies, however, casts doubt on the suggestion that memory profiles in autism and amnesia are similar. Only two of the six cases in an autopsy study reported by Bailey et al. (1998) showed gross hippocampal abnormalities. Ameli et al. (1988) found that 1-minute delay intervals did not differentially affect the visual memory performance of individuals with high-functioning autism as opposed to age-matched normal controls. Minshew and Goldstein (1993) and Bennetto et al. (1996) found close to unimpaired performance in high-functioning autism in the recognition and free recall components of the California Verbal Learning Test (a standardized measure of free recall, immediate and delayed recall, capacity to use cues, proactive and retroactive interference and recognition memory). Renner et al. (2000) found unimpaired performance on free recall and recognition of pictures in subjects with high-functioning autism.
Later positions have described the memory profile in autism as involving a deficit in the organization of information in memory.

As early as 1967, Hermelin and O’Connor showed that children with low-functioning autism produced less semantic clustering than expected in the recall of sequences of the form “Blue, three, red, five, six, white, green, eight”. Similar results were later reported by Frith (1969), Wolff and Barlow (1979), and Tager-Flusberg (1986). Fein et al. (1996) found that both visual and verbal memory were impaired in both high- and low-functioning children with autism. They found the most severe impairments, however, in verbal tasks that required organization of information in memory. Minshew and Goldstein (1993) administered the California Verbal Learning Test to individuals with autism and individuals with typical development and found no significant differences between the two groups on 33 different memory variables. Nevertheless, individuals with typical development outperformed individuals with autism on 30 of these measures. Minshew and Goldstein (1993) interpret these results as indicating a “subtle insufficiency” in the ability to organize information in memory.

Bennetto et al. (1996), who did not find simple recognition and recall skills to be impaired in high-functioning autism, did find impairments in source memory (memory for the particular situation in which a fact was learned) and temporal order memory (memory for the particular order in which information was learned), both of which depend on the organization of items according to context. Renner et al. (2000) found explicit memory to be intact in children with high-functioning autism. However, the children showed only recency effects rather than the typical primacy and recency effects, partly replicating the reduced primacy effects found in immediate free recall of low-functioning children with autism in Boucher (1981a). Renner et al. (2000) concluded that people with autism use different organizational strategies during either encoding or retrieval of memory.

The organizational strategies missing or deficient in people with autism cannot be part of the perceptual representation system, since they impose an organization beyond the perceptual representation of a single item. They are probably not part of semantic memory either, because they are highly context-dependent, grouping together items experienced in particular contexts, e.g., fruits that appeared in the California Verbal Learning Test. It seems likely, therefore, that problems in the use of organizational strategies are associated with impairments within the episodic memory system. Evidence regarding episodic memory in autism is discussed next.

**Autism and Episodic Memory**

Recent studies have produced some direct evidence for episodic memory deficits in autism. Klein et al. (1999) reported impaired access to personal experiences but intact knowledge of personal traits in a young adult with low-functioning autism. Millward et al. (2000) reported impaired memory for events
performed by self as opposed to others in children with high-functioning autism. Bowler et al. (2000) reported more ‘know’ and fewer ‘remember’ responses during recognition in high-functioning autism as compared to controls. These results are consistent with earlier evidence of impaired memory for recent events reported by Boucher (1981b) and Boucher and Lewis (1989) in children with low-functioning autism.

Summary of the Cognitive Memory Profile

The evidence presented in this review is largely compatible with the three predictions derived from the hypothesis of a selective deficit in episodic memory, outlined earlier in the paper.

1. Memory tasks that do not depend on episodic memory but on the perceptual representation system or semantic memory, such as rote memory and memory for facts, show intact performance in subjects with autism. It can be argued that people with high-functioning autism rely more on semantic memory, while people with low-functioning autism rely more on the perceptual memory system. Memory for facts is generally a strength in high-functioning autism. Memory in low-functioning autism is famously rote, restricted and inflexible (e.g. O’Connor and Hermelin, 1988), all hallmarks of the perceptual representation system (Tulving and Schacter, 1990)\(^1\).

2. Memory tasks that are episodic in nature, and which cannot be compensated for using compensatory strategies involving semantic memory or the perceptual representation system, are universally impaired in subjects with autism. Source memory and temporal order memory have been shown to be impaired even in high-functioning autism (Bennetto et al, 1996). Deficits in the organization of information in memory, arguably related to episodic learning, are found consistently in autism (Minshew and Goldstein, 1993; Bennetto et al., 1996; Renner et al., 2000). Memory for personally experienced events seems to be impaired in low-functioning (Boucher, 1981b; Boucher and Lewis, 1989; Klein et al. 1999) as well as high-functioning autism (Millward et al., 2000).

3. Memory tasks that depend partly or wholly on episodic memory, but for which it is possible to compensate using the perceptual representation system or semantic memory, show a mixed pattern of performance in subjects with autism. The level of performance may depend on the cognitive level of the subjects tested. Thus, in low-functioning children with autism, Boucher and Warrington (1976) found delayed free recall to be impaired relative to both normal and ability-matched controls. Recognition, often argued to be less dependent on episodic memory than is free recall, was also impaired, but to a lesser degree.

\(^1\) Asperger Syndrome is a syndrome at the high-functioning end of the autism spectrum. There has been extensive discussion about differences and similarities between Asperger Syndrome and high-functioning autism, including a possible left-hemisphere cognitive profile in Asperger Syndrome vs. a right-hemisphere profile in high-functioning autism (e.g., Delong, 1999). Parts of this difference may involve a more verbal semantic memory in Asperger Syndrome vs. a more pictorial semantic memory in high-functioning autism.
By contrast, Boucher (1981a) found immediate free recall to be intact in low-functioning autism. In high-functioning autism, delayed free recall and recognition are unimpaired or close to unimpaired relative to ability-matched controls (Ameli et al., 1988; Minshew and Goldstein, 1993; Bennetto et al., 1996; Renner et al., 2000).

The difference between immediate and delayed free recall in low-functioning autism can be explained if the perceptual representation system can be used in immediate but not delayed recall. The difference between delayed recall in low- and high-functioning autism might be explained if a higher IQ facilitates the existence and efficacy of semantic compensatory strategies (perhaps similar to the effects of cognitive ability on the ability to perform tasks that require empathy in subjects with autism, Yirmiya et al., 1992).

It was also predicted that there should be qualitative signs of the use of atypical strategies. Reduced or absent primacy effects in the face of intact recency effects have been reported in both high-functioning (Renner et al., 2000) and low-functioning autism (Boucher, 1981a). Performance in high-functioning autism is reduced on the late but not the early trials of the California Verbal Learning Test (Minshew and Goldstein, 1993; Bennetto et al., 1996). Finally, despite similar levels of performance, subjects with high-functioning autism show more ‘know’ responses and fewer ‘remember’ responses in recognition compared to controls (Bowler et al., 2000).

New Insights into the Neuroanatomy of Episodic Memory

Three new findings on episodic memory help relate the emerging memory profile in autism to a selective abnormality in the hippocampus, the medial prefrontal cortex or both.

The first finding involves the effects of early hippocampal damage on episodic memory. In an important paper, Vargha-Khadem et al. (1997) show that early hippocampal damage leads to selective deficits in episodic memory, but does not impair semantic memory (nor, probably, the perceptual representation system) (cf. Prediction 1 above).

The second finding involves the relationship between episodic memory and learning, on the one hand, and the organization of information in memory, on the other. Source memory and temporal order memory are consistently impaired in patients with frontal lobe damage (Shimamura et al. 1991). A recent paper by Savage et al. (2001) highlights the connections among the prefrontal cortex, strategic memory processes and the ability to use organizational strategies in the service of episodic memory. Specifically, these authors found that the level of activity in the ventromedial prefrontal cortex during encoding predicts semantic clustering scores in subsequent free recall, in a task closely modeled after the California Verbal Learning Test (cf. Prediction 2 above).

The third finding involves the role of the hippocampus in the typical serial position curve in free recall. Hermann et al. (1996) examined seventy-seven patients who had undergone hippocampal resection. The patients were administered a list-learning task before and after surgery, and changes in the serial position curve were examined. Such changes were found only in patients
with resection of the left hippocampus, and almost exclusively among patients without hippocampal sclerosis. These patients showed a significant decline in recall from the primacy and middle portions of the list, without any change in the recency portion of the list. Another point of similarity between the patients in Hermann et al. (1996) and individuals with high-functioning autism is reduced performance on the late but not early trials of the California Verbal Learning Test (cf. Prediction 3 above).

The Neuroanatomical Basis of the Memory Profile in Autism

While the above memory profile in autism is largely consistent with a selective deficit in episodic memory, it does not allow localization of the anatomical abnormality to either the hippocampus or the prefrontal cortex. All three predictions are consistent with abnormalities in either of these locations, while specific comparisons with other clinical groups sometimes point to the one and sometimes to the other.

One possible cause of this ambiguity is a variation in the location of the abnormality among individuals with autism (perhaps contributing to some of the variation between the autopsy findings reported by Kemper and Bauman (1993) and by Bailey et al. (1998)).

Another possible source of the ambiguity is the paucity of information about the differential effects of early hippocampal and prefrontal abnormalities on episodic memory. Nevertheless, what the memory profile in autism seems to already suggest is a selective deficit in the limbic-medial prefrontal episodic memory system.

CONCLUSION

Turning back from the domain of memory to the more general issue of cognition in autism, it might be said that the social-emotional and memory profiles in autism are consistent with an abnormality in two systems involving cooperation between the limbic system and the medial prefrontal cortex. The first and probably characterizing system includes the pathway from the amygdala to the medial prefrontal cortex (the intactness of this system is probably the reason why the children in Vargha-Khadem et al. (1997) are not autistic). This system is also probably the one that supports theory of mind. The other system is the one including the pathway from the hippocampus to the medial prefrontal cortex. This system is arguably necessary for episodic memory. It is also probably the system that supports some organizational strategies in episodic learning and perhaps some of the ‘coherence’ impaired in ‘weak coherence’. In the case of both of these systems, it is suggested that autism involves an impairment in the conversion of limbic inputs into medial prefrontal outputs.

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