

Part Seven:

**Neuroscience and
Neuropsychological
Foundations for
Clinical Practice**

Neural Mechanisms in Autism¹

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Currently, there is no reliable evidence as to exactly what are the neural bases for autism. There are no accepted genetic markers, even though there are several candidates (Bailey, Palferman, Heavey, & Le Couteur, 1998; Folstein, Bisson, Santangelo, & Piven, 1998; Szatmari, Zwaigenbaum, & MacLean, 1998). It is also increasingly clear that autism is a heterogeneous disorder, even if it is genetic. There are no objective tests *in vivo* that are specific for the condition. There have been no structural, metabolic, or neuropathologic abnormalities that have been reliably linked to autistic features. There is no accepted animal model of the condition, although infant monkeys with selective brain lesions (Bachevalier, 1991; Bachevalier & Merjanian, 1994) show behavioral features suggestive of autism.

NEUROBIOLOGIC STUDIES

Although no neuropathologic features have been found yet to be characteristic of autism, a number of abnormalities have been reported. Bauman and Kemper (1994) found consistent neuronal changes (“too many, too small”) in the hippocampus, amygdala, and other areas of the limbic system, as well as decreased Purkinje cells in the lateral cerebellum. More recently, Bailey et al., (1998) reported cerebellar, neocortical, and olivary

(but not limbic) changes. These findings may reflect “developmental curtailment” of the cellular connections in the developing cortex (neuropil) that affects information processing and representational memory (in the hippocampal complex); recognition of facial gestures and cross-modal memory (amygdala); and shifting attention, language processing, and motor function (cerebellum). In spite of the limitations of traditional methods inherent in light microscopic studies of autism so far (Rapin & Katzman, 1998), and the paucity of postmortem tissue available for study, these studies have fostered a new era in neurobiological research in autism by other investigators who are using recently developed genetic, neurochemical, and morphological techniques.

Diverse Causes for Similar Defects of “Higher Cortical Functions”

Autism can be caused by a number of different insults and etiologies. These causes may be as diverse as viral infections, dysmorphic syndromes, or genetic abnormalities of intracellular metabolism. In any individual,

¹Condensed with permission from a chapter in Pasquale Accardo (Ed.), *Autism: Clinical and research issues*. Towson, MD: York Press. (2000).

these would produce a fairly unique pattern at the neural level, even though their behavioral outcomes are more similar. There are some aspects of function in which it is possible to make a fairly direct correlation to neuroanatomy, particularly in the fully developed organism. The elementary sensory and motor systems are the best examples. However, higher cognitive abilities, by their very nature, are the product of a number of different underlying mental functions. Each of these functions may have very complex relationships to neural structures. These mental functions may not even be products of structures per se, as much as of their internal dynamics or the dynamics of other systems and structures. Moreover, many of the functions considered to be *higher* abilities are actually *chains* of abilities that unfold over time. The higher functions considered to be most important were unlikely to have sprung up full-blown in phylogeny. More likely, they have been cobbled together out of refined and rearranged combinations of other functions. Therefore, such functions may not have very direct brain correlations. The situation is even more complicated in the case of developmental disorders. Normal mental development proceeds through a cascade of many different processes, which tend to bootstrap each other. The interruption, or just simple delay, in any part of this sequence, can and often does have major effects on the final components and their assembly into a functional whole.

The genetic deficits of autism may be expressed in peculiar patterns that can be related to neurobiologic organization, but not to the functional organization of the nervous system. They also may be expressed at different times in the developing nervous system. Some of these effects may be visible at the time they occur, whereas some may take a long period of subsequent development to be expressed. It is still a reasonable strategy to look as early in

development as possible for clues to the neurobiologic problems. A recent example is the study by Teitelbaum, Teitelbaum, Nye, Fryman, & Maurer (1998), which showed that movement disorders could be retrospectively detected in autistic children as early as ages 4 to 6 months. Of particular relevance to the issues raised here is that the movement disorders were expressed in different movements, and in different ways, among the different children.

Neural Networks

Neuropathological findings in the limbic system, cerebellum, and frontal cortex in autism suggest that disorders in these structures may be important contributors to the autism deficit. Variations in clinical expression among autism spectrum disorders may relate to different types of effects—as well as their distribution—in related structures, such as the basal ganglia (important for motor planning) and prefrontal cortex (motivation, executive functions) (see Figure 1). These regions may be dysfunctional by themselves (e.g., following closed-head injury, stroke, or encephalitis) or may become disconnected from their interactive partners within networks due to their failure to develop, modify, or prune their connections during development of the neuropil (Zilbovicius et al., 1995). For example, the basal ganglia (caudate and globus pallidus) and thalamus are essential subcortical integrating way-stations in networks with prefrontal and anterior cingulate cortex. Abnormalities in subcortical neurotransmission to or from the prefrontal cortex are likely to contribute to executive dysfunction, disinhibition and irritability, and apathy and inertia (Denckla & Reiss, 1997).

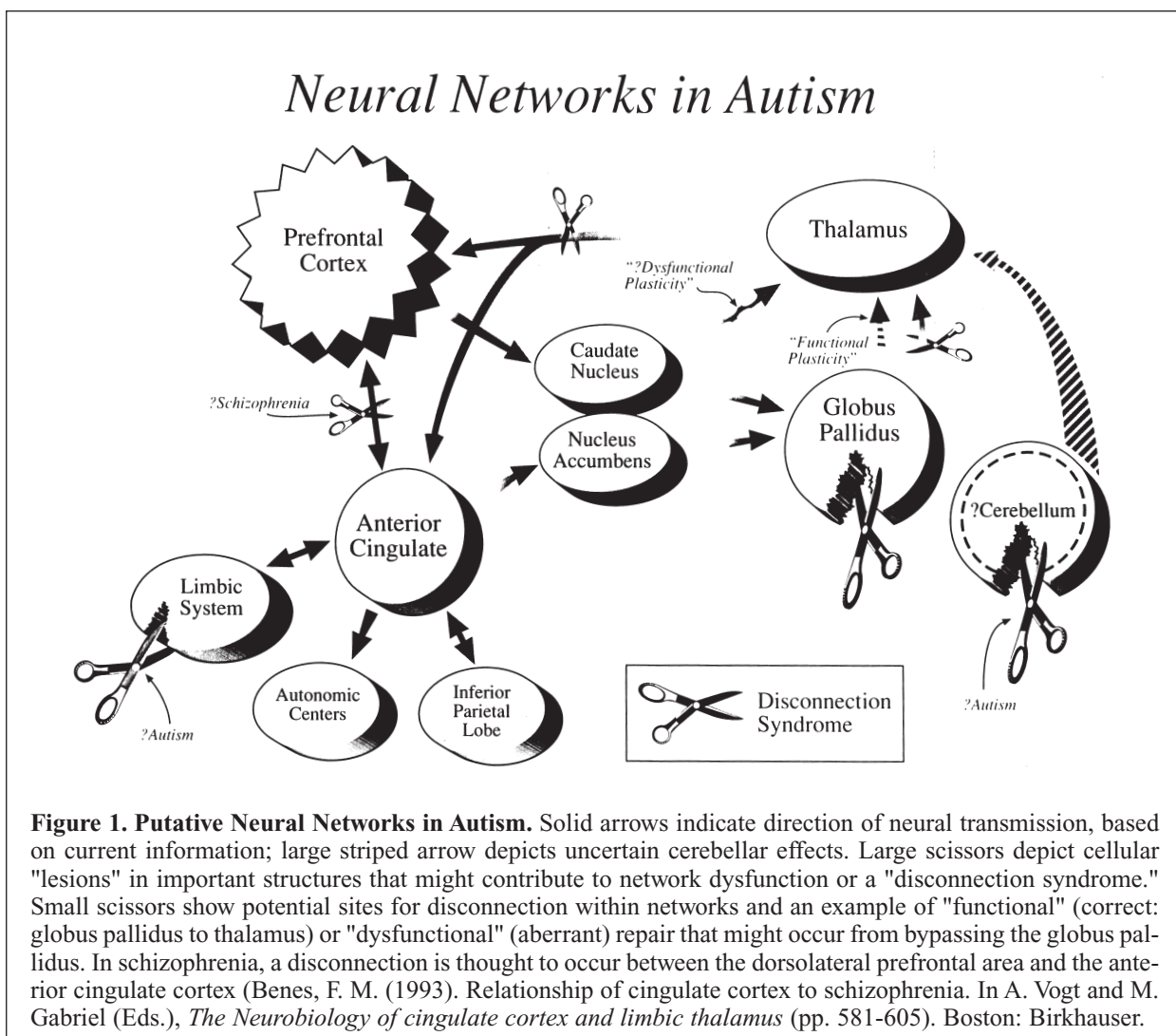
The capacity for repair of, or compensation for, brain lesions (plasticity) is maximal during the early years of development (Jacobson, 1991). Therapeutic programs in

autism may take advantage of this potential for repair (Greenspan & Wieder, 1997; Lovaas, 1987). Although its biological basis is poorly understood, clinically effective repair may depend on the regulation of multiple neurotransmitters, growth, and other trophic factors in the brain while training programs are taking place. (Repair also may occur to some degree with or without training.) Compensation for defective way-station processes (e.g., hippocampal or cerebellar), or disconnection within networks, probably depends on correct forms of rerouting ("functional plasticity," see Fig.1). Plasticity

is functional if it compensates for a disconnection between way-stations (e.g., between globus pallidus and thalamus). "Dysfunctional plasticity" (e.g., from caudate to thalamus) may reduce the efficiency of the repair or even negate its effects if the new route bypasses critical parts of the network (e.g, globus pallidus).

FUNDAMENTAL COGNITIVE AND BEHAVIORAL DEFICITS IN AUTISM

There have been a number of attempts to tease apart the cognitive and behavioral deficits that occur in autism, and to hopefully



identify some as more fundamental than others (for reviews, see Bailey, Phillips, & Rutter, 1996; Happe & Frith, 1996; Rapin 1997; Rumsey, 1996; and Litrownik & McInnis, 1982). A recent example has been attention to the lack of a *theory of mind* in autism. Theory of mind was the term used by Premak & Woodruff (1978) to describe an individual's understanding of the motives, knowledge, and beliefs of others. Frith, Baron-Cohen, and others (Baron-Cohen, 1995; Baron-Cohen & Swettenham, 1997; Frith & Happe, 1994) have noted that autistic individuals do not seem to have such understanding, nor are they able to develop it. Consequently, these authors have posited that a deficit in the primitive functions that form the basis for having a theory of mind could be a major cause of the difficulties in autism. However, just what constitutes a theory of mind, who has it, and whether it is truly impaired in autism has been debated (see, for example, Povinelli & Preuss, 1995).

A different, perhaps more fundamental deficit should be entertained as being present in many persons with autism, particularly if they are low-functioning: a deficit in the ability to selectively manipulate sensory representations, concepts, and thoughts. This manipulatory deficit would be independent of the sensory representations, concepts, and thoughts themselves (although these may also be deficient). In basic terms, this is a problem with the *ability to imagine*. However, it is not a deficit in simple visual imagery; there is self-reported evidence that high-functioning persons with autism not only have visual imaginations but rely upon them (Grandin, 1997). Instead, what is referred to here is the ability to select elements of mental states and manipulate them. Normally, humans are able to focus on different aspects of an object or experience, and even seem to be able to break these aspects

away from the original experience and manipulate them separately. A person can see a red cup and separate out its redness from its shape. Persons with autism, however, are notorious for not being able to do this. They are notorious for context-dependence and for apparently focusing on the "wrong" features of everyday objects.

There is some evidence that, in normal individuals, this ability to select features from otherwise unitary representations is dependent upon the prefrontal cortex (Thompson-Schill, Esposito, Aguirre, & Farrah, 1997). A deficit in such functions would certainly fit with many of the other noted behavioral characteristics of persons with autism: their rigidity, repetitive behavior, and perservation; their lack of symbolic play; and, more elaborately, a theory of mind. Deacon (1997) and others have suggested that this type of mental manipulation, which is essentially symbolic, is one of the important mental prerequisites of humanness.

Within the subgroups of autism, much still needs to be explained. Each of the subgroups (described in Zimmerman & Gordon, 2000) is known to be associated with at least two paradoxes. One is that autistic individuals often have disproportionate mental abilities and skills, in addition to their obvious disabilities. The other paradox is that, despite the clear cognitive and behavioral abnormalities in each of the autistic categories, the underlying neural pathology still seems to resist a consistent description. Going back and reclassifying the pathology of autism into clinical subcategories does not yet result in a more coherent picture. According to published studies, even within these clinical subcategories, reported abnormalities may be present in some individuals and absent (or different) in others. The inability to find beneficial effects of any categorization scheme may simply reflect how conflated these categories

have been in reported studies, and in the impossibility of reconstructing them from the published accounts. It is also very possible that some heterogeneity—in mental functions as well as in neuropathology—will prove to be a fundamental characteristic of each category of autism.

Behavioral Heterogeneity

One of the most striking features of autism is that that it is often accompanied by relative strengths in some areas of cognition, in addition to disabilities in others (Happé & Frith, 1996; O'Connor & Hermelin, 1989). Such patterns are well known in developmental disorders. In Williams syndrome, speech, surface language abilities, and (at times) musical ability, are typically far superior to visual-spatial abilities and to general cognitive abilities (Capirci, Sabbadini & Volterra, 1996; Tager-Flusberg, Boshart, & Baron-Cohen, 1998). Many of the developmental syndromes of mental retardation have relative preservation of visual-perceptual ability (Pulsifer, 1996). However, supranormal islands of ability are much rarer in other conditions compared to autism spectrum disorders (Happé & Frith, 1996). It has been claimed that 10% of the autistic population has “special abilities” (Rimland & Fein, 1988). The supranormal skills that have been described in both autistics and in individuals with other diagnoses include lightning calculation, calendar skills, list learning (Mottron, Belleville, Stip, & Morasse, 1998), visual memory, hyperlexia, puzzle construction, drawing ability, musical memory, and playing by ear and improvisation. (For more complete lists, see Happé & Frith, 1996; O'Connor & Hermelin, 1989.) Regardless of the exact proportion having such abilities, the overabundance of such skills demands some explanation and might even shed some light on the nature and neurobiology

of autism itself, as Frith (1989), O'Connor (1989), and others have suggested.

Not all of the apparently superior skills that have been reported are difficult to explain. Restricted attentional focus, repetitiveness, and the lack of competing thoughts or abilities (Frith, 1989) can certainly account for many apparent abilities. A recent study of atypical memory abilities in one individual (Mottron et al., 1998) is perhaps an example of how superior performance in one area may be accounted for, in some instances, by actual cognitive deficiencies in other areas.

However, there are other examples of apparently superior ability that seem to arise spontaneously (e.g., Selfe, 1977) and do not seem to be easily explained by the absence of normal mental impediments. These often seem to involve implicit learning of rules and patterns (Hermelin & O'Connor, 1986). They also often seem to be remarkably circumscribed. An individual who can do lightning calculations of dates may not even be able to multiply numbers (Happé & Frith, 1996). It may not be unreasonable to ask that any unified account of the neural basis for autism account for these abilities as well as autism's documented disabilities.

NEURAL NETWORK THEORIES

It may be possible to unify both the behavioral heterogeneity—the abnormalities and the supernormalities—as well as the possible neural heterogeneity. To do so requires a digression into neural network theories. (It should be noted that Cohen 1994 raised many of the same hypotheses proposed here.) Neural network theories of cognitive processes posit that many mental operations are carried out through successive sets (layers) of neuronal processing elements. (For a brief overview, see Gordon, 1997.) With the proper

input and training criteria, and the proper learning of rules, such networks have proven to be extremely adept at embodying rules and patterns that are implicit in the data presented to them. However, the accuracy of this extraction is very dependent upon the number of processing elements in the active learning layer (Baum & Hausler, 1989). If there are too few elements, then the network does not learn with very good accuracy: it, in fact, tends to over-generalize. If there are too many elements, then the network learns each specific situation presented to it and doesn't generalize enough. If some number of working elements leads to adequate performance, a somewhat greater number can result in truly superior performance in learning implicit rules and patterns, as long as it avoids becoming too specific.

This observation might be tied in to normal development, and to the abnormal development(s) that occur in autism, in the following way: the normal development of higher cerebral functions in a child's cortex appears to be driven by at least two major influences. One is predetermined connections: the other is activity and use. It has often been noted that the number of genes coding for the brain and neural tissue (~50,000) are insufficient to specify all the connections of the mature brain. Thus, the development of these connections must be guided in part by experience. Edelman (1987) and Intrator and Edelman (1997) have suggested that whether an uncommitted area develops connections with one region or another is based on the outcome of a competition for use. The developing child's brain normally has several primary sensory inputs, including vision, audition, and touch. These inputs are hardwired and fairly compelling. Such sensory inputs will do all they can to recruit whatever upstream neuronal processing resources are not yet committed.

Normally, the multiple influences on a child lead to a balance of forces, with the normal balance of lower and higher processing abilities (and neuroanatomic maps) as a result. The amount of neural tissue that is devoted to each higher function therefore represents a tradeoff between several forces: an attempt to optimize processing, the practical limits on optimization (because of lack of enough experience and training time), and competition with other functions for those same neuronal processing elements.

What if a developing brain had all those same forces at work, but for some reason some processing systems were impaired or delayed in their development? What if the systems in question were those involved in speech perception and speech production? Specific genetic deficits in speech production have been tentatively identified. It is conceivable that there are other deficits or combinations of deficits with more widespread effects on both speech production and speech perception. If the systems related to speech perception and speech production were developmentally impaired, then many higher abilities dependent upon appropriate auditory input and output would never develop properly. Whatever cerebral tissue would have been devoted to those higher functions would then be free to be incorporated into other processes (assuming the tissue itself was not too badly affected by the same defects). If vision were intact, then visual-related abilities would be expected to appropriate the extra cerebral tissue. The result would be a child's brain that was not capable of all of the normal functions of a child, but that was capable of performing some functions superlatively well. The brain would not be capable of those abilities that are related to speech and language capability, such as a long-term component of working memory (the part normally dependent upon an articulatory loop), and perhaps even such

higher functions as the “inner voice” aspects of consciousness. It would, however, be extraordinarily good at wordless visual perception and analysis. Neuropathologically, such a brain might have only a few, apparently nonspecific, abnormalities. It would not have to have fewer neurons than normal. Autistic brains are, if anything, average or larger-than-average in size (Courchesne, Muller & Saitoh, 1999; Lainhart et al., 1997). It might be possible to detect additional territory devoted to visual-related functions, but perhaps not with current behavioral tasks and instrumentation. Autism may therefore represent disorders of activity-dependent plasticity during brain development that occur at several different levels: gene, synapse, neuron, network, and neuronal group.

Hypothesis of Activity-Dependent Plasticity

In broader outline, the hypothesis is this: Either because of genetics or external influences, several regions or neuronal networks of the developing brain are damaged or delayed in their development. Regions involved in social connection and those involved in speech and language seem to be particularly susceptible. (It is not too speculative to imagine that they have a functional linkage and perhaps, therefore, a genetic one as well.) There are two consequences of this primary pathology. Functions that require these inputs cannot develop fully. Functions that were not dependent upon these impaired routes can develop normally, and might well develop supranormally. They would develop supranormally if these functions were normally kept constrained by a competition for neural resources from the functions that were now impaired (with the competition being

either in functional space or perhaps just through simple anatomic proximity).

This hypothesis has several testable consequences. There will be *forme frustes* of autistic disorder—in speech and language and in socialization—representing less extreme forms of the autistic pathology. These types of deficits should be familial. The domino effect on functions should be predictable after research establishes a better understanding of what functions depend upon other functions, in both development and in operation. Finally, it should be possible to identify some *in vivo* correlates of the extra neural tissue that has been adopted for processing (e.g., vision) in these individuals.

This hypothesis does not explain the primary cause or causes of the deficits. It would, however, help to explain why persons with autism tend to have the patterns of disabilities and abilities that they do, and why their neuropathology (in the broadest sense) has been so variable from individual to individual. It might also suggest ways in which functional retraining can try to ameliorate some of their disabilities or take advantage of their particular strengths.

CONCLUSION

The next stages of investigation of neural mechanisms in autism spectrum disorders should first focus on the selection of subjects and clinical definition of subsets. Although well-studied animal models are desirable, high-functioning subjects with autism are more likely to reveal the essential abnormalities in this very “human” disorder. Multiple investigative techniques, from cellular and neurochemical to cognitive neurophysiology, and quantitative and functional neuroimaging, will help to define the neural networks that contribute to autism. ■

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Autism as a Disorder of Complex Information Processing¹

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This chapter reviews the evidence leading to the proposal of the neurobehavioral model, or conceptual construct, of autism as a disorder of complex information processing that spares the visual-spatial system. This model is a multiple primary cognitive deficit model proposing that the pattern of deficits within and across cognitive domains in autism is a reflection of complex information processing demands.

NEUROBEHAVIORAL MODELS IN NEUROBIOLOGIC CONTEXT

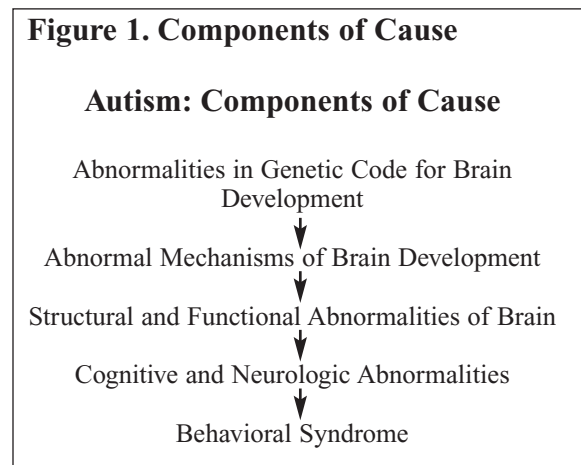
Neurobehavioral models for autism are hypotheses about the cognitive basis of behavior and its neural representation in the brain. Numerous such models have been proposed for autism in the decades since a neurologic origin gained acceptance. These models, and the large body of research they arose from and led to, have resulted in major progress in the characterization of the neurocognitive basis of autism with several major consequences. First, this research has led to substantial improvements in diagnostic criteria, recognition of affected individuals, and treatment. Second, recent developments in the definition of structural and functional abnormalities of the brain have culminated in the recognition that the brain in autism

reflects the unique effects of disruption of the dynamics of brain development. A third milestone resulting from this research has been the recognition of partially affected family members and the resulting appreciation of autism as a family genetic disorder with multiple probable genetic loci. Collectively, these research contributions have led to the current conceptualization of the neurobiology of autism as originating with familial abnormalities in the genome that code for brain development. Multiple families of gene abnormalities are anticipated, reflecting various clinical phenomena. These gene abnormalities are expected to code for various abnormal mechanisms for brain development, which culminate in the structural and functional abnormalities of the brain seen in autism. These functional and structural abnormalities constitute the neural basis for the cognitive impairments underlying the behavior that defines autism (see Figure 1). The achievement of this conceptualization of the neurobiology of autism has been the product of decades of research and has made

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the long-term goal of developing corrective neurobiologic interventions for autism finally conceivable. The eventual attainment of this goal is dependent on achieving a detailed characterization of each of the elements in this neurobiologic chain of events. The continuing investigation of the cognitive and neural basis of autism in future research can be expected to play as significant a guiding role in reaching this goal as it did in making such a goal feasible.

Figure 1. Components of Cause



EVOLUTION IN NEUROBEHAVIORAL MODELS FOR AUTISM

The investigation of the cognitive and neural basis of autism has led to numerous neurobehavioral models in the 35 years since a neurologic origin for autism first gained acceptance (Rimland, 1964). These models reflect a stepwise series of progressively improving approximations of the underlying pathophysiology that resulted from research investigating important hypotheses about the neurocognitive basis of autism. Current neurobehavioral models are a composite reflection of the accumulated knowledge of decades of research as well as the considerable remaining unknowns about autism and about the normal human brain, cognition, and behavior. Neurobehavioral models are thus,

by definition, temporary conceptual constructs that organize existing findings into testable hypotheses for further investigation.

The earliest neurobehavioral models for autism emerged in the 1960s and 1970s and generally proposed a single primary deficit in an aspect of information acquisition as the cognitive basis for this behavioral syndrome. Therefore, the earliest models hypothesized deficits in sensory perception, brainstem attentional or arousal mechanisms, or associative memory. These models were ultimately abandoned when the previously demonstrated abnormalities in post-rotary nystagmus, brainstem auditory-evoked potentials, temporal horn ventricular size on imaging, and associative memory were found to be the result of the inclusion of a substantial number of autistic subjects with coexisting causes for these findings. Repetition of these studies with autistic subjects screened to exclude those with other disorders causing brain damage failed to provide evidence of abnormalities (Campbell, Rosenbloom, & Perry, 1982; Creasey et al., 1986; Courchesne & Lincoln, 1985; Courchesne, Hicks, & Lincoln et al., 1985; Damasio, Maurer, Damasio, & Chui, 1980; Dunn, 1989; Minshew & Goldstein, 1993; Ornitz, Atwell, Kaplan, & Westlake, 1985; Ornitz, Sugiyama & deTraversay, 1993; Prior, Tress, Hoffman, & Bolt, 1984; Rumsey, Grimes, Pikus, Duara, & Ismond, 1984). However, even the latter studies provided little neuropsychologic evidence documenting the status of sensory perception, attention, and associative memory abilities in autism.

A second, shorter-lived group of neurobehavioral models emerged in the 1970s, proposing a left hemisphere-language acquisition defect or a lack of hemispheric specialization as the basis for autism (reviewed in Minshew, 1994). By the mid-1980s, however, neuropathologic (Bauman & Kemper, 1985) and neurophysiologic studies (reviewed in Minshew,

1991) had consistently demonstrated a bilaterally symmetric pattern of brain involvement in autism. In addition, evidence of right hemisphere language deficits involving prosody, gesture, and facial expression was emerging, highlighting the limitations of drawing conclusions about the brain localization for autism based on the localization of a single cognitive deficit.

In 1980, the first formal information processing model for autism was proposed. This model was based on the first report in autism of attenuation or absence of auditory P300 evoked potentials with sparing of visual P300 potentials, which led to the hypothesis of a selective auditory information processing defect (Novick, Kurtzberg, & Vaughan, 1979; Novick, Kurtzberg, Vaughan, & Simpson, 1980). In light of the intact behavioral performance of the subjects, Novick and colleagues (1980) proposed that the neurophysiologic abnormality reflected the reliance by parietal cortex on less efficient neural pathways for the processing of auditory information. The disparity observed between auditory and visual P300 potential abnormalities in autism was replicated by subsequent investigators (Dunn, 1989), and led to questions about the involvement of visual information processing and the posterior regions of the cerebral hemispheres. These neurophysiologic findings were among the first data demonstrating the central involvement in autism of information analysis and evaluation rather than of information acquisition. These data were also of major significance for providing documentation of the consistent and reliable conduction of sensory information to the cerebral cortex and of the consistency of sensory perception by individuals with autism (Minschew, Sweeny, & Bauman, 1997).

In the latter 1980s and early 1990s, several major cognitive findings were reported that led to a number of new neurobehavioral

models. In 1988, a study of neuropsychologic functioning across domains in 10 autistic men with average group mean verbal and performance IQ scores documented a cognitive profile characterized by dramatic deficits in conceptual reasoning abilities, relatively intact language, memory, and motor abilities, and intact sensory perception and visual-spatial abilities (Rumsey & Hamburger, 1988). Based on this profile, Rumsey and Hamburger proposed a core deficit in a broad class of verbal and non-verbal conceptual reasoning abilities, but had difficulty relating this deficit conceptually to the behavioral syndrome of autism. Ozonoff, Pennington, and Rogers (1991) replicated this overall profile and accumulated evidence of executive function deficits, which led to their proposal of an influential executive dysfunction-frontal systems model for autism (Ozonoff, Pennington, & Rogers, 1991). In a second significant study, Ozonoff, McMahon, & Filloux (1994) investigated the specific cognitive components in autism responsible for executive dysfunction on the Wisconsin Card Sorting Test. They identified the cognitive flexibility component as the major source of impaired performance, and the inhibition of prepotent responses as making a modest contribution. Notably, they found that components related to shifting attention between different features of an object and to inhibiting responses failed to demonstrate impairments, leading Ozonoff and colleagues to propose that autistic individuals' perseverative focus of attention on details had a conceptual rather than a perceptual basis. This study was also significant for demonstrating that complex cognitive tasks received contributions from multiple component processes that could be separated with appropriate procedures and that the impaired performance of different neuropsychiatric populations could be traced to dysfunction of different components.

A second major recent contribution to neurobehavioral conceptualizations of autism was the recognition of “theory of mind” deficits as a major cognitive mechanism underlying the abnormal social behavior in autism. The identification of this cognitive ability and its impairment in autism demystified social behavior in autism and brought it clearly into the realm of cognitive psychology. It was also a milestone, and likely the first of many, for having identified a previously unsuspected cognitive ability responsible for an important aspect of human behavior (Tooby & Cosmides, 1995). The model proposed for theory of mind abilities in autism was also notable for highlighting the role of multiple cognitive abilities acting in concert in novel ways to subservise complex human behavior (Baron-Cohen, 1995). Thus, the impairment in the capacity for making inferences about the mental beliefs and knowledge of others was seen as functionally linked to deficits in the social use of eye contact. This model thus converged with reports on autism of deficits in the use of eye contact to achieve shared attention (Sigman, 1996), another newly recognized cognitive or neurologic function contributing to social behavior. These two newly recognized abilities provided clear examples of the many yet-to-be defined cognitive abilities that contribute to the complex cognitive and behavioral competencies impaired in autism, and of the likely need to reconceptualize the cognitive contributions to other impaired abilities in autism as new research findings are reported.

A third major influence on recent neurocognitive models for autism pertains to reports of attentional deficits. Deficits in attention have been proposed repeatedly throughout the course of autism research in an attempt to explain the autistic individual’s intense focus on details, on the one hand, and a lack of interest in people, on the other.

Although recent research studies summarized previously have provided evidence for a conceptual basis for these abnormalities in behavior, deficits in attention continue to be reported and proposed as the primary cognitive basis for behavior in autism. Deficits in selective attention, attention to extra-personal space, and shifting attention have been among those recently proposed (Courchesne et al., 1993; Ornitz, 1988; Townsend & Courchesne, 1994). The first two of these deficits were inferred from neurophysiologic abnormalities in the absence of impairments in cognitive performance and imaging abnormalities involving the parietal lobe, respectively. The shifting attention deficit was documented with a cognitive paradigm, but the paradigm also had substantial executive function and working memory demands in addition to the demand for an attentional shift at the perceptual level. The multiple demands of this task made it impossible to determine the cognitive origin for the impaired performance in autism without investigating these contributions individually. A number of subsequent studies attempted to clarify the role of attentional processes in autism. Collectively, these studies examined the reflexive and voluntary or executive control of attention in individuals with autism of varying levels of ability (reviewed in Burack, Enns, & Johannes, 1997). These studies provided evidence that abnormalities in attentional focus in autism are related to the information processing aspects of the tasks and the voluntary or executive control of attention, and not to deficits in reflexive orienting abilities. These latter studies were also of major importance in highlighting the influence of developmental level or general ability level on the expression of deficits in autism, and the limitations of conclusions about core deficits that did not consider these influences.

Up to this point, neurobehavioral models for autism generally were single primary cognitive deficit models, proposing a clinically apparent deficit in a single cognitive domain or modality as underlying the social, communication, and odd nonsocial behavior in autism. By the early 1990s, however, substantive evidence of deficits in several higher-order cognitive abilities had emerged, posing a major question for the validity of single primary deficit models. As most of the cognitive and neuropsychologic studies in autism had focused on a single cognitive domain, their design precluded the identification of potential deficits in other domains and the consideration of their significance in the various neurobehavioral models.

PROFILE OF NEUROPSYCHOLOGIC FUNCTIONING IN AUTISM

Examination of cognitive functioning across domains within the same subject sample provided an obvious opportunity for addressing the issue of single versus multiple co-existing cognitive deficits in autism. It also provided an opportunity for observing the pattern of these deficits, which itself might contain additional important clues to the underlying neurobiology. One of the first studies to investigate neuropsychologic functioning across domains in a group of autistic subjects screened to exclude those with causes of brain dysfunction other than autism was that of Rumsey and Hamburger (1988). This study was viewed as remarkable for the demonstration of dramatic impairments in the reasoning domain that were not explainable by deficits in other domains. However, less noticed was the characterization of the language, memory, and motor domains as “relatively intact,” whereas sensory perception and visual-spatial abilities were described as intact. Examination of the test

battery revealed only a few tests and mixed results in the language, memory, and motor domains, whereas there were a larger number and broader range of tests for the reasoning domain. The relatively intact domains reflected a combination of good performance on tests of simpler abilities and impairments on tests of more complex abilities, especially in the memory and language areas. A number of investigators subsequently replicated this profile, emphasizing the evidence for executive dysfunction but again relying on few tests in the language and memory domains, with the same mixed results.

One study attempted to address this issue by expanding the memory and language test battery and by separately considering simple and complex abilities at analysis (Minschew et al., 1992). This study of 15 nonmentally retarded individuals with autism revealed intact function on memory tests of simple associative processes and on language tests of basic skills such as word fluency, reading decoding, and spelling. Memory deficits were documented on delayed recall measures, suggesting that information encoding was not sufficiently supported by organizing strategies. Language deficits were documented on tests of higher-order abilities, such as comprehension of idioms, metaphors, and ambiguous sentences. This pattern of findings in the language and memory domains suggested the presence of a dissociation in autism between simple and complex abilities. The second major finding of this study was the absence of impairments on the Wisconsin Card Sorting Test (WCST). Deficits on this test had come to be viewed as a hallmark of the abstraction deficit in autism as a result of the extensive investigation of executive dysfunction based on this test. Instead, abstraction deficits were demonstrated on the Goldstein-Scheerer Object Sorting Test with a test of verbal reasoning and in the capacity

to shift concepts. The absence of deficits on the WCST in this study was attributed to the higher level of function of the autistic subjects compared to prior studies. In these subjects, the deficit was better characterized by deficits on concept-formation tests than by rule-learning tests, such as the WCST. The third significant finding of this study was the presence of deficits on Part A, but not on Part B, of the Trail Making Test. Deficits on Part B are typically viewed as evidence of problems with executive function or shifting attention, as subserved by the frontal lobes. Part A has minimal cognitive demands and serves as practice for Part B; the major demand of part A is on psychomotor skills. The intact performance by the subjects with autism on Part B, but with impairments on Part A, suggested the presence of psychomotor slowing. Review of the Rumsey and Hamburger (1988) Trail Making Test data revealed that their subjects had exhibited greater deficits on Part A than on Part B, as well as exhibiting evidence of psychomotor slowing on a finger-tapping task.

Several of the findings from the preceding study were amplified in follow-up studies. Concept formation ability was investigated further with the Twenty Questions Procedure, which requires subjects to identify a preselected object from an array using a maximum of 20 questions. The most efficient strategy is to formulate constraint-seeking questions that involve characteristics shared by several objects, which can eliminate several alternatives at once and thus progressively narrow the possibilities to the target item. Four trials were administered in a study comparing the problem-solving skills of nonmentally retarded individuals with autism and matched control subjects. The autistic subjects solved significantly fewer of the four trials and used a significantly smaller number of constraint-seeking questions. Their impaired performance on this test of the

concept formation aspect of abstraction was contrasted with their intact performance on tests of the rule-learning aspect of abstraction, a less challenging aspect of abstraction. The mixed pattern of results in the language and memory area in the Minshe et al. study (1992) led to an in-depth examination of the language domain investigating the hypothesis of a dissociation between preserved simple abilities and impaired complex abilities (Minshe, Goldstein, Taylor, & Siegel, 1994; Minshe, Goldstein, & Siegel, 1995). In these studies, the simple language category was comprised of tests of mechanical skills, such as verbal fluency, mechanical reading, word recognition, spelling, phonetic analysis, and simple calculation. The complex language category included tests of interpretive abilities, such as reading comprehension, understanding of the metaphorical aspects of spoken and written language, and verbal reasoning. The performance of high-functioning subjects with autism was compared to that of normal community volunteers matched by age, gender, race, IQ, and socioeconomic status (SES). The results of the study indicated that the autistic subjects did as well and often better than control subjects on the tests of mechanical language skills, but significantly more poorly on tests of complex interpretive skills. These studies provided additional evidence suggesting that subjects with autism had selectively failed to acquire the higher-level interpretive language abilities expected on the basis of their age, verbal IQ score, and basic language skills.

EVIDENCE FOR A COMPLEX INFORMATION PROCESSING DISORDER

In light of these findings, a third study of the profile of neuropsychologic functioning was designed to further characterize the

pattern within and across domains in a large group of rigorously defined subjects with autism and individually matched controls. The test battery was expanded and designed to address the neuropsychologic deficits hypothesized by various neurobehavioral models for autism, as well as to address the hypothesis of selective involvement of higher-order cognitive abilities related to generalized dysfunction of association cortex. The battery was composed of valid and reliable neuropsychologic tests assessing the major cognitive domains of attention, sensory perception, motor function, language, memory, reasoning, and visual-spatial abilities (see Table 1 in the chapter appendix, "Results of Neuropsychological Tests Assessing the Major Cognitive Domains.") The visual-spatial domain was included because its status was important in completing the profile of cognitive functioning in autism, although visual-spatial abilities have long been considered a strength of individuals with autism. A range of abilities was considered within each domain to address the various hypothesized deficits, and both verbal and visual modalities were assessed where appropriate. The large number of measures relevant to the assessment of simple and complex language and memory abilities in both the visual and auditory modalities required subdivision of these cognitive domains into simple and complex categories for separate analysis. In other domains, the number of tests was fewer and individual consideration of the tests within domains was relied upon to characterize the features related to deficits and intact abilities. Tests in each domain were considered as multivariate sets, and stepwise discriminate function analyses were used to evaluate the accuracy of each set in correctly classifying cases into autistic and control groups. Classification accuracy was assessed with Cohen's kappa, an index of strength of

agreement for nominal scales. Tests included and not included in the regression equations and their order of entry provided additional information on which tests had the most discriminatory power. Individual t-tests were computed to clarify performance on tests not included in the regression equations (see Table 2, chapter appendix).

Tests in the attention, sensory perception, simple memory, and visual-spatial domains did not yield satisfactory classification accuracy, providing evidence of intact basic information acquisition abilities and intact information processing in the visual-spatial domain. *Kappa* scores in the fair to good agreement range (0.40-0.75) were obtained for the motor, simple language, complex language, complex memory, and abstract reasoning domains. For the simple language category, the significant *kappa* score reflected superior performance by the subjects with autism relative to control subjects, in contrast to the motor, complex memory, complex language, and reasoning categories where the significant *kappas* reflected impairments.

Examination of tests entered and not entered into the regression equations, order of entry, and individual t-test results provided additional evidence about the nature of the deficit pattern. The attention domain was most notable for the absence of evidence of deficits. Only tests with a motor component—the letter and number cancellation tasks—were entered into the regression equation, and these failed to achieve significant classificatory accuracy. Performance on these two tests was notable for the low rate of errors by both subject groups and the absence of a predilection for any quadrant; thus, there was no support for a hypothesized deficit in attention to extra-personal space. In the motor domain, it was of note that discriminatory accuracy was achieved with the Grooved Pegboard Test and Trail Making Test, Part A,

the two tests of skilled motor sequences. In contrast, there was no difference between subjects with autism and control subjects on the test of simple or isolated motor movements (Finger-tapping Test). T-tests revealed significantly poorer performance on Part A, but not Part B, of the Trail Making Test, which is consistent with prior observations and the assignment of Part A to the motor domain and Part B to the reasoning domain. In the complex language and complex memory domains, test entry was notable for including both verbal and visual tests, thus failing to support the hypothesis of a selective auditory processing deficit in autism. In the reasoning domain, the WCST and the Halstead Category Test (two tests of the rule-learning aspect of abstract reasoning) failed the tolerance test consistent with the previously reported findings in nonmentally retarded individuals with autism (Minshew et al., 1992). The first test passing the tolerance test for the reasoning domain was the Twenty Questions Procedure, which is a concept formation test. This was followed by the Picture Absurdities subtest of the Binet scales, which requires consideration of context and a conceptual framework in order to identify incongruities, and the Trail Making Test, Part B, which challenges working memory and shifting cognitive sets (executive function). The selection of these three tests suggests that the reasoning deficit in autism involves a broad range of conceptual abilities as previously proposed by Rumsey and Hamburger (1988), and that executive dysfunction or cognitive inflexibility might be too narrow to encompass the deficit.

The profile of cognitive functioning in these nonmentally retarded autistic adolescents and adults was therefore defined by deficits in concept formation, complex memory, complex language, and skilled motor abilities and by intact or superior function in

the attention, sensory perception, simple memory, simple language, rule-learning, and visual-spatial areas. The implications of these findings are several.

RESEARCH IMPLICATIONS

The characterization of the cognitive profile in terms of both deficits and intact abilities is significant, as it demonstrates the distinctions between autism and general mental retardation, on the one hand, and the developmental specific learning disabilities, on the other. The two-part characterization also demonstrates the selective impact of autism on higher-order abilities. Thus, the presence of age- and IQ-appropriate performance on tests of spelling, reading, arithmetic, and visual-spatial abilities distinguishes autism from the developmental specific learning disabilities and the nonverbal learning disability syndrome. The intact language, memory, arithmetic, rule-learning and visual-spatial abilities account for the attainment of IQ scores in the average range. The deficits in problem solving, concept formation, complex language and complex memory abilities explain the failure of the average IQ scores to be accurate predictors of adaptive behavior and function in society. This dissociation between intact and deficit skills also explains the clinical observation that abstraction, communication, and social abilities fall rapidly (or disproportionately) with declining IQ in the autistic population as compared to the nonautistic, mentally retarded population, and the lower adaptive function of mentally retarded individuals with autism compared to mentally retarded individuals without autism of the same general level ability.

In addition to demonstrating the selective impact of autism on higher-order cognitive abilities, the documented intact abilities fail to support neurobehavioral models that

hypothesize clinically apparent deficits in sensory perception, attention at the perceptual level, and associative memory as the basis for autism. The integrity of these basic abilities also demonstrates that the deficits documented in concept formation, complex memory, complex language, and skilled motor abilities are not secondary to deficits in more elementary abilities.

A second unique feature of cognitive functioning in the subjects with autism was the pattern of intact simpler abilities in domains demonstrating deficits. Perhaps contrary to expectations, a deficit in the abstract reasoning domain, for example, did not mean that all abstraction was impaired. Rather, deficits in each domain involved the highest level abilities expected on the basis of an individual's age and IQ, while leaving simpler abilities intact or even enhanced. That is, in each domain, deficits appeared to correspond to the highest level tasks, thus depending on the most cognitively advanced abilities, whereas intact function appeared to correspond to the simplest or most basic skills. This pattern conformed to the neurophysiologic pattern reported for autism of impaired, late cognitive potentials and intact earlier potentials. Across domains, complexity also appeared to account for the predilection of deficits for those domains with the highest demands on information processing. The consistency of this pattern within and across domains and with the neurophysiologic pattern suggests that it reflects a neurobiologic feature or principle of brain structure and function.

As one way of probing the validity of this conceptualization or characterization of cognitive functioning in autism, the cognitive profile defined in this study was compared with that reported by Tallal for a disorder of early or simple information processing (Jernigan, Hesselink, Sowell, &

Tallal, 1991; Johnston, Stark, Mellits, & Tallal, 1981; Neville et al., 1993; Tallal & Piercy, 1973; Tallal et al., 1996). This comparison revealed that the cognitive profile in autism was the converse of that described by Tallal for children with developmental specific learning impairment (SLI). As in autism, the neuropsychologic profile in children with SLI involved multiple domains but included the attention domain as well as the sensory perception, motor, memory, and language domains. Unlike autism, the deficits involved the elementary or simple abilities; namely, basic attentional processes, sensory perception, elementary motor, simple memory, and simple language abilities. This profile was found to correspond to a disturbance in early information processing, resulting in the failure to acquire information dependent on the first 100 msec of information processing. In contrast, higher-order interpretative and reasoning skills were intact, and the children could sometimes use these abilities to fill in or infer missing information.

Evidence of a deficit in complex abilities in the motor domain also supports the neurobiologic validity of a complex information processing construct in autism. That is, the presence of a dissociation between simple and complex abilities in an area of minor clinical involvement would also suggest that the dissociation reflects a fundamental feature of the neurobiology. The coexistence of a similar pattern across domains suggests that the deficits are dependent on a common neural substrate or organizing principle of the brain.

In arriving at the characterization of the cognitive profile in autism as reflecting a complex information processing disorder, consideration was given to the ways that complexity is defined. Within cognitive theory, complexity is defined in several ways, including number of elements contained in the stimulus material as well as the multiplicity of

cognitive processes involved in task performance. The latter definition involves emergent abilities that are not directly reducible to simpler elements of cognitive function (i.e., the reductionist fallacy). Thus, the cognitive capacity to comprehend extended blocks of language is not simply reducible to vocabulary and grammar skills, but requires another level of language abilities in order to comprehend the meanings beyond those implicit to vocabulary and the arrangement of words into sentences. The model proposed here does not distinguish between these definitions of complexity, particularly because they are related in the sense that, as the number of elements increases, there is typically an increase in the number of cognitive processes needed for task performance.

The application of a complexity construct to the cognitive profile in autism requires several constraints or specifications to accurately reflect the data from which it was derived. First, the data in this study define deficits by complexity within domains, not independent of domains; thus, the definition of complexity conveyed in this model is domain-related. That is, although any language skill might be viewed from a cognitive perspective as more complex than any motor skill, the deficits found do not conform to a cognitive ranking of relative complexity independent of domain. Rather, the deficit pattern appears to conform to the fact that different cognitive functions are represented by separate neurologic systems in the brain. Second, visual-spatial abilities involve complex information processing but were found to be intact; thus, the disorder of complex information processing in autism must be stipulated to spare the visual-spatial domain. Because the visual-spatial system is a separate neural system, it is reasonable to assume that this neural system could be spared through various neurobiologic mechanisms

without invalidating a complex information processing model for cognitive functioning in other domains. Third, this model was derived from the study of nonmentally retarded adolescents and adults with autism. If it is to be applied to younger or lower-functioning individuals with autism, it is clear that complexity in terms of cognitive function has to be conceptualized in relation to age and IQ. The specific expression of the complex information processing deficit is therefore going to float as a reflection of the age and general ability level of the individual.

Several key aspects of the clinical syndrome of autism were not assessed in this study because of the time-intensive nature of experimental measures or the lack of sufficiently challenging measures for nonmentally retarded individuals with autism. Consequently, the test battery did not assess social or nonverbal language abilities, although deficits in these abilities are implicit to the diagnosis of autism and were documented with the structured instruments used for diagnosis, which were the Autism Diagnostic Interview (LeCouteur et al., 1989; Lord, Rutter, & LeCouteur, 1994) and the Autism Diagnostic Observation Schedule (Lord, Rutter, & Goode, 1989). Nonetheless, the deficits in these areas can be conceptualized within a complex information-processing model. Theory of mind skills are therefore viewed as a higher-order inferential, cognitive ability. Similarly, the modulation of eye contact and facial expression for communication purposes and the comprehension and expression of satire, irony, and innuendo in prosody are likewise viewed as higher-order complex, information-processing skills. On the other hand, deficits were found in complex memory skills that are not obviously related to the clinical criteria for autism. The data supporting their presence is clear, so the issue is how such an impairment might relate

to the clinical deficits. The evolution of theory of mind abilities in relation to autism provides a model for considering the existence of a previously unrecognized cognitive contribution to the clinical manifestations of autism (Baron-Cohen, 1995). The memory data from the present study provided evidence of intact rote memory for simple information in limited amounts but a reduced capacity for remembering information as its complexity increased. This reduced memory capacity applied to an increasing number of units of the same kind, such as words in a sequence and branch points in a maze, as well as to an increase in the intrinsic complexity of the material, as in the case of stories and the Rey-Osterreith complex figure (Minsheu et al., 1996). Thus, these subjects with autism have difficulty remembering increasing amounts of information and discerning the intrinsic organizational structure of information that normally supports memory. Given that social interactions, communication, and problem-solving situations typically involve the presentation of large amounts of information, it would seem likely that a memory impairment of the type found would contribute to impaired function. As proposed by Toobes and Cosmides (1995) in their foreword to Baron-Cohen's book describing the evolution of the theory of mind data and construct in autism, there are many as-yet-undescribed cognitive abilities that are performed so automatically that their existence is not suspected. The theory of mind model described by Baron-Cohen further suggests that cognitive abilities also may act in concert in ways not currently described to support complex capabilities in humans, and that these interactions may also be disrupted in autism. Consistent with this, it has been proposed that the social and language systems must interact in order for communication to be related to a social context and that

these interactions are disrupted in autism. Such an interaction provides a cognitive and neural basis for the use of language for communication. Similarly, it is probable that the memory system interacts at a cognitive and neural systems level with the social, language, and reasoning systems to support the cognitive functions impaired in autism. Ultimately, these relationships will be explored and elucidated with experimental cognitive procedures and fMRI.

SUMMARY

In summary, this study of neuropsychologic functioning in autism provided evidence of the co-existence of deficits in multiple domains within a single-subject group, supporting a multiple primary cognitive deficit model for the cognitive basis of behavior in autism. No evidence was found of deficits in attention, sensory perception, or associative memory to support neurobehavioral theories hypothesizing clinically apparent deficits in these abilities as the basis of behavior in autism. Within affected domains, impairments consistently involved the most complex tasks dependent on higher-order abilities whereas intact or superior function was found on simpler abilities within the same domains. Across domains, complex information-processing demands also provided an explanation for the particular constellation of deficits that define autism; that is, those domains with the highest complex information-processing demands. The neuropsychologic profile for autism characterized in this study is consistent with the evoked potential pattern of abnormal late, endogenous potentials and preserved earlier potentials, and the converse of the neuropsychologic and neurophysiologic pattern described for a simple or early information-processing disorder. The presence of such a

common denominator within and across domains would suggest that impairments are dependent on a common feature of neuronal organization. As such, there is likely to be a larger class than currently appreciated of yet-to-be-defined cognitive abilities impaired as a result of this disturbance in neuronal organization. Theory of mind abilities and the deficits in complex memory identified in this study are examples of the unknown features of the cognitive basis of autism to be defined in future research. Both of these impairments also highlight the emerging recognition of the importance of disruption in the interactions between different cognitive functions and neural systems as the basis for certain aspects of behavior in autism. ■

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Appendix

RESULTS OF NEUROPSYCHOLOGIC TESTS ASSESSING THE MAJOR COGNITIVE DOMAINS

Table A1. Discriminant Analysis Results By Domain and By Order of Entry

Domain	Tests Failing Tolerance Test	Tests Passing Tolerance Test	% Correct	% Jackknife	Kappa ¹
Attention	Serial Digit Learning; Digit Span; Continuous Performance	Letter Cancellation; Number Cancellation	66.7	66.7	.33
Sensory Perception	Luria-Nebraska Tactile Scale: Touch, Position, Finger Position and Stereognosis items	Finger Tip Writing; Luria-Nebraska Sharp/Dull Tactile Scale item	64.6	62.5	.29
Motor	Finger Tapping; Developmental Test of Visual Motor Integration	Grooved Pegboard; Trail Making A	75.8	75.8	.52 ¹
Simple Language	WAIS-R Vocabulary	K-TEA Reading Decoding; K-TEA Spelling; WRMT-R Word Attack; Controlled Oral Word Association	71.2	66.7	.42 ¹
Complex Language	WRMT-R Passage Comprehension; TLC- Metaphoric Expression	K-TEA Reading Comprehension; Verbal Absurdities; Token Test	72.7	65.2	.45 ¹
Simple Memory	Paired Associates; 3 Word Short Term Memory; Maze Recall	CVLT Trial 1	65.2	65.2	.30
Complex Memory	Paired Associates-Delayed; CVLT Long Delay	NVSRT-Consistent Long Term Retrieval; WMS-R Logical Memory- Delayed Recall; Rey Figure-Delayed Recall	77.3	75.8	.55 ¹
Reasoning	Category Test; Wisconsin Card Sort Test	20 Questions; Picture Absurdities; Trail Making B	75.8	72.7	.52 ¹
Visual-Spatial	WAIS-R Picture Completion, Object Assembly	WAIS-R Block Design	56.1	56.1	.12

¹Indicates a significant between-group difference in performance.

Table A2. Psychometric Data Used for Discriminant Analysis

Tests Entered into Prediction Equations	Autistic Group		Control Group		p
	<u>M</u>	<u>SD</u>	<u>M</u>	<u>SD</u>	
<u>Attention Domain</u>					
WAIS-R Digit Span	9.88	3.81	10.52	2.46	.424
Serial Digit Learning-Correct Responses	16.52	8.17	17.42	7.91	.648
Continuous Performance Test-Mean Reaction Time Correct Responses	0.34	0.62	0.23	0.66	.487
Letter Cancellation-Omissions	1.09	1.63	0.45	1.00	.061
Number Cancellation-Omissions	3.27	4.03	4.39	5.38	.342
<u>Sensory Perception Domain</u>					
Luria-Nebraska Tactile Scale:					
Simple Touch Errors	0.29	0.55	0.17	0.48	.407
Stereognosis Errors	0.46	0.59	0.21	0.42	.096
Sharp-Dull Discrimination Errors	0.88	0.80	0.58	0.72	.189
Position Sense Errors	0.00	0.00	0.08	0.41	.328
Finger Position Errors	0.67	1.27	0.46	1.02	.535
* Halstead-Reitan: Fingertip Number Writing-Errors	5.38	4.30	2.79	2.84	.019*
<u>Motor Domain</u>					
Finger Tapping-Dominant Hand	44.27	13.78	45.19	16.24	.805
Developmental Test of Visual-Motor Integration-Total Points	15.42	32.43	22.18	31.69	.465
* Grooved Pegboard-Dominant Hand-Time in Seconds	86.73	18.30	70.67	16.03	.000*
* Trail Making A-Time in Seconds	31.52	15.81	20.45	7.99	.001*
<u>Simple Language Domain</u>					
Controlled Oral Word Association (FAS)-Number of Words	36.00	13.31	34.00	16.18	.586
WAIS-R Vocabulary	9.45	3.02	9.70	2.26	.713
K-TEA Spelling	102.58	16.93	100.91	11.50	.642
Woodcock Reading Mastery-Word Attack	107.24	11.55	103.52	15.53	.273
K-TEA Reading Decoding	97.48	13.60	102.79	10.19	.078

Continued

Table A2. *Continued*

Tests Entered into Prediction Equations	Autistic Group		Control Group		p
	<u>M</u>	<u>SD</u>	<u>M</u>	<u>SD</u>	
<u>Complex Language Domain</u>					
Token Test (number correct)	18.03	2.19	18.42	5.19	.690
* K-TEA Reading Comprehension	91.36	14.43	103.06	12.45	.001*
* Woodcock Reading Mastery-Passage Comprehension	92.27	15.04	104.27	14.34	.002*
* Test of Language Competence-Metaphoric Expression (scaled score)	6.85	3.25	9.42	3.70	.004*
* Binet Verbal Absurdities-Raw Score	9.30	3.64	12.48	3.97	.001*
<u>Simple Memory Domain</u>					
Maze 1 Recall (correct/incorrect)	0.42	0.61	0.52	0.57	.534
3 Word Short Term Memory-Number of Correct Sequences	3.24	3.04	2.91	3.15	.663
Paired-Associate Learning-Number Correct	42.55	23.13	48.76	24.21	.290
CVLT A List-Trial 1 Number Correct	4.50	3.90	6.30	3.90	.072
<u>Complex Memory Domain</u>					
Paired-Associates-Delayed Recall	16.00	7.46	17.45	6.13	.390
CVLT A List-Long Delay	7.00	5.49	9.00	5.55	.146
* WMS-R Logical Memory-Delayed Recall-Elements	5.58	5.79	8.45	6.02	.052*
* Nonverbal Selective Reminding-Consistent Long-term Retrieval	19.94	15.09	37.39	16.09	.000*
* Rey-Osterrieth Figure-Delayed Recall-Number of Elements	16.83	8.58	21.94	7.49	.012*
<u>Reasoning Domain</u>					
Halstead Category Test (errors)	46.24	28.71	40.73	22.46	.388
Wisconsin Card Sorting Test-Perseverative Errors	16.45	15.48	13.27	11.13	.342
Trail Making B (time in seconds)	65.48	37.19	52.42	23.31	.093
* Binet Picture Absurdities (raw score)	20.00	11.46	27.52	6.12	.002*
Questions (% constraint seeking)	35.49	23.82	56.08	14.02	.000*
<u>Visual-Spatial Domain</u>					
WAIS-R Picture Completion	8.76	2.22	9.21	2.27	.415
WAIS-R Object Assembly	9.88	3.63	9.73	2.88	.852
WAIS-R Block Design	10.79	3.25	9.70	2.14	.113
Rey-Osterrieth-copy score	31.30	4.80	33.09	3.75	.096

Autism: Clinical Features and Neurobiological Observations¹

Margaret L. Bauman, M.D.

Since its first description in 1943 (Kanner, 1943), autism has intrigued clinicians and scientists alike, largely because of its association with significant disturbances in cognition and behavior in the absence of obvious physical and brain dysmorphology. For many years, parenting and environmental factors were believed to be to blame for the social aloofness, obsessive need for sameness, perseverative and stereotypic behaviors, and impaired language that characterize this disorder. However, with the advent of improved neurobiological technology and with the awareness of the high incidence of seizures (Deykin & MacMahan, 1979) and abnormal electroencephalograms (Small, 1975) within the autistic population, evidence for neurological basis for the disorder began to mount.

In any consideration of the clinical deficits exhibited by autistic children, disturbances in language development are usually the first concern and are the symptom that most frequently brings the child to the attention of a physician (Rapin, 1991). Initially, some autistic children may appear deaf, failing to respond to being called by their name or to follow simple commands. Rapin and Allen (1987) have suggested that many (if not most) autistic children have impaired comprehension of language and that some may

exhibit a verbal-auditory agnosia or word-deafness (Rapin, Mattis, Rowan et al., 1977).

In the majority of autistic children, expressive language also is significantly delayed, and a significant proportion of these fail to develop any meaningful communication skills (Rutter, 1978). Approximately one-fifth of autistic children appear to develop language at the appropriate time, some of which development can seem to be precocious and associated with an exceptional vocabulary. However, these skills undergo regression, usually between 12 and 18 months of age, following which language development in these children is similar to that of autistic children whose verbal output was delayed from the beginning (Kurita, 1985).

Those children who eventually do develop language display a wide variation in the quantity and quality of communication patterns exhibited. Frequently, little spontaneous language is exhibited, and expressive output is obtained with the assistance of verbal or physical prompts. Some children will demonstrate rote patterns of counting, reciting the alphabet, or repeating scripts they have acquired from television, videotapes, books,

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or parents with little understanding of their meaning. Echolalia may be present, and children perseveratively may repeat a word or the last several words of a sentence just heard. For those children who become fluent speakers, abnormalities of prosody or the melody and intonation of speech may substantially impair communicative intent. Their verbal output may have a sing-song or monotone quality, and they may have difficulty in modulating the volume of their voice. Some highly verbal autistic children may speak pedantically to others, particularly on a favorite topic, with little appreciation of the interest of the listener. Many of these children can appear to have little need of a conversational partner, and social language often is impaired. Typically, they have difficulty in maintaining a topic of conversation, particularly if it is a topic which they themselves have not chosen. They have difficulty with conversational turn taking, do not easily establish or use eye contact during communication, and typically interpret poorly the body language, tone of voice, or facial expression of others (Rapin, 1991).

Nonverbal communication also is impaired in autistic children. They rarely use a pointing response, nor do they exhibit joint attention. Rather than gesture, autistic children will lead the hand of an adult to a desired object or obtain the object themselves (Minshew & Payton, 1988).

Though it is now acknowledged that autistic individuals exhibit a wide range of intellectual abilities, estimates suggest that approximately 75% function within the retarded range [Diagnostic and Statistical Manual of Mental Disorders (fourth edition) (DSM-IV)]. Regardless of the level of function, the profile of cognitive development tends to be uneven (DSM-IV). Many are very concrete, and even very intelligent autistic individuals may experience difficulty with concept formation, reasoning, abstract thought, and insight (Rapin,

1991). Typically, autistic children tend to have better nonverbal than verbal skills and tend to be better visual learners than auditory learners (Rapin, 1991). They tend to have an exceptional memory for details and tend to overgeneralize rules. In contrast, autistic individuals often have difficulty with the processing of information related to the integration and generalization of concepts and the development of abstract thought (Minshew & Payton, 1988). Some autistic persons have shown superior skills for a narrow range of abilities, such as calendars, calculations, music, drawing, and rote verbal tasks, despite otherwise impaired cognitive abilities (Rapin, 1991).

During early childhood, the majority of autistic children demonstrate significant deficits in imaginary or symbolic play. In the high-functioning adult, this deficit may contribute to the inability to develop generic notions in regard to abstract concepts, such as justice, beauty, or jealousy (Grandin, 1995).

Along with language and cognitive impairments, social deficits are one of the most striking clinical manifestations of autism. During infancy, autistic children may be extremely passive babies requiring little attention, or they may be very irritable, difficult to feed, have irregular sleep patterns, and resist cuddling. As young children, they appear to be socially aloof, seemingly unaware of the presence or feelings of others. Alternatively, some autistic children can be overly and inappropriately affectionate, even with strangers. They can become excessively attached to and clingy with one parent and tolerate separation poorly. Autistic children do not know how to make friends or to engage others in their activities or play. They tend to be rigid and do not easily learn socially appropriate behavior, such as initial greetings. Some basic social skills can be taught, but only rarely do they become automatic and used with total ease. The extent to

which socialization abilities are related to or interdigitate with either language or cognitive functioning remains unknown.

Nearly all autistic children appear to have difficulty with the regulation of attention (Dawson & Lew, 1989). Many are easily distractible and hyperactive, rarely giving any task or toy more than momentary interest. Alternatively, others may become hyperfocused and “lock into” a task of particular interest to them, such as the computer, lining up objects, or twirling string. In this case, shifting or transitioning their attention to another activity often is difficult and leads to disruptive behavior (Kinsbourne, 1991).

Although autistic children initially were believed to be motorically normal, more careful observation has found that many demonstrate a generalized hypotonia with hyperextensibility of some of the joints. Posture tends to be poor. Though most of these children meet their developmental gross motor milestones on time, a significant proportion walk late. Gait patterns may lack fluidity, and bilateral motor coordination for such skills as skipping and cutting with scissors may be executed poorly. Some children walk on their toes, but whether this practice is related to a dysfunctional motor pattern or to excessive sensitivity on the bottoms of the feet (or both) is unclear. Refined fine motor skills, such as buttoning, controlling a pencil, or tying shoes, often are exceedingly difficult and (in some cases) are never achieved. In addition, a deficit may be possible in the ability to imitate motor movements and automatically to execute skilled motor tasks or to perform these tasks in a demand situation, suggesting the presence of motor dyspraxia in these children (Rapin, 1991). Poorly executed oral-motor movements can be associated with drooling, poor articulation (resulting in reduced intelligibility), and difficulty in chewing. Repetitive and stereotypical motor

movements are seen in approximately one-third of autistic children. Although the disorder frequently is termed “self-stimulatory” behavior, its etiology and functional significance remains a matter of debate.

Many autistic children appear to have difficulty in modulating the input of sensory information. Some appear to be particularly sensitive to auditory stimuli, such as mechanical noises, school bells, a baby’s cry, or the subtle noises made by fluorescent lighting. Some are particularly sensitive to light touch, such as tags in their shirts, seams in their socks, haircuts, and new unwashed clothing that is perceived as scratchy. Alternatively, these same children may appear impervious to pain, failing to cry even when severely hurt. Some seek comfort from the sensation of pressure and may be found contentedly curled up between two mattresses in their bedroom. Occasionally, some autistic children also appear to be excessively sensitive to odors and others to food textures, which may result in restricted dietary intake.

NEUROPHYSIOLOGICAL STUDIES

Given the variety and complexity of symptoms with which the autistic child presents, some benefit derives from considering possible brain mechanisms that may underlie some of the clinical features of the disorder. Some of the earliest studies that attempted to address this question were neurophysiological investigations that demonstrated abnormal auditory-nerve and brainstem-evoked responses (Student & Schmer, 1978; Tanguay, Edwards, Buchwald, Schwofeld, & Allen, 1982) and rapid eye movement sleep patterns (Tanguay, Ornitz, Forsythe, & Ritvo, 1976). However, in retrospect, these abnormalities were found to be related primarily to the heterogeneity of the study population and to methodological factors. Subsequent investigations on well-documented

autistic subjects have failed to confirm the original reports (Rumsey et al., 1984; Courchesne et al., 1985a).

P300 and negative component (Nc) have been the most common event-related potentials (ERPs) studied in autism. P300s are believed to originate from the modality-nonspecific association cortex in the parietal lobes and are thought to be dependent on the intact connectivity between this cortical region and the hippocampus and limbic cortex (Wood et al., 1984). Nc is believed to originate from the frontal cortex. ERPs are of cortical origin and depend on the brain's intrinsic processing of sensory information, not on the stimulus.

Small or absent auditory P300s and visual P400s have been recorded in autistic subjects who were required to detect random missing stimuli from a regular series of auditory or visual stimuli (Novick, Kurtzberg, & Vaughan, 1979). Because the subjects were able to detect the missing stimuli, the authors suggested that the attenuated ERPs were related to a disturbance in information storage secondary to a dysfunction in the circuitry connecting the inferior parietal cortex with the entorhinal cortex and hippocampus, not to motivational or attentional factors. Further, cross-modulation studies involving both auditory and visual stimuli have suggested an impairment in information processing (Novick et al., 1979). This hypothesis was revised in 1980 when the same authors reported significantly smaller auditory P200 and P300 potentials in autistic subjects in response to pitch changes and deleted stimuli (Novick et al., 1980). It was noted that the depression in the late potentials occurred during tasks that required direct sequential comparison of auditory stimuli and was not limited to conditions in which a temporal interval must be registered. Based on these findings, the authors hypothesized that the abnormalities

were not related to a dysfunction in information storage as previously proposed but to a disturbance in the processing of auditory information and that the abnormality most likely was located in the parietal association cortex. Subsequently, Courchesne et al. (1985b) noted the absence of Nc to novel visual or auditory stimuli in autistic subjects, despite normal task performance and sustained attention, suggesting abnormalities involving the frontal cortex. Thus, evidence appears to point to neurophysiological abnormalities in the parietal and frontal association cortices in autism; they have been hypothesized to be related to inefficient cortical auditory processing or to dysfunctional cortical handling of selective attention (Minschew, 1991).

POSITRON EMISSION TOMOGRAPHY AND FUNCTIONAL IMAGING STUDIES

Relatively few positron emission tomographic (PET) studies have been reported in autism. In 1985, Rumsey et al. noted increased 2-fluoro-2-deoxy-D-glucose uptake throughout the cerebral cortex, hippocampus, thalamus, and basal ganglia in a series of adult high-functioning male autistic subjects. However, substantial overlap occurred in the data between the control and autistic groups in this study. When these data later were subjected to correlation analysis, reduced frontal-parietal intercorrelations were found in the autistic individuals and were hypothesized to be related to an imbalance in mutually inhibitory neuronal circuits associated with attention (Horwitz et al., 1988). Two additional studies have failed to show any statistically significant differences between the autistic and control subjects (De Volder et al., 1987; Herold et al., 1988). More recently, Chugani et al. (1996) studied serotonin synthesis with PET in 10 normal adults in comparison with

4 adult autistic subjects. The results of this study demonstrated significantly higher serotonin synthesis in normal female subjects as compared to male subjects and increased serotonin synthesis in the autistic subjects in comparison with that in controls. These preliminary findings are intriguing and warrant further investigation.

Using (31)P nuclear magnetic resonance spectroscopy, Minshew et al. (1994) reported a decrease in phosphocreatine and adenosine triphosphate levels, borderline decreased phosphomonoesters, and increased phosphodiesterases in the dorsal prefrontal cortex in a group of high-functioning autistic adolescents and young adults, suggesting neuronal membrane alteration and altered energy metabolism in the frontal cortex. The authors hypothesize that these preliminary findings may be reflective of inefficient information processing in autism.

IN VIVO NEUROANATOMY

The first imaging study to suggest a neuroanatomical basis for autism was a pneumoencephalographic study performed on 18 children who presented with retarded language development and autistic behavior (Hauser, DeLong, & Rosman, 1975). Enlargement of the left temporal horn was noted in 15 cases, with some subjects showing enlargement of both temporal horns or mild enlargement of the lateral ventricles, more pronounced on the left. On the basis of these observations, the authors suggested that abnormalities involving the medial temporal lobe structures might play a role in the symptomatology of autism.

The introduction of computed tomography (CT) in the mid-1970s resulted in numerous attempts to further define brain abnormalities in autism. In 1979, Hier, Lemay, and Rosenberger reported a reversal

of the normal left-right parietal-occipital asymmetry in 57% of the autistic subjects who were studied in comparison with mentally retarded and neurological control groups. On the basis of these findings, the failure of normal language development in autism was speculated possibly to be related to the morphological inferiority of the left hemisphere. However, subsequent CT studies failed to replicate these initial findings (Damasio et al., 1980; Tsai, Jacoby, & Steward, 1983; Rumsey et al., 1988). Further CT studies focused on observations of ventricular size (Jacobson et al., 1988; Rumsey et al., 1988) without documentation of consistent abnormalities.

With the emergence of magnetic resonance imaging (MRI) technology, *in vivo* morphometrical studies of the brain have focused on the analysis of specific brain regions. The major focus of these studies has been on the cerebellum (following the initial reports of Courchesne et al. in 1987 and 1988) and on a remeasurement of the same cases in 1989 (Murakami et al., 1989), indicating a selective hypoplasia of lobules VI and VII of the vermis on midsagittal images in autistic subjects. However, five well-designed subsequent studies have failed to replicate these findings (Ritvo & Garber, 1988; Holttum et al., 1992; Filipek et al., 1992; Kleiman, Neff, & Rosman, 1992; Piven et al., 1992). In 1994, Courchesne et al. reanalyzed data from previously published MRI vermian measurements in 78 autistic subjects. Although the majority of the patients were found to demonstrate hypoplasia of lobule VI and VII as originally reported, a small subgroup was noted to have hyperplasia of these same lobules. The authors concluded that, because of the presence of both vermian hypoplasia and hyperplasia and the averaging of these measurements, cerebellar midline abnormalities were not detected in several of

the previously reported series. However, given that only a single midsagittal section was measured, they did not address the possibility that the shape and total volume of the cerebellum, age, intelligence quotient, and other factors unrelated to autism may be significant variables. Further studies involving large numbers of carefully matched subjects will be needed before the significance of cerebellar findings on MIR can be resolved.

Other areas of the brain also have been studied by MRI in autism, including the brainstem and more recently the parietal lobe and corpus callosum (Gaffney et al., 1988; Filipek et al., 1992; Piven et al., 1992). So far, the findings in these studies have been inconsistent, and their significance at this time is uncertain.

HISTOANATOMICAL OBSERVATIONS OF THE BRAIN

Relatively few neuropathological studies have been reported in autism. In large part, this has been due to the limited availability of post-mortem material for study and to the fact that, in most cases, the brains appear to be grossly normal, giving few clues to the location and nature of the neuropathology that underlies this disorder. On the basis of the clinical features of autism, and extrapolating from observations derived from clinical and animal research, a variety of candidate sites of abnormality have been hypothesized. These have included the basal ganglia (Vilensky, Damasio, & Maurer, 1981), the thalamus (Coleman, 1979), the vestibular system (Ornitz & Ritvo, 1968), and structures of the medial temporal lobe (Boucher & Warrington, 1976; Delong, 1978; Damasio & Maurer, 1978; Maurer & Damasio, 1982). Despite these considerations, early neuropathological studies failed to determine any consistent morphological abnormalities (Aarkrog, 1968;

Darby, 1976; Williams et al., 1980; Coleman et al., 1985).

Using the technique of whole-brain serial section (Yakovlev, 1970), the brains of nine well-documented autistic patients have been systematically studied in comparison with identically processed age- and sex-matched control material (Bauman & Kemper, 1995). All cases studied to date have shown no abnormalities of external brain structure or myelin. With the exception of the anterior cingulate gyrus, microscopical analysis of multiple cortical regions in all the autistic brains also have shown no abnormality of cortical lamination, neuronal size or number, or cellular migration consistent with the findings of Coleman et al. (1985). In addition, a systematic survey of the basal ganglia, thalamus, hypothalamus, and basal forebrain failed to delineate any differences from the controls.

Areas of the forebrain that were found to be abnormal were confined to the hippocampus, subiculum, entorhinal cortex, amygdala, mammillary body, anterior cingulate cortex, and septum. These structures are known to be related to each other by interconnecting circuits and make up a major portion of the limbic system of the brain. In comparison with controls, these areas showed reduced neuronal cell size and increased cell-packing density (number of neurons per unit volume), which appeared to be equal bilaterally. Using the rapid Golgi technique, pyramidal neurons of areas CA1 and CA4 of the hippocampus showed reduced complexity and extent of dendritic arbors (Raymond, Bauman, & Kemper, 1996). In the amygdala, small cell size and increased cell-packing density was most pronounced medially in the cortical, medial, and central nuclei, whereas the lateral nucleus appeared to be comparable to controls. The exception to this profile was observed in the brain of a 12-year-old autistic boy with a history of serious behavioral disturbances but

with documented average intelligence. In this case, the findings of small cell size and increased cell-packing density was less robust in the hippocampal complex, compared with that of more severely impaired subjects, but the entire amygdala was diffusely abnormal.

In the septum, reduced cell size and increased cell-packing density were similarly observed in the medial septal nucleus in all cases. However, a different pattern of abnormality was found in the nucleus of the vertical limb of the diagonal band of Broca (NDB). Compared with controls, unusually large but otherwise normal-appearing neurons, present in adequate numbers, were found in all the autistic patients younger than age 12. In contrast, these same neurons were noted to be small and markedly fewer in all the autistic patients older than age 22.

Outside of the forebrain, additional abnormalities in the autistic brains have been limited to the cerebellum and related inferior olive. In all cases, a marked reduction in the number of Purkinje cells was observed throughout the cerebellar hemispheres, most dramatically in the posterolateral neocerebellar cortex and adjacent archicerebellar cortex, with sparing of the vermis (Arin, Bauman, & Kemper, 1991; Bauman & Kemper, 1996). Abnormalities also have been found in the globose, emboliform, and fastigial nuclei located in the roof of the cerebellum which, like the findings in the septum, appear to differ with age. Small pale neurons that are reduced in number are seen in these nuclei in all the autistic patients older than age 22. However, in all the younger autistic subjects, these same neurons and those of the dentate nucleus are enlarged and present in adequate numbers (Bauman & Kemper, 1994).

No evidence of atrophy or cell loss was found in the principal inferior olivary nucleus

of the brainstem in any of the autistic brains, areas known to be related to the abnormal regions of the cerebellum (Holmes & Stewart, 1908). Because of this close relationship, neuronal cell loss and atrophy of the inferior olive invariably have been noted in human neuropathology after the perinatal and postnatal loss of Purkinje cells (Norman, 1940; Greenfield, 1954). In the three oldest cases, the olivary neurons were small and pale but exhibited no evidence of cell loss. In all the younger subjects, these same neurons were enlarged but otherwise normal-appearing.

IMPLICATIONS OF LIMBIC SYSTEM ABNORMALITIES FOR AUTISM

Microscopical analysis of the brain in autism has shown abnormalities that have been confined consistently to the limbic system, the cerebellum, and the related inferior olive. The findings of decreased neuronal cell size and increased cell-packing density that characterize the limbic system are consistent with a pattern of developmental curtailment involving this circuitry. This concept is supported further by the presence of decreased complexity and extent of dendritic arbors observed in the pyramidal cells of the hippocampus.

Given its extensive network of interrelated circuits and widespread connections to other parts of the brain, abnormalities of the limbic system could disrupt significantly the function of the limbic and sensory association neocortex and the reticulate core of the brain. Lesions in experimental animals involving the structures of the medial temporal lobe have shown pronounced effects of emotion, behavior, motivation, and learning, many of which effects resemble the clinical features of autism. Purposeless hyperactivity, severe impairment in social relatedness, hyperexploratory behavior, and the inability to remember or recognize the significance of

visually or manually examined objects have been observed in monkeys after bilateral surgical ablations of the medial temporal lobe (Kluver & Bucy, 1939). Similar behaviors have been noted after comparable neurosurgical lesions in humans (Terzian & Delle-Ore, 1955).

Selective lesions involving specific medial temporal lobe structures, introduced experimentally in adult animals, have provided further insight into the function of each of these individual regions. In the rat, bilateral ablations of the hippocampus produced hyperactive animals with stereotypical motor behavior and unusual responses to novel stimuli (Roberts, Dember, & Brodwick, 1962; Kimble, 1963). Similar surgical lesions in monkeys, confined to the amygdala, resulted in animals who exhibited loss of fear of normally aversive stimuli, compulsive indiscriminate examination of objects, and withdrawal from formerly socially rewarding situations (Mishkin & Aggleton, 1981). Further, these same animals showed a reduced ability to attach meaning to new environments based on past experience, resulting in poor adaptability to novel situations. When ablations were confined to the most medially located amygdalar structures (the central, medial, and cortical nuclei), the influence of familiarization on learning was reduced significantly (Vergnes, 1981). Further evidence for the importance of the amygdala for learning has been supplied by Murray and Mishkin (1985). In these studies, monkeys experienced a severe impairment of cross-modal associative memory after bilateral ablations of the amygdala. These animals failed to recognize visually an object that had been examined previously by taste or touch. These observations suggests that one of the major functions of the amygdala may be the integration and generalization of information that is processed by multiple sensory systems

in the brain, a skill that is typically difficult for autistic individuals.

In 1991, Squire and Zola-Morgan reconsidered the hypothesized relationship of medial temporal lobe structures to memory. They noted that the severe memory loss previously attributed to bilateral combined lesions of the amygdala and hippocampus was the result of inadvertent surgical damage to the cortical regions adjacent to the amygdala, not to the inclusion of the amygdala, as previously believed (Mishkin, 1978). Thus, it appears that structures involved in the medial temporal lobe memory system include the hippocampal formation and related entorhinal, perirhinal, and parahippocampal cortices and that the amygdala is not a component of this system.

Studies in human and nonhuman primates have suggested the presence of at least two memory systems: representational or associative memory, and procedural or habit memory (Mishkin & Appenzeller, 1987; Murray, 1990; Squire & Zola-Morgan, 1991). Representational memory is believed to involve all sensory modalities and mediates the processing of facts, experiences, and events and the integration and generalization of information that leads to higher-order cognition and learning. In contrast, habit memory is involved in skill learning and automatic connections between stimulus and response. The two systems are believed to be anatomically separate, representational memory depending on the hippocampus, amygdala, and areas related to them, whereas the anatomical substrate for habit memory is believed to reside in the striatum and neocortex of the cerebral hemispheres. Neuropathological studies of the brain in autism have shown no abnormalities of the striatum and, with the exception of the anterior cingulate cortex, the neocortex likewise is unremarkable. In contrast, the hippocampal complex, amygdala, entorhinal cortex, septum,

and medial mammillary body have shown significant abnormalities. Thus, the substrate for representational memory appears to be selectively abnormal in the autistic brain, whereas the structures responsible for habit memory appear to be spared.

Though the effect of an early disturbance to the limbic system structures is unknown, likely curtailment of development and prenatally acquired lesions in these regions could disrupt or distort the acquisition and interpretation of information. Such a disturbance in the processing of information could lead to the disordered cognition, social interaction, and language characteristics of the autistic child. In contrast, the preservation of the habit memory system could account for the need for sameness and preoccupation with a narrow range of interests and activities and for the outstanding memory for rote information observed in some autistic individuals.

Studies have suggested that these two neural systems mature at different times in both human and nonhuman primates, the habit system being functional early in life, though the representational system develops later in childhood (Bachevalier & Mishkin, 1991; Overman et al., 1992). Given this pattern of cognitive maturation, possibly a developmentally dysfunctional neuronal circuitry involving the limbic system would have little impact during the first 1 to 2 years of life. However, with development, the effect of this dysfunctional circuitry gradually may become evident, leading to what appears to be social, language, and cognitive deterioration—features frequently reported as part of the early history of childhood autism.

IMPLICATIONS OF CEREBELLAR ABNORMALITIES

Areas of abnormality outside the forebrain in autism have been confined to the cerebellum

and related inferior olive. Marked reduction in the number and size of Purkinje cells has been noted, primarily in the posterior and inferior regions of the hemispheres, with sparing of the vermis and without the presence of significant gliosis. The absence of glial hyperplasia suggests that the lesions have been acquired early in development. Animal studies have shown a progressively decreasing glial response after cerebellar lesions at increasingly early ages (Brodal, 1940).

The preservation of the neurons of the inferior olive further support an early origin for the cerebellar abnormalities. Retrograde loss of olivary neurons regularly occurs after cerebellar lesions in immature postnatal and adult animals (Brodal, 1940) and neonatal (Norman, 1940) and adult humans (Homes & Stewart, 1908; Greenfield, 1954), presumably because of the close relationship of the olivary climbing-fiber axons to the Purkinje cell dendrites (Eccles, Ito, & Szentagothai, 1967).

In the fetal monkey, prior to establishing their definitive relationship with the Purkinje cells dendrites, the olivary climbing fibers have been shown to synapse in a transitory zone beneath the Purkinje cells called the *lamina desiccans* (Rakic, 1971). In the human fetus, this zone is no longer present after 30 to 32 weeks' gestation (Rakic & Sidman, 1970). Therefore, in the absence of retrograde cell loss in the olive in the presence of a marked reduction in the number of Purkinje cells, likely the cerebellar cortical lesions seen in autism have their onset at or before this time.

The relationship of the cerebellar findings to the clinical features of autism is unclear. Dysfunction of the cerebellum beginning before birth may be associated with few if any neurological symptoms (Norman, 1940; Adams, Corselis, & Duchon, 1984). Studies in adult animals have demonstrated both a pathway between the fastigial nucleus of the

cerebellum and the amygdala and septal nuclei of the limbic system and a reciprocal connection between this nucleus and the hippocampus, suggesting that the cerebellum may play a role in the regulation of emotion and higher cortical thought (Heath & Harper, 1974; Heath et al., 1978). The cerebellum also has been implicated in the regulation of affective behavior (Berman, Berman, & Prescott, 1974) and in functional psychiatric disorders (Heath et al., 1979).

More recently, studies in animals and humans have suggested a role for the cerebellum in cognition, including mental imagery and anticipatory planning (Leiner, Leiner, & Dow, 1987) and in some aspects of language processing (Peterson et al., 1989). Further, the cerebellum has been implicated in the control of voluntary shift of selective attention between one sensory modality and another, for example, shifting between auditory and visual attention (Akshoomoff & Courchesne, 1992; Courchesne et al., 1994). Also, the cerebellum has been suggested to play a possible role in cognitive planning, a function independent of memory and most significant in novel situations (Grafman et al., 1992). More recently, studies in monkeys have established that the dorsolateral prefrontal cortex, believed to be involved in spatial working memory, is the target of output from the dentate nucleus of the cerebellum (Middleton & Strick, 1994). This relationship to the prefrontal cortex suggests that the cerebellum may be involved in the planning and timing of future behavior. Thus, a growing body of evidence suggests that the cerebellum is important in the regulation of the speed, consistency, and appropriateness of mental and cognitive processes and in the control of motor and sensory information and activity (Schmahmann, 1991). Therefore, it is likely the anatomical abnormalities observed

in the cerebellum in autism contribute to many of the atypical behaviors and disordered information-processing characteristic of the syndrome. However, the precise functional significance of these abnormalities, their relationship to the findings observed in the limbic system, and their impact on the specific features of autism remain to be elucidated.

CONCLUSION

Although science has made significant advances in our understanding of autism, particularly within the last 15 years, numerous challenges remain. Most now accept that autism is a disorder of neurological development probably occurring or beginning before birth. The most obvious anatomical abnormalities of the brain appear to be selective and appear to be confined to the limbic system and to the cerebellum and related inferior olive. Although now genetics appears possibly to play a significant etiological role, the pathogenic mechanisms for the disorder remain unknown. Future research undoubtedly will be directed toward elucidating the genetic profile associated with autism, thereby offering opportunities for prenatal and more precise and earlier postnatal diagnosis. Equally important will be the pursuit of *in vivo* functional imaging studies and neurochemical analysis of autopsy material, with a particular emphasis on the parts of the brain identified as being abnormal. Autism also is a disorder that offers the clinical investigator an unusual opportunity to study multiple aspects of atypical cognition, emotion, social awareness, language, and behavior from a developmental perspective, and likely, science ultimately may have a better understanding of normal development as the result of these present and future research efforts. ■

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The “BOLD” Approach: A Multimodal Format for Understanding Communication and Learning Disorders

Mark Rosenbloom, M.D., and Galina D. Kitchens, M.A.

Communication and learning disorders, similar to other disorders, are multiply determined and influenced by interacting and interdependent levels of genetic, physiological, social, and behavioral processes. The BOLD approach presents a multimodal format to identify, assess, treat, and guide research of these disorders. This approach takes into account the broad context of interlocking influences on communication and learning disorders, including **B**iological milieu, **O**riginal traits, **L**earned behaviors, and **D**erived behaviors (or BOLD). Although there has been an explosion of information, research, and analysis in the field of communication and learning disorders, there has been a lack of consistency in approach, presentation, and structure. The BOLD format was developed to address this lack by facilitating comparisons of ideas across disciplines and to expedite recommendations and evaluations of relevant research.

The BOLD format was developed by a physician and parent to synthesize, analyze, categorize, and interpret the vast array of emerging knowledge about communication and learning disorders. In developing this approach, its creator, Mark Rosenbloom, found it useful to (1) summarize current knowledge, (2) clarify research needs and

directions, (3) evaluate a child by clearly delineating individual behaviors and looking for underlying determinants of these behaviors, and (4) identify, implement, and evaluate appropriate interventions. The purpose of this chapter is to introduce the concepts and uses of the BOLD format.

There are numerous categorical diagnostic labels, such as attention deficit hyperactivity disorder (ADHD), autistic spectrum disorders (ASD), pervasive developmental disorder (PDD), and dyslexia, as well as specific learning disorders. Innovative investigators may use these syndromes as a window to making new observations. Over-adherence to these formal syndromes as fixed categories with expected (but not fully identified) biological pathways, however, may lead the field to overlook the significance of multiple determinants and interlocking, systematic influences within each disorder. Such limitations often result in offering unitary treatment approaches to patients labeled with one of the preceding diagnoses. As discussed in other chapters of this book, a broader, functional approach is needed to include more eclectic intervention and more treatment options, and to accommodate individual needs of children who display unique patterns of functional deficits.

In Chapter 3, “Clinical Practice for Principles of Assessment and Intervention,” it was pointed out that at the current level of knowledge and understanding, a fixed, syndrome-based approach overstates the current evidence with regard to communication and learning disorders. These disorders do not appear to have a single, fixed biological pathway. There is a tendency, however, to focus on specific behavior symptoms without sufficient attention to the full range of the underlying biological differences. In fact, the same behavior can often be caused by the opposite patterns. For example, one “autistic” child may bang his head as an attempt to drown out overwhelming sensory input. Another may engage in the same behavior in order to create sensation because he is afflicted with sensory deficits and wants to break through the extreme sensory insensitivity. Hypothetically, from a biological standpoint, the same behavior may be caused by a serotonin deficiency *or* a serotonin excess.

There is understandable pressure to go beyond existing data and oversimplify categorization of developmental and learning disorders with children who, at present, do not have identifiable fixed etiologies. The goal of the BOLD approach is to consider the multiple factors that influence communication and learning disorders with a focus on relating recent neuroscience research (see the prior two chapters) in the context of different biological levels (e.g., genetics, constitutional, and developmental patterns) with different levels of observed behavior (e.g., different levels of adaptation and maladaptation). It attempts to look relatively more microscopically at the interface between biology and experience as part of the overall Developmental-Individual differences-Relationship-based (DIR) model described in other chapters.

Research has indicated that communication and learning disorders result from complex

dynamics between genetic and environmental factors (Folstein & Rutter, 1988; Troittier, Srivastava, & Walker, 1999). The BOLD approach may prove helpful in that it addresses the factors that serve as modifiers at each of four levels. These levels include: **B**iological milieu, **O**riginal or primary traits, **L**earned or secondary behaviors (simple “coping mechanisms”) and **D**erived or tertiary behaviors. Interactions between a level and its modifiers result in changes at subsequent levels. Thus, the dynamic of environmental factors modifying the first level, biological milieu, leads to the second level of the model, original traits. Even though the second level is closely related to genetic composition, it is not purely genetic. Instead, various influences of the chemical and physical environment result in expression of particular genes. Likewise, the original traits level is modified by basic stimulus-response type interactions of the child with caregivers and others resulting in level three, learned behaviors. This level is represented by an array of “coping mechanisms,” basic in nature and rudimentary in structure. Finally, the fourth level of the model, derived behaviors, results from a dynamic interplay between a child’s learned behaviors (level three) and the response of the child’s complex social environment to his or her learned behaviors. However, unlike the third level, derived behaviors go beyond basic coping mechanisms. They are highly complex, goal directed, and require higher processing. The interconnectedness among the four levels of the model stipulates a multimodal approach for organizing a large amount of information and for assessment and treatment. What follows is a more detailed description of each level of the model.

LEVEL ONE: BIOLOGICAL MILIEU

Genes, biochemistry, and fundamental structural components of the human body,

along with their environmental influences, constitute the biological milieu level. This includes the central and peripheral nervous systems and their interface with all other body systems. Although certain aspects of this level may be predictable or preventable at earlier stages of development, the structural aspects of the biological milieu are commonly thought of as essentially unchangeable in standard forms of current therapy. As knowledge expands and technology improves, modifications of biological components are becoming more possible. However, once the medical evaluation is complete for any particular child and no correctable abnormalities have been found, therapists are likely to regard biological characteristics as unmodifiable. Specific biological components that need to be addressed in connection with communication and learning disorders include, at a minimum, the basic genetic structure, central and peripheral nervous systems, neurotransmitters, the immune system, and the digestive system.

A strong genetic component of communication and learning disorders has been consistently supported by research (Folstein, Bisson, Santangelo, & Piven, 1998; MacLean et al., 1999). A 60% to 91% concordance rate for autistic spectrum disorders was found among monozygotic twin pairs, while the concordance rate among dizygotic twins was significantly lower, between 3% and 5% (Bailey et al., 1995; Gillberg, 1998; Steffenburg, 1989). In 25% of cases, autism appeared to be associated with genetic disorders, such as fragile X syndrome. Although it has been speculated that more than one gene may be involved in the etiology of the developmental disorders, the exact genetic mechanisms have not been identified. However, some advances have been made in identifying the connection between certain autism markers of brain development (three markers of the c-Harvey-

ros oncogene) and homeobox gene EN2, and between ADHD and the D² and D⁴ dopamine receptors genes and the dopamine transporter gene (Faraone & Biederman, 1998; Trottier, Srivastava, & Walker, 1999). Investigations in this area continue and are expected to provide more important information about autism and other developmental disorders. Most researchers agree that genetic predisposition may be necessary but not sufficient to cause autism and that environmental insult plays an essential role in the development of the disorder (Folstein & Rutter, 1988; Trottier, Srivastava, & Walker, 1999). This notion will be addressed further in the discussion of biological milieu modifiers.

Research has further demonstrated an association between communication and learning disorders and certain structural abnormalities in the brain. Thus, intrinsic, neocortical dysfunction as well as structural anomalies in cerebellar hemispheres and vermian lobules, parietal lobe, and the posterior regions of the corpus callosum were found in association with autistic spectrum disorders (Minshew, Luna, & Sweeney, 1999; Saitoh & Courchesne, 1998). Structural anomalies were also detected in the corpus callosum and the midsagittal surface of dyslexic children (Robichon & Habib, 1998). Many children with autism display altered evoked-response potential and conduction time and about 50% have abnormal electroencephalograms (Trottier, Srivastava, & Walker, 1999). In addition, children with ADHD exhibited abnormalities in frontal cortex activation patterns (Baving, Laucht, & Schmidt, 1999; Faraone & Biederman, 1998; Zametkin et al., 1990). However, because virtually all of the studies in this area are correlational by nature, no definite conclusions can be made at this time about whether these abnormalities are causes or effects of the disorders.

Positron emission tomography (PET) studies have focused on examining brain

function in addition to the simple brain structures. These studies demonstrated abnormalities in language and auditory functioning, such as reversed hemispheric dominance during verbal auditory stimulation, reduced activation of auditory cortex during acoustic stimulation, and reduced cerebellar activation during nonverbal auditory perception (Muller et al., 1999). Hypometabolic and neuronal migration anomalies were also detected in other areas of the brain (Schifter et al., 1994). In addition, individuals with ADHD exhibited working memory patterns that were different from those displayed by controls (Schwitzer et al., 2000). Neurochemical studies have investigated the role of neurotransmitters in communication and learning disorders. It appears that levels of glutamate, dopamine, serotonin, epinephrine, norepinephrine, and beta-endorphins are altered in autism, ADHD, and other developmental disorders (Carlson, 1998; Chugani et al., 1999; Leboyer et al., 1999; Vallone, Picetti, & Borrelli, 2000). In addition, alternative hypotheses implicate an overactive brain opioid system and changes in oxytocin neurotransmission (Trottier, Srivastava, & Walker, 1999).

The biological milieu is continuously influenced by physical environmental factors. For example, an association between autism and virus serology and brain autoantibody suggested that a virus-induced autoimmune response may play a causal role in autism (Singh, Lin, & Yang, 1998; Connolly et al., 1999). This hypothesis was further supported by an increased rate of autoimmune disorders found in relatives of children with autism (Comi, Zimmerman, Frye, Law, & Peeden, 1999). A number of research studies have focused on other relationships between various environmental events and communication and learning disorders (Barton & Volkmar, 1998; Bolte, 1998; Carlson, 1998; Kobayashi & Murata, 1998; Patzold, Richdale, & Tonge, 1998).

Factors that appear to be associated with and to influence these disorders are referred to in the BOLD format as modifiers. At the biological milieu level (level one), these include pregnancy variables, delivery, neonatal complications, diet, pollution, illness, medical interventions, and other insults as yet unidentified.

By examining obstetrical records, researchers of a number of studies have investigated various associations between pregnancy, delivery, neonatal experiences, and developmental disorders (including autistic spectrum disorders and ADHD) (Bolton et al., 1997; Lord, Mulloy, Wendelboe, & Schopler, 1991; Milberger, Biederman, Faraone, Guite, & Tsuang, 1997). In spite of some controversy, most researchers agree that the following events were significantly higher among individuals with communication and learning disorders in comparison to the general population: rates of prenatal, perinatal, and neonatal complications and insults (e.g., bleeding, smoking, illicit drug use, family problems, or viral infections during pregnancy), birth complications, use of anesthetics during delivery, low birth weight, and seizures at birth (Knobloch & Pasamanick, 1975; Milberger et al., 1997; Ticher, Ring, Barak, Elizur, & Weizman, 1996; Torrey, Hersh, & McCabe, 1975). Furthermore, an association was found between pregnancy and delivery complications and the development of tardive and withdrawal dyskinesia in children with autism who were treated with haloperidol (Armenteros, Adams, Campbell, & Eisenberg, 1995). Further research is needed to explore relationships between communication and learning disorders and such teratogenic factors as malnutrition, stress, prescribed and illicit drugs, various diseases, and radiation exposure. Despite the significant excess of total obstetric complications observed in connection with developmental disorders, no single event or combination of adversities could reasonably

account for any large number of cases of a particular disorder (Deykin & MacMahon, 1980).

Diet may also modify, in various ways, the biological milieu in terms of developmental disorders. For example, some researchers suggest that abnormal levels of glutamate in children with autism may be dietary by origin, and dietary interventions have been demonstrated to be beneficial for children with ADHD (Boris & Mandel, 1994; Moreno-Fuenmayor, 1996). Ecological conditions, such as air, water, and ground pollution, have been considered in association with the etiology of autism (Sanua, 1986). Medical illnesses such as epileptic seizures and viral diseases, especially when experienced in early childhood, have also been found to be associated with developmental disorders (Kobayashi & Murata, 1998).

Of course, there are biological milieu modifiers that are intentional, such as surgery or medications directed toward symptom reduction of the communication and learning disorder. Studies suggest that more than 50% of patients are treated with one or more medications and that this treatment results in some symptom relief for many of them (Aman, Van Bourgondien, Wolford, & Sarphare, 1995). In addition, reduction in autistic symptoms was reported in patients who underwent epilepsy-related brain surgery (Gillberg, Uvebrant, Carlsson, Hedstrom & Silfvenius, 1996). It has also been suggested that some of the medical interventions not targeted at developmental disorders, such as antibiotics or vaccinations, may be affecting the biological milieu. Indeed, research indicates that a significant percentage of individuals with autism have a history of extensive antibiotic use. Inasmuch as oral antibiotics disrupt protective intestinal microbiota and create a favorable environment for colonization by opportunistic pathogens, it is feasible that some of these pathogens (e.g., *Clostridium tetani*) may

result in production of neurotoxins that disrupt neurotransmission (Bolte, 1998). However, the literature remains controversial in reference to the hypothesized link between vaccines (particularly MMR) and developmental disorders (Boyles & Key, 1998; Duclos & Ward, 1998). Additional biological milieu modifiers are likely to be identified as research in this area continues.

As previously noted, biochemical interventions (medications) can be significant modifiers of level one, biological milieu, and can affect level two, original traits, as well as subsequent levels. Ideally, assessment and treatment of the communication and learning disorder should begin at level one in order to impact effectively upon original traits and address the “core” problem, especially if treatment involves biochemical interventions. Unfortunately, medications are often utilized without assessment at this primary level. Instead, they are utilized in response to symptoms at later levels. For example, Ritalin is often utilized to “control” problems at the later behavioral levels. This can result in other expressions of the primary problem, other problematic behaviors, or a compromising of a child’s ability to learn appropriate behavior without the use of medication.

LEVEL TWO: ORIGINAL/PRIMARY TRAITS

Original or primary traits are the functional, operating, core determinants of the individual’s behavior. They are the biologically based individual differences in terms of the child’s motor, sensory, cognitive, and affective patterns. As noted previously, these traits are not purely genetic; they emerge as a result of interactions between one’s genetic makeup and the immediate chemical and physical environment that promotes expression of some genes while hindering that of others.

Whether original traits are modifiable depends on a child's current developmental stage in the biological life cycle. The earlier an intervention occurs, the more likely it is to result in successful modification of original traits. While evaluating and treating communication and learning disorders, a number of original traits can be considered in terms of the child's strengths or weaknesses in respective areas. These traits include but are not limited to visual and auditory acuity and processing, sensory modulation, motor planning/sequencing and kinesthetic processing, affective processing, cognitive functioning, and memory processing.

Research literature highlights a number of differences in original traits that distinguish individuals with communication and learning disorders from the general population. Thus, abnormalities in visual acuity and processing were consistently detected among children with autism (Scharre & Creedon, 1992). A nonnegligible number of children with autism were also found to have peripheral hearing impairments (Kiln, 1993). For children with learning disabilities, hearing loss compounded a significant part of their communication and educational problems (Welsh, Welsh, & Healy, 1996). Stereotypical behaviors, specifically behavioral rigidities, often displayed by children with developmental disorders were found to be associated with tactile defensiveness (Baranek, Foster, & Berkson, 1997). Some anomalies in sensory processing and sensorimotor functioning were detected among children with autism as early as at 9-12 months of age (Baranek, 1999). Multichanneled sensory processing and remarkably detailed memory for past events were reported in high-functioning individuals with autism (Cesaroni & Garber, 1991). Children with autism showed reduced expression of positive affect while interacting with their family members (Joseph & Tager-Flusberg, 1997). Finally, children with

autism did not appear impaired on metamemory tasks but rarely made spontaneous use of memory strategies (Farrant, Boucher, & Blades, 1999).

A number of these and other anomalies in original traits can be referred directly to the biological characteristics described in the previous section. For example, neurological impairments within the brain stem, the cerebellum, the midbrain, and the frontal lobe could be associated with deficits in affective processing, sensory processing, motor planning, and cognitive flexibility (Huebner, 1992). More specifically, abnormal hippocampal system function leads to the disrupted integration of information known as *canalesthesia*. Abnormal amygdaloid system function disrupts affect association and results in impaired assignment of the affective significance to stimuli. Impaired oxytocin system function flattens social bonding and affiliativeness, and abnormal organization of temporal and parietal polysensory regions yields aberrant overprocessing of primary representations, leading to extended selective attention (Waterhouse, Fein, & Modahl, 1996).

Modifiers of original traits include sensory stimuli from the child's environment. The nature of the environmental stimuli will affect the child's ability to progress normally through subsequent developmental stages. A child with adequate ability to process the sounds, sights, movements, events, and circumstances impinging upon her senses from the surrounding environment will progress adequately unless the environmental stimuli are inadequate, depriving, excessive, threatening, overly harsh, erratic, unusual, or inconsistent. Developmental delay, or even a disorder, may then result. The child's ability to advance adaptively to the level of learned behaviors or derived behaviors may also be compromised inasmuch as there is diminished ability to respond appropriately to

normal patterns of learning contingencies, modeling, and interaction. A child with inadequate processing abilities may, of course, also experience developmental delay or disorder even in a “normal” environment. A normal environment may be excessive or depriving for a child with abnormal processing abilities. Modifying the environment specifically to target abnormalities in processing may result in adequate compensations and allow for normal development. Of course, the interactions between environmental stimuli that are depriving or excessively harsh and sensory abilities that are inadequate place a child at highest risk for communication and learning disorders or delays, especially at particular critical stages of development.

LEVEL THREE: LEARNED/SECONDARY BEHAVIORS

Various types of learned behaviors emerge as a result of interaction between the child’s original traits and rudimentary sensory environmental stimuli with caregivers, family members, peers and therapists, the media, the computer, and other visual, auditory, gustatory, olfactory, and tactile stimuli. These learned behaviors can best be described as basic “coping mechanisms.” They are generally connected to spoken and written language (e.g., in children diagnosed with ASD, dyslexia, and specific learning disabilities), memory and attention (e.g., in children with ADHD and ASD), impulsivity (e.g., in children with ADHD, autism, and other developmental disorders), and social interactions (especially in children with ASD) (Berger & Posner, 2000; Hardan & Sahl, 1997; Jolliffe & Baron-Cohen, 1999).

All of the learned behaviors can be divided into three broad categories: executive developmental functions, adaptive coping behaviors, and maladaptive coping behaviors.

Executive functions are behaviors that serve to organize a series of events over a long period of time. They include prolongation, or a person’s ability to hold and evaluate events in working memory; separation; regulation of affect based on his ability to distinguish facts from feelings; internalization of language; and reconstitution, which involves analysis and synthesis of events. The development of these functions are often impaired or delayed in children with learning and communication disorders (Pennington & Ozonoff, 1996). This leads to a number of problems, including deficient self-regulation of mood and behavior, impaired ability to organize and plan behavior over time, inability to direct behavior toward the future, and diminished social effectiveness and adaptability (Houghton et al., 1999; Pennington & Ozonoff, 1996; Vig & Jedrysek, 1995).

Some of the research on autism has posited an association between failure to learn adaptive social behavior and autistic children’s lack of a “theory of mind” (Baron-Cohen, 1996; Happe, 1995, 1997). “Theory of mind” is a term used to describe one’s understanding of the motives, knowledge, and beliefs of others. This includes understanding of the mental states of self and others, including wanting, feeling, believing, and thinking (Bartsch & Wellman, 1995; Baron-Cohen, Leslie, & Frith, 1985). Such understanding is achieved and usually inferred by normally developed individuals through the acquisition of the ability for affective signaling between an infant and her caregiver and such related skills as eye contact and joint attention (Greenspan, 1995, 1997). It has been proposed that children with communication and learning disorders may be delayed in acquiring abilities related to the theory of mind and that they may have problems generalizing these abilities due to a deficient sense of “self” and/or the absence of healthy social contexts and inadequate community

contacts (Hadwin, Baron-Cohen, Howlin, & Hill, 1997; Sparrevoorn & Howie, 1995). However, in many cases, such apparent delays or deficiencies may actually only signify insufficient means of assessment. Examples of a more appropriate assessment model will be presented later in this chapter.

As far as the adaptability of these learned behaviors or coping mechanisms, it may be suggested that if all the child's biological milieu, original traits, and their modifiers were known, the so-called "maladaptive" behaviors could be understood in terms of their origin and purpose. This would make them not only predictable but also elucidate how the behaviors may be attempts at adaptation. Unfortunately, syndrome diagnoses are often made based on limited information about learned behaviors and in the absence of a broader picture of levels one and two. However, since the same maladaptive coping behaviors may originate from different combinations of biological milieus, original traits, and their modifiers, such generalized diagnoses may be misleading in reference to the choice of interventions. In order for the intervention strategies to be successful, all levels must be considered.

Modifiers of learned behaviors include the responses of other people in the child's environment. For example, abnormal behaviors tend to evoke responses from parents, relatives, caregivers, teachers, and the community, which may modify the learned behaviors toward better adjustment or toward further abnormality. These responses from others to the developing child's learned behaviors will tend to modify them therapeutically in proportion to available knowledge about the child's specific biological milieu, environmental modifiers, and other levels of the model noted in earlier sections. In turn, learned behaviors may be modified negatively due to ignorance about the dynamics of these multilayered and interconnecting levels.

This may include professional interventions that over-focus on one dynamic or ignore important interacting variables. Some inappropriately interventions may include sole use of medications to control behavior, inappropriate rigid reliance upon any one-dimensional treatment strategy, isolating a child in a locked facility, or restricting him to a special needs environment where there are no "typical" children. Of course, the responses from people in a child's environment to his learned behaviors lead, in turn, to further responses from the child that are called "derived behaviors," or level four, of the BOLD model. These behaviors will be even more disruptive if responses, including interventions, toward abnormally learned behaviors are shortsighted, narrow, or otherwise inappropriate.

LEVEL FOUR: DERIVED BEHAVIORS

Derived behaviors are represented by children's responses to the initial reactions that their original traits and learned behaviors evoke in other people and society. These are multidimensional patterns of behaviors that are far more complex than the rudimentary coping mechanisms referred to at the third level. Because they can be particularly disruptive or dysfunctional, derived behaviors represent the most obvious, and usually the most alarming, symptoms of the learning and communication disorder. This is the level at which evaluation and diagnosis frequently occur, and the level likely to be targeted by treatment interventions. Unfortunately, derived behaviors are often so far removed from the biological milieu and original traits that it becomes very difficult, if not impossible, to properly assess a child solely at this fourth level and to implement appropriate intervention strategies. Examples of derived behaviors may be easily recognized as commonly assessed symptoms of numerous syndromes

falling under the category of learning and communication disorders. These behaviors may include head-banging, rocking, spinning, continuous self-stimulation, and other stereotypical behaviors. Also, there may be aggressiveness toward others expressed in biting, kicking, head-butting, or spitting. Other problem behaviors may include idiosyncratic rituals and compulsions, inappropriate yelling out, continuous seeking out of attention by inappropriate acting out, severe temper tantrums, angry outbursts, social isolation, withdrawal, and lack of development of spoken language.

Modifiers of these behaviors include various intervention programs. A number of such programs have been developed (Rogers & Lewis, 1989; Schopler, Mesibov & Hearshey, 1995; Strain & Hoyson, 1988). Some programs are highly structured and have a behavioral orientation; others are multidisciplinary and have a relational focus (Campbell, Schopler, & Hallin, 1996; Greenspan & Wieder, 1998; Lovaas, 1981, 1987; Robinson, 1997; Wieder, 1992, 1996). Such programs work on modifying derived behaviors through a variety of means, including facilitating communication, decreasing inattention and irritability, improving cognitive and social skills, and promoting generalization and maintenance of new adaptive behaviors (Bondy & Peterson, 1990; DeGangi & Greenspan, 1997; Greenspan, 1992; Greenspan & Wieder, 1997, 1998; Olley, Robbins, & Morelli-Robbins, 1993; Stokes & Osnes, 1988).

Many intervention programs have traditionally remained self-contained by including only the population of children with communication and learning disorders, with no emphasis on providing them with opportunities to socialize with children from general populations. Research seems to indicate, however, that development of many of the maladaptive derived behaviors could be prevented by placing the children in an environment that

includes adaptive peers (Bricker & Cripe, 1992; Fewell & Oelwein, 1990; Giangreco, Dennis, Coninger, Edleman, & Shattman, 1993). Such an environment may allow them to learn positive social roles and communication skills by observing and imitating their peers. Mesibov (1984) suggested that many children with communication and learning disorders exhibit social deficits due to the lack of friends and positive role models. This suggestion is confirmed by research findings that children with learning and communication disorders benefited from opportunities to interact with their more typically developed peers (Mahoney & Powell, 1992; Odom & McEvoy, 1988). Their gains were more significant than those of children in self-contained programs, and included increased social behavior as a result of being actively engaged in social interaction by their more typically developed peers. Also, children with learning and communication disorders gained enhanced development of language as well as improved cognitive, social, motor, and other age-appropriate skills (Mahoney, Robinson, & Powell, 1988; McHale, 1993; Peck, Odom, & Bricker, 1993; Roeyers, 1996; Strain & Kerr, 1981; Strain, Kerr, & Ragland, 1979; Yoder, Kaiser, & Alpert, 1991). Effective and creative curricula that ensure inclusion of both children with developmental disorders and their more typically developed peers are currently available (Jorgensen, 1997; Onosko & Jorgensen, 1997; Sizer, 1992).

USING THE BOLD APPROACH TO ENHANCE ASSESSMENT

As previously noted, the BOLD format was developed as a multimodal approach to communication and learning disorders. What follows is a breakdown of how this approach may enhance one of these applications; namely, the assessment of communication

and learning disorders. Looking at the different levels contributing to a child's challenges may help in asking the additional questions that will reveal the different "contributors" to the child's behaviors.

A comprehensive, team-based approach to assessment can use the different levels as reminders of the different functions involved and the relationship among them. The biological milieu—that is, all relevant biological areas, including individual physical differences and possible modifiers of this level (e.g., birth complications, medical interventions)—is a basic level. Assessment may then proceed sequentially to original traits (functional developmental level) and corresponding modifiers (e.g., various sensory and environmental stimuli), then learned behaviors and modifiers (e.g., responses of caregivers), and, finally, derived behaviors and modifiers (e.g., therapeutic interventions at home, family, and school interactions).

Assessment of the biological milieu (level one) can rule out possible metabolic abnormalities, seizure activity, brain lesions, neurological disorders, immune disorders, and other likely influences on communication and learning disorders. The child's biochemical makeup, genetic structure, and central and peripheral nervous systems can be assessed by means of standard medical evaluations, pediatric neurological evaluations, metabolic/endocrine screenings, nutritional and genetic screenings, MRIs, PET scans, and EEGs.

Modifiers of the child's biological milieu, such as pregnancy complications, birth complications, medications, surgery, diet, and contaminants, can also be evaluated by these and other procedures. Assessments of the modifiers of the biological milieu are important because some modifiers, such as diet, medications, and pollutants, may be preventable or reversible. Moreover, such assessments may shed light on

different expressions of the same genetic structure, for example, as seen in identical twins.

Assessment of original traits (level two) should examine functional strengths and/or weaknesses in auditory reception and processing, visual-spatial perception, and processing, olfactory, gustatory, tactile, and other sensory input/processing modes, basic cognitive abilities, and memory. Specialists in pediatrics, ophthalmology, audiology, and other processing areas may rule out abnormalities in vision, hearing, perception, and sensorimotor processing. Psychological testing may rule out cognitive processing, memory deficits, and other complications.

As noted previously, a child's ability to advance adaptively to subsequent developmental levels may be compromised, even with normal original traits, if these traits (hearing, vision, and others) are abnormally modified by an environment that is depriving, excessive, threatening, or otherwise harsh. Thus, a child may unfortunately not experience normal patterns of learning contingencies, not respond to conditioning stimuli and reinforcement, nor be able to benefit normally from social modeling. Assessment of the status of the child's environment may include psychosocial histories, immediate observations of child-caregiver interactions, and on-site evaluations at the child's home or school.

Likewise, assessment of learned behaviors (level three) may include on-site observation of learning contingencies in the child's usual environment to rule out possible inadequate social interactions, parenting styles, or deficient preschool or academic conditioning. The child's developmental level of functioning (e.g., age appropriateness) is assessed at this level and may also include formal tests, such as psychological evaluations, behavior checklists, and tests for learning disabilities. Also included may be tests to rule out abnormalities in spoken and/or written communications,

impulse control problems, attention deficits, low frustration tolerance, inability to postpone immediate gratification, deficits in mood regulation, faulty cognitive responses to stress that may influence affect (e.g., overgeneralizing or “catastrophizing”), empathy (“emotional quotient”), and social skills delays.

Assessment of modifiers of learned behaviors involves evaluations of others’ reactions or interventions to the child’s problematic learned behaviors. The responses of parents, relatives, peers, and the child’s community to his learned behaviors may modify those behaviors therapeutically or even worsen them. It will be important to assess what kinds of informal and formal interventions have been applied or are currently in place. Of course, this can be done by taking a thorough history of previous clinical interventions and *in vivo* observations of the child in his natural environment at home, in school, at clinics, and in the community. Assessment may rule out responses or interventions that are ignorant of the interacting dynamics of the various levels affecting communication and learning disorders. Interventions or responses that are not comprehensive, over-focus on only one dynamic, or are too narrow or shallow may be uncovered.

Assessment of derived behaviors (level four) involves ascertaining the child’s responses, in turn, to the interventions or reactions of others toward her learned behaviors. These responses of the child are often the alarming or stereotypical behaviors that are the hallmark of the communication and learning disorders, such as head-banging, chronic self-stimulation, rocking, spinning, aggressive outbursts, and withdrawal. Assessment of these may include matching the problem behavior to antecedent stimuli or triggers (e.g., child bangs head when intervention is isolation from peers). Also, assessment will ascertain and list the quantity or number of behaviors

and their type and severity. This may be done through direct observations, anecdotal reports from others, use of checklists, narrative descriptions, and other means.

Finally, assessment of modifiers of derived behaviors involves assessment of the interventions applied toward the most problematic behaviors. The interventions may be assessed in terms of observed effectiveness, short- or long-range effectiveness, whether they generate further problems, and whether they make use of multiple influencing variables. Assessment of modifiers of derived behaviors can identify whether interventions are unitary, multimodal, comprehensive, shortsighted, or too self-contained. The assessment may evaluate if interventions are increasing communication, attention, social interest, mood regulation, and cognitive skills, and whether interventions are making use of beneficial interactions with normal peers. At times, an intervention may over-focus on a particular behavior and undermine the more important relationship and positive feelings a child has with a caregiver, therapist, or teacher. Although the child may change specific behaviors, the results of missing the most important component of the intervention may show up in negative changes in the child’s mood, flexibility, and overall thinking and problem-solving capacities.

As new research in the field of communication and learning disorders becomes available, the BOLD format may serve as a framework to channel and organize new knowledge on the understanding between different biological levels of organization (genetic, constitutional, and developmental) with various levels of observed behavior. As a multimodal approach, it may sort comprehensive new information for the purpose of meaningful synthesis with established knowledge and prompt new directions in research and intervention. ■

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