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Autism: A Neurological and Sensory Based Perspective

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Autism is defined as a Pervasive Developmental Disorder (PDD) that typically occurs in the first three years of life. More specifically, the Diagnostic and Statistical Manual (DSM- IV, American Psychiatric Association, 1994) defines it as “the presence of markedly abnormal or impaired development in social interaction and communication and a markedly restricted repertoire of activity and interests”. Some of the most common symptoms include sensory processing difficulties (Baranek 2002; Dawson and Watling 2000), limited social interaction (Gevers et al. 2006), deficits or delays in language development (Smith et al. 2004), and unusual or problematic behaviors (Horner et al. 2002). One in 150 children in the United States today are diagnosed with autism, which is double the incidence of ten years ago (Centers for Disease Control and Prevention (CDC) 2007). Parents of infants with autism often report sensory peculiarities early in development. These reports are among the most salient feathers of autism in the first two years of life (Dahlgren and Gilberg 1989). Most researchers agree that autism is caused by either abnormal brain structure, abnormal “organization” within the CNS or both. Because of the heterogeneity of symptoms, the wide range in their severity and the spectrum of functional deficits, the term Autism Spectrum Disorders (ASDs) is now being used to account for the differences seen in these children (Wing 1997). Although several theories remain regarding what causes autism, much more specific information is now available about the genetic and neurological abnormalities that exist.

Causes of Autism

Genetics

No one gene has been linked to autism (Vastag 2004), but it has long been theorized that it might be an x-linked disorder because of a high ratio of males (Skuse 2000). Only one out of five children with autism is female. Most researchers today believe that autism may begin with a combination of genetic vulnerabilities and environmental triggers (Miller-Kuhaneck & Glennon 2004). Autism however is believed to be prenatal in its origin. Many have suggested that there is a genetic mutation (or mutations) that underlie or cause autism. Statistics suggest that there is a 60-90% chance of having a sibling with an ASD if another child is affected. Geneticists studying autism have discovered specific abnormalities on chromosomes 2, 5, 7, 11, 15, and 17 (Auranen et al. 2002; Badner, Gershon 2002; Buxbaum et al. 2001; Gallagher, Becker, Kearney 2003; Hutcheson, Bradford, Folstein et al. 2003). They believe there may be abnormalities on many more genes. These findings have strongly supported that autism is heterogeneous and that different symptoms, behaviors, and levels of severity displayed by the children may be representative of different types of autism. Today, federal funding for autism research, much of which is genetic in focus, has reached $100 million dollars (Cray 2006).

Neurotoxins

There are also several neurotoxins currently being studied in an effort to determine their possible influence in the development of autism since parents have believed that there was some "substance" that caused their child's autism. A study was completed that examined tissue samples obtained from 700 children with autism to test for the presence of heavy metals (ex. Mercury) due to the "vaccine" theory of autism. While it has been suspected that an immune system response was activated as a result of the injections since some children show chronic inflammation in their brains (Singh, et al. 1998), this theory has not been supported as a cause (Fombonne, Chakrabarti 2001; Hviid, Stellfeld, Wholfahrt, Melbye 2003; Miller 2003; Taylor, Miller et al., 2002; Wilson, Mills, Ross, McGowan, Jadad, 2003). Tissue from children with autism has also been tested for pesticides and other toxic chemicals as possible triggers for autism, with varying levels of evidence which has led to a lack of a definitive conclusion (Edelson, Cantor, 1998).

The influence of opioids has also being examined due to their association with being a by-product of gluten and casein in the diet (Lucarellli et al. 1995). Increased levels of these substances have been found in the urine of some children with autism (Reichelt, Ekrem, & Scott 1990; Reichelt & Kniysberg 2003).

Neurological

It is clearly evident today, as substantiated by both Magnetic Resonance Imaging (MRI) (including functional MRIs) and Positron Emission Technology (PET) scan studies, that the brains of children with autism are different. Electroencephalograms (EEGs) and Magnetoencephalograpy (MEG) have also been used to measure fluctuations in electrical and magnetic responses generated by neural activity in the brain. The evidence suggests that there are abnormalities in both the structure and the function of the brains of individuals with autism. Recent studies have shown that the brains of children with autism are larger (Brambilla et al, 2003; Fidler, Bailey, & Smalley, 2000; Hardan, Minshew, Mallikarjuhn & Keshavan, 2001). This increase in size and growth becomes evident at approximately 6 to 14 months of age Ccourchesne, Carper, & Akshoomoff 2003). This may be due to an excessive number of neurons. Rapid head growth has therefore been suggested as one of the early warning signs. Abnormalities in structure, growth and function have been substantiated in many of the structures of the brain in individuals with autism (Brambilla, et al. 2003). In describing these differences from the lower brain structures to the higher brain structures, differences in the structure and transmission of information have been noted.

The Brainstem

The brainstem is one of the first relay stations for transmitting sensory messages up to higher areas of the brain (Ayres 1972; Bear, Connors, Paradiso 2001). It is where basic integration of information begins. What the brainstem does is below our level of consciousness. The brainstem contains a structure called the reticular formation which has two parts (Bear, Connors, Paridiso 2001). One part of the brainstem is descending and sends messages down through lower levels of the central nervous system. The other part of the reticular formation is ascending and sends messages up to higher structures of the brain. The descending fibers of the reticular formation in the brainstem are concerned with vegetative or autonomic responses and send messages to target organs that are necessary for our survival. The descending fibers are also involved in postural responses involving position, equilibrium and movement. The ascending reticular fibers (also known as the reticular activating system) are concerned with degrees of consciousness and alertness (Noback, 2005). Many of the major sensory pathways -for example for touch, pressure, and movement have axons that end at the nuclei of the reticular activating system. Several studies have suggested that there is an increase in the transmission time of incoming information into the brainstems of children with autism (Akshoomoff et al. 2002). Hashimoto et al. (1995) have shown that the brainstems of the children with autism that they studied were smaller. In a study of ten children with autism and two control groups with ten children each, the children with autism displayed an average of four soft neurological signs, which the authors felt was suggestive of brain stem involvement (Jones, Prior 1985).

The Thalamus and Hypothalamus

Above the brainstem is an area of the brain called the diencephalon which is divided into the thalamus and hypothalmus. The thalamus is also a main relay center for the nervous system, channeling information to and from the motor cortex (Bear, Connors, Paradiso 2001). The hypothalmus has control over the autonomic nervous system (Bear, Connors, Paradiso 2001) which includes the parasympathetic system that maintains homeostasis and calms and organizes us, (Mangelsdorf, Shapiro, Marzolf, 1995: Porges, 1996) and the sympathetic nervous system that responds when we feel we are under threat. It provides us with the flight or fight response (Bear, Connors, Paradiso 2001). The child with a high activity level, who perhaps is hyper-responsive to sensory input, is thought to be dominated by their sympathetic nervous system. This results in frequent flight or fight reactions. So- even though this system is designed to increase our readiness to respond, it can also result in persistent stress responses for the individual who is dominated by this system.

The Cerebellum

In typical people, the cerebellum is a primary site for the integration and modulation of sensory and motor activity. It receives significant amounts of ascending sensory input from the tactile (touch), vestibular (movement - with which it has a direct connection), and proprioceptive (body awareness) systems. The cerebellum also receives signals that are being sent down to the muscles from the motor cortex and helps to modulate that information for postural control before it travels down into the brainstem. It fine tunes motor responses, and helps to control the smoothness with which we move (Bear, Connors, Paradiso 2001). The cerebellum in some children with autism has been found to have an excess of axons within it (Brambilla et al., 2003; Harden, Minshew, Harenski, Keshavan 2001) but their distribution is abnormal. There has also been research that has suggested a reduction in size of the cerebellum (Hashimoto et al. 1995). In addition, the links that should be made from the cerebellum to other structures appear to be decreased (Cray 2006). There are also fewer Purkinje cells in the cerebellum (Bauman , Kemper 1985; Rapin, Katzman 1998). One of the functions of these cells is to arouse the reticular nuclei, which stimulates the arousal of muscle tone and helps a person to change the focus of their attention (Townsend et al. 2001).

The Cerebrum

Within the cerebrum is a structure called the hippocampus. It lies deep within the middle of the brain and is one of the structures that assist us with remembering new information (Bear, Connors, Paradiso 2001). It is slightly larger than normal in some children with autism (Brambilla et al. 2003).

The amygdala which is located in the cerebrum, is part of the limbic system which is involved in emotional responses and helps us to determine what is important and what is not important. The amygdala specifically is associated with arousing us and helping us to determine threatening situations (LeDoux, 1996). The response when activated, is emotional (Brodal, 1992). The amygdala is enlarged in some children with autism (Howard et al., 2000). Research has also shown that the amygdala is activated in children with autism when in social situations and when looking directly at faces (Dalton, Nacewicz, Johnstone, Schaefer, et al. 2005). It is not activated sufficiently in the parietal or frontal lobes where paying attention to faces is normally processed. Several authors have theorized that avoidance of eye contact may be a self-regulatory mechanism that compensates for difficulty with modulating visual input. Others have reported that children with ASD often inspect objects and people in an unusual way with their peripheral vision (LeCouteur et al. 1989; Lord et al. 1994). The conclusion therefore seems to be that here are neurological reasons for lack of eye contact in individuals with autism.

Another area of the cerebrum found to have some abnormalities in its structure, is an area called the basal ganglia. This structure which lies deep within the cerebral hemispheres, serves to connect the cerebellum with the cerebrum in order to regulate automatic movement. The basal ganglia contain a structure called the caudate nucleus. The caudate nucleus in children with autism is enlarged. Increased size of the caudate nucleus in the basal ganglia has been associated with compulsive behaviors, difficulty with changes in routine, and stereotypical motor movements (Sears et.al 1999).

The corpus collosum is an area in the middle of the brain that links the left and right sides for communication between the two hemispheres. It is smaller in children with autism (Harden, Minshew, Keshavan 2000;; Piven, Bailey, Ranson, Arndt 1997) and the neuronal activity that occurs between the two hemispheres of the brain is erratic and poorly connected. Because the corpus collosum links the left and right sides of the brain, there are a number of implications for this abnormality in size and function, including language development, the development of a dominance, and the ability to use bilateral integration.

The Cerebral Cortex

The Cerebral Cortex contains four lobes. These include the frontal, parietal, occipital, and temporal lobes. The somatosensory cortex- which is the ultimate destination for sensory input is located in the parietal lobe. It contains the sensory homunculus which represents and interprets the sensory information that is received by the various body parts (Bear, Connors, Paradiso, 2007). A study by Courchese et al. (1993) showed some volume loss in the parietal lobes of individuals with autism.

The motor cortex - is contained in the frontal lobe of the cerebral cortex (Bear, Connors, Paradiso 2001). It contains the motor homunculus which controls motor function, and is where the tracts for voluntary muscle control originate. The frontal lobes in some children with autism are larger due to an increased number of axons within them (Carper et al., 2002). But despite this increase in the number of axons within the frontal lobes, the connections between them and the parietal (sensory) lobes, and between both of these areas with the thalamus, (a major relay station of the brain), are disrupted.

Summary of Neurological Findings

Although there are several more studies and theories on the neurological causes of autism that are reported in the literature, based on the findings reported in this paper, some major conclusions can be made. It has been suggested that there is an excess of axons in specific areas of the brain which results in over-connection in these areas. However, their links to other areas of the brain appear to be weak (Herbert 2005). There seems to be a lack of coordination among brain regions. There is a lack of synchronization between the various areas of the brain, which seem to impact function. People with autism have difficulty bringing different cognitive functions together in an integrated way. Individuals with autism have problems in planning and organization (Prior, Hoffman 1990; Ozonoff et al. 1991; Hughes et al. 1994). Coordinating volition with movement and sensation can be difficult for some (Cray 2006). In autism each area of the brain seems to do its own thing (Just, Cherkassky, Keller, Minshew 2004). Integration of information therefore does not occur as it should.

Neurological links to sensory processing difficulties in children with autism

Some of the earliest as well as some of the most current theories on autism are based on the premise that children with autism process sensory information differently from others (Brock, Brown, Boucher 2002; Frith 1989; Hermelin, O'Connor 1970; Happe 2005; Just, Cerkassky & Keller 2004). Initial clinical reports of atypical reactions to sensory input date back to Kanner (1943) who first described autism. The first theories on the causes of atypical behaviors among children with autism were based on observations of hypo- or hyper-arousal and unusual reactions to sensory input (Hutt, et al., 1964; Kootz, Marinelli,Cohen 1982; Ornitz 1974). These early reports have since been corroborated by numerous clinical, parental, and first person reports form individuals with autism who have reported unusual attention to, or avoidance of sensory input from various sensory systems (Grandin, 1992; Cesaroni, Garber 1991, O'Neill, Jones, 1997; Williams 1994). Grandin (1995) wrote of her experiences as a person with autism and noted for example that certain textures of clothing could make her anxious, distracted, and fidgety. Based on a review of research that included anecdotal and clinical reports, the prevalence of sensory processing deficits among children with autism is estimated between 42 and 88% (Barenek 2002; Greenspan, Weider 1997; Kientz and Dunn 1997; LeCouteur et al. 1989; Watling, Deita, White 2001) suggest that approximately 39% of children with ASD are under-responsive to sensory input, 20% are hypersensitive, and 36% show a mixed pattern of hypersensitivity and hyposensitivity. Kientz and Dunn (1997) in their study of 3- 13 year old children with autism found that when compared with typical children - the children with autism had significantly more (85% of the responses) on the Sensory Profile to be either hypo or hyper. Rogers et al. (2003) studied 21-50 month-old children with autism and found significant difficulties in tactile sensitivity, taste/smell sensitivity, underactive/seeks stimulation, auditory filtering, and low energy, weak muscle areas of the Sensory Profile. When individuals have deficits in processing and integrating sensory input, problems can occur in learning, behaving, and moving. Poor sensory processing can impact on their ability to participate in social, school, and home activities. Children with autism often demonstrate an extreme aversion to (hyper-responsiveness) or excessive seeking out of sensory input (hypo-responsiveness). (Cesarone, Garber 1991; O'Neill, Jones 1997). From a clinical perspective, the sensory related behaviors exhibited by persons with autism are thought to assist them in coping with their sensory environments by either generating or avoiding sensory input (Erner, Dunn 1998). The effect is that the child is extremely limited in their ability to participate functionally in school, home, or play activities. However when children with sensory integrative dysfunction are given the opportunity to receive appropriate input within the context of meaningful activity, the ability of the CNS to process and integrate sensory input can often be improved - and learning, movement, and "behavior" have the opportunity to be enhanced (Ayres 1972).

Neuroscience research has shown that when animals and humans are allowed to explore and interact with environments that are interesting and meaningful to them, there are significant increases in the formation of synapses. As a result of interacting with the environment and integrating the sensory input that is received, there is an increase in the synaptic connections between the neurons that send the messages and there is also an increase in their efficiency. Animal studies have shown that appropriate sensory input can, and does make positive changes in the synapses (Kandel, Schwartz, Jessell 1995; Kempermann, Gage 1999). These changes are most pronounced when the child is actively engaged rather than passively exposed. In sensory integration theory, an adaptive and automatic response (a successful response) to an environmental change or some form of sensory input is what is expected (Ayres 1972). The children however need assistance through the selection of appropriate activities that correspond to their needs Bundy, Murray 2002). Sensory integration intervention generally provides activities that elicit appropriate responses to tactile, vestibular and proprioceptive input. On the sensory processing spectrum a child can be hypo or hyper-responsive to this input (Dunn 1999). Our knowledge of how the child processes this information is based on careful observation and assessment of his or her responses and behaviors (Ayres 1979).

References

American Psychiatric Association 1994. Diagnostic and statistical manual of mental disorders. 4th ed. Text rev. Washington (DC): Author.

Akshoonoff N, Pierce K, Courchesne E. 2002. The neurological basis of autism from a developmental perspective. Developmental Psychopathology 14(3):613-634.

Ashburner J, Ziviani J, Rodgers S. 2008. Sensory processing and classroom emotional, behavioral and educational outcomes in children with autism spectrum disorder. American Journal of Occupational Therapy 62:564-573.

Auranen M, Vanhala R, Varilo T, et al. 2002. A genomewide screen for autism spectrum disorders: Evidence for a major susceptibility locus on chromosome 3q25-27. American Journal of Human Genetics 74(1):777-790.

Ayres AJ. 1972. Sensory integration and learning disorders. Los Angeles: Western Psychological Services.

Ayres AJ. 1979. Sensory integration and the child. Los Angeles: Western Psychological Services.

Badner JA, Gershon ES. 2002. Regional meta-analysis of published data supports linkage of autism with markers on chromosome 7. Molecular Psychiatry 7(1): 56-66.

Baranek GT. 2002. Efficacy of sensory and motor interventions for children with autism. Journal of Autism and Developmental Disorders. 32:397-422.

Barenek GT, Foster LG, Berkson G. 1997. Tactile defensiveness and stereotyped behaviors. American Journal of Occupational Therapy 51:91-95.

Bauman ML, Kemper, TL. 1985. Histoanatomic observations of the brain in early infantile autism. Neurology 35: 866-874.

Bauman ML, Kemper, TL. 1994. Neuroanotomic observations in autism. In: ML Bauman, TL Kemper, editors. The neurobiology of autism. Baltimore: John Hopkins University Press. p. 119-145.

Bear MF, Connors BW, Paradiso MA. 2007. Neuroscience: Exploring the Brain. Baltimore: Lippincott, Williams & Wilkins.

Boddaert N, Zibovicius M. 2002. Functional neuroimaging and childhood autism. Pediatric Radiology 32(1):1-7.

Brambilla P, Harden A, diNemi SU, Perez J, Soares, JC, Barale F. 2003. Brain anatomy and development in autism: Review of structural MRI studies. Brain Research Bulletin 61(6):557-569.

Brock J, Brown G, Boucher J. 2002. Free recall in Williams Syndrome: Is there a disassociation between short and long term memory 42(3):366-375.

Brodal P. 1992. The Central Nervous System: Structure and Function. 3rd ed. New York: Oxford University Press.

Bundy AC, Lane S, Murray. 2002. Sensory Integration: Theory and Practice. 2nd ed. Philadelphia: FA Davis Co.

Buxbaum JD, Silverman, Smith CJ, et al. 2001. Evidence for susceptibility gene for autism on chromosome 2 and for genetic heterogeneity. American Journal of Human Genetics 68:1514-1520.

Carper RA, Moses P, Tigue ZD, Courchesne E. 2002. Cerebral lobes in autism: Early hyperplasia and abnormal age effects. Neuroimage 16(4):1038-1051.

Case-Smith J, Bryan T. 1999. The effects of occupational therapy with sensory integration emphasis on preschool children with autism. American Journal of Occupational Therapy 53(2):489-497.

Centers for Disease Control and Prevention 2007. CDC releases new data on autism spectrum disorders (ASDs) from multiple communities in the United States. Available from: http://www.cdc.gov/od/oc/media/pressrel/2007/r070208.

Cesaroni L, Garber M. 1991. Exploring the experience of autism through firsthand accounts. Journal of Autism and Developmental Disorders 21(3):303-313.

Courchesne E, Press GA, Yeung-Courchesne R. 1999. Pariental lobe abnormalities detected with MR in patients with infantile autism. American Journal of Roentgenology 16:387-393.

Courchesne E, Carper R, Akshoomoff N. 2003. Evidence of brain overgrowth in the first year of life of autism. Journal of the American Medical Association 290(3):337-444.

Dalton KM, Nacewicz BM, Johnstone T, Schaefer HS, Gernsbacher MA, Goldsmith HH, Alexander AL, Davidson RJ. 2005. Gaze fixation and the neural circuitry of face processing in autism. Nature Neuroscience 8(4):519-526.

Dahlgren SO, Gilberg C. 1989. Symptoms in the first two years of life: A preliminary population study of infantile autism. European Archives of Psychology and Neurological Sciences 238(3):169-174.

Dawson G , Watling R. 2000. Interventions to facilitate auditory, visual, and motor integration in autism: A review of the evidence. Journal of Autism and Developmental Disorders 30:415-421.

Dunn W. 1999. The Sensory Profile. San Antonio: The Psychological Corporation.

Edelson SB, Cantor, DS. 1998. Autism: Xenobiotic influences. Toxicological and Industrial Health 14:553-563.

Ermer J, Dunn, W. 1998. The Sensory Profile. A discriminant analysis of children with and without disabilities. American Journal of Occupational Therapy 5:283-290.

Escalona A, Field, T, Singer-Strunck R, Cullen C, Hartshorn K. 2001. Brief report: Improvements in the behavior of children with autism following massage therapy. Journal of Autism and Developmental Disorders 3:513-516.

Fidler DJ, Bailey JN, Smalley SL. 2000. Macrocephaly in autism and other pervasive developmental disorders. Developmental Medicine and Child Neurology 42(11):737-740.

Field T, Lasko D, Mundy P, Henteleff T, Kabat S, Talpins S, et al. 1997. Brief report: Autistic children's attentiveness and responsivity improve after touch therapy. Journal of Autism and Developmental Disorders 36:567-571.

Folstein SE, Piven J. 1991. Etiology of autism. Pediatrics 87:767-773.

Fombonne E, Chakrabarti S. 2001. No evidence for a new variant of measles-mumps-rubella-induced autism. Pediatrics 108(4):E58.

Frith 1989. Autism: Explaining the enigma. Hoboken (NJ): Wiley-Blackwell.

Gallaher L, Becker K, Kearney G. 2003. Brief report: A case of autism associated with del(2)32q.1q3.2) or (q32.2q32.3). Journal of Autism and Developmental Disorders 33(1):105-108.

Gevers C, Clifford P, Mager M, Boer, F. 2006. Brief report: A theory of mind-based social cognition training program for school aged children with pervasive developmental disorders. Journal of Autism and Developmental Disorders 36(4):567-571.

Gilberg C, Coleman M. 2000. The biology of autistic syndrome. London: Cambridge Press.

Gilberg C, Ehlers S, Schaumann H, Jakobsson G, Dalgren SO, Lindblom R, et al. 1990. Autism under age 3 years. A clinical study of 28 cases referred for autistic symptoms in infancy. Journal of Child Psychology and Psychiatry 31:921-934.

Gomot M, Bernard FA, Davis MH, Belmonte MK, Ashevin C, Bullmore ET, et al. 2006. Change detection in autism: An auditory event-related MRI study. Neuroimage 29:475-484.

Grandin T. 1995. Thinking in pictures: My life with autism. New York: Doubleday.

Grandin T. 1992. An inside view of autism. In: Schopler E, Mesibov GB, editors. High functioning individuals with autism. New York: Springer. p. 105-124.

Greenspan SL, Wieder S. 1997. Developmental patterns and outcomes in infants and children with disorders in relating and communicating: A chart review of 200 cases of children with autism spectrum diagnoses. Journal of Developmental and Learning Disorders 1:87-141.

Happe F. 2005. The weak central coherence account of autism. In: FR Volkmar, R Paul, A Klin, DJ Cohen, editors. Handbood of autism and pervasive developmental disorders. Vol 1: Diagnosis, development, neurobiology, and behavior. New York: John Wiley and Sons. p. 640-649.

Harden AY, Minshew NJ, Keshavan MS. 2000. Corpus callosum size in autism. Neurology 55(7):1033-1036.

Harden AY, Minshew NJ, Mallidarjuhn M, Keshavan MS. 2001. Brain volume in autism. Journal of Child Neurology 16(6):421-424.

Hashimoto T, Tayama M, Murakawa K, Yoshimoto T, Muyazaki M Harada M, Kuroda Y. 1995. Development of the brainstem and cerebellum in autistic patients. Journal of Autism and Developmental Disorders 25(1):1-18.

Herbert MR. 2005. Large brains in autism: The challenge of pervasive abnormality. Neuroscientist 11:417-440.

Hermelin B, O’Connor N. 1970. Psychological experiments with autistic children. Pergamon.

Homer R, Car E, Strain P, Todd A, Reed H. 2002. Problem behavior interventions for young children. Journal of Autism and Developmental Disorders 32: 423-426.

Howard MA, Cowell PE, Boucher J, Broks P, Mayes A, Farrant A et al. 2000. Convergent neuroanatomical and behavioral evidence of an amygdala. Neuroreport 1(13):2931-2935

Hutchinson HB, Bradford Y, Folstein SE, et al. Defining the autism minimum candidate gene region on chromosome 7. American Journal of Medical Genetics: Neuropsychiatric Genetics 117b(1):90-96.

Hutt C, Hutts J, Lee D, Ounsted C. 1964. Arousal and childhood autism. Nature 204:908-909.

Hughes C, Russell J, Robbins TW. 1994. Evidence for executive dysfunction in autism. Neuropsychologia 34(4):477-492.

Hviid A, Stellfeld M, Wohlfahrt J, Melbye M. 2003. Association between thimerosol-containing vaccine and autism. Journal of the American Medical Association 290(13):1763-1766.

Jones V, Prior M. 1985. Motor imitation abilities and neurological signs in autistic children. Journal of Autism and Developmental Disorders 15(1):37-46.

Just MA, Cherkassky VL, Keller, TA, Minshew NJ. 2004. Cortical activation and synchronization during sentence comprehension in high-functioning autism: Evidence of underconnectivity. Brain 127(8):1811-1821.

Kandel ER, Schwartz JH, Jessell TM. 1995. Essentials of Neuroscience and Behavior. Burr Ridge (IL): McGraw Hill.

Kanner L. 1943. Autistic disturbances of affective contact. Nervous Child 2:217-250.

Kemperman G, Gage FH. 1999. Experience dependent regulation of adult hippocampal neurogenesis: Effects of long term stimulation and withdrawal. Hippocampus 9(3):321-332.

Kientz MA, Dunn W. 1997. A comparison of the performance of children with and without autism on the Sensory Profile. American Journal of Occupational Therapy 51:530-537.

Kootz JP, Marinelli BC, Cohen DJ. 1982. Modulation of response to environmental stimulation in autistic children. Journal of Autism and Developmental Disorders 12(2):185-193.

Lainhart JE, Piven J, Wzorek M, Landa R, Santangelo SL, Coon H, et al. 1997. Macrocephaly in children and adults with autism. Journal of American Academy of Child and Adolescent Psychiatry 36(2):282-290.

Lamb JA, Moore J, Bailey A, Monaco AP. 2000. Autism: Recent molecular genetic advances. Human Molecular Genetics 9(6):861-868

LeCourteur A, Reuter M, Lord C, Rios P, Robertson S, Holdgrafer M, et al. 1989. Autism Diagnostic Interview: A standardized investigator based instrument. Journal of Autism and Developmental Disorders 19:363-387.

LeDoux JL. 1996. The Emotional Brain. In: JM Jenkins, K Oatley, NL Stein, editors. Human Emotions: A Reader. Malden (MA): Blackwell Publishers, Inc. p. 98-111.

Lord C, Rutter M, LeCoutier A. 1994. Autism Diagnostic Interview-Revised: A revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. Journal of Autism and Developmental Disorders 24:659-685.

Lucarelli S, Frediani T, Zigoni AM, Ferruzi F, Giardini O, Quintieri F, et al. 1995. Food allergy and infantile autism. Panminerva Medicine 37:137-141.

Mangelsdorf S, Shapiro J, Marzolf D. 1995. Developmental and temperamental differences in emotion regulation in infancy. Child Development 66:1817-1828.

Miller E. 2003. Measles-mumps-rubella vaccine and the development of autism. Seminars in Pediatric Infectious Diseases 14(3):199-206.

Miller H. 1996. Eye contact and gaze aversion: Implications for persons with autism: Sensory Integration Special Interest Newsletter 19:1-3.

Noback CR, Strominger NL, Demarest RJ, Ruggiero DA. 2005. The Human Nervous System. New York: Humana Press.

O'Neill MO, Jones RSP. 1997. Sensory-perceptual abnormalities in autism: A case for more research? Journal of Autism and Developmental Disorders 27(3):283-293.

Ornitz EM. 1974. The modulation of sensory input and motor output in autistic children. Journal of Autism and Childhood Schizophrenia 4(3):197-215.

Ozonoff S, Roger SJ, Pennington BF. 1991. Asperger's syndrome: Evidence of an empirical distinction from high-functioning autism. Journal of Child Psychology and Psychiatry 32(7):1107-1122.

Piven J, Bailey J, Ranson BJ, Amdt S. 1997. An MRI study of the corpus collosum in autism. American Journal of Psychiatry 154:1051-1056.

Porges SW. 1996. Physiological regulation in high- risk infants: A model for assessment and potential intervention. Development and Psychopathology 8:43-58.

Prior M, Hoffman W. 1990. Brief report: Neuropsychological testing of autistic children through an exploration with frontal lobe tests. Journal of Autism and Developmental Disorders 20(4):581-590.

Rapin I, Katzman R. 1998. Neurobiology of autism. Annals of Neurology 43(1):7-14.

Reichelt KL, Ekrem J, Scott H. 1990. Gluten, mild proteins and autism: Dietary intervention effects on behavior and peptide secretion. Journal of Applied Nutrition 42:1-11.

Reichelt KL, Knivsberg AM. 2003. Can the pathophysiology of autism be explained by the nature of the discovered urine peptides? Nutritional Neuroscience 6:19-28.

Rogers SJ, Hepburn S, Wehner E. 2003. Parent reports of sensory symptoms in toddlers with autism and those with other developmental disorders. Journal of Autism and Developmental Disorders 33(6):631-642,

Rutter M. 2000. Genetic studies of autism: From the 1970s into the millennium. Journal of Abnormal Child Psychology 28(1):3-14.

Sears LL, Vest C, Mohamed S, Bailey J, Ranson BJ, Piven J. 1999. An MRI study of the basal ganglia in autism. Progress in Neuro-Psychopharmacology and Biological Psychiatry 23(4):613-624.

Singh VK, Lin SX, Yang VC. 1998. Serological association of measles virus and human herpes virus-6 with brain autoantibodies in autism. Clinical Immunology and Immunopathology 89(1):105-108.

Smith C, Goddard S, Fluck M. 2004. A scheme to promote social attention and functional language in young children with communication difficulties and autistic spectrum disorder. Educational Psychology in Practice 20:319-333.

Skuse DH. 2000. Imprinting, the X-chromosome, and the male brain: Explaining sex differences in the liability to autism. Pediatric Research 47(1):9-16.

Taylor B, Miller E, Farrington, CP, Petropoulos, MC, Favot-Mayaud, I, Wright, PA. 1999. Autism and measles, mumps, and rebella vaccine; No epidemiological evidence for a causal association. The Lancet 353:2026-2029.

Taylor B, Miller E, Lingam R, Andrews N, Simmons A, Stowe J. 2002. Measles, mumps, and rubella vaccination and bowel problems or developmental regression in children with autism: Population study. British Medical Journal 324(7334): 393-396.

Townsend J, Westerfield M, Leaver E, Makeig S, Jung T, Pierce K, et al. 2001. Event-related brain response abnormalities in autism: Evidence for impaired cerbello-frontal spatial attention networks. Brain Research and Cognitive Brain Research 11(1):127-245.

Turner M, Barnby G, Bailey A. 2000. Genetic clues to the biological base of autism. Molecular Medicine Today 6(6): 238-244.

Vandenberg NL. 2001. The use of weighted vests to increase on-task behavior in children with attention difficulties. American Journal of Occupational Therapy 55(6):621-628.

Vastag B. 2004. National autism summit charts a path through a scientific, clinical wilderness. Journal of the American Medical Association 291(1):29.

Volkmar FR, Klin A, Pauls D. 1998. Nosological and genetic aspects of Asperger's syndrome. Journal of Autism and Developmental Disorders 28:457-462.

Wallace C. 2006. Inside the autistic mind. Time.

Watling RL, Deitz J, White O. 2001. Comparison of Sensory Profile scores of young children with and without autism spectrum disorders. American Journal of Occupational Therapy 55(4):416-423.

Williams D. 1994. Somebody somewhere. London: Doubleday.

Wing L. 1997. The autism spectrum. Lancet 350:1761-1766.

Wilson K, Mills E, Ross C, McGowan J, Jadad A. 2003. Association of autism spectrum disorder and the measles, mumps, and rubella vaccine: A systematic review of current epidemiological evidence. Archives of Pediatric and Adolescent Medicine 157(7):628-634.