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Autism: An Experiment of Nature

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A newborn with autism, usually physically normal, often good looking, appears to be the healthy baby that the parents may have expected and is also declared to be so by the health professionals. It is only over a period of months that the reality manifests gradually. Parents with little experience in handling infants often do not perceive or may ignore the earliest warning signs of the disorder. If they do notice that their child behaves differently from the normal infant, they may be unsure of their observation or may even run the risk of being labeled over-anxious.

The earliest indications in the form of lack of eye contact, head turning or reaching out for objects may soon progress to speech delay, oddities in behaviour, and solitariness that indicate the presence of the disorder. At this juncture, the world for parents, comes apart.

Autism is a neurobiological disorder which is behaviourally defined. In his seminal work, Leo Kanner who provided the beautiful description of "autistic disturbances of affective contact" deeply rooted in Gessel's theory of normal social development of children.[1] Kanner described the lack of social interaction in the autistic child as a constitutionally determined, biologically driven feature and referred to it as "autism," a term he borrowed from Bleuler's concept of autism in schizophrenia. Autistic children were described to have a self-centred quality of affect and thinking that was associated with social withdrawal. Autism was characterized by a failure of development whereas schizophrenia represented regression. Kanner's description had profound influence on clinicians' and researchers' conceptualizations of autism.

Kanner observed that these children had difficulties in social communication and resistance to change; and he believed that patterns of parenting had an etiological role in the illness. This premise was later refuted. It is now clear that interactional problems originate in the child and not in parents. Due to the severity of the disorder and use of the term 'autism,' for quite some time, the illness was considered to a psychosis of childhood.[2] Kindred clinical entities proposed by clinicians and researchers were Heller's dementia infantilis or disintegrative disorder of childhood;[3] Mahler's symbiotic psychosis;[4] Asperger's disorder,[5] and Rett's disorder.[6] It was much later that the pathogenetic pathways of these disorders which appeared very early in development of the child were recognized. In DSM I and DSM II, the term childhood schizophrenia was

used to describe autistic children. It was only when Rutter[7] and Kolvin[8] described the natural history and course of autism that it became clear that autism is not an early form of schizophrenia. Thereafter, the entire concept and understanding of autism changed. Today we know much more about the neurobiology, molecular biology, cognitive neuroscience and psychology and genetics of autism and that makes us wonder at this biggest and most intriguing experiment of nature.

Cardinal features of autism

Based on his research findings and Kanner's descriptions, Rutter[9] gave what became the cardinal features of autism: onset by age 2 ½ yrs; impaired and distinctive social development; impaired and distinctive communication; and unusual behaviours such as repetitive sameness, rigidity, resistance to change, stereotypies, mannerisms and so on. To this list, Edward Ritvo[10] added the disturbances in rates and sequences of development; response to sensory stimuli; speech, language, cognition and nonverbal communication; and capacity to relate appropriately to people, events and objects. All these features were later incorporated into the official classificatory systems (DSM, ICD).

Autistic children have developmental difficulties in social; language and communication; attention, arousal and regulation; emotional; and cognitive functioning.

Social development: These children have very limited interest in social environment. They are interested in inanimate aspects of the environment such as objects; remain engaged in solitary activity; and fail to respond to persons. Symptoms may be less severe in high functioning autism. However, impaired social reciprocity; lack of eye contact; failure to use non verbal cues; and lack of attachment, emotions, or intimacy; remain the hallmarks of the disorder. These features manifest very early in infancy. Social functioning may improve with age but does not become normal. These children remain odd, emotionally cold, passive, and aloof. Social problems seen in autism include gaze avoidance and absence of joint attention (sharing with caregiver the experience of third object); deficits in imitative play and absence of reciprocal social play; lack of symbolic/make believe play; deficient or odd attachment; deficits in recognition and imitating emotions; lack of empathic response; and lack of pragmatics in language (not used in social contact meaningfully).

Various authors have proposed that specific deficits undergird the social dysfunction seen in autism. These include the lack of theory of mind or "mind blindness" (the inability to from mental representation of other people's mind)[11,12]; and the "strategic social behaviour" model which proposes that recognition of caregiver as a source of sustenance and nurturance is maintained but "affiliative social behaviour" involving affective and social relationship aspects are missing[13]. These deficits point towards involvement of the limbic system (motivational and emotional behaviour), the oxytocin systems (social attachment and affiliation), the amygdala (empathy and the theory of mind), and the orbitofrontal cortex (emotional regulation and attachment behaviour). The theory of mind hypothesis is the most recent and powerful hypothesis invoked for understanding autism. It is evolutionary in concept and it proposes that the lack of theory of mind may be an attribute that autistic children share with non human primates, who lack metacognitive abilities.

Language and communication: Severe delay in language and comprehension characterizes autistic children. Normally communicative behaviour in children appears at 12 months and it rapidly increases in content and complexity. Autistic children begin to speak late and pick up language at a slower rate. They do not respond to being called, and

do not speak as required for communication. They may have difficulties in articulation, intonation, style, or in usage of words. Echolalia and pronoun reversal are common.

Two theoretical approaches have been described to account for language and communication deficits in autistic children. The first one is the lack of theory of mind, meta representation or ability to understand persons, and lack of central coherence; and the second is the impairment in executive functioning and higher order cognitive processes that lead to deficits in acquisition of meaningful words. Impaired language leads to impaired social interaction. Deficits in autism lie at intersection between cognition and social interaction e.g. play creates an internal world derived from external social world and language provides the cognitive schema. There is double deficit in autism; there is delay and also deviance.

Attentional difficulties: Attention is central to all processes involved in cognition and information processing within the realm of cognitive neurosciences. Components involved in normal attention are arousal, sustained attention, orienting, gazing, and filtering. With high arousal, low intensity stimulus elicits attention and with low arousal intensity of stimulus has to be high. When attention is sustained on a particular task, one allocates cognitive and sensory resources as exclusively as possible. Orienting is aligning of sensory receptors in the direction of the sudden stimulus. Orienting response can be exogenous (stimulus driven, involuntary, peripheral reflex) or endogenous (based on information which is voluntary and central in origin). Gazing involves the use of the mind's eyes in an attentional gaze that is centered on one location at a time (the gaze is highest in the center and there is a decreasing gradient in the surroundings). Filtering or gating involves responses to perceptual stimuli that are driven by certain characteristics of objects (size, colours, shape etc) or scenes, to the exclusion of others.

Autism may be characterized by underarousal;[14] attention turned inwards[15] and faulty modulation of arousal.[16] Deficits in sustained attention seen in autistic children are largely dependant upon their developmental level, IQ, motivation and interest in the task. Reflexive orienting of both types i.e. physical or (overt) and of mind's eye (covert) seems to be impaired in autistic children as they continue to look at idiosyncratic stimuli and do not get distracted or disengaged easily. They cannot shift attention from one task to another. Research points towards spatial orienting deficit in autism, whereas reflexive orienting may be intact. Autistic children lack the ability and voluntary control over attentional gaze required for a particular task. They have what can be called as "tunnel vision", very narrow attentional gaze, ignoring and excluding the other stimuli in the environment. Deficits in filtering in autism are seen more often in lower levels of development and IQ. Autistic children show slower reaction time and errors in filtering task when competing stimuli are presented. Overall, research on attentional difficulties in autism is at an early stage. Both, qualitative as well as quantitative differences in attentional tasks between autistic and normal children have been noted.

Cognitive processing: Autistic children do not exhibit abnormalities, across the entire gamut of cognitive functions. Autistic children are able to learn functions of objects, to discriminate and to memorize material. However, deficits are seen in translation of information derived from other people and about other people into symbolic or mental representation. They fail to learn from social environment. They do not recognize that other people have thoughts, feelings and viewpoints. Autistic children fail to attribute intentions or emotions to other people and therefore do not respond to their gestures or facial expressions. Whether the origin of this deficit lies in problems related to social

cognition is a question that is yet to be answered. It is proposed that autistic children have deficits in both cognitive and affective domains. They fail to develop empathy, which restricts development of social relationships.

All the human qualities that constitute the psyche i.e. cognition, emotions, personality, language, social relationships are rooted in the central nervous system. Study of biological factors that explain the stereotypic features common to all individuals, as well as environmental and psychological experiences that explain the uniqueness or the individual differences during the course of development is necessary. It will involve the study of genetics, molecular and cellular biology, and neural systems; of the family and the environment to uncover the mysteries of development. Development is neither merely linear nor transactional alone. Development involves interactive and self-manipulative components of the gene and environment.

Developmental biology of autism

Autism, dyslexia, schizophrenias and attention deficit hyperactivity disorder are developmental in origin. There are adult disorders, which produce symptoms akin to these developmental disorders. However understanding of deficits in these adult disorders does not automatically provide understanding of the childhood onset disorders. For example, deficits in executive functions seen in autistic children are known to occur in frontal lobe pathologies in adults. Yet fetuses and infants who have lesions in frontal cortex do not develop autism. There are two ways of resolving these discontinuities. One is to study the end products of maldevelopment, e.g. the causes of the theory of mind deficit, arousal deficit, “mind blindness”, abnormal eye movements etc., which means working backwards. This approach attempts to construct a theory to explain common deficits seen in disorders of adults and children, however, it has not worked well. The second approach involves working forward to observe the unfolding of the events from the beginning. This approach promises to uncover the origin of many developmental disorders.

Let us now discuss the principles and mechanism involved in normal and abnormal development. Normal development is a self-organizing phenomenon. Initially there is over abundance of neurons, synapses and axonal connections. During development, some of these neural elements are selectively eliminated and others are retained - “Neurons that fire together wire together”. It is a dynamic process, which is shaped through individual specific experiences. Inactive axon terminals compete with the active ones for nerve growth factors and will eventually shrink. Ultimately, this dynamic process of emergence and transformation leads to a complex, highly specialized, stable neural network and all intermediate neural states and operations are eliminated during the development. Thus different individuals with similar neuro-developmental starting point, may experience differences in gene-environment interactions leading them into divergent developmental paths. There can also be convergent developmental path, where in, similar neuro-behavioural end products may be derived from different developmental origins.

Abnormal development too is a self-organizing phenomenon, which incorporates some degrees of mis-organization. Developmental process may be perturbed due to “alterations in ecological balance” leading to chaos. This can set off a cascade of growth and functional changes in the direction of irrevocable deviation from the normal. Ultimately abnormal neural networks and organizations are formed. These perturbations are in the form of neuronal migration error, lesions, receptor deficits, sensory defects and so on. Abnormal functional activity may determine what neuronal elements are retained

and what are eliminated e.g. retinal blocking causes hypoplasia of primary visual cortex. Structural or functional mis-organisations may lead to effects at sites distant from the site of abnormality e.g., neuronal loss in a particular location will trigger loss in additional locations distant from the primary site. In 43% of autistic adolescents or adults, there is atrophy of posterior parietal, somatosensory and motor cortex on magnetic resonance studies. Early developmental abnormalities lead to aberrant neural circuitry and permanent behavioural abnormalities. Thus, abnormalities of the thalamic magnocellular system observed in the lateral and medial geniculate occurring in early prenatal development may underlie the perceptual processing impairments in autism. Small cell size and disorganization of magnocellular system is likely to affect the development of language areas of brain, or quality of sensory experience by slowing the speed of information processing along this pathway. This may lead to problems in language acquisition and reading.

With the developments in advanced neuroimaging techniques, it is possible to study noninvasively, the myelo-architectonic features of cerebral cortex in living human brain. Developmental changes in more than 50 cortical areas of brain can be studied for their structural as well as functional integrity. However, the absence of clear biochemical or genetic marker for autism presents a formidable challenge to researchers.

Gaps in spatial and temporal contiguity interfere with the ability to discern causal relationships and joint social attention; leading to fragmented representation of the environment and consequential inability to acquire social communication and language. This is the core model in which abnormalities of cerebellum and parietal cortex underlie the primary dysfunction in attention, information processing, and social communication that characterize autism. However, it is still uncertain whether cerebellum is the primary site of damage or is it preceded by damage at some other site. Two decades of research has shown that the loss of Purkinje cells in posterior cerebellum causes failure of modulation of cerebellar output and chaotic excitatory output to parts of the brain. As there are cerebellar connections to brain areas involved in attentional processes (e.g. reticular activating system, posterior parietal cortex, prefrontal cortex, cingulated gyrus etc.), unmodulated cerebellar output produces attentional impairments seen in cerebellar lesions “i.e. attentional asynergia.” The same process may lead to structural abnormalities in parietal cortex leading to parietal lobe dysfunction in autism. Attentional impairments from cerebellar damage which are slowness to shift or reorient attention can cause temporal and spatial gaps in information processing in autistic infants.

With these developments, gene therapy has become possible. Neural transplants with embryonic Purkinje cells have been carried out in ‘pcd’ mouse in which cerebellar Purkinje cells die early in postnatal life due to a genetic defect. The grafted Purkinje cells migrate, grow, differentiate and form normal cerebellar connections.

Neocerebellar hypophasia seen in autism is caused by abnormal cell migration occurring between 3-5 months of gestation. Neocerebellum and hypocampus and other parts of limbic system undergo neurogenesis at the same time. Neuronal migration continues to occur postnatally in both structures unlike the rest of the brain. Thus, both neocerebellum and limbic system, are vulnerable to embryonic insult due to genetic or environmental causes. CT and MRI studies have found lesions in frontal lobes, other cortical lobes, basal ganglia, limbic system and corpus collosum, and enlargement of lateral ventricles in autism. Migration defects leading to malformations in cerebellum, limbic system and cortex are consistently seen in autism. Metabolic deficits have been demonstrated on magnetic resonance spectroscopic studies in the prefrontal cortex and

could also be present in other brain areas. Hypometabolism points towards the possibility of less efficient or less integrated information processing. Studies have revealed lack of correlation and coordination between cortical (frontal and parietal cortex) and subcortical (thalamus, candate nucleas and lenticular nucleus) structures in autism.

Recent neuropsychological theories of autism focus on three areas:

1. Frontal lobe disorder and executive functions and working memory abnormality.
2. Primary deficit in attention/arousal modulation due to cerebellar dysfunction (e.g. chronic autonomic overarousal and different orienting response to novel stimuli leave autistic children with a very narrow range for optimum stimulation).
3. Limbic disorder causing deficits in long term, episodic memory. There may be developmental amnesia due to damage to limbic memory structures e.g. frontal amnesia (deficit in encoding of memory). Limbic amnesia involves impaired declarative memory. Overall damage to limbic structures can produce autistic symptoms.

Thus, there is no single, consistent morphological or functional correlate of autism. The widespread abnormalities reveal the possibility of involvement of distributed neuronal systems responsible for integration of behaviour.

Cerebellar damage in autism occurs between second trimester of gestation and first year of postnatal life.[17] These primary abnormalities of cerebellum lead to further brain abnormalities in the form of abnormal organization of arousal, attention, and memory; and in reciprocal connections between cerebellum and limbic, sensory, hypothalamic, serotonergic, dopaminergic, noradornergic and motor systems.[18, 19] In autism, there is increased sulcal width in the superior parietal region whereas frontal and temporal lobes are judged to be normal. This accounts for deficits in spatial attention seen in autistic children. It is again during the late prenatal and early postnatal period of life when parietal lobes develop.

Several factors can be attributed as causes for these perturbations and developmental psychopathologies, e.g. genetic mutations, exposure to development altering agents like viruses, toxins, alcohol, lead, neuro-pharmacological agents.

Biological basis of theory of mind is yet to be fully described although it is known that limbic and orbital-frontal structures play a special role in social behaviour. Both, the theory of mind and executive dysfunctions are hypothesized to be manifestations of prefrontal dysfunction. Research in autism is now focused on cognitive neuroscience, developmental neurobiology and developmental psychopathology. This research lies in the frontiers of neurobiology and is filled with extreme challenge as well as excitement.

Newer findings

Theory of mind and Face Processing: Normally children develop the key mental states i.e. understanding desire and intention by the age of 2 years. Intention is a plan of action to fulfill the desire. Younger children attribute intention to most events even of accidental occurrence where as by 4 years of age they can distinguish acts ‘done on purpose’ from those happening by chance. Children begin to exhibit pretend play be 10-18 months of age, which also incorporates capacity for meta-representation. Children can infer what other person can see by age of 2 years. They can also infer how the object appears to the other person by about 3-4 years of age. On the other hand, autistic children failed the test on understanding beliefs of others (e.g. baby is thinking). The theory of mind, which young children acquire effortlessly, is severely impaired in autism.

Infants show strong preference for human faces by 1 month of age; they attend to movement such as a nod or a smile. A stationery face evokes distress in the infant as young as 2 months old. Eye contact is established by about 4 weeks of age, and at 2-3 months of age, the infant looks at the face that has eyes open rather than closed, moving eyes rather than fixed eyes. By focusing on the face and eyes, the infant learns to recognize faces, discriminate one from another and establish identities. Face processing plays a key role in developing the theory of mind. Infants by 2-7 months of age begin to look to the direction in which the eyes of the adult are pointing. This is called joint attention on 'eye pointing'. This develops into other behaviours such as pointing to the objects by 10-14 months of age. During this process, the child would have processed the face and eyes of the other person, directed his attention and shared a common perception. All this is impaired in autism. Autistic children do not focus on eyes, do not understand the mental significance of eyes.

Autism children have impaired face processing, impaired recognition of facial expressions of emotions, and impaired processing of complex emotions such as surprise. Simple emotions such as happiness or sadness may be understood.

Etiological models

It is now believed that autism has a biological origin. However, of the various kinds of brain damage shown to occur in autism, the specific ones that cause the disorder is not clear. Further, evident damage itself had a pathophysiology. Genetic causes account for more than 80% of phenotypic variance and are themselves likely to be heterogenous.[20] Viral disease is considered to be an additional or independent cause.[21]

Some theories suggest that autistic child's cognitive and emotional states, which are biologically determined, evoke a response in the caregivers which disrupts parental boding. Psychodynamic theory emphasizes the role of interpersonal factors as both the cause and the effect of autism. How these interpersonal factors contribute to casualty is not entirely clear.

It has been stated that the causal link between biological factors and the resulting behavioural impairments require cognition at the intervening level.[22] It is proposed that all autistic disorders have in common a single cognitive deficit which gives rise to the core symptoms during development. According to this cognitive theory autistic children do not imitate spontaneously. Imitation or modeling is essential to learning in children and contributes to child's development of awareness of self and others. Autistics do not mentalize or in other words they lack the ability to explain behaviour in terms of mental states such as belief, wish, desire, intent, and pretense. These mentalizing deficits explain the three core features of autism.

Finally, according to the Hobson's "affective theory", primary deficit in autism is a disturbance of affective contact, which has biological origin.[23] However, it is difficult to explain all symptoms of autism just on affective disturbance without involving cognitive deficits.

Concluding comments

Autism is a life long condition that causes severe burden and impairment. The child may apparently look very normal but most of the deficits and dysfunctions manifest early during the course of development. Such a child evokes anger, frustration, pity, sympathy, and rejection in the mind of parents and society from time to time. The child too finds himself in a state of serious conflict and pressure. He doesn't know why others don't understand him and vice versa. A clear and definite diagnosis can break this

impasse and struggle. However, then the issue of how to bring up, teach or train such a child arises.

With all that is known and understood about autism so far, it is extremely difficult to point at any one cause or the mechanisms the underlie it. What derails the development of brain remains an enigma. But once it happens it leads to cascade of neurobiological consequences and behavioural manifestations. Study of autism has provided a paradigm for research on normal development of social cognition, emotional cognition, information processing, theory of mind and so on. To that extent, autism can be considered as an experiment of nature, which is most awe inspiring, challenging and painful.

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