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NEUROBIOLOGY OF ASPERGER'S SYNDROME: A CASE STUDY AND OVERVIEW

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ABSTRACT

Asperger's syndrome is an autistic spectrum disorder, which has engendered lesser attention in comparison to autism. Recent literature has focused on the involvement of cortical areas of the brain in this syndrome. We report a case of Asperger's syndrome in which an extensive work-up, including neuropsychological, neurophysiological and neuroimaging procedures, were undertaken. The findings of the various investigative procedures are discussed and literature supporting the neurobiological basis of Asperger's syndrome is highlighted. Finally, we briefly touch upon the 'Theory of Mind' construct in autistic spectrum disorders.

Key words : Asperger's syndrome, neuropsychology, P 300, theory of mind.

Asperger's syndrome (AS) is an autistic spectrum disorder characterized by qualitative impairment in social relationships, restricted range of interests and impairment in verbal and non-verbal communication, especially in the pragmatics of social communication (Szatmari, 1991). Of uncertain nosological status till recently, this disorder is said to have a prevalence of 1 in 10,000 (Volkmar and Klin, 2000). Though not believed to be as uncommon as before, AS is usually diagnosed late in the course of illness due to lack of awareness about the condition amongst the clinicians. Before AS was introduced to the English speaking world by Lorna Wing (Wing, 1981), this entity was only anecdotally cited. However, with the appearance of consensus guidelines for the diagnosis of this condition in the current classificatory systems, more studies on AS have appeared in the last two decades.

No definitive aetiology for this syndrome exists, though there are a number of hypotheses, one of which is an underlying neurobiological dysfunction. While much research has been done in the neurobiology of childhood autism, probably because of higher incidence of mental retardation and seizures, comparable literature on AS is lacking. There exist only a handful of case reports citing structural anomalies in AS. Besides this, a few studies have assessed neuropsychological functions in AS (Scott, 1985; Wolff and Barlow, 1979; Pomeroy and Friedman, 1987; Szatmari et al, 1990; Klin et al, 1995). But there is no consistency in observations from either the neuroimaging or the neuropsychological studies. We report a case of AS who underwent a detailed neurobiological evaluation which included neurological examination, Strub and Black battery, PGI-Battery of Brain Dysfunction, assessment of soft neurological signs, Luria Nebraska Neuropsychological Battery (LNNB), evoked potentials, quantitative EEG, and MRI. Such an exhaustive neurological work-up for a case of AS has not been reported before. Moreover, to our knowledge, this represents the first case of AS in which both LNNB and evoked potentials have been utilized.

CASE REPORT

Patient SB, a 22-year-old male, had his first psychiatric consultation for the complaints of inability to sustain interpersonal relationships, circumscribed areas of interests, oddities of speech with a peculiar intonation, repetitive patterns of behaviour and an awkward gait since the age of four years.

Patient was described as a 'difficult' child by the parents. A product of uncomplicated pregnancy and delivery, he had normal developmental milestones. His speech initially had a stammer, which later disappeared. Though having a good vocabulary and grammar, he developed a peculiar intonation in his voice which remained loud and pedantic. He would repeat phrases and questions in a stereotypic fashion often to the limit of irritating others. His gait was awkward as he swayed from side to side while walking. Typically he also exhibited difficulty in tying up knots and never could, till now, tie shoelaces.

At school, patient had no close friends and would often refuse to follow the teachers' instructions. At the age of 10 years, patient became fond of chess, which he quickly excelled in and was soon playing with people elder to him. He would often challenge people to play with him and then place bets with them and would become irritable if somebody did not comply with the bet. This presentation had continued till his present consultation. Family history revealed a bipolar illness in maternal grandmother while father had some deficits in fine motor coordination as evinced by his inability to tie knots. Keeping in view the typical presentation and the lack of other features suggesting an alternative diagnosis such as schizoid personality disorder, a diagnosis of Asperger's syndrome in accordance with ICD-10 (World Health Organization, 1992) was entertained Following the diagnosis, the patient underwent a comprehensive battery of investigations for assessing neurocognitive functions. His routine blood investigations were in the normal limits. The neurobiological assessment included the following:

1. Neurological examination : Other than bilateral myopia and an awkward gait, patient displayed no focal neurological deficits.
2. Soft Neurological Signs : For assessing soft neurological signs, Cambridge Neurological Inventory was employed (Chen et al, 1995). On it, the patient showed deficit in the area of motor coordination.
3. Intelligence : IQ was tested using Wechsler Adult Intelligence Scale (WAIS). The verbal IQ was 132 and performance IQ was 108, with full scale IQ being 121.
4. Strub and Black Mental Status Examination in Neurology (Strub and Black, 1993) : The patient had geographical disorientation and impaired alternative motor patterns, which suggested the involvement of parietal and frontal lobes (prefrontal cortex).
5. PGI- Battery of Brain Dysfunction (Pershad and Verma, 1989) : This battery did not indicate any cognitive deficits on the whole. However; some impairment was noticed on individual tests such as Bender visual motor gestalt test and Nahor-Benson test, which indicated dysfunction in visuo-motor coordination, spatial abilities and visuo-spatial activity. This translated into possible involvement of right parieto-occipital region.
6. Luria Nebraska Neuropsychological Battery (Golden et al, 1985) : Next the patient was administered LNNB which was done under the supervision of a clinical psychologist having extensive experience with this battery (A.N.). Findings on LNNB suggested involvement of temporo-parietal and right frontal regions.
7. Neurophysiological studies : The patient underwent a quantitative (q) EEG and evoked potential studies, namely P300 and bereitschafts potential. A consultant trained in qEEG and evoked potentials (S.H.N.) interpreted these. While the qEEG and bereitschafts potential did not reveal any abnormality, patient had delayed P300 latency (500 msec; normal 250-400 msec) over the Fz electrode position and reduced P300 amplitude over Cz and Pz electrode positions of the 10/20 system of electrode placement.

8. Brain MRI : This did not reveal any abnormality.

DISCUSSION

This report is the first of its kind to undertake such a comprehensive evaluation in a case of AS. Some interesting observations emerge when the findings of individual investigations are integrated. Evaluation of soft neurological signs showed deficits in motor coordination. These signs depend on the integration within the motor or sensory system or between the motor and sensory system (Griffiths et al, 1998). Motor coordination is said to heavily involve the frontal lobes (Heinreichs and Buchanan, 1988). Frontal lobe involvement was also revealed by the Strub and Black battery and LNNB. Besides this, parietal lobe involvement was indicated by the Strub and Black battery, PGI-BBD, and LNNB. Support for the involvement of frontal and parietal regions was evident by the impaired P300 variables. The increased latency over Fz location indicated slowed cognitive efficiency during initial stimulus evaluation implicating the frontal region. The shortened amplitude over the Cz and Pz locations indicated a deficit in temporal and parietal lobe activation which meant an impairment in later attentional resource and memory processes that store stimulus information (Polich, 1999). Although patient showed motor incoordination on assessment of soft neurological signs, a normal bereitschafts potential, which is a neurophysiological marker of voluntary movement planning, made the involvement of frontal-subcortical circuits unlikely (Tanji, 1994; Duggal, 2000).

Overall, evidence for the involvement of frontal lobe was the most robust followed by that for parietal lobe. Specifically, the right frontal lobe dysfunction as revealed by the LNNB was commensurate with the patient's non-verbal difficulties and impaired pragmatics of speech. A normal bereitschafts potential precluded the involvement of supplementary motor and primary motor areas of the frontal lobe, which are the neuroanatomical correlates of this preparatory motor potential. This when viewed in the light of finding on the Strub and Black battery indicated towards involvement of the pre-frontal cortex which is in concert with earlier reports implicating this brain region in AS (Ozonoff et al, 1990a). Parietal lobe involvement as revealed by the neuropsychological tests was in tandem with the patient's impaired visual-spatial abilities which are known to occur in patients with AS (Klin et al, 1995; Volkmar et al, 2000). Thus, AS may predominantly involve the right pre-frontal cortex and the parietal lobe. Further validation of these observations by a systematic study on a comprehensive neuropsychological battery is desirable.

We now briefly review the literature available on the neurobiological basis of AS. Scott (1985) compared adults with AS to chronological age-, sex- and education-matched controls and found deficits in non-verbal aspects of communication, including recognition and production of emotional expressions. In addition, a few studies have assessed neuropsychological functioning in patients with AS vis-à-vis autism. While two of these studies found no difference in neurocognitive functioning between patients of autism and AS (Wolff and Barlow, 1979; Szatmari et al, 1990), others showed significant difference between the two groups on visual-perception subtests (Pomeroy and Friedman, 1987; Klin et al, 1995), executive functions and verbal memory (Ozonoff et al, 1991b), fine and gross motor skills, visual memory, and non-verbal concept formation (Klin et al, 1995). As regards to IQ, it has been shown that patients with AS have a significantly higher verbal IQ than performance IQ (Ozonoff et al, 1991b; Volkmar et al, 2000). The above findings are in concert with our observations in this case. It is important to note that the finding of verbal IQ> performance IQ is in contrast to autism (not associated with mental retardation), in which, typically, non-verbal skills are more likely to be higher than or at par with verbal skills (Sparrow, 1997). This observation helps a clinician to distinguish autism from AS but this distinction gets somewhat blurred when comparing high

functioning autism and AS (Szatmari et al, 1990). In neuroanatomical terms, lower performance IQ may indicate involvement of right parietal lobe as highest level of increased metabolic activity occurs in right parietal lobe during performance skills (Kaplan and Sadock, 1998).

Neuroimaging studies have implicated various brain regions in AS. A MRI study of concurrent Tourette's syndrome and AS suggested that structural cortical and sub-cortical abnormalities are common in these patients (Berthier et al, 1993). SPECT scanning in three patients of AS (McKelvey et al, 1995) demonstrated right hemisphere dysfunction in all the subjects. In addition, there exist case reports implicating various structures in the brain in AS such as the corpus callosum (David et al, 1993; Berthier, 1994), frontal lobe (Volkmar et al, 1996), temporal lobe (Jones and Kerwin, 1990; Piven et al, 1990, Volkmar et al, 2000), and left hemisphere and cerebellum (El-Badri and Lewis, 1993) There have been no reports of evoked potential abnormalities in AS while comparable data on autism reveal attenuated P300 amplitude in an auditory paradigm (Novick et al, 1980). Non-specific abnormalities in EEG have also been cited, though infrequently, in patients with AS (Bankier et al, 1999).

Though we did not assess the 'Theory of Mind' (TOM) deficits in our patient, this is an impressive construct which has garnered much attention recently both in the West and our country (Muris et al, 1999; Lalitha et al, 2001). This postulate refers to the child's ability to ascribe thoughts, feelings, ideas and intentions to others and to employ this ability to anticipate the behavior of others. TOM has thus been described as a prerequisite for the understanding of the social environment and for engaging in socially competent behavior. A study showed no significant difference between TOM deficits between patients with AS and controls whereas the same patients with AS performed better on TOM tasks as compared to patients with high functioning autism (Ozonoff et al, 1991b). This better performance by AS patients has been attributed to better verbal abilities in these patients (Sparrevohn and Howie, 1995). These TOM deficits are correlated with deficits on executive function and hypothesized to occur due to dysfunction of the prefrontal cortex (Ozonoff et al, 1991a). Utilization of TOM tasks in autistic spectrum disorders with Indian norms is encouraged.

In conclusion, a growing body of evidence underscores the neurobiological basis of AS. While similar literature in autism is comparatively abounding, there is a need to explore these dimensions in AS. This report, it is hoped, would provide substantial leverage in fostering future research in the neurobiology of AS.

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