SHORT COMMUNICATION

Cerebral Perfusion Abnormalities in Children with Autism and Mental Retardation: A Segmental Quantitative SPECT Study

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Autism is a severe developmental disorder, the biological mechanisms of which remain unknown. Hence we conducted this study to assess the cerebral perfusion in 10 children with autism and mental retardation. Five age matched normal children served as controls. These cases were evaluated by single photon emission computed tomography (SPECT) using Tc-99m HMPAO, followed by segmental quantitative evaluation. Generalized hypoperfusion of brain was observed in all 10 cases as compared to controls. Frontal and prefrontal regions revealed maximum hypoperfusion. Subcortical areas also indicated hypoperfusion. We conclude that children with autism have varying levels of perfusion abnormities in brain causing neurophysiologic dysfunction that presents with cognitive and neuropsychological defects.

Keywords: *Autism, Cognitive deficit, SPECT, Tc-99m HMPAO.*

Autism is a behavioral syndrome, defined by the presence of pervasive social deficits, communication abnormalities, and restricted, repetitive, and stereotyped patterns of behavior(1), leading to a severe developmental disorder. Despite a general agreement that autism has a biological basis(2,3) rather than being a psychological disorder, the biological study of the underlying brain abnormalities and of putative genetic mechanisms has received little attention(4). *In vivo* neuroimaging studies of brain in autism have demonstrated an abnormal cerebral perfusion pattern in cortical and subcortical areas of brain by many workers(3,5-7). It has been observed that in the resting state, a direct relation exists between the cerebral energy demand i.e. local cerebral metabolic rates for glucose (LCMRglc; measured in terms of cerebral perfusion) and total membrane surface area(8,9).

We conducted this study to assess the quantitative segmental cerebral perfusion in cortical and subcortical areas of brain, in children with autism and mental retardation, using Single Photon Emission Tomography (SPECT).

METHODS

We enrolled 10 autistic children with mental retardation (autistic group) between the age of 4-8 years. Infantile autism was diagnosed using the criteria of DSM-IV (American Psychiatric Association, 1994)(10). Five normal age matched children (control group) were also selected to serve as control. In both groups, only those children were selected, whose EEG and MRI were normal. Informed consent was taken from parents. The study was approved by the Ethical Clearance Committee of Krishna Ram Ayurvigyan Shodh Sansthan (KRASS).The IQ was measured by using Wechsler Preschool and Primary Scale of Intelligence and also

cross checked by Raven's Colored Progressive Matrices.

The patients were evaluated by single photon emission computed tomography (SPECT) (9) using Technetium-99m *d*, *l,* hexamethylpropyleneamine oxime [^{99m}Tc] HMPAO. A dose of 25 mCi was injected intravenously into an antecubetal vein. SPECT perfusion studies of brain were conducted using dual head GE Millennium MG device. Software used was Xeleris version 1.1234. Reconstruction of images was done by FBP using filter Butterworth with critical frequency 0.5 power 10. The Collimeter used was LEHR. Initiation of imaging was done 1 hour after injection. Analyses for perfusion studies were conducted using segmental quantitative method by using the xeleris brain SPECT segmental analysis application.

RESULTS

Mean age of the patients was 6±1.5 years (4.5-8). The mean IQ was 49 (SD=12.5) in the autistic group and 87 (SD=13.5) in the control group.

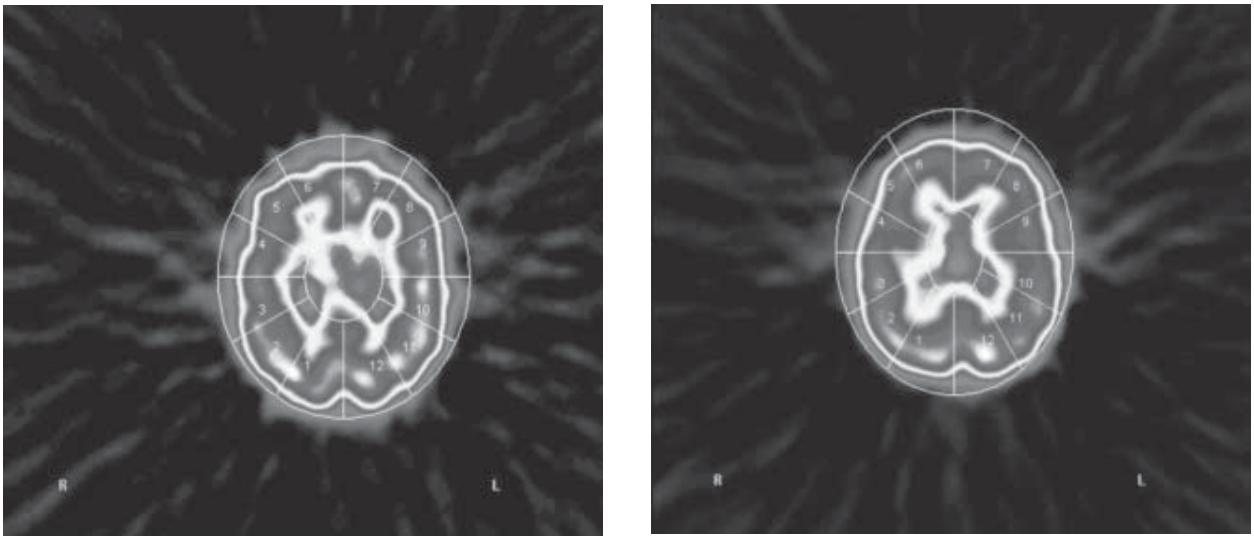
Results of quantitative segmental analysis of SPECT study were represented by graph between segments and mean values of counts in all cases (cases and controls). A representation is given in ***Fig.* 1*a*** (case of autism) and ***Fig.*1*b*** (control).

The average of the mean counts on SPECT quantitative segmental analysis in 10 cases of autism and 5 control cases is depicted in ***Table* I**. The results reveal a lower count values (30 to 40) in autistic children in comparison to control group (75-85), indicating a generalized hypoperfusion. Frontal and prefrontal region were showing the maximum hypoperfusion. The other areas where hypoperfusion was observed were parietotemporal region. Significant hypoperfusion (P<0.05) was also observed in subcortical areas viz. cerebellum, thalamus and basal ganglion.

DISCUSSION

We documented varying levels of perfusion abnormalities in cortical and subcortical areas in brain of autistic children with mental retardation. These abnormalities of the different areas of central nervous system may lead to neurophysiological dysfunction and eventually present with cognitive and neuropsychological deficit.

It has been reported that any altered cerebral perfusion in cortical areas especially in the left medial prefrontal cortex is associated with impairments in communication and social interaction(11,12). The altered perfusion at left anterior cingulate gyrus has been reported to be



(*a*) (*b*)

FIG. 1 *Quantitative segmental analysis of SPECT brain (a) Case of autism with mental retardation; (b) Control.*

WHAT THIS STUDY ADDS?

- Cerebral hypoperfusion was the most common abnormality on SPECT scan in children with autism and mental retardation.

TABLE I MEANS OF COUNTS ON SPECT QUANTITATIVE SEGMENTAL ANALYSIS

Segment	Controls (*n*=5)	Cases (*n*=10)
1	80.4	38.7
2	78.8	38.2
3	72.3	30.6
4	68.2	28.2
5	72.3	31.7
6	68.3	29.0
7	71.3	30.0
8	68.7	27.6
9	71.3	28.9
10	63.1	30.8
11	75.1	36.3
12	84.5	38.5

All differences between the two groups significant (P<0.05). Segment representation (respectively right and left): 1 & 12 occipital cortex; 2 & 11 parieto occipital; 3 & 10 parietal; 4 & 9 parietotemporal; 5 & 8 frontal and 6 & 7 frontal & prefrontal.

associated with impairments in communication and social interaction(4,6). Autistic individuals have significant perfusion deficits in ventral brain areas such as the basal and inferior temporal-occipital regions, and in subcortical structures such as the thalami and left basal ganglia(13). Sears, *et al.*(14) reported significant correlations between subcortical dysfunction in stereotyped and ritualistic behaviour in low-functioning autistic individuals. Pandya and Yeterian(15) recently suggested that ventral temporal and middle prefrontal areas as well as paleocortically derived regions of the thalamus and basal ganglia may provide response modulation, planning and sequencing, means of holding events "online," and attention resources.

Significant hypoperfusion was observed at cortical and subcortical areas of brain in autistic subjects, suggesting that the structural abnormalities of these brain areas may result in reduced cortical activity(13), thus causing dysfunction of these brain areas, and eventually producing some of the emotional and behavioral disorders usually described in autistic subjects. These SPECT findings may help to explain several behavioral features of autism, such as impulsive and aggressive behaviours (to self and others), motor disinhibition (such as stereotypic and manneristic movements and echophenomena), and deficits in planning, sequencing and attention(8).

Though this study contributes to the explanation for cognitive dysfunction, abnormal responses to sensory stimuli, obsessive desire for sameness, impairment in communication and social interaction observed in cases of autism, but this study does not distinguish effects of autism from mental retardation (MR) on SPECT findings. That may serve as a major limitation to this study design.

Contributors: SKG provided the study design and was responsible for literature review, data collection and interpretation of results. BVR conducted SPECT study, carried out segmental quantitative analysis and interpreted the results.

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Competing interests: None stated

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