SUMMARY

Aggressive behavior and mood disorders frequently appear in childhood. There is often lack of objective data to support a specific clinical diagnosis. Ultimately it is likely that alterations in production, concentration, storage, release, reuptake and degradation of neurotransmitters such as serotonin, dopamine, acetylcholine and gamma-aminobutyric acid play key roles in the manifestations of mood disorders. We sought to determine if more gross anatomic patterns of regional brain activation in a "baseline" state might also supply an objective means of verifying the presence of a mood disorder characterized by anger or aggressive behavior.

We studied 8 patients, 3 girls and 5 boys, ages ranging from 6 to 12, referred for SPECT brain imaging with the diagnosis of an attention deficit disorder or autism. All had been reported as having temper problems on the routine questionnaire completed by the parents prior to SPECT imaging. The patients, who were not sedated, had absolute cerebral blood flow measured by the xenon 133 gas inhalation technique followed by intravenous injection of Tc-99m HMPAO with an administered dose calculated according to patient age and weight. One hour following the injection, high resolution brain SPECT imaging was performed using a Picker triple headed camera with fan beam collimators.

We analyzed the brain SPECT studies using 3D volume rendered semi-transparent images with dual cut off windows of 88% (high) and 60-65% (lower value depending on the patient absolute mean cortical blood flow), as well as the traditional transverse, coronal and sagittal sections. The dual window 3D display helped demonstrate increased perfusion or activation of either or both right and left temporal lobes in all 8 of the patients. This pattern was not seen in children with similar clinical diagnoses but whose parents did not report temper problems. These preliminary findings support the proposition that an increase in perfusion to the temporal lobes may be associated with oppositional or aggressive behavior. They suggest that Brain SPECT with images displayed to emphasize the presence of regions of increased blood flow may be useful in objectively confirming the presence of mood disorders and perhaps in guiding appropriate therapy.

Key words: SPECT, aggression, children, behavior, mood disorders, increased regional cerebral blood flow.

BACKGROUND

The temporal lobes play an important role in the processing of language, word retrieval, memory and emotions. Problems associated with temporal lobes
abnormalities result in deficiencies including inability to understand and process language, memory loss (both long and short term), aggression (irritability and violent thoughts), and anxiety, as well reading and auditory difficulties.

A number of reports indicate that many of these neurological deficits are related to abnormalities in production, concentration, release, degradation or reuptake of common neurotransmitters. These small molecular transmitters act relatively quickly.\(^{(1)}\) For example, alteration in regional concentrations of serotonin, that like all the others small molecule transmitters, is synthesized and packaged for use in the axon terminals may be linked to anxiety, mood and eating disorders.

Regional alterations in dopamine have been associated with schizophrenia and in excess may cause hallucinations. Deficits in acetylcholine may be associated with Alzheimer’s disease. Gamma-aminobutyric acid has proved helpful in the treatment of anxiety disorders. Interestingly, all of these small molecule transmitters, or their main components, are derived from the food that we eat.

The concentration of these transmitters and their level of activity may be significantly related to diet. Ultimately, the distribution and concentrations of these molecular transmitters are probably the factors most directly related to emotional disorders, but tools for meaningful routine clinical evaluation of neurotransmitter concentrations are presently lacking.

It is well known that the temporal lobes are related not only to memory and language functions, but also to anger and temper control. We explored whether routine SPECT brain imaging could be helpful in objectively characterizing this mood disorder. The main purpose in this study was to observe any common or unique changes in the distribution of the radioactive tracer in the temporal lobes.

We were particularly interested in whether the use of a semitransparent surface rendered 3D image presentation which emphasized the presence of regions of increased blood flow could be helpful. We compared the results of patients who had reported temper problems with patients who had the same clinical diagnosis, but who didn’t have any temper problems reported by their family. This was ascertained using routine questionnaire filled out by the families of all patients. The questionnaire included the question: "Are there any problems with temper?".

**PATIENT POPULATION**

Eight patients were studied ages ranging 6-12, (3 girls and 5 boys). All were physician referrals for assessment of cerebral blood flow and activity levels in the brain:

Two, one boy and one girl were referred for attention deficit hyperactivity disorder (ADHD). The boy had problems with temper and the girl possibly frequent feelings of sadness or depression. One boy had the diagnosis of ADD without hyperactivity.

Two patients, one boy and one girl were diagnosed with pervasive developmental disorder (PDD). They were reported to experience temper problems.

Three patients were diagnosed with autism, two boys and one girl. Two of them had difficulties in concentration, reported by their parents, and the other had temper problems. All were referred with a diagnosis of neuro-cognitive dysfunction. The results of these patient’s brain SPECT studies were compared with 10 other randomly selected children referred having similar clinical diagnoses, but whose parents’ had answered “no” to the question of whether there was a problem with temper.

**MATERIAL AND METHODS**
CLINICAL DATA

In addition to the referring physician’s clinical diagnosis, a questionnaire was routinely completed for each child by the parents. This was in a simple “yes” or “no” format, with opportunity for amplification or comment. One of the questions was, “Is there a problem with temper”. All parents answered this question.

IMAGING

All eight patients had measurement of absolute mean cortical cerebral blood flow using Kanno and Lassen’s modification of Obrist’s method measuring regional washout of inhaled xenon-133 gas. (3,4) This was followed by intravenous injection of freshly prepared Tc 99m-HMPAO, with the patients in a resting state in a dim, quiet room. No sedation was used. High resolution brain SPECT Imaging was performed one hour post injection using the Picker 3000XP triple headed camera with fan beam collimators. The scan time was 20 minutes in the continuous mode; the matrix size was 128x128, angular range of 120 CCW, angular step 3.00, and 30 sec/step, 120 total acquisitions.

All the studies were processed using a preset brain program. Image attenuation correction was done using the Chang method, and reconstruction was performed using a Low Pass filter (Butterworth) with an order of 8.0 and a cut-off ranging between 0.20 and 0.23. We obtained a transverse, coronal and sagittal slices. A slice thickness of 2 pixels, 4.4 mm, was selected using the Picker preset program for oblique reformatting.

ANALYSIS

We visually analyzed 3-D volume rendered images, together with traditional, transverse, sagittal and coronal images. A 3-D surface program is used to render and view surfaces in 3-D from any direction. Designated thresholds define surface deficits. This particular program only works in filtered transverse or oblique reformatted files. (Picker, Nuclear Med, manual). One set of the traditional “opaque” volume rendered 3-D images was created with only one cut-off or threshold of 60-65% of the maximum value, depending on the mean absolute cortical blood flow obtained using the Xe-133 inhalation technique prior to the Tc-99m injection. This display method provides an excellent means for anatomic localization of cortical perfusion deficits.

A second set of 3-D images had two thresholds set. The high one was set the same for all patients at 88%. It was used to identify areas that had a relative perfusion within 12% of the maximum cortical blood flow. These areas were presented in blue. Both cortical as well as sub-cortical areas of relatively high blood flow can be seen in this display form, since the cortex is displayed as a see-through lattice. The lattice points join regions with a second, lower cut-off value that was the same as used in the first 3-D image. These values fluctuate between 60-65% of the maximum value. The cortical areas corresponding to these values were connected by a red lattice-work like a Buckyball. The 3-D images, were presented in 5 standard views: anterior, left and right lateral, as well as the vertex views allowed ready appreciation of alteration of perfusion in the temporal lobes. In addition, analysis was made directly from the computer monitor that allowed rotation of any of the 3D volume rendered images about all three axes of the model.

FINDINGS

We found no temporal hypoperfusion in the 3-D images with only one cut-off or threshold of 60-65% of the maximum value in children with or without temper problems (Figure 1). Nor did we find any temporal hyperperfusion in the dual threshold 3D images in children without temper problems, although areas of increased flow could...
often be seen in the prefrontal, and posterior parietal cortex as well as in the cingulate gyrus (Figure 2 A). The location of the increased perfusion was more difficult to ascertain on the transverse views (Figure 2 B).

Figure 1. Volume rendered 3D surface images of a child with temper problems. No cortical temporal lobe change is appreciated. There is a non-specific cortical deficit in the vertex in the region of the paracentral lobules adjacent to midline.

Figure 2 A  Figure 2B
**Figure 2 A.** Dual level 3D images. The red lattice work represents normal cortex that has perfusion of between 65-87% of maximum. The blue areas represent regions of highest perfusion ranging between 88-100% of maximum pixel counts. The vertex view (center image) shows high blood flow in the left frontal parietal region as well as in the anterior and posterior cingulate gyrus. The anterior view (top image) shows the increased blood flow in the anterior cingulate gyrus as well as the left superior pre-frontal region. The lateral images show the separation of the regions of high flow in the pre-frontal area from the anterior cingulate gyrus. The anterior (top) and posterior (bottom) views show the right cerebellar hemisphere has higher blood flow than the left. The temporal lobe blood flow is not increased. The transverse sections, B, show areas of highest flow as white with the transition between red and yellow at 60% of maximum roughly corresponding to gray and white matter demarcation. Increased flow can be seen in the region of the left insula (section number 20), the anterior and posterior cingulate, the left dorsal fronto-parietal region as well as the midline prefrontal area, the right parietal area and visual cortex. This child had no temper problems.

By contrast, in the dual threshold 3-D images with the upper cut-off of 88% and the lower cut-off of 60-65%, we observed an increase in the perfusion or activation in the region of the superior gyrus of either one or both temporal lobes (Figure 3A). It was also often striking on the transverse views as well (Figure 3B). This was detected in all of the eight patients with temper problems. It did not matter what clinical diagnosis they received from the referring physician. Increased perfusion in the temporal lobe was not seen in 10 patients with the same clinical diagnoses, but who did not have temper problems reported.

**Figure 3A.** Marked increased in blood flow can be seen in the dual level 3D images beginning in the dorsal pre-frontal cortex, affecting the superior temporal gyri bilaterally as well as the anterior and posterior portions of the cingulate gyrus. Activity in the cerebellar hemispheres is symmetric. The basal ganglia and thalami can be readily seen on the anterior (top) and vertex (center) views. The transverse views, B, show the increased blood flow (white is the highest value) ringing the cortex and affecting the temporal lobes in section 19. This child had temper problems.

**CONCLUSION**

Increased perfusion to the temporal lobes is significant because it has been reported that altered perfusion in the temporal lobes can be an indication of aggressive
behavior.

These findings support the proposition that brain SPECT may be useful in categorizing functional problems in the brain. This can help in the early diagnosis and timely, appropriate treatment of behavioral problems. A dual window 3D display is well suited to identifying and localizing cortical or subcortical regions of increased perfusion.

REFERENCES