CASE REPORT:

Brain Imaging: Evoked Potential, Quantitative EEG and SPECT Abnormalities in Schizophrenia

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The case of a nineteen-year-old female with a three-year history of psychiatric symptomatology clinically consistent with the DSM-III-R diagnosis of schizophrenia is presented. Neurophysiologic assessment using topographic brain mapping demonstrated auditory evoked potential P300 asymmetry with left temporal inactivation and increased latency, while EEG frequency analysis was remarkable for left hemispheric slow wave predominance as well as increased left temporal beta activity. Single photon emission computed tomography (SPECT) using hexamethylpropyleneamine oxime (HMPAO) in the same patient revealed radionucleide uptake reductions in the frontotemporal cortical regions. The clinical presentation of schizophrenia in the context of these imaging correlations is reviewed.

Keywords: schizophrenia, imaging, topographic mapping, SPECT.

Attempts to delineate the neurobiological substrates of schizophrenia are resulting in a rapidly expanding area of research as the definitive etiology of this disorder remains unclear. Current hypotheses include perinatal trauma, toxic exposures in early development, primary metabolic dysfunction, hereditary encephalopathy, infection or post-infectious state, autoimmune disorder, predilection to enviromental injury and/or a manifestation of the developmental spectrum (Kendler 1986; Weinberger 1987).

Brain imaging is being increasingly recognized as a useful tool for identifying psychiatric disorders such as schizophrenia. Topographic surface-distribution maps of evoked potential and quantitative EEG data are now available to aid clinical assessment (Knight 1985). Single photon emission computed tomography (SPECT) is another imaging technique which involves the measurement of radiopharmaceutical distribution in the brain as a way of evaluating regional cerebral blood flow (Nakano et al 1989). Each of these modalities thus provide specific indications of functional brain activity. We report the case of a young schizophrenic adult who demonstrates evoked potential, quantitative EEG and SPECT abnormalities which are confirmatory of the clinical psychiatric diagnosis.

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CASE REPORT

This nineteen-year-old female presented with a pervasive history of being isolative and withdrawn from social interaction since early childhood. She also had episodes of emotional lability, hypervigilance and suspiciousness. For at least three years, psychiatric reports described her as having frank psychotic symptoms. She demonstrated ongoing frequent complaints that unspecified people were out to kill her and insisted that the entire local police force be available to ensure her safety. Referential thoughts included delusions that TV broadcasts ridiculed her and signified danger. Some delusions focused on the concern that someone was trying to run her over with a car. Thought insertion and auditory hallucinations were also present during the course of symptom evolution. The patient met the diagnosis of chronic paranoid schizophrenia via DSM-III-R criteria.

Her past medical history included an uneventful prenatal course and birth. Developmental milestones were also within

normal limits. While the patient was described as being "somewhat detached" growing up, a relatively unremarkable childhood ensued. The family history was remarkable for episodic depression in the biological mother while the biological father suffered from chronic paranoid schizophrenia. Initial diagnostic studies performed prior to the initiation of neuroleptic medication included screening for metabolic abnormalities, CT head scan and a routine EEG all of which were within normal limits. The patient's IQ testing revealed average intelligence. It was also determined that she was right handed.

All topographic brain mapping was performed with the Biologic Brain Atlas III. The target auditory evoked potential was conducted using the Donchin paradigm (Donchin 1978) and visually compared to a normative group of subjects. This assessment was remarkable for asymmetric P300 topography with displacement to the right consistent with poor activation in the left hemisphere (Figure 1). Subsequent EEG data (eyes open) were collected, and 32 artifact free epochs (defined via lead referencing) were combined for spectral analysis. Using the fast Fourier transformation, the data were divided into component frequency ranges. Visual inspection in comparison to normal subjects revealed a predominance of slow wave delta activity in the left hemispheric region with a relative increase in left temporal beta activity (Figure 2).

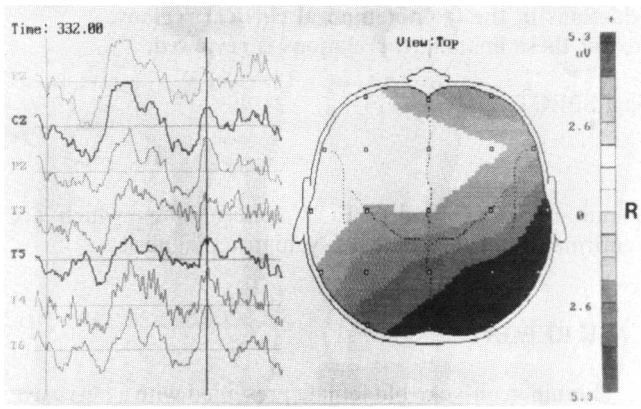

Fig. 1: P300 maxima demonstrates reduced amplitude, increased latency and asymmetrical attenuation with peak amplitude over the right parieto-occipital region.

The SPECT scan was performed using a Siemens Orbiter gamma camera under conditions of ambient light, sound and stimulation. No premedication was administered as the patient remained conscious during the scan. Hexamethylpropyleneamine oxime (HMPAO) was the radiopharmaceutical used for measurement of regional cerebral blood flow. A standardized HMPAO dose was administered intravenously, and imaging was initiated 30 minutes later. The data was collected in a 64 x 64 array with a 360 degree acquisition at 64 stops. A Sophy G+ computer was used for image reconstruction. After applying center of rotation and uniformity corrections, a Butterworth 4/16 filter was used to generate transverse brain images. Fifty percent thresholding was performed with spatial resolution essentially at 10-11 mm. Semiquantitative visual interpretation of the scan in comparison to normal controls revealed a prominent reduction in left frontotemporal HMPAO activity (Figure 3). A smaller decrease in right frontotemporal activity was also evident.

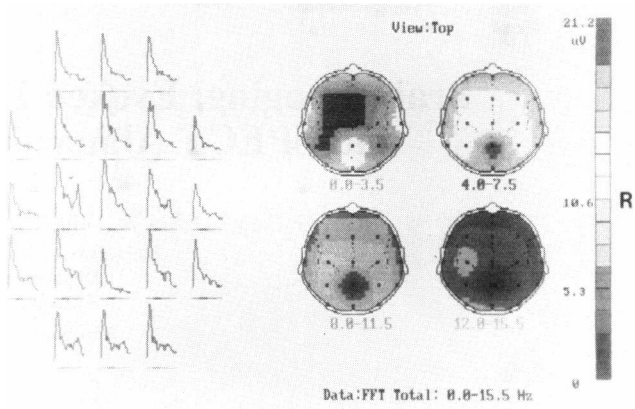

Fig. 2: EEG frequency analysis demonstrates left hemispheric predominance of delta activity (0.0 - 3.5 Hz). A relative increase in left temporal beta activity (12.0 - 15.5 Hz) is also present.

DISCUSSION

The auditory evoked potential findings presented in this case are consistent with findings previously reported in schizophrenia. While P300 topography in normal subjects usually demonstrates maximal amplitude over the midline centroparietal region (Knight 1985), the P300 of schizophrenic patients generally shows reduced amplitude and increased latency with a deficit of activity in the left temporal region resulting in asymmetrical displacement of the maximal amplitude to the right (Faux et al 1988; Morstyn et al 1983a). The P300 waveform is theorized to be involved in giving subjective significance to events and appears to occur in association with tasks that involve the processing of unusual or unexpected stimuli. Increases in latency or decreases in amplitude are associated with increased difficulty of task assessment. These abnormalities indicate the likelihood of mismatching between the subjective consciousness and perception of events where a failure in the planning and execution of selective listening leads to inabilities to be focally attentive and ignore irrelevant exteroceptive as well as interoceptive stimuli (Donchin 1978; Morstyn 1983a). With the hypothesis that the P300 derives from the temporal lobe and hippocampus, these results are consistent with electrophysiological dysfunction in these left sided limbic structures (McCarley et al 1989; Okada et al 1983).

With regard to the quantitative EEG results, the prominence of delta activity in the left hemisphere and increased left temporal beta activity observed in our patient are

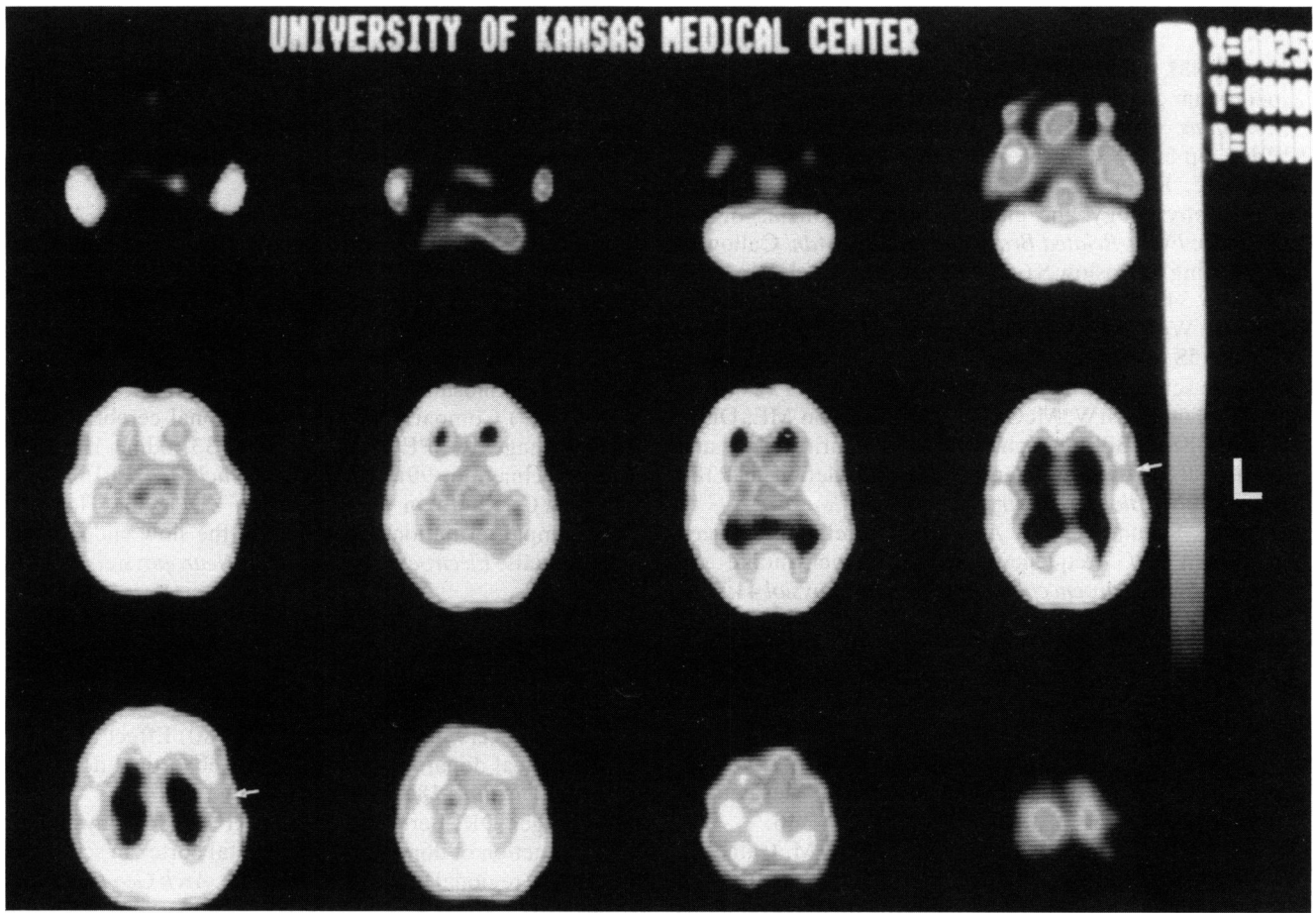

Fig. 3: SPECT transaxial brain images reveal a significant decrease in left frontotemporal HMPAO activity (arrows). A smaller decrease in the right frontotemporal region is also evident.

comparable to previous findings observed in schizophrenic patients (Morihisa et al 1983; Morstyn et al 1983b). Explanations for the diffuse delta pattern include impairments of cognition and/or arousal (Ingvar et al 1976; Morstyn et al 1983b). Left temporal increases in beta activity suggest the possibility of an irritable cortical focus which also may account for the auditory P300 shift away from this region (Ingvar et al 1976; Morstyn et al 1983b).

HMPAO SPECT brain imaging demonstrates bilateral frontotemporal hypoperfusion in our patient. These findings are consistent with other SPECT and PET studies which indicate abnormally reduced perfusion and metabolism (more markedly on the left side) in the frontal lobes of schizophrenics (Farkas et al 1984; McEwan et al 1989). It has been postulated that an early developmental abnormality or insult to the frontal cortex leads to dopaminergic pathway dysfunction (Weinberger et al 1986). Animal studies support this hypothesis as selective prefrontal cortical dopamine leisions enhance mesolimbic dopamine transmission which would theoretically lead to psychotic symptoms in humans (Pycock et al 1980).

Collectively, the evoked potential, quantitative EEG and HMPAO SPECT findings consistently suggest frontotemporal physiologic brain abnormalities in our schizophrenic patient. Although comparisons of topographic mapping and SPECT abnormalities are rare, one previous report indicates that in most cases decreases in radionucleide uptake correlate with auditory evoked potential aberrancies as well as delta predominance on quantitative EEG analysis (Preston et al 1989). Both electrophysiologic techniques of assessment measure processes which critically affect cortical blood flow (Branston et al 1978). The degree of hemodynamic hypoperfusion as visualized via HMPAO SPECT may well depend on the degree of electrophysiologic abnormality which is synaptically based possibly reflecting associated impairments of neurotransmitter synthesis and/or reuptake. Furthermore, histopathological abnormalities such as those described by Kraepelin in the frontal and temporal lobes of those with "dementia praecox" are likely to have some relationship to the physiologic dysfunction. Neurophysiologic imaging thus aids in the delineation and understanding of psychiatric disorders such as schizophrenia.

REFERENCES

Branston NM, Symon L (1978) Cortical EP blood flow and potassium changes in experimental ischaemia. In: *Evoked Potentials.* Barber C (ed). Baltimore: University Park Press, pp 527-530.

Donchin E, Rilter W, McCallum WC (1978) Cognitive psychophysiology: the endogenous components of the ERP. In: *Event-Related Brain Potentials in Man.* Calloway E, Tueting P, Koslow S (eds). New York: Academic Press Inc., pp 349-432.

Farkas T, Wolf AP, Jaeger J, Bradie JD, Christman DR, Fowler JS (1984) Regional brain glucose metabolism in chronic schizophrenia. *Arch Gen Psychiatry* **41**:293-300.

Faux SF, Torello MW, McCarley RW, Shenton ME, Duffy FH (1988) P300 in schizophrenia: confirmation and statistical validation of temporal region deficit in P300 topography. *Biol Psychiatry* **23**:776-790.

Ingvar DH, Sjolund B, Ardo A (1976) Correlation between dominant EEG frequency, cerebral oxygen intake and blood flow. *Electroencephalogr Clin Neurophysiol* **41**:268-276.

Kendler KS (1986) Genetics of schizophrenia. In: *Psychiatry Update, American Psychiatric Annual Review.* Hales RE, Frances AJ (eds). Washington, D.C.: APA Press, pp 42-67.

Knight RT (1985) Electrophysiology in behavioral neurology. In: *Principles of Behavioral Neurology.* Mesulam M (ed). Philadelphia: F.A. Davis Co., pp 327-346.

McCarley RW, Faux SF, Shenton M, LeMay M, Caine M, Ballinger R, Duffy FH (1989) CT abnormalities in schizophrenia: a preliminary study of their correlations with P300/N200 electrophysiological features and positive/negative symptoms. *Arch Gen Psychiatry* **46**:698-708.

McEwan AJ, Blackman H, Paterson W, Hooper HR (1989) Quantification of hexamethylpropyleneamine oxime (HMPAO) distribution in pediatric psychiatric patients. *J Nucl Med* **30**:812.

Morihisa JM, Duffy FH, Wyatt RJ (1983) Brain electrical activity mapping (BEAM) in schizophrenic patients. *Arch Gen Psychiatry* **40**:719-728.

Morstyn R, Duffy FH, McCarley RW (1983a) Altered P300 topography in schizophrenia. *Arch Gen Psychiatry* **40**:729-734.

Morstyn R, Duffy FH, McCarley RW (1983b) Altered topography of EEG spectral content in schizophrenia. *Electroencephalogr Clin Neurophysiol* **56**:263-271.

Nakano S, Kinoshita K, Jinnouchi S, Hoshi H, Watanabe K (1989) Comparative study of regional cerebral blood flow images by SPECT using xenon 133, iodine-123 IMP, and technetium-99m HMPAO. *J Nucl Med* **30**:157-164.

Okada YC, Kaufman L, Williamson SJ (1983) The hippocampal formation as a source of the slow endogenous potentials. *Electroencephalogr Clin Neurophysiol* **55**:417-426.

Preston DF, Gaffney GR, Bergh JR, Maurer RG, Robinson RG (1989) SPECT iofetamine scans in clinical child psychiatry and comparison with findings of "BEAM" brain mapping. *J Nucl Med* **30**:966.

Pycock CJ, Kerwin RW, Carter CJ (1980) Effect of leision of cortical dopamine terminals on subcortical dopamine in rats. *Nature* **286**:74-77.

Weinberger DR, Berman KF, Zee RF (1986) Physiologic dysfunction of dorsolateral prefrontal cortex in schizophrenia. I: regional blood flow evidence. *Arch Gen Psychiatry* **44**:114-124.

Weinberger DR (1987) Implications of normal brain development for the pathogenesis of schizophrenia. *Arch Gen Psychiatry* **44**:660-669.