The brainstem auditory evoked responses were studied in 19 opioid dependent subjects and 20 normal healthy volunteers. The absolute latencies of wave III, V and the interpeak latencies I-III, III-V and I-V were significantly prolonged in the experimental group. Implications are discussed.

Key Words: Opioid dependence, BAER

The psychoactive drugs are known to alter the brain's response to the sensory stimuli. Some change the perception of the stimuli, some alter the cognitive processing and some the emotional response to them (Barret et al., 1987). In order to study these effects non-invasive methods like brainstem auditory evoked responses (BAER) can be performed to study the functional integrity of various areas of the brain.

This study was undertaken to determine brainstem auditory evoked responses in opioid dependent patients.

MATERIAL AND METHOD

The study was conducted at the AllMS, New Delhi. All patients registered at the deaddiction centre on the outpatient days of one of the authors (R.L) during the period Jan. 1995 to June 1995 were screened. Those diagnosed as opioid dependence syndrome; currently using the substance (F 11.24) according to ICD-10 (WHO, 1992) in the age group 16-45 years were included in the study. Patients using other psychoactive substance were also included provided an opioid was the primary drug and the patient was not currently dependent on the other substance. An informed consent was obtained from all the patients. A detailed history and physical examination was done to rule out concurrent chronic medical illness; a haematological screening to rule out diabetes, hepatic and renal damage was also done (blood sugar, blood urea, serum creatinine, SGOT, SGPT) and it was ensured that the patient was not on any long term medications.

The controls were all healthy subjects, who were not dependent on any drug. There was no history of head injury, vertigo, deafness, alcohol or opioid intake in the controls.

Recording procedures: BAER: This was performed using the Viking II equipment. The auditory stimuli (click) were delivered through the headphones in a quiet room. The click rate was 11/sec and intensity of 65dB above the hearing threshold. The hearing threshold was determined for all, at the onset of recording in order to eliminate any peripheral hearing defect. The band pass was between 100-3000 Hz. Recordings were made between Cz and Ai. Two separate trials of 2000 responses were recorded and superimposed. Absolute latencies of wave I,III,V and interpeak latencies I-III, III-V, and I-V were noted. These were compared to values obtained
from controls. Mean±SD was calculated and student t test was used to determine statistical significance.

RESULTS

There were 19 subjects in the experimental group, heroin dependence-16, buprenorphine-2, opium-1. All the subjects were males in the age range of 20-43 years (29.9±6.4). The duration of opioid use ranged from 2 months-14 years. The control group consisted of 20 normal healthy volunteers (22-44 years; mean= 28 years).

BAER. The absolute latencies of wave III-V and the interpeak latencies l-III, III-V and I-V were all significantly prolonged in the opioid dependent subjects. Details are shown in table.

| TABLE | VER & BAER (MEAN±S.D., p VALUE) IN CONTROLS AND OPIOID DEPENDENT SUBJECTS |
|-------|--------------------------------------------------------------------------|
| Controls | Opioid dep | p value |
| P 100 (ms) latency | 96.0 | 96.4 | 8.7 | NS |
| AMP P100 (uV) | 72.17 | 3.43 | 2.7 | <0.001 |
| BAER I (ms) | 2.74 | 1.74 | 0.20 | NS |
| BAER III (ms) | 2.74 | 3.82 | 0.32 | <0.001 |
| BAER V (ms) | 5.5 | 5.90 | 0.43 | <0.01 |
| BAER I-III (ms) | 2.0 | 2.2 | 0.26 | <0.01 |
| BAER III-V (ms) | 1.8 | 2.06 | 0.46 | <0.01 |
| BAER I-V (ms) | 3.8 | 4.1 | 0.50 | <0.05 |

DISCUSSION

The brain-stem auditory evoked response (BAER) occurring within the first 8-10 ms following the click stimulus are due to activation of the brainstem auditory structures (Markand, 1994).

Auditory evoked potential (BAER) have two major clinical applications: 1) the assessment of peripheral auditory function and 2) the assessment of the integrity of the central auditory pathways. The wave I reflects the compound action potential in the peripheral portion of the eighth nerve. Subsequent waves are believed to originate in the auditory pathways in the brainstem. Wave II represents activity in the ipsilateral cochlear nucleus. Wave III is generated in the caudal pons. The major sources of wave V are considered to be lateral lemniscus and inferior colliculus on both sides. (Stockard et al., 1977; Oh et al., 1981). The assessment of the brainstem can be achieved through measures of the intercomponent conduction times (waves I-III, III-V or I-V) in addition to the measure of absolute latencies of waves I, III and V. The present study revealed significant prolongation of waves III (p<.001) arising from pons and V (p<.01) arising from midbrain respectively. Earlier studies revealed prolongation of wave I, with no significant difference in the latencies of later components (Dabic-Jeftic & Mikula, 1944).

All the interpeak latencies (I-III, III-V and I-V) were also prolonged significantly. This has also been seen in association with chronic exposure to alcohol (Chu et al., 1982), but no reports, to our knowledge, exists of this abnormality in subjects with opioid dependence. This signifies an impaired conduction in the auditory pathway along lower and upper brain stem. The pathogenesis of these abnormalities in evoked responses remains uncertain. These abnormalities may suggest demyelination or neuronal loss in the brain stem. Corresponding imaging studies may help to establish the exact pathology. However it does provide some insight into the functional disturbances of the brain. Whether these changes are reversible after abstinence, as reported in alcoholism (Chu, N.S et al., 1982) and the effect of vitamins, still remains to be worked out.

The auditory evoked responses are abnormal in subjects with opioid dependence, suggestive of dysfunction in auditory conduction. This non-invasive technique helps
to assess the functional integrity of the brain-stem. Thus, it could be a useful tool to investigate the extent of central nervous abnormalities in opioid dependent subjects. Whether these changes are temporary or permanent and the relationship with duration of substance use needs to be evaluated. The answers to all these would help us to understand the functional disturbance of the brain in the population of opioid dependent patients. Thus these tests could provide insight into the pathophysiology and detrimental effects of the opioid, which may not be clinically discernible.

ACKNOWLEDGEMENTS

We are thankful to Mr. M.S. Bisht and R.S. Arya for their technical assistance.

REFERENCES

Barret, Q., Neshige, R. & Shibasaki, H. (1987) Human auditory and somatosensory event-related potentials Effect of response conditions and age. *Electroencephalog Clin Neurophysiol*, 66, 409-519.

Chu, NS., Squires, K. & Starr & A. (1982)

Auditory brainstem responses in chronic alcoholic patients. *Electroenceph Clin Neurophysiol*, 54, 418-425.

Dabic-Jeftic, M. & Mikula, I. (1994) Brainstem auditory evoked potentials (BAER) in drug addicts. *Alcoholism*, 30, 1-2.

Markand, O.N. (1994) Brainstem auditory evoked potentials. *J. Clinical Neurophysiology*, II, 3, 319-342.

Oh, S.J., Kuba, T., Soyer, A., Choi, S. Bonikowski, RP. & Vitek J. (1981) Lateralization of brainstem lesions by brainstem auditory evoked potentials. *Neurology*, 31, 14-18.

Stockard, J.J. & Rossiter, V.S. (1977) Clinical and pathologic correlates of brainstem auditory response abnormalities. *Neurology*, 27, 316-325.

Stockard, J.J., Stockard, P.J.E. & Sharbrough, F.W. (1992) Brainstem auditory evoked potentials in neurology. In Methodology, interpretation and clinical application, Edn 3, (Ed) Aminoff, M.J., pp 503-531, New York: Churchill Livingstone.

World Health Organisation (1992) International classification of diseases, 10th edition, chapter V. Geneva: WHO.

R. LAL*. Additional Professor, Department of Psychiatry. M Bhatia, Assistant Professor & I/C Officer Electrophysiology lab, Department of Neurology, AIIMS, New Delhi-110 029.

*Correspondence