Nootropic Effect of BR-16A (Mentat), a Psychotropic Herbal Formulation, on Cognitive Deficits-induced by Prenatal Undernutrition, Postnatal Environmental Impoverishment and Hypoxia in Rats

Bhattacharya, S.K.
Department of Pharmacology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India.

ABSTRACT
Subchronic administration of BR-16A (Mentat), a compound herbal formulation, and the nootropic agent, piracetam, augmented learning acquisition and retention of learning in normal rats, as well as in states of cognitive deficits induced by prenatal undernutrition, postnatal environment impoverishment and sodium nitrite hypoxia. The test paradigms used were step-down latency in a passive avoidance test and transfer latency in elevated plus maze. The drugs were administered orally once daily for 7 days, behavioural testing being done 1 hr after the last administration on day 7. Post-trial performances of the rats at 24 hr and after another 7 days was assessed as indices of learning acquisition and retention of learning (memory), respectively. Mentat (100 mg/kg) and piracetam (100 mg/kg) induced statistically significant nootropic effect in all the test parameters. However, the lower dose (50 mg/kg) of Mentat did not significantly augment learning acquisition in normal rats and in induced states of cognitive deficits, but significantly improved retention of learning in normal rats and in animals with cognitive deficits, but significantly improved retention of learning in normal rats and in animals with cognitive deficits. Acute single administration of either Mentat (100 mg/kg, orally) and piracetam (100 mg/kg, orally) did not exhibit any discernible nootropic effect in any of the paradigms or parameters investigated. The results indicate that Mentat, like piracetam, can facilitate learning and memory, and can be categorised as a nootropic agent. They also corroborate clinical reports on the memory-facilitative effect of Mentat and earlier experimental evidence of its nootropic activity in mice.

BR-16A (Mentat), is a herbal formulation consisting of: Brahmi (Bacopa monnieri), Mandookparni (Centella asiatica), Ashwagandha (Withania somnifera), Jatamansi (Nardostachys jatamansi), Shankhpushpi (Evolvulus alsinoides), Tagar (Valeriana wallichii), Vach (Acorus calamus), Guduchi (Tinospora cordifolia), Malkangni (Celastrus paniculatus), Kuth (Saussurea lappa) Amla (Embelica officinalis) and the other ingredients of Triphala (Terminalia chebula and Terminalia belerica)\(^1\). Some of these plants namely, B. monnieri, C. asiatica, W. somnifera, N. jatamansi, E. alsinoides, V. wallichii, A. calamus, T. cordifolia and C. paniculatus, have been classified in Ayurveda as Medharasayanas and claimed to improve memory and intellect\(^2\). Compound formulations are generally used in Ayurveda, based on the concept that such combinations provide synergistic therapeutic effect. They also contain ingredients, which are said to minimise the likely adverse effects of the major drugs.
Mentat has been reported to improve memory quotient in normal individuals belonging to different age groups\(^3\), increase memory span and attenuate fluctuation of attention in normal adult students\(^4\) and improve learning ability in children with behavioural problems or minimal brain damage\(^5\). Experimental findings have corroborated these clinical data and Mentat has been shown to improve acquisition and retention of learning in normal mice and attenuate the amnesic effects of scopolamine and electro-convulsive shock\(^6,7\). The present study was undertaken to confirm the nootropic status of Mentat by using cognitive deficits induced by prenatal malnutrition, postnatal environmental impoverishment and hypoxia. The animal models of impaired cognitive functions have been extensively used to evaluate nootropic activity\(^8-11\) and it has been proposed that they are more 'physiological' than drug or electroshock induced cognitive deficits\(^12\).

**MATERIALS AND METHODS**

**Animals** - Inbred litter mate Charles Foster albino rats, of either sex, were used for the undernourishment and environmental impoverishment studies, whereas male Charles Foster rats (150-180 g) were used for the hypoxia studies.

Undernutrition was induced by giving pregnant rats half the amount of diets (Hindustan Lever rat feed normally consumed by an adult rat\(^13\) from day of conception, as evidenced by presence of sperms in vaginal swab until parturition. This regimen has been shown to induce undernutrition in the pups born to mothers underfed during gestation\(^8,10,14\). At birth the litters were culled to 8 pups per dam and those from restricted and normally fed mothers were designated as undernourished and normally nourished respectively. The pups were weaned at 21-22 days of age and behavioural testing was done at 9 to 10 weeks of age.

Environmental impoverishment was induced by rearing pups, of either sex, individually for 5 weeks before behavioural testing in small cages covered on three side. This ensured that the rats were isolated and deprived of outer environmental stimulation\(^15\). Control rats of this group were reared in large steel cages (45x65x60 cm) with wire mesh walls, which ensured that the rats were exposed to external stimulation. Furthermore, these rats were allowed to play with manipulative objects like wooden blocks, balls, ladders etc. for 4 hours each day in groups of 10 to 12 animals\(^15\).

Chemical hypoxia was induced by administration of sodium nitrite (75 mg/kg, sc), immediately after acquisition training\(^16\).

**Drugs** - Drugs used were BR-16A (Mentat) (Himalaya Drug Co., India) and piracetam (Biddle Sawyer, India). The drugs were suspended in distilled water and administered orally, through an orogastric tube, in a volume of 1 ml/100 g once daily for 7 days, the last dose being administered 1 hr prior to behavioural testing. Control animals received equivalent volume of distilled water through the same route for the same time period. However, in the hypoxia group, the rats received one more drug or vehicle administration along with sodium
nitrite after the acquisition trial. Mentat was administered at two dose levels, 50 and 100 mg/kg, while piracetam was administered in a dose of 100 mg/kg.

Methods - The following methods were used to assess learning acquisition and retention of learning:

Passive avoidance test: The method used was essentially the same as described earlier. Briefly, the rat was placed on the elevated platform situated in the centre of the passive avoidance box and the latency to step down was recorded. Immediately after stepping down, the rat received electric shock (0.5mA) of 3 sec duration through the grid floor, and was then returned to its home cage. On the following day (24 hr retention interval) the rat was once again placed on the platform and the step-down latency was recorded. Electric shock was not administered at this time. If the rat remained on the platform for the 5 min test duration, it was assigned a maximum score of 300 sec. Latency to step down was again assessed a week later on day 9 in order to assess the retention of passive avoidance learning. The results have been expressed as retention scores after 24 hr or one week for each rat by calculating the inflexion ration by the formula:

\[
\text{Inflexion ratio} = \frac{(L_1 - L_0)}{L_0}
\]

where \(L_0\)=initial step down latency (sec) and \(L_1\)=step down latency (sec) after 24 hr or 1 week.

Transfer latency in elevated plus-maze: The plus-maze consisted of two opposite open arms (50x10 cm), crossed with two closed arms of the same dimensions with 40 cm high walls. The arms were connected with a central square, 10x10 cm to give the apparatus the appearance of a plus sign. The maze was elevated 70 cm above the floor and placed in a dimly illuminated room. Rats were placed individually at one end of an open arm, facing away from the central square. The time taken for the rat to move from the open arm and enter one of the closed arms was recorded as transfer latency. On day 1 the rat was allowed to exposed the maze for 30 sec after recording transfer latency. Transfer latency was again recorded 24 hr later and on day 9 for retention of learning. The method used was that of Itoh et al., adapted for use in rats.

Statistical analysis - The data was initially analysed by a one-way analysis of variance (ANOVA) followed by the two-tailed Student's t-test. A 0.05 level of probability was accepted for recording statistical significance.

RESULTS

Acute single administration of Mentat (100 mg/kg) and piracetam (100 mg/kg) did not induce any discernible effects on either learning acquisition or retention of learning: per se in normal animals and in states of induced cognitive deficits (data not shown).

Prenatally induced undernutrition
Passive avoidance test: Mentat (100 mg/kg) and piracetam (100 mg/kg) administered subchronically for 7 days augmented learning acquisition and retention of the learned task as tested 24 hr and 7 days later, respectively, in normal rats after initial trials. However, the lower dose of Mentat (50 mg/kg) had little effect on learning acquisition but promoted retention of learning in normal animals. The step-down latency of prenatally undernourished rats at 24 hr and 7 days post-trial test was significantly lower than that of their normally nourished counterparts, indicating the existence of cognitive deficit induced by this manoeuvre. Sub-chronic administration of Mentat (100 mg/kg) and piracetam (100 mg/kg) induced qualitatively comparable reversal of the decrease in step-down latencies induced by undernutrition at both these test time periods, indicating that both the drugs exerted significant nootropic activity. However, the lower dose of Mentat (50 mg/kg) reversed only the undernutrition induced deficit in retention of learning, the reversal of learning acquisition deficit remaining statistically insignificant (Table 1).

<table>
<thead>
<tr>
<th>Treatments (mg/kg)</th>
<th>n</th>
<th>Retention intervals</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>24 hours</td>
<td>p</td>
<td>1 week</td>
<td>p</td>
</tr>
<tr>
<td>Normal nutrition environment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vehicle</td>
<td>20</td>
<td>3.64 ± 0.8</td>
<td>–</td>
<td>5.52 ± 1.4</td>
<td>–</td>
</tr>
<tr>
<td>Mentat (50)</td>
<td>8</td>
<td>5.24 ± 1.4</td>
<td>NSa</td>
<td>7.36 ± 0.9</td>
<td>&lt;0.05a</td>
</tr>
<tr>
<td>Mentat (100)</td>
<td>8</td>
<td>8.98 ± 1.4</td>
<td>&lt;0.01a</td>
<td>9.96 ± 1.6</td>
<td>&lt;0.01a</td>
</tr>
<tr>
<td>Piracetam (100)</td>
<td>6</td>
<td>9.86 ± 1.6</td>
<td>&lt;0.01a</td>
<td>10.84 ± 1.5</td>
<td>&lt;0.01a</td>
</tr>
<tr>
<td>Undernourishment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vehicle</td>
<td>8</td>
<td>1.65 ± 0.8</td>
<td>&lt;0.01a</td>
<td>3.28 ± 0.9</td>
<td>&lt;0.01a</td>
</tr>
<tr>
<td>Mentat (50)</td>
<td>8</td>
<td>3.42 ± 1.2</td>
<td>NSb</td>
<td>8.76 ± 1.6</td>
<td>&lt;0.01b</td>
</tr>
<tr>
<td>Mentat (100)</td>
<td>8</td>
<td>7.76 ± 1.2</td>
<td>&lt;0.001b</td>
<td>11.08 ± 1.8</td>
<td>&lt;0.001b</td>
</tr>
<tr>
<td>Piracetam (100)</td>
<td>6</td>
<td>8.98 ± 1.6</td>
<td>&lt;0.001b</td>
<td>12.09 ± 1.2</td>
<td>&lt;0.001b</td>
</tr>
<tr>
<td>Environment improvement</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vehicle</td>
<td>8</td>
<td>2.04 ± 0.6</td>
<td>&lt;0.05a</td>
<td>3.96 ± 0.12</td>
<td>&lt;0.05a</td>
</tr>
<tr>
<td>Mentat (50)</td>
<td>6</td>
<td>3.98 ± 1.2</td>
<td>NSb</td>
<td>6.43 ± 0.14</td>
<td>&lt;0.01b</td>
</tr>
<tr>
<td>Mentat (100)</td>
<td>6</td>
<td>5.56 ± 1.6</td>
<td>&lt;0.05b</td>
<td>8.74 ± 1.9</td>
<td>&lt;0.05b</td>
</tr>
<tr>
<td>Piracetam (100)</td>
<td>6</td>
<td>7.42 ± 1.3</td>
<td>&lt;0.001b</td>
<td>10.5 ± 1.8</td>
<td>&lt;0.001b</td>
</tr>
</tbody>
</table>

a Comparison of data with normal nutrition environment vehicle-treated group.
b Comparison of data with respective cognitive deficit vehicle-treated group.

Elevated plus-maze test: The results obtained with Mentat and piracetam, in this paradigm, were similar to those obtained in the passive avoidance test. Thus, prenatally induced under nutrition induced significant cognitive deficits, as evidenced by increase in the transfer latency during acquisition and retention trials. Mentat (100 mg/kg) and piracetam (100 mg/kg) decreased transfer latencies at both test periods, in normal animals, and reversed the effect of under nutrition on acquisition and retention of learning. However, the lower dose of
Mentat (50 mg/kg) had insignificant effect in normal animals but significantly reversed cognitive deficit induced by under nutrition (Table 2).

**Postnatal environmental impoverishment**

Passive avoidance test: Rats subjected to environmental impoverishment showed cognitive deficits when compared to their normally reared counterparts with significant decrease in step-down latencies during acquisition and retention trials. Subchronic administration of Mentat (100 mg/kg) and piracetam (100 mg/kg) significantly reversed both these deficits, whereas the effect of the lower dose of Mentat (50 mg/kg) was restricted to learning retention (Table 1).

### Table 2: Effects of Mentat and piracetam on transfer latency in elevated plus-maze in normal, prenatally undernourished and environmentally impoverished rats (values are mean ± SE)

<table>
<thead>
<tr>
<th>Treatments (mg/kg)</th>
<th>n</th>
<th>24 hours</th>
<th>Transfer latency (sec)</th>
<th>1 week</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal nutrition environment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vehicle</td>
<td>16</td>
<td>58.2 ± 5.8</td>
<td>–</td>
<td>42.3 ± 4.8</td>
<td>–</td>
</tr>
<tr>
<td>Mentat (50)</td>
<td>8</td>
<td>42.9 ± 6.9</td>
<td>NS&lt;sup&gt;a&lt;/sup&gt;</td>
<td>32.7 ± 5.6</td>
<td>&lt;0.5&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Mentat (100)</td>
<td>8</td>
<td>28.8 ± 4.4</td>
<td>&lt;0.05&lt;sup&gt;a&lt;/sup&gt;</td>
<td>24.2 ± 2.6</td>
<td>&lt;0.01&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Piracetam (100)</td>
<td>8</td>
<td>22.6 ± 3.8</td>
<td>&lt;0.01&lt;sup&gt;a&lt;/sup&gt;</td>
<td>20.9 ± 2.9</td>
<td>&lt;0.01&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Undernourishment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vehicle</td>
<td>8</td>
<td>86.9 ± 9.6</td>
<td>&lt;0.01&lt;sup&gt;a&lt;/sup&gt;</td>
<td>80.4 ± 6.2</td>
<td>&lt;0.001&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Mentat (50)</td>
<td>8</td>
<td>43.9 ± 5.3</td>
<td>&lt;0.001&lt;sup&gt;b&lt;/sup&gt;</td>
<td>39.4 ± 4.9</td>
<td>&lt;0.001&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Mentat (100)</td>
<td>8</td>
<td>31.6 ± 4.8</td>
<td>&lt;0.001&lt;sup&gt;b&lt;/sup&gt;</td>
<td>26.8 ± 3.7</td>
<td>&lt;0.001&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Piracetam (100)</td>
<td>6</td>
<td>25.4 ± 3.2</td>
<td>&lt;0.001&lt;sup&gt;b&lt;/sup&gt;</td>
<td>23.2 ± 2.9</td>
<td>&lt;0.001&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Environment improvement</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vehicle</td>
<td>8</td>
<td>69.4 ± 6.2</td>
<td>NS&lt;sup&gt;a&lt;/sup&gt;</td>
<td>73.2 ± 6.8</td>
<td>&lt;0.01&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Mentat (50)</td>
<td>8</td>
<td>49.4 ± 9.2</td>
<td>NS&lt;sup&gt;a&lt;/sup&gt;</td>
<td>47.8 ± 8.2</td>
<td>&lt;0.01&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Mentat (100)</td>
<td>8</td>
<td>39.6 ± 6.4</td>
<td>&lt;0.01&lt;sup&gt;b&lt;/sup&gt;</td>
<td>33.7 ± 5.8</td>
<td>&lt;0.001&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Piracetam (100)</td>
<td>6</td>
<td>32.9 ± 8.4</td>
<td>&lt;0.01&lt;sup&gt;b&lt;/sup&gt;</td>
<td>30.6 ± 3.9</td>
<td>&lt;0.001&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Comparison of data with normal nutrition environment vehicle-treated group.

<sup>b</sup> Comparison of data with respective cognitive deficit vehicle-treated group.

NS – Data statistically non-significant.

Elevated plus-maze test: Like in the passive avoidance test, rats subjected to environmental impoverishment, exhibited significant cognitive deficit, as indicated by an increase in transfer latencies during acquisition and retention trials. Mentat (100 mg/kg) and piracetam (100 mg/kg) reversed these cognitive deficits, whereas the effect of the lower dose of Mentat (50 mg/kg) was restricted to reversal of learning retention deficit only (Table 2).

**Sodium nitrate induced hypoxia**

Passive avoidance test: Sodium nitrite (75 mg/kg, sc) induced marked cognitive deficit as indicated by significant decrease in step-down latencies during acquisition (24 hr) and retention (7 days) trials.
Mentat (100 mg/kg) and piracetam (100 mg/kg) significantly reversed the hypoxic deficits of both acquisition and retention of learning. The effect of the lower dose of Mentat (50 mg/kg) on these parameters, though evident, remained statistically non-significant (Table 3).

Elevated plus-maze test: Like in the passive avoidance test, hypoxic rats, in this paradigm, exhibited significant cognitive deficit, as shown by the marked increase in transfer latencies during acquisition and retention trials. Both Mentat (100 mg/kg) and piracetam (100 mg/kg) reversed these deficits, following sub-chronic administration. However, the effect of the lower dose (50 mg/kg) of Mentat on these parameters though discernible, remained statistically non-significant (Table 3).

DISCUSSION
Nootropic agents are known to facilitate learning and memory, and prevent impairment of cognitive functions induced by diseases and brain insults. Piracetam is the prototype of this class of psychotropic agents. There is extensive experimental evidence that piracetam and its analogues can facilitate learning acquisition, and its analogues can facilitate learning acquisition and retention of that learning, as memory, in a variety of animal models of impaired cognitive functioning including learning deficits in aged animals\textsuperscript{8,19}. However, despite several encouraging clinical reports\textsuperscript{19}, the therapeutic utility of available nootropic agents, including piracetam and related drugs, remains questionable and controversial\textsuperscript{19}.

The methods used to induce experimental cognitive deficits have been extensively validated in this laboratory and elsewhere\textsuperscript{8-11,20}. Apart from experimental evidence, there is conclusive evidence, which indicates that prenatally-induced malnutrition is likely to induce more severe memory deficits in the offspring, as compared to malnutrition existing postnatally\textsuperscript{21}. Though there is insufficient clinical evidence, substantial experimental data confirms that rats reared in isolation, resulting in environmental impoverishment exhibit substantial cognitive deficits as compared to normally reared counterparts\textsuperscript{8-10}. Likewise, chemical hypoxia induced by administration of sodium nitrite, resulting from reduction in the oxygen carrying capacity of blood with conversion of hemoglobin to methaemoglobin has been validated as an experimental model for manipulation of brain energy metabolism\textsuperscript{11}. It has been postulated that this model simulates hypoxic amnesia noted in old age and in brain ischaemia\textsuperscript{11}. Piracetam, and related nootropic agents, have been reported to attenuate memory deficits induced by these three models of cognitive dysfunction used in this study\textsuperscript{8-11,20}.

In the present study, Mentat, a compound herbal formulation of several Medharasayana medicinal plants\textsuperscript{2}, was found to improve learning acquisition and retention of the learned task in normal rats with no cognitive deficit, when administered subchronically. The effects were comparable to those induced by an equivalent dose of piracetam. This indicates that Mentat meets a major criterion for nootropic activity, namely improvement of memory in the absence of cognitive deficits\textsuperscript{19}. The putative nootropic activity was further evidenced by its ability to...
reverse cognitive deficits induced by undernutrition, environmental deprivation and hypoxia, similar to the reversal induced by piracetam given in equivalent dosage and for similar time schedule. Unlike the effective higher (100 mg/kg) dose of Mentat, a lower dose (50 mg/kg) of the drug was ineffective in facilitating learning acquisition and reversing induced by under nutrition, environmental deprivation and hypoxia, similar to the reversal induced by piracetam given in equivalent dosage and for similar time schedule. Unlike the effective higher (100 mg/kg) dose of Mentat, a lower dose (50 mg/kg) of the drug was ineffective in facilitating learning acquisition and reversing induced deficits in learning, but promoted learning retention in normal animals and attenuated induced deficits in memory consolidation. This difference in the activity of the two doses of Mentat may be related to dosage but may also reflect the postulate that acquisition of learning, and the consolidation of the learning as memory, involve dissimilar neurochemical mechanisms which are differentially affected by the lower and higher dose of the drug. The ineffectiveness of acutely administered piracetam, and that of Mentat, to exhibit discernible nootropic activity is consonant with experimental and clinical reports indicating that memory facilitation is best exerted after sub-chronic administration of these drugs.

The results of the present study lend relevance to clinical reports, which have indicated that Mentat is effective in promoting memory in normal subjects and in patients with cognitive deficits. They also corroborate earlier experimental studies, demonstrating the nootropic effect of Mentat in normal mice and in learning deficits, in this species, induced by scopolamine and electroshock.

Behavioural studies, using similar doses and treatment schedules adopted for this study, indicate that Mentat exerts significant anxiolytic and antidepressant effects in rodents. The drug has also been shown to attenuate anxiety following ethanol withdrawal in mice. It had earlier been summarized, based on the amnesic effect of benzodiazepine, that anxiolytic activity and memory deficits were inter-related. However, this hypothesis was proved wrong when non-benzodiazepine anxiolytics, including ondansetron, a 5-HT receptor antagonist, and tianeptin, which promotes the re-uptake of serotonin into its neurons were shown to facilitate learning and memory. The effect of Mentat in promoting cognition in environmentally deprived isolated rats can be correlated to its attenuation of anxiety evidenced in the social interaction test, using paired previously isolated rats. Apart from its anxiolytic activity, the antidepressant activity in Mentat may also contribute to its nootropic effect. Cognition perturbations are very often associated with depressive illness and newer antidepressants, devoid of anticholinergic activity, have been found to improve cognitive functions, both experimentally and clinically.

It would be presumptuous, at this stage, to hazard a cogent neurochemical basis for the observed nootropic activity of Mentat, given the fact that, despite intensive research, the mechanism of action of conventional nootropics, including piracetam, remains controversial and equivocal. However, the earlier observations that Mentat can reverse the amnesic effects of the anticholinergic agent, scopolamine and that of electroshock, indicate that the
central cholinergic system may be involved. There is extensive and conclusive evidence to link central cholinergic mechanisms to cognitive functions. Impairment of cholinergic function invariably leads to cognitive dysfunction while, conversely facilitation of central cholinergic activity is associated with improvement in learning and memory. The reversal of cognitive deficits induced by electroshock convulsions by piracetam and active principles of *W. somnifera*, one of the major constituents of Mentat, has been shown to be associated with attenuation of rat brain acetylcholine depletion induced by electroshock.

Apart from central neurotransmitters, impairment of cerebral metabolism and cerebral blood flow are known to induce cognitive deficits, and, it is proposed that the beneficial effect of nootropics may be the result of improvement in cerebral circulation and brain metabolism. The reversal by Mentat, comparable to that exhibited by piracetam, of cognitive deficits induced by under nutrition and hypoxia, indicate that similar mechanisms involving brain metabolism and blood flow may be associated with the observed experimental and clinical nootropic effect of Mentat. However, further studies are required for elucidating the basis of nootropic activity of this formulation.

ACKNOWLEDGEMENT
Grant-in-aid from the Himalaya Drug Co., Bombay is acknowledged.

REFERENCES