Chapter V

Results and Discussion

The results of the present investigation have been presented and discussed in the following section:

A multigroup design experiment was conducted to study the effect of VP on morphine induced amnesia. After training in a passive avoidance task, the animals were given two successive injections of VP, morphine or saline (S+S, M+S, S+VP or M+VP). Retention tests were taken after 1, 2 and 7 days.

Table 1

Showing the mean latency scores of the four groups (S+S, M+S, S+VP and M+VP) on the three retention tests.

<table>
<thead>
<tr>
<th>Retention tests</th>
<th>I (S+S)</th>
<th>II (M+S)</th>
<th>III (S+VP)</th>
<th>IV (M+VP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>150.077</td>
<td>20.800</td>
<td>244.875</td>
<td>192.25</td>
</tr>
<tr>
<td>II</td>
<td>99.138</td>
<td>10.308</td>
<td>197.184</td>
<td>135.817</td>
</tr>
<tr>
<td>III</td>
<td>25.908</td>
<td>3.754</td>
<td>199.542</td>
<td>74.608</td>
</tr>
</tbody>
</table>

From the means it appears that morphine has an inhibitory effect on retention, since the Group II (M+S) scores are lower than that of the saline group (Group I)
on all the three retention tests. The mean scores of the other two groups, Group III (S+VP), Group IV (M+VP) are higher than that of the saline indicating that not only does VP facilitate retention, but it also counteracts the morphine induced amnesia. In order to determine whether the differences between the means were due to the experimental manipulations or just due to chance error, they were statistically analysed.

The present investigator diverted from the usual practice of applying analysis of variance (ANOVA) to test the significance of difference between the means of a multigroup experiment. After applying ANOVA, even if an insignificant F value is obtained, all the possible mean differences have to be tested individually, since it is possible that two thirds of the means might be significantly different. Therefore, Duncan's Range test, which is an alternative to the parametric analysis of variance (McGuigan, 1978), and is more economical, was employed.

Table 2

<table>
<thead>
<tr>
<th>Group</th>
<th>Retention II (M+S)</th>
<th>Retention I (S+S)</th>
<th>Retention IV (M+VP)</th>
<th>Retention III (S+VP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>20.800</td>
<td>150.077</td>
<td>192.250</td>
<td>244.875</td>
</tr>
<tr>
<td>II</td>
<td>10.308</td>
<td>99.138</td>
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</tr>
</tbody>
</table>
FIG. 3. SHOWING THE MEAN LATENCY PERIODS OF THE S+S, M+S, S+VP AND M+VP GROUPS ON THE FIRST RETENTION TEST.
The statistical analysis indicates that the mean latency scores of the morphine injected group (Group II, M+S) are significantly different from the saline (Group I) on the first two retention tests. Even on the third retention test, the Group II score is 85.51% less than that of Group I, but the difference fails to be statistically significant. The other two groups (Group III and IV) are significantly different from Group II on all the three retention tests.

The present results are in congruence with those obtained by Staubli and Huston (1980), Izquierdo (1980), Sunita (1983) and Monisha (1985) who also observed an amnestic effect of morphine at the same dose (3 mg/kg) in a passive avoidance task. A number of earlier investigators have reported that opiate agonists which mimic the action of the endogenous opiate peptides, have a dose dependent effect (U-shaped relationship) on retention (Jensen et al., 1978; Gallagher and Kapp, 1978; Messing et al., 1979; Monisha, 1985).

This contention receives support from a number of investigations in which it has been demonstrated that opiate antagonists which release the cholinergic and catecholaminergic neurotransmitter systems from the opiate mediated inhibitory influences (Izquierdo and Grandenz, 1980; Jhamandas and Sutak, 1983).
FIG. 4. SHOWING THE MEAN LATENCY PERIODS OF THE S+S, M+S, S+VP AND M+VP GROUPS ON THE SECOND RETENTION TEST.
reverse the opiate induced amnesia (Castellano, 1975; Messing et al., 1981; Sunita, 1983).

The facilitative effect of VP is also evident from the present results (Figure 3, 4 and 5). The latency score of the VP injected group (Group III, S+VP) is significantly different from the saline as well as the morphine injected group on all the three retention tests.

A number of earlier investigators have reported that VP acts on the brain as a neuromodulator and exerts an important influence on acquisition and retention (de Wied, 1966, 1969, 1972, 1975; van Wimersma, 1975; Gold and van Buskirk, 1976). The present findings are in line with those of Gold and van Buskirk (1976) who also reported a facilitative effect of VP at the same dose (3 I.U./Kg). Kovacs et al., 1979 also agree with the fact that VP, which has a varied neurochemical effect i.e., influence on synthesis of brain proteins, increase in cerebral phosphorylases and modulation of neurotransmitter systems especially the noradrenergic system, plays an important role in learning and memory.

It has been recently proposed that VP acts by increasing behavioural arousal (the state of alterness, or wakefulness) which in turn has an inverted U shaped relationship with performance (Sahgal, 1983 a,b; Sahgal et al., 1982; Sahgal and Wreight, 1983). This hypothesis
FIG. 5. SHOWING THE MEAN LATENCY PERIODS OF THE S+S, M+S, S+VP AND M+VP GROUPS ON THE THIRD RETENTION TEST.
suggests that administration of VP immediately after the learning trial increases arousal which facilitates acquisition and consolidation.

A physiological interaction has also been reported between VP and the endogenous opiate peptides. Intravenous administration of β-endorphin caused the release of VP (Weitzman et al., 1977), and VP potentiates the release of β-endorphin (Jones and Hillhouse, 1977; Vale et al., 1979). Distinct fiber like process within the neurohypophysis also reacted to enkephalin antiserum (Bloom et al., 1978). Administration of an opiate antagonist (Nalaxone) also reverses the effect of VP on memory (DeVito and Brush, 1984). These researches suggest a role of opiates in the modulation of the release of VP and its facilitative effect on learning and memory.

Thus the first two hypotheses which predicted that immediate post training administration of morphine/VP would have an inhibitory/facilitative effect on retention of an aversive learning task are verified.

The present investigator had also hypothesised that the amnestic effect of morphine, which causes behavioural depression (Castellano, 1973) would be counteracted by administration of VP. This fact is supported by the present results depicted in Figure 3, 4 and 5.
The mean latency scores of the M+VP group (Group IV) are significantly higher than those of the M+S group on all the three retention tests. In fact, the scores of this group (M+VP) are even higher than those of the saline (S+S) groups on all the three retention tests, although a significant difference it observed only on the last retention test.

These results indicate that the amnesia induced by morphine (Group I) has been counteracted by administration of VP (after 5 minutes). In fact the dose of VP utilized in the present experiment appears to be slightly more potent than that necessary to eliminate the morphine induced amnesia, since the latency scores of the M+VP group animals are higher than those of the saline (S+S) group. Since morphine exerts an inhibitory effect on the noradrenergic synapses via the opiate receptors (Castellano, 1975; Messing et al., 1979) and VP releases these systems from the inhibitory influence (Quartermain, 1975; Flexner et al., 1977), the observed reversal of morphine might be due to opiate-catecholaminergic interactions. In 1978, Gold and van Buskirk reported that hypo or hyper secretion of NE at the adrenergic synapses results in amnesia and moderate secretions are positively correlated with a high level of retention. Thus the amnesic effect of morphine might be due to reduction in the secretion of NE at the synapse and VP counteracts this
amnesia by restoring the optimal levels. This view is further supported by the fact that both VP and morphine have a dose dependent effect on retention. While morphine facilitates retention when administered in extreme doses and inhibits retention in moderate doses (3 mg to 12 mg), the effect of VP is the reverse. Since VP and morphine have opposing influence on the secretion of NE at the 
\text{\textsuperscript{\textalpha}A} synapses, their dose dependent effects are also inverse.

Alternatively the reversal of morphine induced amnesia by VP might be simply due to the additive effect of the exogenously administered morphine and the endogenous \text{\textbeta}-endorphin released due to administration of VP (De Vito and Brush, 1984). Since the opiate agonists inhibit retention only in moderate doses, the administration of VP immediately after administration of an amnestic dose of morphine might result in an elevation in the neural level of the opiate peptides, thereby reversing the morphine induced amnesia.

We may now sum up the findings of present investigation. A multigroup design experiment was conducted to study the antagonistic effect of VP on morphine induced amnesia. It was hypothesised that posttraining administration of morphine would inhibit retention of a passive avoidance
task while VP would reverse the morphine induced amnesia. Results support these hypotheses. It appears that the opiate-catecholaminergic interactions are involved in the amnesia induced by the opiate peptides.

Implication of the present work

1. Since amnesia induced by a depressant-morphine is reversed by administration of VP, this hormone might help in treatment of depression or other affective disorders.

2. Earlier researches indicate that a number of psychiatric disorders, such as Alzheimer's disorder, Karaskoff's syndrome (Bohus et al., 1975; Celestian et al., 1975; Oliveros et al., 1978; Anderson et al., 1979; Ehrensing et al., 1982), are due to imbalances in the neurohumoral systems. Thus restoration of the neuroendocrine balance should help in treatment of these patients.

Suggestions for further research:

1. Further experimentation can be done to determine whether the facilitative effect of extreme doses of morphine are also reversed by administration of VP.

2. Experimentation can be done at the human level also to determine whether depression induced amnesia can be reversed by administration of VP.