CHAPTER I

INTRODUCTION
The first demonstration of electroconvulsive therapy (ECT) was given in Medical Academy of Rome in May, 1938 (Cerletti and Binni). Despite the warning against possible electrocution by the editors of the Journal of American Medical Association (Kalinowsky, 1970), this method soon spread to the other countries. Soon it captured much of the attention of the researchers and many studies were conducted to understand the seizure process and to improve its safety.

ECT is a highly economical and useful therapy. It is effective over a wide range of affective disorders, including psychotic depression, mania and catatonia. There is no decrement in its efficacy with age. Results are likely to be better in patients with an acute onset of illness, short duration of decompensation and greatest severity of disturbance.

Along with the benefits, the effects of ECT are linked with various side-effects. Death, fractures, panic, fear, post-seizure delirium, spontaneous seizures and cardiovascular complications are generally described to accompany ECT administration. But the most common and extensively studied side effect of ECT is amnesia. Amnesia is so prominent with convulsive
therapy that some investigators concluded that impairment in memory was central to its mode of action. The amnesic effects of ECS were more marked when hypoxia was accepted as a part of therapeutic processes. After this, Holmberg (1955, 1963) demonstrated that the amnesia was still found when inhalation of oxygen prevented hypoxia.

**Amnesia**

Amnesia accompanied by ECS depends on many factors. Its severity and duration is determined by time of administration, quality of the stimulus and mental status at the time of learning. Learning is essential for the recall of any event. Depressed patients have an impairment in learning which may selectively affect the recall of little personal meaning or those that were not clearly defined so that the individual failed to attend to the event for its learning and later recall. Emotionally important, familiar, and easily assimilated events are recalled more easily than complex and unfamiliar events (Williams, 1950 a, b, 1966). Therefore, at the time of recall, familiarity, reminders and other clues may be helpful in eliciting the material that was learnt. There is an evidence suggesting that the amnesia of painful memories is more prevalent than the amnesia of non-painful
The effects of ECS on memory also vary with the modality (auditory, tactile or visual) and the content (verbal and nonverbal). The changes in current path resulting from varying electrode placements affect modality and content differently, indicating that brain response is not unitary to a seizure but is quite varied. The sensitivity of the memory process to seizures is different for different learning tasks. The subjects find recognition tasks the easiest to accomplish and this task is least sensitive to impairment. Recall, particularly after an interpolated delay (as with the learning and recall), is the most difficult task and is most sensitive to impairment by ECT.

Variation in the degree of amnesia has also been observed with the variation in the type of Psychopathology. Amnesia is usually less in non-depressed patients who may be resistant to the amnesic effects of seizures. Whether this is a reflection of their young age or a difference in brain responsivity is yet unclear.
Besides this, performance on memory tasks decays with each successive seizure during the course of treatment. After the first seizure, memory impairment is observed for a few hours; after four to six seizures, it is observed for 48 hrs. and longer; after eight to 10 seizures, it has been observed to last for 4 to 7 days and even longer (Brengelmann, 1959; Goldman et al., 1972; Squire et al. 1975).

The severity of amnesia differs when repeated seizures spaced hours apart in one day or when induced on a daily basis. It is comparatively less severe than the impairment when an equal number of seizures is given in one sitting. The amnesic effects of ECT partly seem to be a result of the currents of the seizures that pass through the body (Fink, 1979).

Changing electrode placement alters the cerebral path of electric currents. With unilateral electrode placements, memory is disrupted less than with bilateral placements. This is true whether the electrodes are placed over the dominant or non-dominant hemisphere.
The asymmetry of the localization of cerebral function also provides a basis for the earlier discussed different effects of the stimulating electrodes on modality and content of memory tests. Unilateral placement allows a greater effect of the current on the tissues under and between the electrodes. The effects on verbal tasks are greater when electrodes are placed over the dominant hemisphere than on nonverbal and visual tasks when the electrodes are placed over the non-dominant hemisphere (Dornbush, 1972).

The disruption in performance on verbal memory and auditory tests is most severe with dominant unilateral electrode placements, next with the bilateral and least with non-dominant unilateral treatments. For the non-verbal and visual tests, disruption is more severe with non-dominant unilateral treatments and least with dominant unilateral treatment (Zamora and Kaelbling, 1965).

ECS disrupts both the memory for the events experienced before (retrograde) and after (anterograde) the seizure. Russel and Nathan (1946) have made a careful distinction between retrograde amnesia, where the forgetting involved events prior
to the trauma and anterograde amnesia where the forgetting involved events subsequent to the trauma. The distinction between the two can be done on the basis of presentation of interfering agent. The inhibition would be proactive and retroactive on the basis of whether the interference appears before learning or after learning respectively. Therefore, when the forgetting is typically for subsequent events, it is termed as anterograde amnesia.

There are some qualitative differences between anterograde and retrograde amnesia associated with ECT. Both the types of amnesias were observed in Frith et al’s (1987) experiment. However, the presentation of cues eliminated anterograde amnesia and they did not affect retrograde impairments. These results confirm those of Mortensen (1980) who found no effects of cues on retrograde and those of Squire and his colleagues (1978, 1985) who found that cues eliminated anterograde amnesia. So anterograde amnesia is very similar to amnesia from other sources in that priming eliminates the defect. This is not in the case of retrograde amnesia. Cohen (1984) has suggested that there are two kinds of memory—procedural and declarative. Procedural memory is spared in most of the cases of amnesia as it is related to
cues (such as time, place, specific facts etc.) Mortensen (1980) suggests that there is retrograde effect of ECT on procedural memory since cued recall is impaired. However, anterograde effect of shock is on a task involving recognition but not a task involving primes (Squire et al., 1985).

Anterograde and retrograde amnesia can be considered to be linked deficits joined by the fact that the neural system damaged in amnesia prevents learning from being established and also prevents recently formed memories from becoming fully consolidated. In other words, new representations cannot be established because of unavailability of a critical neural system.

Anterograde amnesia so aroused, is not permanent and has been demonstrated as early as 6 weeks after administration of treatment (Squire and Chace, 1975; Squire, 1977, and Weeks, 1980).

Anterograde amnesia induced by ECS also disappears as the time interval between training and testing is lengthened. So the experiences immediately after ECS are more affected and the experiences far away from administration of electroconvulsive
shock are less affected. Such a conclusion has been drawn by authors like Kopp et al. (1968) and Zerbolio (1969). The former found no effects on memory if ECS was administered 24 hrs. prior to training. However the same ECS administered 1-4 hours prior to training caused retention deficits. A similar retention failure was apparent on administration of ECS just five minutes before training and ECS delivered one hour before training did not cause impairment (Zerbolio, 1969). The significance of training treatment interval was also evident when Ikegami (1972) stated that ECS administered 15-30 minutes before information processing reduced short-term-learning significantly but ECS administered 2-4 hours before training had no significant effect.

The above differences in the findings which seem to be caused by temporal variations in ECS administration could also be due to changes in number of methodological factors such as ECS frequency, its intensity and duration of passive avoidance parameters like intensity of foot shock and time of testing.

Regarding ECS frequency, a cumulative effect of repeated ECS on anterograde memory function was supported by the presence
of intact retention after ECS1 with the increasing severity of impairment from ECS2 on. Hence impairment of memory increases with the increasing number of treatments.

Similarly ECS intensity should be sufficiently high to produce memory impairment (Lerer et al., 1985). A significant memory loss has been found in various studies when the intensity of ECS was increased in comparison to low ECS administrations. Infact higher the intensities, higher would be the amount of current that passes through the brain and body, resulting in more severe disturbance than the low intensity.

The other type of ECS induced amnesia i.e. Retrograde amnesia (RA) has always been of particular interest to the researches in the field of memory. Retrograde amnesia is specifically associated with the forgetfulness of remote events. Names of persons and places are particularly vulnerable (Brody, 1944) and many persist for a long time after a series of treatments have been completed.

Electroconvulsive shock causes retrograde amnesia in which the events forgotten are usually independent of their
psychological importance. The mechanism underlying ECS effects is also not clear. It is, however, plausible to study the mechanism, as it helps to understand how it disrupts the material learned. Overall, there are three major proposals advanced to explain the effects of ECS on memory. The most frequent explanation seems to be based on consolidation processes that involve the transfer of short-term memory to long term memory.

Consolidation Hypothesis

The basic consolidation hypothesis was advanced in 1900 but the technical means for conducting experimental investigations of it date-back to 1938 when electroconvulsive shock was introduced into clinical practice by Cerletti and Bini. According to this hypothesis, memories are initially in a labile stage, and they are vulnerable to destruction with time. ECS, thus, may interfere with neural "reverbratory activity" and neural fixation processes that transform the acquired material into permanent structural changes. However, the learned material becomes increasingly resistant to disruption when the time is reached at which it is said to be consolidated. But the exact time that a memory takes to be consolidated (RA gradient) is, however, in dispute. It has been reported to be as short as 10-30 sec (Chorover and Schiller,
1965) and possibly as long as 6 hr. (Kopp et al., 1968). Duncan (1949) suggests that it takes somewhere between 15 minutes and one hour for the structured modification to set. He stated that if consolidation is allowed to complete after each trial before administering ECS, the performance is better on subsequent trials.

Several investigators have suggested that the wide range of RA gradients are due, not to a unitary disruption of consolidation, but rather to two qualitatively different events. The short RA gradient of approximately 30 seconds is assumed to reflect "true" amnesia. The long RA gradients are assumed to reflect not the decreasing susceptibility to disruption of memorial events, rather an increase in the strength of avoidance response (Pinel & Copper, 1966; Spevack & Suboski, 1969). McGaugh and Dawson (1971), on the other hand, maintained that RA curves seem to be best interpreted as indicating that memory storage processes become decreasingly susceptible to interference with time following training. The processes initiated by training remain labile for a fairly long interval (several hours) following training.
The length of consolidation period may be determined by various training conditions (Miller, 1970) like tasks (Chorover, 1965) and training procedures (Davis, 1966). However, several attempts to study direct relationship between ECS and amnesia suggest that the ECS parameters like its intensity and duration play a crucial role in determining the quantity and quality of amnesia. For example, stronger ECS is generally more effective in disrupting consolidation at any given stage of the consolidation process. Thus, whether, a long or short estimate for the consolidation period is found in a particular experiment may depend substantially on the strength of the ECS used.

The evidence that a stronger (high intensity and / or long duration) ECS is effective in disrupting consolidation over a longer period than a weaker ECS (Alpern and McGaugh, 1968; Miller, 1968) suggests indirectly that an ECS treatment does not invariably stop the consolidation process. Instead, it appears possible that with weak ECS treatment, the interference with consolidation is not total and there is a continuation of consolidation after the ECS treatment. Albert (1966) has provided some direct evidence that consolidation can continue following an amnesic treatment. He found that a brief period of cortical
spreading depression was not in itself sufficient to impair retention. But it enabled a later period of spreading depression to produce a loss of retention at a time at which the second spreading depression treatment by itself would normally be ineffective. Albert suggested that the first period of spreading depression was not sufficient to impair retention. It did disturb consolidation in a latent way which allowed the second period of spreading depression to actually stop the consolidation process and prevent retention.

Another view holds that ECS disturbs the conditions for consolidation rather than to destroy the information being stored. If the conditions essential for consolidation can be re-established following an amnesic treatment (ECS), the development of long-term memory would be possible. In case, the required consolidation conditions are not destroyed, it appears to continue. The continuation of consolidation process after single ECS evident from intact retention after 5 minutes of training and the memory impairment after second ECS enabled Mah et al. (1971) to suggest that the conditions for consolidation are not completely destroyed by the first ECS or are re-established spontaneously.
This shows that stronger ECS is generally more effective in disrupting consolidation at any given stage of the consolidation process. It is also assumed that if ECS of sufficient intensity prevents consolidation than the amnesia produced should be permanent. However the permanence of amnesia is a matter of controversy. Many investigators have suggested a recovery from ECS - induced amnesia.

**Permanence of Amnesia**

Reappearance of an avoidance response previously abolished or attenuated by Electroconvulsive shock has been demonstrated by Zinkin and Miller (1967) with repeated testings of convulsed animals. Therefore, permanence of ECS-produced retrograde amnesia has been questioned.

No one has explicitly tested the assumption of permanence of amnesia. Even Zinkin and Miller appear to have examined only the effect of repeated exposures to the experimental situation on retrograde amnesia. To examine the stability of ECS produced amnesia, repeatedly tested, convulsed animals must be compared with subjects that are tested for the first time at an interval (after ECS) equal to that at which the repeatedly tested animals
receive their last test. In Zinkin and Miller study this would be at 72 hours, when repeatedly tested subjects evidenced apparent recovery from amnesia.

However, Herz and Peeke (1968) found amnesia on first retention test i.e. 24 hours after ECS that largely disappeared on two subsequent retention tests (at 48 hr and 72 hrs). However, true recovery may not have occurred since there was a gradual adaptation to the experimental situation after repeated exposures. The animals tested for the first time at 72 hours, however, showed degrees of retrograde amnesia equal to or greater than that observed in the subjects tested for first time at 24 hours. This observation appears to indicate that re-exposure to experimental situation is a necessary condition for recovery.

However, no recovery from amnesia with repeated tests over periods as long as one month was concluded later on (Lutiges and McGaugh, 1967). Recovery was reported to be a function of procedural or task variables.

A statement, that memories apparently lost might be restored by appropriate means, challenged the permanence of
amnesia (Lewis et al., 1968). However, the conditions for recovery were rather limited (Quatermain, McEwen and Azmitia, 1970). The efforts were done to restore memory for footshock by giving a reminder shock before testing in an environment different from that of the training. No recovery was obtained.

Recovery was also found to be a function of time, indicating that time is a great healer. Some investigators found that the original loss of memory was due to suppression of conditioned emotional response (CER) which latter reappeared as a lapse of time, manifesting itself as a recovery from amnesia (Young and Gallusico, 1971).

However, the events which are very close to the treatment may be permanently lost. The impairment is worse for the recent events extending to the information that occurred 4 to 7 years before but not to the information occurred 8 to 16 years before (Squire et al., 1976a). The deficit persisted up to two weeks after the last treatment. Further they stated that information acquired 2 to 20 years prior to bilateral ECT was temporarily lost but fully recovered by 6 months retesting. Information
acquired in the week prior to treatment may be permanently lost; that acquired from 1 week to 2 years prior to treatment appears to be recovered by 6 months retesting (Squire, 1977).

Above discussion regarding the permanence of amnesia shows that the memory loss caused by ECS may not be stable. A temporary loss refers to interference with retrieval processes rather than consolidation of information (Nielson, 1967).

While discussing the possible explanations underlying the causes of ECS-induced memory disruption, one must discuss the contribution of Coons and Miller (1960). They suggested that single ECS induces fear which is sufficiently intense to disrupt behavioral performance. This concept became popular as Fear Hypothesis.

**Fear Hypothesis**

The supporters of this hypothesis believed that the response decrements after ECS are a result of interference with performance of the response rather than a memory loss; the interference arises from fear or conflict caused by ECS treatment.
ECS had some distracting effect on memory as it add to the effect of shock by suppressing the avoidance response (Coons and Miller, 1960). It was confirmed from their results which indicated that ECS aroused fear due to that the information acquired was lost.

However, this fear hypothesis was soon contradicted by some investigators. Madsen and McGaugh (1961) did not find the summated effects of ECS and footshock in their experiment. Lewis and Adams (1963) also rejected fear and conflict hypothesis by giving a different explanation for poor retention. They argued that certain aspects of convulsion become conditioned to the surrounding stimuli as a result of which the Ss are unable to reproduce the information acquired.

Infact ECS produces a massive inhibition, part of which becomes associated with the environmental stimuli present at the time of ECS administration. The conditioned inhibition in turn, is purported to produce a reduction in fear when the subject is returned to environment where ECS was administered (Lewis and Maher, 1965).
However, the effects of ECS on memory could be comparatively vividly explained on the basis of memory modulation hypothesis.

**Memory Modulation Hypothesis:**

This hypothesis suggests that memory may alter as a result of changes in arousal level, autonomic function, neuroendocrine activity or such biological adaptive responses to training. In untreated animals memory may be modulated by endogenous systems which are sensitive to subsequent hormonal responses after training (Gold, Van Buskirk, and Haycock, 1977). Many endogenous substances are released on administering ECS.

The facilitation of dopaminergic neurotransmission by ECS was suggested by Evans et al. (1976). He stated that pre-treatment with a series of daily ECS caused hyperactivity response to be increased indicating that dopaminergic neurotransmission has been facilitated. The ability of ECS to enhance dopamine and 5HT - mediated behaviour could be due to effects on neuronal systems modulating behavior through monoamine receptors. Green et al. (1978) reported that ECS pre-treatment increased Gama-aminobutyric acid (GABA) concentrations and reduced its turnover. This alteration might potentiate dopamine and
SHT-mediated behaviour. In addition, high affinity binding to acetylcholine receptors was determined as these systems may modulate behavioural responses to dopamine and 5HT agonists. However, there is evidence that some of the behaviours elicited by MAO I + C-dopa may be mediated by serotonin release, since putative 5HT antagonists attenuate some components of behavior (Jacobs, 1974; Deakin and Green, 1978).

ECS has been shown to affect several biochemical parameters of the central nor-adrenergic system. Eden and Modigh (1977) have reported ECS-potentiation of behavioural and growth hormone responses to the alpha-receptor agonist clonidine. In contrast, Vetulani and Sulser (1975) report reductions in nor-adrenaline sensitive adenylate cyclase activity in brain membrane from ECS-pretreated animals.

Similarly ECS affects the level of brain content of endorphins. Hong et al., 1979) and Kartz and Schmaltz (1980) observed that ECS reduced the ability of morphine to induce hyperactivity. One explanation of later finding is that the opiate receptors become desensitized in ECS-treated animals and this hypothesis was directly examined by measuring opiate receptor
binding in the stratum (an endorphin rich area) in rats which received ECS. The involvement of endogenous opioids in memory processes is also evident from the studies showing facilitation of retrieval of behavior measured after one or more days after training (Messing et al., 1969; Izquiredo and Graudenz, 1980).

Opioid peptides interfere with the release of catecholamines in various brain regions. It is clear from Izquiredo and Graudenz’s (1980) suggestion that opioid antagonists act by releasing central dopaminergic and $\beta$-noradrenergic systems. However, ECS also alters noradrenaline release (Modigh, 1976). Infact, ECS has been shown to affect several biochemical parameters of central nor-adrenergic (NA) systems. It increases the activity of tyrosine hydroxylase (Musacchio et al., 1969), endogenous NA concentrations (Kety et al., 1967) and decreases the high affinity uptake of NA into synaptosomes.

There is also evidence to suggest that brain levels and turnover of serotonin increase in animals following a series of ECS (Baldessarini, 1975).
The possibility that ECT is effective to the extent that it stimulated the secretion of ACTH was tested by direct ACTH administration, but the results were disappointing. However, the plasma ACTH increase 10 minutes after ECT was found by Delitala et al., 1977). A similar increase occurred in cortisol, the increase varied inversely with initial levels (Stokes, 1972).

Similarly ECS is followed by number of other neurohormonal and hormonal changes among which are increase in prolactin (Meco et al, 1978), Urinary gonadotropin (Ettiggi and Brown, 1977), Vasopressin (Soelberg, Hammer and Bolwing, 1982). The alterations in the level of such endogenous substances may create memory deficit.

The fact that the above explained endogenous substances altered by ECS mediate memory processes seems to be true because (a) the external administration of these substances and/or (b) the drugs (a particular dose) simulating their action at same receptor sites aroused a memory loss.

Therefore, when amnesia is produced, the chemical substances with in the body especially in brain arouse a state
which is different from the normal brain state. Thompson and Neely (1970) suggest that it is the difference in the brain states at the time of testing and training that actually arises amnesia. However, the recovery may be observed if the unique patterned brain state present at the time of memory formation is reproduced or at least approximated at the time of retrieval. In other words, memory may be produced by creating the dissociate state present at the time of training. So it is a state dependent phenomenon.

**State-Dependent-Effect**

State-dependent effect or dissociation learning occurs when learning is acquired under specific condition and is thereafter, best elicited if the same condition is re-established. The deterioration of performance established in any abnormal state but tested under normal conditions seems more paradoxical. The most convincing demonstration of state-dependent performance has been provided by the observation that an organism behaves adaptively in specified situation under both normal and abnormal conditions. But the type of behavior displayed at a moment is determined by the particular state imposed at that time.

State-dependent effect supports the convention that the observed changes in performance levels are often due to alteration
in the crucial states of central nervous system related to the processing of information, brain excitability state present at the time of learning or recall may have an impact on ECS induced amnesia (Nielson, 1967). When learning occurs at one state of brain excitability, and the animal is tested for retention of that learning in different state of brain excitability, the animal fails to show that learning. A similar state of brain excitability at the time of testing exhibits the best recall of material learned. This suggests that neurological aspect of learning may involve changes in brain excitability. The retention implies a maintenance and reconstruction of these modifications of brain excitability, and the failure of retention implies when brain excitability is modified away from that established by training procedure.

**Effect of brain lesions and drugs on state-dependent effect:**

A peculiar type of state dependent effect that is related to species typical behaviour tendencies can be observed. For example, damage to the posterior neocortex of the rat has the effect of eliminating aversions to light or to bright stimuli in visual discrimination tasks. Infact rats learn to approach the black stimulus more readily than the white stimulus in such
problems. After posterior neocortical damage, this deferential case of learning is lost, and it is just easy to learn to go to the white stimulus as to the black stimulus. Meyer (1973) has suggested that this change in behavior often hides the fact that relearning a brightness discrimination after neocortical damage is more difficult than before surgery since animals are usually trained to approach the white stimulus.

This species typical tendency to approach to dark places or stimuli could be the basis on which same discriminations are acquired. Animals may learn to do what they feel bad. If lesions eliminate the basis of some species typical behavior then postoperatively there may be no basis for performance on such problems. An appropriate control for lesion induced state-dependent effect is difficult to devise. Perhaps the best approach would be to keep the possibility to such effects in mind when interpreting the data from all the experiments and when appropriate to control for changes in arousal levels in experimental design.

Another way in which brain lesion could affect behavior would be by altering an animal's orientation to its surroundings.
Lesions of the several brain regions, especially amygdala and hippocampus, altered methods used to search the environment and perhaps spatial orientation as well. Depending upon the nature of task requirements, these changes could impair or facilitate the performance.

State dependent phenomena are now a common place in the study of the effects of drugs upon behavior (Overton, 1971). In essence state-dependency refers to the fact that any discrimination of memory is contingent upon possible differences between the state of subject during acquisition and that during testing. Learning of many problems occurs in either a drugged or non-drugged state, but later expression of learning depends upon reinstatement of condition existing during acquisition. State-dependent phenomena are different from changes in sensory or procedural processes in that they can not be explained on the basis of peripheral changes induced by drugs. Presumably they depend upon alteration of central neural mechanism.

Girden (1940) was the first to propose a specific neural model for state-dependent phenomena. He proposed that both cortical and sub-cortical systems of the dog could subserve the
acquisition of behavioral task. In normal dog the neocortex was presented to be predominant, and its actions were through to inhibit subcortical system. However, if the cortex was induced inactive by a drug (erythroidine), the subcortical systems could be used to acquire the task.

When the cortex was relieved from the drug's effects, it inhibited the subcortical mechanisms again and the animal behaved as if it had not been trained. Girden found that decortication eliminated the dissociation effect, but more recent research has shown neocortical destruction in the rat does not eliminate state-dependent behaviors induced by Phenobarbital (Overton, 1971).

It seems likely that any damage to the central nervous system can produce a chronological different state of individual which could be similar to the temporarily different states produced by same drugs. This new state might interfere with the expression of previously acquired responses.
Many of the drugs that are most effective in inducing state-dependent effect are hypnotics, and this suggests that changes in arousal level could form at least one part of the basis of the dissociation effect.

Like drugs, Electrical brain stimulation may produce state-dependent learning. Electrical brain stimulation of Caudate nucleus has been shown to produce state-dependent learning of an inhibitory avoidance response (McIntyre and Gunter 1979). However, such a state dependent learning test of amygdala with electrical stimulation proved negative (McIntyre and Gunter, 1979), suggesting that memory disruptive effects of post-trial amygdala electrical brain stimulation may represent true consolidation failure.

The critical difference between state-dependent and consolidation hypothesis is that the later explains that memory for a conditioning trial just preceding electro-convulsive-shock is formed while under state-dependent effect amnesia is observed because ECS produces a brain state which is incongruous with the retention of memories acquired in a dissociate state.
A dissociation between the neural mechanism responsible for convulsive movement and those presumably involved in the mediation of ECS-induced RA is implied by earlier findings. In addition RA is not prevented when the overt convulsive reaction to ECS is blocked by drugs (Ottoson, 1960; Weissman, 1965; McGaugh and Alpern, 1966). However, what was not known earlier and what the present results indicate that such a dissociation may also occur in intact, unanesthetized, unrestrained rats and that it may develop as a natural consequence of prior stimulus events. This dissociated state affects the information stored in such a manner that retrieval is seriously impaired unless the ECS condition is reinstated (Thompson and Neely 1967; Devietti and Hopfer, 1973).

With this introduction and background about the state-dependent-effect we would discuss the next chapter pertaining to the literature related to Amnesia as a result of ECS and its recovery.