Respected members of the chair and distinguished colleagues, I am proud to address you at this august forum. Before I commence with my text, I have a few pleasant duties to perform. I acknowledge with gratitude Professors Venkoba Rao and Parvathi Devi for having instituted this award, and pay my humble respects to the memory of their son, the late Tilak Venkoba Rao, whose promising career was tragically aborted by an unfortunate road accident. I thank my mentor and colleague, Dr. B. N. Gangadhar, who has guided me in much of my ECT research. Finally, I wish to pay a special tribute to all my teachers, down the decades, some of whom I am privileged to have in my audience today; few amongst us can claim to be entirely self-made, and I unreservedly acknowledge my personal and professional indebtedness to the teaching profession.

The efficacy of ECT is established in depression and mania (Gangadhar et al, 1990a); there is also evidence for its usefulness in schizophrenia and other psychiatric disorders, and possibly in certain neurological and medical conditions as well (Weiner and Coffey, 1988a; Andrade and Gangadhar, 1990a).

Depression is the single largest indication for ECT. In depression, the superiority of ECT over antidepressant drugs is mooted on several counts with only Rifkin (1988) sounding a note of caution. Recovery is faster with ECT than with antidepressant drugs (Gangadhar et al, 1982, 1985a); with drugs, onset of therapeutic action is usually delayed to about 2 weeks after commencement of therapy, and peak response may not obtain until at least a month has elapsed, even granted absence of requirement for dose adjustments; with ECT, however, response is seen from the first treatment itself (Rich and Black, 1985; Andrade et al., 1989a), and the patient is usually adequately recovered with 2-3 weeks treatment (Kendell, 1981). This differential rate of response becomes more pronounced with depressions of greater severity, and is important not just because ECT alleviates suffering faster, but because the patient is suicidal (if at all) for a shorter period (note also that a depressed patient can take an overdose of antidepressant drugs, but can not attempt suicide using ECT.), and because the time-cost-energy expenditure on the parts of both clinician and patient are less (Markowitz et al., 1987) with ECT. Further, ECT is more effective than antidepressant drugs in depression with psychotic features, and often succeeds when drugs fail (Consensus Conference, 1985).

This advantage for ECT over drugs may not be at the cost of increased side effects; Calev et al. (1989) showed that the cognitive adverse effects of ECT and imipramine differ qualitatively rather than quantitatively, while Gangadhar et al. (1982) and Gangadhar (1985) found ECT-treated patients to report fewer subjective side effects than imipramine-treated patients, indices of organic brain
impairment being comparable in the 2 groups in the intermediate and long term.

The posited superiority of ECT over drugs does not mitigate the disadvantages of ECT not all patients treated with ECT respond, and virtually all patients receiving ECT experience some (albeit mostly minor) of side effects. Today, there is hence a tendency to employ ECT not as a positive indication but when depression is very severe, when psychotic features are present, or when antidepressant drug therapy fails.

The tendency to underutilize ECT can be combated by the development of strategies for rational prescription and reduction in morbidity; my address will focus on the evaluation of such strategies. 'Rational prescription' is concerned with the maximization of the percentage of responders while 'reduction in morbidity' is concerned with the minimization of adverse effects. In my presentation, I will discuss the frontiers of research in these areas; rather than extensively review the field, I will focus on issues of practical importance and topics of personal interest.

(A) STRATEGIES FOR RATIONAL PRESCRIPTION

However careful the selection and however optimum the treatment procedure, some depressives treated with ECT fail to respond. Fink (1979) observed that over 80% of depressives treated with ECT show some degree of response while Stromgren (1984) opined that some 20% of endogenous depressives fail to respond to ECT. Most other authors cite similar figures.

Looking at individual studies, however, startling differences emerge. Sackeim et al. (1987a) found responders to comprise just 28% of a population of depressives treated with one form of ECT, while we (Andrade, 1986) found 93% of depressed patients to respond to another form of ECT. The findings of most other studies lie in between these two extremes. The reasons for these divergent figures presumably lie in the selection of cases for ECT, in the ECT technique itself, and in the post-ECT psychiatric care. Accordingly, strategies for rational prescription may be considered under the headings of response prediction, response facilitation and relapse prevention.

(I) Prediction of response of depression to ECT

Problems in the interpretation of research

Several problems cloud the interpretation of studies in this and in later sections. One is that different authors define response differently. This is unfortunate as, for example, predictors of outcome may vary in the same population depending on the outcome measure defining response (Coryell and Zimmerman, 1984). While Abrams (1989), discussing various outcome analysis procedures, has proposed a mathematical model as an alternative to the definition of response, a consensus definition is nevertheless needed to make results of studies comparable and clinically relevant (Andrade and Gangadhar, 1989).

Another problem is the placebo effect. Although selection biases may explain the high proportion of sham-ECT responders in some studies (Kendell, 1981), many sham-ECT-treated patients undeniably improve (Johnstone et al., 1980). Any group of ECT responders, therefore, also includes depressives who may have responded to sham ECT. Hence predictors of response that have been developed actually predict response to true and/or sham ECT, or merely identify good prognosis depression. The Northwick Park group, to-date, has been the only group to attempt prediction of response to true ECT alone (Clinical Research Centre, 1984).

Yet another problem is the diagnostic category addressed. Studies on depressives unselected by diagnosis (e. g. Mendels, 1965a) obviously yield results applicable only to depressives unselected by diagnosis. Although
such studies are of limited relevance presently, their heuristic value in their day was undeniable as they were conducted in an era in which the nosology of depression was in flux. Recent studies on specific depressive diagnostic subcategories of course yield results applicable only to such depressives. Regrettably, studies have been conducted on ‘depressives referred for ECT’ without diagnosis-based selection (e.g., Robin and de Tissera, 1982). Also, many authors select patients diagnosed as Major Depressive Disorder (DSM III/DSM III R), which diagnosis is probably a heterogeneous category, and which, from experience in our country, includes a number of patients whom we understand to be neurotic. Results from such studies understandably cannot be generalized.

Finally, despite the production of comparable motor seizures, all ECT may not be therapeutically equal. Therefore, variations in ECT Technique, or in any aspect of methodology or analysis, could make results difficult to interpret or compare.

**Categories of response prediction**

Clinical, psychological, physiological, electroencephalographic, neurochemical, neuroendocrine and other predictive measures have each been described (Fink, 1979, 1982 & 1986; Hamilton, 1982; Abrams, 1982 & 1988; Scott, 1989). Unfortunately, few predictors (if any) have been consistently validated, and an opinion has even been expressed that once an endogenous syndrome is defined, little variance remains to be explained on the basis of other predictors (Abrams, 1989, personal communication).

This is an era of sophistication in technology, and a dazzling array of investigations has been described in the attempt to predict the outcome of depression with ECT. Few of these, however, are relevant to our country because of unavailability, inaccessibility or unaffordability. Therefore, at our centre we addressed clinical predictors of response to discover whether further refinement in prediction could be obtained after an endogenous was defined.

**The clinical prediction of response of endogenous depression to ECT**

In an endogenous population, sociodemographic variables such as age and sex do not differentiate responders from non-responders, nor do illness variables such as episode number and duration (Andrade et al., 1989b); with a few exceptions (no doubt results of chance distributions), these have never been seriously considered as outcome predictors (Dunn and Quinlan, 1978; Rich et al., 1984a; Coryell and Zimmerman, 1984; Prudic et al., 1989).

Interestingly, we found bipolarity to significantly predict response (Andrade et al., 1989b). A possible interpretation is that the diagnostic criteria for endogenous depression are not sufficiently precise to define a biological (or, at least, an ECT-responsive) illness, and that a past history of mania refines a ‘clinically endogenous’ sample to a ‘biologically endogenous’ one. There is unfortunately poor support for this finding in literature (Abrams et al., 1973; Abrams and Taylor, 1974; Pande et al., 1988), possibly because the sample in these studies was not rigorously screened for endogenosity.

The presence of psychotic features (delusions, hallucinations, stupor) indicates ECT as the preferred treatment. However, there is no evidence that presence of psychotic features promises a greater likelihood or degree of response (Rich et al., 1984a & 1986; Solan et al., 1988; Black and Winokur, 1989), or that presence of reactive factors, concurrent medical illness, or personality disorders augurs poorly (Tich et al., 1984a; Zimmerman et al., 1986). Interestingly, endogenous symptoms are not more likely to respond to ECT than non-endogenous symptoms (Prudic et al., 1989). These studies do not imply that endogenous or psychotic depressions are not good prognosis indicators, but that certain
patients referred for ECT may be good responders even if endogenous or psychotic features are absent or other primary/associated features or diagnoses are present.

Nosological systems admit other depressive subcategories (e.g., schizodepression, postpsychotic depression, reactive psychotic depression secondary depression etc.), but, to-date, no research has satisfactorily addressed the efficacy of ECT in such depressions or the prediction of outcome thereof. A study on drug-resistant depression found that only 60% of patients responded to ECT; responders differed from non-responders in that they were less depressed initially; in no other clinical, sociodemographic or seizure parameters did differences obtain (Shapira et al., 1988a).

Non-nosological aspects of symptom profile also fail to predict outcome. We found that negative symptom and social disability profiles do not differ between ECT responders and non-responders (Andrade et al., 1990a). While certain studies (e.g., Pande et al., 1988), including ours (Andrade et al., 1990a) find individual symptoms to differ in initial severity between ECT responders and non-responders, no symptom is consistently associated with response; such findings are best considered to be due to chance in view of the large number of symptom comparisons being made. Delusions, however, but no other characteristic, have specifically been identified to predict good prognosis with real ECT (Clinical Research Centre, 1984).

Many studies have associated lesser initial severity of depression with good response (Pande et al., 1988; Shapira et al., 1988a), which has been our observation as well (Andrade et al., 1989b). The application of this finding is obscure, given the low margin of difference in mean initial ratings of severity between responders and non-responders in these studies. The direction of this findings is unfortunate as less depressed patients are more likely to receive drugs, while more depressed patients are more likely to be treated with ECT. This finding, however, does not indicate that ECT should not be used in more depressed patients, for, although ECT may be less effective in these as compared with lesser depressed patients, it may yet be more effective than pharmacotherapy.

Many prognostic scales have been proposed to predict the outcome of ECT-treated depression; these are listed elsewhere (Clinical Research Centre, 1984; Pande et al., 1988). Since these scales were developed in an era in which the nosology of depression was unclear, it has been opined that the scales do little beyond defining an endogenous syndrome (Abrams, 1982). However, many items in the scales differ from indices considered to define endogenity (e.g., see Carney et al., 1965). We hence sought to discover whether superimposition of certain of these scales upon an endogenous (R.D.C.) population refined prognostication. Using Holson's (1953), Mendels' (1965b; 1967) and the Newcastle Prognostic and Diagnostic (Carney et al., 1965; the latter was applied with the hypothesis that superimposition of the Newcastle endogenous depression concept upon the RDC endogenous depression concept would identify a core endogenous group likely to respond well to ECT) indices scored qualitatively (using the authors’ cut-offs) and quantitatively as these indices may be more meaningful if considered as continuous variables), we found the Newcastle Prognostic Index to identify ECT responders with high specificity but disappointingly low sensitivity, while the other indices, by virtue of indiscriminately classifying all/almost all patients as responders, were high in sensitivity but low in specificity. The indices failed to differentiate responders from non-responders when quantitatively analyzed, nor did 'heightening' of endogenity using the Newcastle Prognostic Index refine prediction (Andrade et al., 1988a, 1989b & 1990a). These findings suggest a utility for only the Newcastle Prognostic Index scored using the authors' cut-
off), and only when one wishes to be as certain as possible that no patient unlikely to respond will be exposed to ECT.

While many have found these indices unhelpful in unselected depressives (e.g. Abrams et al., 1973), some (e.g. Katona and Aldridge, 1984) support our observations of the specificity with which the Newcastle Prognostic Index identifies ECT responders in an endogenous cohort. In contrast to our findings, however, Katona and Aldridge (1984) obtained a high sensitivity for the Newcastle Prognostic Index. No good reason is apparent for the lack of agreement between the 2 studies.

Sensitivity versus specificity apart, these indices suffer from limitations related to operationalization of constructs and to meaningfulness. When exactly, for example, is a personality previously ill-adjusted (Hobson, 1953), or how does one accurately evaluate neurotic traits in childhood (Mendels, 1965)?

ECT prognostic indices are hence unhelpful once an endogenous population has been defined; a guarded exception may be made for the Newcastle Prognostic Index, but reevaluation of its sensitivity and specificity is required.

As a responder to ECT is likely to improve from the first treatment itself, we studied whether response to the first ECT could reliably predict outcome. We found a significant difference in depression scores between ECT responders and non-responders after the first ECT, severity of depression being comparable in the 2 groups prior to treatment; 15% or greater attenuation of initial depression scores identified ECT responders with high specificity and, once ‘doubly depressed’ patients were excluded, high sensitivity as well (Andrade et al., 1989a). If future research confirms our findings, ‘trial ECT’ for endogenous depression may become a viable predictor. Our conclusion is indirectly supported by the work of Rich and Black (1985) which showed that the first ECT produces the maximum antidepressant response. ‘Trial ECT’ may however be unacceptable to patients and clinicians and, even if accepted, difficulty in ensuring patient (from whom informed consent would have been taken) and rater blindness to the purpose of the exercise may complicate interpretation of scores.

Finally, allied to the prediction of good response to ECT is the prediction of poor response. This has received virtually no research attention no doubt on the spurious grounds that one who is not predicted to be a good responder must necessarily be a poor or non-responder. The identification of non-response is useful to ensure that no patient unnecessarily receives ECT. To date, no satisfactory guidelines are available beyond the clinical dicta that ‘neurotic’, ‘reactive’ and ‘secondary’ depressions are not indicated for ECT: some studies have however found that absence of endogenous or psychotic symptoms, or presence of associated medical or personality disorder, or secondary or reactive status of the depression do not predict poor response (Rich et al., 1984a & 1986; Zimmerman et al., 1986; Solan et al., 1988; Black and Winokur, 1989).

With the exception of the prognostic scales, predictors of response have by and large been considered univariately. It is possible, however, that presence or absence (or degree thereof) of one predictor may alter the predictive potential of another predictor. Therefore, large sample multivariately analyzed studies are necessary to evolve fresh response predictors with relative weights specified (as had been done, for example, by Carney et al., 1965), to refine prognostication in the light of recent research.

Good response to ECT must be considered vis-à-vis good response to pharmacotherapy in the identification of response predictors—else, merely good prognosis depression will have been identified (no mean goal itself, actually), and not specifically ECT-responsive depression. Alternatively, it must be
acknowledged that predictors of good response to ECT also include predictors of good response to drugs.

(II) Facilitation of response of depression to ECT

The practice of ECT is not standardized and different procedures yield different results. Seizure duration, electrode placement, stimulus waveform and electrical dose are factors implicated in such differences. Each is considered in turn.

Seizure duration

The central seizure is an essential therapeutic ingredient of ECT: modification of the peripheral seizure does not inhibit antidepressant action; non-convulsive stimuli are ineffective; all seizures have antidepressant action whether electrically induced, chemically induced or spontaneous in origin; lidocaine-abbreviated seizures are sub-therapeutic (Kendell, 1981). These findings together with the observation that supraliminal stimuli are not more therapeutic than conventional ones (Ottoson, 1960), prompted the myth that the seizure is an all or none phenomenon, and that as long as a seizure is induced, the dose of electrical stimulus delivered does not matter to the efficacy of the treatment. Hence (as higher electrical doses were recognized to produce more adverse effects, a trend developed to use minimal, individually-titrated electrical stimuli to induce a convolution. The fallacies herein will be taken up later (also see Robin and de Tissera, 1982): it suffices to state here that all convulsions are not therapeutically equal; a certain minimum seizure duration is necessary for the seizure to be therapeutic, and the cut-off point for 'adequacy' is generally stated to be 25 secs. (Freeman et al., 1989).

What then of shorter or longer seizures?

Seizures 25 secs. in duration are not considered adequate; if 15 secs. in duration, restimulation is recommended (Freeman et al., 1989). In our experience, seizures between 15 and 25 seconds in duration are possibly also therapeutic (manuscript in preparation); at the other extreme seizures 100-120 secs. in duration are associated with unacceptable risks for cognitive and other adverse effects. It is not known whether deliberate prolongation of seizures (achieved chemically, or by increased stimulus doses vide infra) beyond 25 secs. increases therapeutic efficacy, although seizures should last for 25—100 secs., there is no evidence to date to suggest that this range for the individual seizure is a therapeutic window in terms of efficacy or efficiency.

Instead, it appears that once the minimum duration is defined for adequacy, seizure duration is not a reliable index of the therapeutic potency of the convolution. While several strands of evidence lead to this conclusion (e.g., Rich and Black, 1985; Weiner et al., 1986a), the most telling evidence perhaps, derives from studies which have demonstrated that seizures produced by different ECT techniques may be comparable in duration but are disparate in efficacy (Sackein et al., 1987a; Andrade et al., 1988b). An explanation is that the pattern and extent of neuronal activation (which varies with ECT technique even though seizure durations may be comparable—e.g., see Robin et al., 1985; Swartz and Larson, 1986; Abrams, 1986) is probably more closely linked to therapeutic potency than seizure duration itself; that the seizure is not a therapeutic all or none phenomenon is hence established.

Maletzky (1978) suggested that the ECT dose is associated with a therapeutic window in terms of cumulative seizure duration, and set this window at 210—1000 secs. Since Maletzky failed to demonstrate the superiority of cumulating seizure duration over cumulating number of treatments administered, his contention is open to the criticism that he
has counted seizures in an unnecessarily elaborate way (for, granted that Maletzky's average seizure was 85 secs in duration, his work suggests little beyond the obvious fact that treatment response is seen between the third and the twelfth ECT). While the cumulative seizure duration therapeutic window concept seems to be falling into oblivion, one must recognize that counting ECTs by number may be quantifying the ECT dose in an unnecessarily simplified way; to-date, however, there is no better alternative (manuscript in preparation).

Several methods have been used to measure seizure duration. Electroencephalography (e.g. Scott et al., 1989) is commonly employed in the West, but there is controversy about its usefulness as inter-rater reliability in assessments (e.g. occurrence and duration of seizures, or the endpoints thereof) has been reported to be low (e.g. Guze et al., 1989; McCreadie et al., 1989). The cuff method (Addersley and Hamilton, 1953), an index of the duration of the motor seizure, is also commonly employed, but tends to underestimate the EEG seizure by 10-30% (Fink and Johnson, 1982; Liston et al., 1988). While controversy dogs the cuff method as well (e.g. Barrington, 1987), this is generally the reference method for definiton of adequacy of seizure duration. Other techniques to estimate seizure duration include electro-cardiography (measuring ECT-induced tachycardia—e.g., Larson et al., 1984) and electrodermography (measuring galvanic skin response—e.g. Guze et al., 1988). The cuff method is easy, convenient and reasonable reliable in application, and may be recommended for routine use in our country.

Routine seizure monitoring is necessary to identify missed or incomplete (abortive) seizures. Such are commoner in the elderly and in males, for seizure threshold is higher in these populations (Sackeim et al., 1987c; Pettinati and Nilssen, 1987); after several ECTs, for seizure threshold increases with successive ECTs, especially in responders (Sackeim et al., 1987b & c); when the skin is greasy or when the electrodes are not firmly applied, for poor electrode-skin contact increases electrical impedance and hence decreases the effective stimulus intensity (Gangadhar and Andrade, 1989a & b); when the electrical stimulus is low in intensity, for the seizure threshold may not be crossed; with bilateral electrode placement, which is associated with greater seizure thresholds (Sackeim et al., 1987c); with unilateral electrode placement at low stimulus doses, for generalization of the seizure may fail to occur (Weiner, 1986a); as a result of hypoxia, anaesthesia or concurrence benzodiazepine or anticonvulsant therapy, all of which raise the seizure threshold (Fink, 1987).

The immediate management of a missed/incomplete seizure is to hyperventilate and hyperoxygenate the patient (to decrease the seizure threshold—see Rasanen et al., 1988 and Chater and Simpson, 1988), ensure a low impedance electrode-skin interface, re-administer the muscle relaxant (if required) and redeliver the stimulus at the next higher setting (the choice of which will depend on the ECT technique employed—see Gangadhar and Andrade, 1989a).

In a few patients, missed/incomplete seizures are a recurrent problem; increasing stimulus dose to the maximum predisposes to increased cognitive and other morbidity and may yet not yield an adequate seizure. Many strategies are available to manage such a problem (Fink, 1987; Freeman et al., 1989). These include eliminating concurrent benzodiazepines, hyperventilating and hyperoxygenating before each treatment, reducing the dose of barbiturate anaesthesia or switching to ketamine or etomidate (but not propofol—see Rampton et al., 1989), using unilateral electrode placement, 'double stimulating', or using drugs to facilitate seizure prolongation. Such drugs include concurrent antidepressant drugs (e.g. trazodone—see Hohly
and Martin, 1986), oral phenothiazines (Freeman et al., 1989) and intravenous caffeine sodium benzoate (Shapira et al., 1987; Coffey et al., 1990). Use of other xanthine alkaloids (e.g., theophylline and aminophylline) may not be advisable because of the risk of status epilepticus (Devanad et al., 1988; C. Edward Coffey, personal communication). Sleep deprivation, which facilitates epileptiform activity in the EEG, does not prolong seizure duration (Kellner and Malcolm, 1988). Dispensing with anaesthesia is unethical and should not be resorted to unless all other options fail.

**Electrode placement**

There is controversy about the ideal electrode placement for facilitation of response to ECT. Scanning the literature, Welch (1982) and Weiner (1986b) failed to find convincing evidence for the posited superiority of bilateral (BL) over unilateral (UL) ECT; Weiner (1986b) observed that with increased rigor in methodology, the therapeutic equivalence of UL and BL ECT becomes more pronounced. Stromgren (1984) has even queried whether BL ECT is ever indicated.

Provided that the work can be replicated, much of the literature on this controversy has recently been rendered redundant. Since routine trials are biased in favour of UL ECT as seizure threshold is less with UL than with BL electrode placements (hence, in fixed ECT electrical dose trials, resulting in UL patients receiving materially more suprathreshold stimuli than BL patients), Sackeim et al. (1987a) comparing UL (nondominant) and BL ECT with stimulus dose titrated to the individual patient's seizure threshold at each ECT setting, found that BL ECT was overwhelmingly superior to UL ECT. Tandon et al. (1988), who did not titrate for the seizure threshold also found an advantage for BL ECT.

UL (non-dominant; UL dominant ECT is seldom given and is discussed later) ECT causes less cognitive disturbance than BL ECT. Hence, if the UL ECT technique is improved such that its efficacy in depression is on par with that of BL ECT, UL ECT would become the procedure of choice. Weiner (1986a) has suggested the following improvements: with UL ECT, the d'Elia electrode placement is best; the electrode-scalp interface must be particularly prepared to ensure low electrical impedance; the seizure must be monitored to ensure both generalization and adequacy in duration; the stimulus dose must be moderately suprathereshold (vide Sackeim et al., 1987a). A problem here is the operationalization of 'moderately suprathereshold', for the closer the stimulus is to 'considerably suprathereshold', the greater the cerebral disturbance and possible loss of safety advantage (Weiner et al., 1986a) without the advantage of therapeutic gain (Cronholm and Ottoson, 1960). Next, as seizure threshold varies widely across subjects and across time (Sackeim et al., 1987c), what is moderately suprathereshold for one patient may be barely suprathereshold for another and highly suprathereshold for a third. Seizure threshold will hence have to be identified for each patient several times during the ECT course, potentially exposing the patient either to subconvulsive stimuli (necessitating restimulation) or to seizures with barely threshold stimuli, neither of which favours the purpose of the exercise as one predisposes to cognitive morbidity while the other predisposes to impaired therapeutic efficacy.

With these modifications, Weiner et al. (1986a & b) found UL ECT to be as effective as but less cognitively 'toxic' (in the short and long term) than BL ECT. If this study can be replicated, reservations about the efficacy of UL ECT (see also Abrams, 1996) may be dispelled.

It is suggested that a subgroup of patients may exist who do not respond to UL brief-pulse (BP) but who do subsequently respond
to BL sinusoidal wave (SW) ECT (McAllister et al., 1985; Price and McAllister, 1986; McAllister and Price, 1986). As the stimuli were not described in these reports, it is not possible to conclude whether this hypothesis is indeed correct or whether the UL BP non-responders actually had high seizure thresholds and were not adequately stimulated. Continuation of UL ECT (Andrade et al., 1987a) with the recommendations of Weiner (1986a) may well have evoked response. If these findings are, however, not an artefact of ECT technique, effort is needed to identify state of trait markers of non-response to UL BP ECT, and to eliminate the confounding influence of waveform-electrode placement interactions.

The efficacy of UL ECT with sparing of certain cognitive functions indicates that not all parts of the brain require stimulation for the ECT to be therapeutic. Hence, techniques for selective stimulation of specific brain structures may, if developed, suffice for therapy, thus maximizing efficacy while minimizing adverse effects and removing the need for a convolution.

Finally: with UL ECT, the non-dominant hemisphere is usually selected for stimulation because dominant ECT causes prominent cognitive deficits (negating the very purpose of UL stimulation) and may also be less therapeutic (Weiner, 1986b). Recently, however, Abrams et al. (1987) found that right-sided EEG slowing was associated with right UL ECT and with less therapy, while left-sided EEG slowing was associated with BL ECT and with more therapy, suggesting a therapeutic advantage for left hemispheric stimulation, which hypothesis was confirmed by Abrams et al. (1989) who reported that right UL ECT was associated with slower response than left UL ECT. The revolutionary implications of this latter study must be tempered by the observations that the authors used very high (fixed) stimulus doses, that the margin of difference between right and left UL ECT, while statistically significant, was clinically small, and that differences were obtained only in rate and not in degree of response.

Stimulus waveform

The cardinal difference between sinusoidal wave (SW) and brief-pulse (BP) ECT is that the latter induces convulsions with lesser stimulus doses; the electrical aspects of stimulus waveform have recently been reviewed (Gordon, 1982; Weaver and Williams, 1982; Gangadhar and Andrade, 1989a).

Scanning available studies, Weiner (1986b) found SW and BP ECT to be comparable in efficacy with an advantage for SW found only when an inefficient BP stimulus (Pulse width <0.5 msec.) was used. We, however, (Andrade et al., 1987b; 1988b) reported more endogenous depressives to respond to BL SW (93%) as compared with BL BP (60%) ECT. The work of Price and colleagues, proposing a subgroup of depressives to be responsive to BL SW but not ULBP ECT has already been discussed. Anand et al. (1986) and Price et al. (1986) reported on patients who responded to SW ECT after unsuccessful ‘adequate’ courses of BP ECT (electrode positioning remaining unchanged). The common limitation in all these studies (except the UL BP vs BL SW reports, where stimulus details were not provided) and most of the case reports is that pulse widths <0.75 msecs. and possibly also minimally (BP) suprathreshold doses, were used, both of which may be suboptimum (Weiner and Coffey, 1989; R. J. Russell, personal communication). The work of Weiner et al. (1986 a & b), demonstrating therapeutic equivalence of SW and BP stimuli under optimum procedural conditions, is signal towards re-establishing the credibility of the BP stimulus.

No study has compared different doses of SW ECT. Greatly suprathreshold pulse stimuli are not superior to moderately suprathreshold (albeit described as ‘liminal’ by
CHITTARANJAN ANDRADE

the authors) ones (Cronholm and Ottoson, 1960).

Of note: the vast majority of ECT instruments available and in use in India utilize the unmodified sinusoidal waveform obtained from the electricity mains.

Electrical dose

From the previous discussions, one may conclude that (1) moderately suprathreshold stimuli (at least with right UL BP ECT) are more effective than liminal stimuli but not less effective than greatly suprathreshold stimuli (2) pulse widths \( \leq 0.75 \) msecs. may be less effective than those between 1 and 1.5 msecs. (3) the rate of stimulus delivery (in electrical terms, power) may also be characterized by a therapeutic range (Weaver et al. (1985); Swartz and Larson (1989) have further found longer stimulus trains to be superior in seizure elicitation at a constant stimulus dose.

The above 3 optimizations are all possible without an efficacy-adverse effect trade-off. There is little doubt that the search for the ideal stimulus in terms of seizure-elicitation with energy economy (Hyrman et al., 1985) is illusory in the absence of description of satisfactory therapeutic benefit.

The realization of the importance of the electrical dose has led to increasing sophistication in ECT instrumentation; 'second generation' instruments have been developed (Keaver and Williams, 1987). These offer the clinician an extensive range of stimulus specifications. Constant current instruments are gradually replacing constant voltage ones as the former permit dosimetric precision in prescription; with constant voltage instruments, at fixed stimulus settings the dose delivered is an inverse function of the impedance. Electrical aspects of ECT and instrumentation are discussed elsewhere (Railton et al., 1987; Weiner and Coffey, 1988b; Swartz, 1989a & b; Gangadhar and Andrade, 1989 a & b).

We have advanced the following hypotheses to explain the relationship between electrical dose and therapeutic response. The argument is adduced in 2 steps. First, there is evidence to suggest that the pattern and extent of neuronal activation with ECT is a function of the ECT stimulus (e.g. Robin et al., 1958; Swartz and Larson, 1986; Weiner et al., 1986a). It is hence reasonable to presume that the neurochemical changes (elicited by the neuronal activation) which mediate recovery from depression are also a function of the ECT stimulus, a.v., the recovery process may be favourably sensitive to increases in current delivery over and above the seizure threshold. A therapeutic window in terms of electrical dose may thus exist for each individual for each ECT. The lower limit of this window is the seizure threshold (or a hypothetical response threshold—see below). This is because the ECT stimulus is a brief one and is unlikely to in itself evoke therapeutic neuronal/neurochemical change, while the seizure-activation of neuronal tissue is prolonged and hence perhaps responsible for the persistent stimulation of structures responsible for reversal of depression. This logic is in line with the observations that subconvulsive stimuli are non-therapeutic, and that convulsive BP stimuli are therapeutic while non-convulsive SW stimuli, although greater in intensity, are non-therapeutic. The upper limit of such a therapeutic window is not clearly defined but is unlikely to exceed a 'moderately' suprathreshold dose as such stimuli are not less therapeutic than grossly suprathreshold stimuli.

Second, just as there exists a seizure threshold which varies across individuals, so too may there exist a hypothetical electrically quantifiable response threshold (situated above the seizure threshold—see above) which similarly varies across individuals. A given stimulus may not be therapeutic (even if it elicits a seizure) unless it exceeds this response threshold. The response threshold may be
either 'all or none' in therapeutic terms or may reflect the lower limit of a therapeutic window as discussed above but located above the seizure threshold.

Integrating these arguments, we hypothesize that ECT stimuli differ in efficacy and efficiency (i.e., degree and rate of response elicited) depending on whether or not they exceed a hypothetical response threshold situated at or above the seizure threshold \( \text{Response Threshold—All or None Hypothesis} \) or depending on the degree to which they exceed a hypothetical response threshold situated at or above the seizure threshold \( \text{Response Threshold—Therapeutic Window Hypothesis} \).

With the 'all or none' construct, the distance between the lowest and highest therapeutic stimuli consists solely of inter-individual variation while with the therapeutic window construct it comprises intra-individual variation as well.

These hypotheses have been progressively refined, albeit in small steps, over the years (Andrade, 1986; Andrade et al., 1987b; Andrade et al., 1988b; present version). Sackeim and co-workers (Malitz et al., 1986; Sackeim et al., 1987a) have also proposed a therapeutic window to characterize at least right (non-dominant) UL ECT. It must be stressed that the evidence for these hypotheses is presumptive and not empirical, and careful studies need to be conducted to test them.

Other issues

Ergoloid mesylates (Sachs et al., 1989) or antidepressants (Nelson and Benjamin, 1989, but not Haskett, 1982) administered concurrently with ECT may enhance therapeutic benefit. Antidepressants drugs alone or lithium augmentation thereof may remit ECT-resistant depression even in those depressed who were resistant to pre-ECT pharmacotherapy; this suggests that ECT may alter the sensitivity of refractory patients to antidepressant drugs (Shapira et al., 1988b).

(III) Prevention of relapse of depression following ECT

ECT should never be prescribed as a course but should be continued until further response is unlikely. Controversy dogs the definition of the treatment endpoint; once this endpoint is reached, though, care is warranted to preclude relapse, of which about 50% (the exact figures vary across studies) risk exists within 6 months of discontinuing ECT.

Formerly, +2, +\( \frac{n}{3} \) or +\( \frac{n}{2} \) ECTs were recommended after \( n \) ECTs produced the desired response. Barton et al.'s (1973) report is widely cited as evidence of the lack of prophylactic benefit of 2 extra ECTs but the study has methodological shortcomings and the data, even as they stand, are capable of being differently interpreted. Yet, the non-necessity of extra ECT can be justified on the grounds that antidepressant drugs or lithium, prescribed after completion of the ECT course, ensure prophylaxis (Abou-Saleh and Coppen, 1988); these should hence be routinely employed.

In some patients, especially those in whom (pre-ECT) pharmacotherapy had failed (Sackeim et al., 1989), maintenance drug therapy fails; here, maintenance ECT, administered weekly to monthly for several months, may be successful (Decina et al., 1987; Fink et al. 1989). Other predictors of relapse possibly include presence of DSM III Axis II personality disorders (Zimmerman et al., 1986) and a diagnosis of delusional depression (Spiker et al., 1985). Clearer identification of predictors of relapse is required, and possible ECT (e.g. ECT maintenance therapy) or other strategies for the management thereof. A problem is the differentiation of relapse (of the same episode from recurrence (of a fresh episode), and the differential management thereof.

(B) STRATEGIES FOR REDUCTION IN MORBIDITY

Cognitive impairment in depression (see
Price, 1982 a&b) is improved by ECT (e.g. Mackenzie et al., 1985). However, ECT itself produces cognitive impairment distinct from that due to depression, and which develops as depression-related impairment wanes (e.g. Squire et al., 1979; Mackenzie et al., 1985). This impairment is functional, not structural (Weiner, 1984; Selected Staff, 1985; Dam, 1985; Kolbeinsson et al., 1986; Pande et al. 1990).

While every ECT-treated patient may experience minor cognitive disturbance (often detected only on structured psychological testing), the incidence of severe impairment may be as little as 0.5% (Fink, 1979). Varying—sometimes alarming—incidences have been cited of ECT-induced subjective/objective cognitive deficits [Price, 1982 a&b]; these must be tempered by the realization that no study has ensured patient or (often) rater blindness. Given negative public impressions of ECT, the possibility must be considered that sham ECT also yields subjective/objective short or long-term cognitive 'dysfunction' which contaminates the true magnitude of that produced by real ECT.

Certain Strategies for minimizing ECT-induced cognitive dysfunction are discussed.

(I) Reduction in ECT requirement

An important recent concept is that ECT may produce time-dependent therapeutic change. Preclinical single ECT studies have described dopamine autoreceptor and alpha-2 adrenoceptor subsensitivity (both suggested to underlie antidepressant action) occurring coincidentally in time with the emergence of similar effects with serial ECTs. (Chiodo and Antelman, 1980; Tepper et al., 1982). We have found single ECT to produce time-dependent effects (Andrade et al., 1990b) but not as earlier described (Andrade and Pradhan, 1990a; Gangadhar et al., 1990b), thus refuting the possibility that a single ECT may suffice to treat depression.

Yet, clinical work has indicated possible benefit with a single ECT. Rich and Black (1985) observed that the first ECT in a series is the most therapeutic, and suggested that further benefit with successive treatments may reflect a carryover effect of the first treatment. In a preliminary (unpublished) double-blind, sham ECT-controlled study, we found many single ECT-treated depressives to show satisfactory improvement as compared with 3/week ECT-treated patients, at the end of the 3-week trial.

Less revolutionary but also on the time-dependent theme is the proposal that 2/week ECT produces the same results as 3/week ECT (see Lerer and Shapira, 1986). In fact, in many centres 2/week ECT is conventional. In our laboratory, we have demonstrated that 3 alternate day ECTs comparably subsensitize alpha-2 adrenoceptors as 6 daily (conventional schedule in animal experiments) ECTs (manuscript in preparation).

McAllister et al. (1987), comparing 2/wk and 3/wk ECT-treated depressives, found the former to require fewer ECTs and experience less cognitive dysfunction than the latter. However, Shapira et al. (1989) found that in the 2 schedules the same number of ECTs were required to attain a specified degree of recovery (the 2/week patients hence improved slower). Even if 2/week ECT necessitates the same number of treatments as 3/week ECT, cognitive morbidity may be less with the former—consider, for example, that 3/week ECT is cognitively less 'toxic' than daily ECT (Freeman et al., 1989).

The time-dependent hypothesis is in theoretical opposition to the concept that a set number of treatments (or a set cumulative seizure duration) is required for therapy, or that response may be hastened by more frequent ECT (Stromgren, 1975; Maletzky, 1987).

Concurrent antidepressant drugs do not decrease ECT requirement (Haskett, 1982) but Sachs et al. (1986) found yohimbine to do so by hastening recovery. Other adreno-
facilitatory drugs may similarly, on theoretical grounds, be of use as such may facilitate postsynaptic beta adrenoceptor down-regulation, which change is suggested to underlie a mechanism of antidepressant action.

Finally, unnecessary ECT can be avoided by optimum definition of treatment endpoint and termination of the ECT course.

(II) Hastening of response to ECT
Quicker response to ECT means less suffering, less risk for suicide and less time-cost-energy expenditure. Further, ECT requirement and hence (presumably) cognitive morbidity would be less.

SWECT, high energy BP ECT, or, in general, higher electrical doses are suggested to purvey faster recovery than BP ECT, lower energy BP ECT or lower electrical doses respectively (Robin, 1981; Robin and de Tissera, 1982; Robin, 1988). These findings have however not been confirmed (Weiner et al., 1986a & b; Andrade et al., 1988c; Fox et al., 1989). Similarly, the claim that BL ECT hastens recovery relative to UL ECT (Gregory et al., 1985; Abramset al., 1987; Tandon et al., 1988) remains in doubt (Weiner et al., 1986 a & b; Sackeim et al., 1987a). Dominant, as compared with nondominant unilateral ECT, may be associated with faster response (Abrams et al., 1989). Multiple ECT, wherein several ECTs are given in each treatment session to hasten recovery (Maletzky, 1986) is as yet unevaluated for benefit and risk in double-blind, prospective studies. Administering 3 or 4 ECTs/week may hasten recovery relative to 2 ECTs/week, possibly without recourse to increased total ECT requirement (Stromgren, 1975; Shapiro et al., 1989); this too is in dispute (McAllister et al., 1987). Besides being questionably effective, these strategies to hasten recovery may increase cognitive dysfunction as will be discussed later. The role of yohimbine in hastening recovery has already received mention.

Interestingly, Dinan and Barry (1989) found that in tricyclic non-responders augmentation with lithium elicited response faster than did ECT, the low rate of ECT response however suggests that the ECT technique used may have been suboptimum.

(III) Prediction of fast response to ECT
Most depressives require 6-8 ECTs, but some respond quicker and others, slower (Kendell, 1981). Cases have been described of dramatic ‘melting’ of symptoms with ECT (Rich, 1984; Keisling, 1984; Andrade et al., 1987c). The prospective identification of potential slow/fast responders is poorly researched and is necessary to ensure that ECT is not discontinued prematurely in slow responders or late in fast responders, and that, if sparing of cognitive function is vital, slow responders receive ECT only if such is unavoidable.

It is not known whether rate of response to ECT is state-or trait-dependant (or linked more to ECT practice-vide supra !). Hilberto, only clinical differentiation of slow and fast responders has been attempted. In a limited analysis, Barton (1973) found that depression >6 months in duration was associated with either fast (requiring 2-4 ECTs) or slow (requiring 9-12 ECTs) response. We (Andrade et al., 1988d) however observed no relationship between duration of depression and rate of response; instead, male sex, and greater age associated with lesser initial severity of depression were associated with faster response (requiring ≤ 5 ECTs for full response), while, interestingly, no such association was found for features suggested to predict good outcome with ECT. Our findings contrast with the opinion of Freeman et al. (1989) (possibly based on the reports of Price et al., 1978 and Rich et al., 1984b, which were methodologically quite different from ours) that older patients and men may require more treatment.

(IV) Stimulus-related issues for minimizing cognitive deficits
BP ECT, even at moderately suprather-
shold doses, produces less acute cognitive morbidity than SW ECT; this advantage for BP ECT is lost in subsequent weeks (Weiner, 1986b; Weiner et al., 1986b), or is even absent acutely if the BP stimulus is too intense (Squire and Zoumounis, 1986). SW but not BP dose variations correlate with cognitive morbidity, implying that as long as stimuli are not more than moderately suprathreshold, BP but not SW stimuli may be below a cut-off for intensity related effects on ECT-induced cognitive dysfunction (Weiner et al., 1986b). However, Pettinati et al. (1989) found that subjects with most forgetting after UL BP ECT were responders who had received higher stimulus doses. Non-cognitive subjective side effects and subjective global memory ratings do not differ between SW and BP groups (Andrade et al., 1990c; Weiner et al., 1986b).

UL non-dominant (ND) ECT, as compared with BL ECT, spares many cognitive (particularly verbal) functions (Price, 1982a & b) and is associated with fewer subjective side effects (Sackeim et al., 1987d) in the acute post-ECT phase. Weiner et al. (1986a & b) have found that personal memory loss with BL but not UL ECT extends for as long as 6 months post-treatment; indices of impairment are least with UL BP and most with BL SW ECT; this, coupled with earlier noted evidence of the therapeutic equivalence of SW and BP ECT, and of UL and BL ECT, recommends UL BP ECT for routine practice in most depressions.

UL ND electrode positions may not differ in cognitive effects (Widepalm, 1987), but UL ND ECT is unquestionably more benign than UL dominant ECT (Price, 1982a & b). Current densities in the brain tissue lying in and around the interelectrode axis are much greater with UL than with BL ECT (Weaver and Williams, 1982), but the fear that these currents may be unacceptably high (Kris et al., 1978; Breggin, 1986) has not been substantiated in cognitive and other studies. Interaction with reality are largely biased for verbal content; hence, UL ND ECT, which relatively spares verbal cognition, is superior to BL ECT. What, then, of musicians, artists and other persons to whom integrity of ND hemisphere functioning is paramount? Might the advantage of UL ND ECT be lost due to the production of higher current densities in the ND hemisphere? While available evidence is reassuring, imaginative cognitive assessment is yet to be conducted in suitably designed studies.

(V) Minimizing cognitive deficit: other strategies

Missed or incomplete seizures are a frequent problem, and the clinician's reflex, when such occur, is to raise a stimulus setting and re-seizure. While this is not incorrect, other strategies can ensure an adequate convulsion at the same stimulus settings; these have been discussed earlier. While many strategies are innocuous (e.g. ensuring adequate electrode-skin conductance) or even beneficial (e.g. switching from BL to UL ECT), certain (e.g. caffeine-prolongation of seizures) have to be evaluated against stimulus dose-augmentation in terms of benefits and cognitive adverse effects. Coffey et al. (1990) demonstrated that caffeine-augmented low electrical dose UL BP seizures are associated with comparable efficacy and adverse effect profiles as seizures produced by higher stimulus doses. Unnecessary elevation in electrical doses should be avoided, while prolongation of an otherwise adequate seizure may not be desirable as such may enhance adverse effects without improving the efficacy or efficiency (Miller et al., 1985).

Anticholinergic drugs impair cognition, but substitution of glycopyrrolate for atropine in ECT premedication does not lessen cognitive deficit (Sommers et al., 1989). Piracetam (Ezzat et al., 1985), possibly ergoloid mesylates (Sachs et al., 1989) and vasopressin (Mett et al., 1989 & 1990; but not ACTH and naloxone (Fredericksen et al., 1985; Nasrallah et al., 1986) have tentatively been suggested to attenuate ECT-induced cognitive dysfunction in
various degrees. Suedfeld et al. (1987 & 1989) found restricted environmental stimulation therapy (wherein the patient is placed in a quiet, dimly lit room for 2-4 hours after ECT) to benefit subjective but not objective memory function after ECT. This, actually, suggests a placebo and not a true therapeutic effect.

Hitherto, ECT parameters have alone been considered as independent variables in ECT-induced cognitive impairment. Might state- or trait-dependant patient variables also be relevant? An attempt to identify patients at high risk for the development of cognitive dysfunction with ECT is warranted.

**CONCLUDING REMARKS**

In the West, legislation and adverse public opinion shackles the practice of ECT, and this important treatment is relegated to application in very severe and medication-resistant illness. By contrast, in India use of ECT is optimized to situations in which it is indicated positively and not merely by exclusion. With increased utilization of psychiatric services accompanying progress in the implementation of the National Mental Health Plan, use of ECT could conceivably increase to manage in a time-cost-energy effective way the burden of the mentally ill from a population in excess of 800 million. These are very good reasons why India should lead in standards of ECT practice and in clinical research. This has been a major objective in the subject and content of my address to you.

Late this year, we will organize and host at NIMHANS a national level ECT Symposium to discuss advances in theoretical and practical aspects of ECT as a belated tribute to the year 1988, the Golden Jubilee Year of ECT, which passed by without a whimper from the Indian scene. Details about this Symposium will be announced in the Indian Journal of Psychiatry.

Finally, communication between psychiatrists in our country is poor. On the subject of ECT at least, I offer to share the expertise that we have developed in our Institute by way of mailing reprints to requesters, providing guidelines, offering suggestions and collaborating in research wherever possible. Our country is rich in clinical material, and I repeat that where practising standards and clinical research in ECT are concerned, India must lead.

**REFERENCES**

Abou-Saleh, M. T. and Coppen, A. J. (1988). Continuation therapy with antidepressants after electroconvulsive therapy. Editorial. Convulsive Therapy, 4, 263-268.

Abrams, R. (1982). Clinical prediction of ECT response in depressed patients. Psychopharmacology Bulletin, 18(2), 48-50.

Abrams, R. (1986). An hypothesis to explain divergent findings among studies comparing the efficacy of unilateral and bilateral ECT in depression. Convulsive Therapy, 2, 253-256.

Abrams, R. (1988). Electroconvulsive Therapy. New York: Oxford University Press.

Abrams, R. (1989). A reply to Andrade and Gangadhar. Convulsive Therapy 3, 191-194.

Abrams, R. and Taylor, M. A. (1974). Unipolar and bipolar depressive illness: Phenomenology and response to electroconvulsive therapy. Archives of General Psychiatry, 30, 320-321.

Abrams, R.; Fink, M. and Feldstein, S. (1973). Prediction of clinical response to ECT. British Journal of Psychiatry, 122, 457-460.

Abrams, R.; Taylor, M. A. and Volavka, J. (1987). ECT-induced EEG asymmetry and therapeutic response in melancholia: relation to treatment electrode placement. American Journal of Psychiatry, 144, 327-329.

Abrams, R.; Swartz, C. M. and Vedak, C. (1989). Antidepressant effect of right versus left unilateral ECT and the lateralization theory of ECT action. American Journal of Psychiatry, 146, 1190-1192.

Adleskey, D. and Hamilton, M. (1953). Use of succinylcholine in ECT. British Medical Journal, 1, 195-197.

American Psychiatric Association (1978). Task Force Report 14: Electroconvulsive Therapy. Washington, DC: APA.

Anand, M. M.; Weller, R. A. and Parke, M. P. (1986). Patients who do not respond to brief-pulse ECT. American Journal of Psychiatry, 143, 531.

Andrade, C. (1986). Outcome of Endogenous Depression with Electroconvulsive Therapy (ECT): Assessed on Different ECT Parameters. Unpublished Thesis. Bangalore University : Bangalore.
Andrade, C. and Gangadhar, B. N. (1989a). When is an ECT responder an ECT responder? Convulsive Therapy, 5, 190-191.

Andrade, C. and Gangadhar, B. N. (1989b). Electroconvulsive shock and dopamine postsynaptic receptor: clinical implications of time-dependent change. Paper received the Bhagwat Award at the 41st Annual Conference of the Indian Psychiatric Society, Cuttack.

Andrade, C. and Gangadhar, B. N. (1990a). Use of electroconvulsive therapy in non-affective disorders. In: Syed Mohammed, P. M., Mohandas, E. and Michael, A. (Eds.): Current Trends in Neurology and Psychiatry (in press).

Andrade, C. and Gangadhar, B. N. (1990b). Current issues in electroconvulsive therapy, Editorial, SJMC Journal of Medicine (in press).

Andrade, C. and Gangadhar, B. N. (1990c). Electroconvulsive therapy: Realities and myths. Health Action (in press).

Andrade, C. and Pradhan, N. (1990). Adrenergic receptor effects of a single electroconvulsive shock. Indian Journal of Psychological Medicine (in press).

Andrade, C. and Pradhan, N. (1990d). Somatic therapies in pregnancy and lactation: theoretical issues and clinical guidelines for psychiatric practice. In: Syed Mohammed, P. M., Mohandas, E. and Michael, A. (Eds.): Current Trends in Neurology and Psychiatry (in press).

Andrade, C.; Swaminath, G. and Gangadhar, B. N. (1987a). Unilateral brief-pulse and bilateral sinusoidal ECT. Journal of Clinical Psychiatry, 48, 30-39.

Andrade, C.; Gangadhar, B. N.; Soshadri, S.; Jain, S.; Swaminath, G. and Channabasavanna, S. M. (1987b). ECT variables: Impact in depression. Presented at 39th Annual Conference of the Indian Psychiatric Society, Calcutta.

Andrade, C.; Gangadhar, B. N. and Channabasavanna, S. M. (1987c). Unusual sensitivity to ECT. Pharmacology, 117, 16-17 & 119-140.

Andrade, C.; Gangadhar, B. N. and Channabasavanna, S. M. (1990). Mania associated with electroconvulsive therapy. Journal of Clinical Psychiatry, 48, 303-304.

Andrade, C.; Gangadhar, B. N.; Swaminath, G. and Channabasavanna, S. M. (1988a). Predicting the outcome of endogenous depression following electroconvulsive therapy. Convulsive Therapy 4, 169-174.

Andrade, C.; Gangadhar, B. N.; Subbakkrisna, D. K.; Channabasavanna, S. M. and Pradhan, N. (1988b). A double-blind comparison of sinusoidal wave and brief-pulse electroconvulsive therapy in endogenous depression. Convulsive Therapy, 4, 297-303.

Andrade, C.; Gangadhar, B. N.; Channabasavanna, S. M. and Pradhan, N. (1988c). Does ECT stimulus waveform influence rate of recovery in endogenous depression? NIMHANS Journal, 6, 121-126.

Andrade, C.; Gangadhar, B. N.; Subbakkrisna, D. K.; Channabasavanna, S. M. and Pradhan, N. (1988d). Clinical prediction of rate of response of endogenous depression to electroconvulsive therapy. Indian Journal of Psychiatry, 30, 381-387.

Andrade, C.; Gangadhar, B. N.; Swaminath, G. and Channabasavanna, S. M. (1988e). Mania as a side-effect of electroconvulsive therapy. Convulsive Therapy, 4, 81-83.

Andrade, C.; Gangadhar, B. N.; Vythilingam, M.; Channabasavanna, S. M. and Pradhan, N. (1989a). Initial response to ECT as a predictor of outcome in endogenous depression. Indian Journal of Psychiatry, 31, 293-295.

Andrade, C.; Gangadhar, B. N.; Channabasavanna, S. M. and Pradhan, N. (1989b). Clinical characteristics of endogenous depressives who respond to ECT. NIMHANS Journal, 7, 119-122.

Andrade, C.; Gangadhar, B. N. Channabasavanna, S. M. and Pradhan, N. (1990a). The clinical identification of endogenous depressives who respond to electroconvulsive therapy. Presented at 42nd Annual Conference of the Indian Psychiatric Society, Chandigarh.

Andrade, C.; Gangadhar, B. N.; Meena, M. and Pradhan, N. (1990b). Dopaminergic effects of restricted schedules of electroconvulsive shock. Convulsive Therapy (in press).

Andrade, C.; Gangadhar, B. N.; Channabasavanna, S. M. and Pradhan, N. (1990c). Subjective side effects of electroconvulsive therapy in endogenous depression. 42nd Annual Conference of the Indian Psychiatric Society, Chandigarh.

Andrade, C.; Arunasmitha, S. and Pradhan, N. (1990d). Serial electroconvulsive shock: Acute and sustained effects on alpha-2 adrenergic receptors. 42nd Annual Conference of the Indian Psychiatric Society, Chandigarh.

Andrade, C.; Arunasmitha, S. and Pradhan, N. (1990e). Apomorphine-induced time-dependent potentiation of dopamine postsynaptic receptor response. NIMHANS Journal (in press).

Barrington, P. and Lambourn, J. (1990). Monitoring the occurrence and duration of electroconvulsive fits. British Journal of Psychiatry, 151, 118-119.

Barton, J. L.; Metha, S. and Smith, R. P. (1973). The prophylactic value of extra ECT in depressive illness. Acta Psychiatrica Scandinavica, 49, 362-392.

Black, D. W. and Winokur, G. (1989). Psychotic and non-psychotic depression: Comparison of response to ECT. Journal of Clinical Psychiatry, 50, 181.

Breggin, P. R. (1986). Brain damage from non-do-
minant ECT. American Journal of Psychiatry, 143, 1320-1321.

Calev, A.; Ben-Tivi, E.; Shapiro, B.; Drexler, H.; Carasso, R. and Lerer, B. (1989). Distinct memory impairments following electroconvulsive therapy and imipramine. Psychological Medicine, 19, 111-119.

Carney, M. W. P.; Roth, M. and Garside, R. F. (1965). The diagnosis of depressive syndromes and the prediction of ECT response. British Journal of Psychiatry, 111, 659-674.

Chater, S. N. and Simpson K. H. (1988). Effect of passive hyperventilation on seizure duration in patients undergoing electroconvulsive therapy. British Journal of Anaesthesia, 60, 70-73.

Chioldo, L. A. and Antelman, S. M. (1990). Electroconvulsive shock: Progressive dopamine autoreceptor subsensitivity independent of repeated treatment. Science, 210, 799-801.

Clinical Research Centre, Division of Psychiatry (1984). The Northwick Park ECT trial: Predictors of response to real and simulated ECT. British Journal of Psychiatry, 144, 227-237.

Coffey, C. E.; Figiel, G. S.; Weiner, R. D. and Saunders, W. B. (1990). Caffeine augmentation of electroconvulsive therapy. American Journal of Psychiatry (in press).

Consensus Conference (NIMH-NIH) (1985). Electroconvulsive Therapy. Journal of the American Medical Association, 254, 2103-2108.

Coryell, W. and Zimmerman, M. (1984). Outcome following ECT for primary unipolar depression: A test of newly proposed response predictors. American Journal of Psychiatry, 141, 862-867.

Cronholm, B. and Ottoson, J. O. (1960). Experimental studies of the therapeutic action of electroconvulsive therapy in endogenous depression. Acta Psychiatrica Scandinavica (Suppl), 35, (145), 69-141.

Dam, A. M. (1986). Quantitative neuropathology in electrically induced generalized convulsions. Psychopharmacology Bulletin, 22, 479-482.

Decina, P.; Guthrie, E. B.; Sackheim, H. A.; Kahn, D. and Malitz, S. (1987). Continuation ECT in the management of relapses of major affective episodes. Acta Psychiatrica Scandinavica, 75, 559-562.

d'Elia, G. (1970). Unilateral ECT. Acta Psychiatrica Scandinavica (Suppl), 215, 5-98.

d'Elia, G. and Raotma, H. (1975). Is unilateral ECT less effective than bilateral ECT? British Journal of Psychiatry, 126, 83-99.

Devanand, D. P.; Decina, P.; Sackheim, H. A. and Prudic, J. (1988). Status epilepticus following ECT in a patient receiving theophylline. Journal of Clinical Psychopharmacology, 8, 153.

Dinan, T. G. and Barry, S. (1989). A comparison of electroconvulsive therapy with a combined lithium and tricyclic combination among depressed tricyclic non-responders. Acta Psychiatrica Scandinavica, 80, 97-100.

Dunn, C. G. and Quinlan, D. (1978). Indicators of ECT response and non-response in the treatment of depression. Journal of Clinical Psychiatry, 39, 620-622.

Ezzat, D. H.; Ibraheem, M. M. and Makhowy, B. (1985). The effect of piracetam on ECT-induced memory disturbances. British Journal of Psychiatry, 147, 720-721.

Fink, M. (1979). Convulsive Therapy: Theory and Practice. New York: Raven Press.

Fink, M. (1982). Predictors of outcome in convulsive therapy. Psychopharmacology Bulletin, 18(2), 50-57.

Fink, M. (1986). Neuroendocrine predictors of electroconvulsive therapy outcome. Annals of the New York Academy of Sciences, 462, 30-36.

Fink, M. (1987). New technology in convulsive therapy: A challenge in training. Editorial. American Journal of Psychiatry, 144, 1193-1198.

Fink, M. (1989). Maintenance ECT is a continuing saga. The Psychiatric Times/Medicine and Behaviour, April 1989, pg. 13.

Fink, M. and Johnson, L. (1982). Monitoring the duration of electroconvulsive therapy seizures. Archives of General Psychiatry, 39, 1189-1192.

Fox, H. A.; Rosen, A. and Campbell, R. J. (1989). Are brief-pulse and sine-wave ECT equally efficient? Journal of Clinical Psychiatry, 50, 432-435.

Frederiksen, S. O.; d'Elia, G. and Holsten, F. (1985). ECT, ACTH and cognition. European Archives of Psychiatry and Neurological Sciences, 234, 291-294.

Freeman, C.; Crammer, J. L.; Deakin, J. F. W.; McClelland, R.; Mann, S. A. and Pippard, J. (1989). The Practical Administration of Electroconvulsive Therapy (ECT). Report of the ECT sub-committee of the Research Committee of the Royal College of Psychiatrists, London: Gaskell.

Gangadhar, B. N. (1985). Side effects of somatic therapies in depression: A double-blind comparison of ECT and imipramine. NIMHANS Journal, 3, 13-16.

Gangadhar, B. N. and Andrade, G. (1989a). Electrical aspects of electroconvulsive therapy: A review. I. Electrical issues. Indian Journal of Psychological Medicine, 12(1), 53-60.

Gangadhar, B. N. and Andrade, G. (1989b). Electrical aspects of electroconvulsive therapy: A review. II. Clinical and practical issues. Indian Journal of Psychological Medicine, 12(1), 61-66.

Gangadhar, B. N. and Andrade, G. (1990). Iatrogenic dysfunction and ECT. In: Keshavan, M. S., Prasad, A. and Kennedy, J. (Eds.): Drug-Induced Dysfunction in Psychiatry: Diagnosis and Management. Kluwer. Hemisphere Publications (in press).

Gangadhar, B. N.; Kapur, R. L. and Kalyanasunderam, S. (1982). Comparison of electroconvulsive therapy
with imipramine in endogenous depression: A double-blind study. British Journal of Psychiatry, 141, 367-371.

Gangadhar, B. N.; Chaudhary, J. R. and Channabasavanna, S. M. (1983). ECT and drug-induced Parkinsonism. Indian Journal of Psychiatry, 25, 212-213.

Gangadhar, B. N.; Kapur, R. L. and Kalyanasunderam, S. (1983). Effect of ECT in endogenous depression: A double-blind comparison with imipramine. NIMHANS Journal, 3, 7-12.

Gangadhar, B. N.; Lakshmanana, G.; Subbakrishna, D. K. and Channabasavanna, S. M. (1985b). Impedance measurements during electroconvulsive therapy. NIMHANS Journal, 3, 135-139.

Gangadhar, B. N.; Pradhan, N. and Maynard, C. S. K. (1987). Dopamine autoreceptor down-regulation following repeated electroconvulsive shock. Indian Journal of Medical Research, 86, 787-791.

Gangadhar, B. N.; Levanna, G.; Andrade, C.; Janakiramaiah, N. and Channabasavanna, S. M. (1988). The NIMHANS Model ECT Instrument: A technical report. Indian Journal of Psychiatry, 30, 247-251, and 31(2), 1.

Gangadhar, B. N.; Ramadevi, G.; Andrade, C. and Pradhan, N. (1989). Dopaminergic effects of repeated electroconvulsive shock. Convulsive Therapy, 5, 157-161.

Gangadhar, B. N.; Andrade, C. and Janakiramaiah, N. (1990a). Electroconvulsive therapy: Theory and practice. In: Vyas, J. N. (Ed.). Postgraduate Psychiatry (in press).

Gangadhar, B. N.; Ramadevi, G.; Andrade, C. and Pradhan, N. (1990b). Dopaminergic effects of a single electroconvulsive shock. Paper presented at 12th Annual Conference of the Indian Psychiatric Society, Chandigarh.

Gordon, D. (1982). Electroconvulsive therapy with minimal hazard. British Journal of Psychiatry, 141, 12-13.

Gregory, S.; Shawcross, C. R. and Gill, D. (1983). The Nottingham ECT study: A double-blind comparison of bilateral, unilateral and simulated ECT in depressive illness. British Journal of Psychiatry, 116, 520-521.

Guzo, B. H.; Liston, E. H. and La Rue, A. (1980). Monitoring electroconvulsive therapy by galvanic skin response. Convulsive Therapy, 4, 84-87.

Guzo, B. H.; Liston, E. H.; Baxter, L. R.; Rieheimer, S. H. and Gold, M. E. (1989). Poor inter-rater reliability of MECTA EEG recordings of ECT seizure duration. Journal of Clinical Psychiatry, 50, 110-112.

Hamilton, M. (1982). Predicting the response of depression to ECT. In: Abram, R. and Essman, W. B. (Eds.): Electroconvulsive Therapy: Biological Foundations and Clinical Applications, Lancaster: MTP Press Limited, 113-127.

Hamilton, M. (1987). Electrodermal response as a monitor in ECT. British Journal of Psychiatry, 151, 539. 

Haskett, R. F. (1982). Factors affecting outcome after successful electroconvulsive therapy. Psychopharmacology Bulletin, 18(2), 75-78.

Hobson, R. F. (1939). Prognostic factors in ECT. Journal of Neurology, Neurosurgery and Psychiatry, 16, 273-281.

Holdy, E. K. and Martin, R. L. (1986). Increased seizure duration during ECT with trazodone administration. American Journal of Psychiatry, 143, 1326.

Hyman, V.; Palmer, L. H.; Cernik, J. and Jetelina, J. (1985). ECT: The search for the perfect stimulus. Biological Psychiatry, 20, 63-645.

Jain, S.; Seshadri, S. and Gangadhar, B. N. (1989). Monitoring the seizure during ECT. NIMHANS Journal, 7, 117-117.

Janakiramaiah, N. (1987). Lithium and post-lithium developments at NIMHANS in the somatotherapy of mania. In: Channabasavanna, S. M. and Shah, S. A. (Eds.): Affective Disorders: Recent Research & Related Developments. Bangalore: NIMHANS, 119-127.

Janakiramaiah, N.; Channabasavanna, S. M. and Narasimha, N. S. (1982). ECT/chlorpromazine combination versus chlorpromazine alone in acutely schizophrenic patients. Acta Psychiatrica Scandinavica, 66, 361-470.

Johnstone, L. C.: Deakin, J. F. W.; Lawler, P.; Frith, C. D.; Stevens, M.; McPherson, K. and Crow, T. J. (1980). The Northwick Park ECT Trial. Lancet, ii, 1317-1320.

Kataoka, C. L. E. and Akridge, C. R. (1984). Prediction of ECT response. Neuropharmacology, 23(2), 281-283.

Keishing, R. (1984). Successful treatment of an unidentified patient with one ECT. American Journal of Psychiatry, 141, 148.

Kellner, C. H. and Malcolm, R. L. (1988). Failure of sleep deprivation to prolong seizures in ECT. American Journal of Psychiatry, 145, 330.

Kendell, R. E. (1981). The present status of electroconvulsive therapy. British Journal of Psychiatry, 139, 265-283.

Kluza, S.; Gangadhar, B. N.; Sinha V.; Rajendra, P. N. and Channabasavanna, S. M. (1989). Electroconvulsive therapy in obsessive-compulsive disorder. Convulsive Therapy, 4, 314-320.

Kolbeinsson, H.; Arnaldsson, O. S.; Petursson, H. and Skulason, S. (1986). Computed tomographic scan in ECT-patients. Acta Psychiatrca Scandinavica, 73, 28-32.
McAllister, T. W. and Price, T. R. P. (1982). Short- and long-term cognitive effects of ECT: Part I—Effects on Memory. Psychopharmacology Bulletin, 18(1), 81-91.

Price, T. R. P. (1982a). Short- and long-term cognitive effects of ECT: Part I—Effects on Memory. Psychopharmacology Bulletin, 18(1), 81-91.

Price, T. R. P. (1982b). Short- and long-term cognitive effects of ECT: Part II—Effects on non memory associated cognitive functions. Psychopharmacology Bulletin, 18(1), 91-101.

Rauscher, F. F. and Sattin, A. (1987). Effects of ECT given two vs. three times weekly. Psychiatry Research, 21, 63-69.
Phillipson, M. (1982). ECT response in psychotic

Rich, C. I.; Spiker, D. G.; Jewell, S. W.; Neil, J. F. and

Rich, C. I., and Black, N. A. (1983). The efficiency

Rich, C. I., (1984). Recovery from depression after

Rasanen, J.; Martin, D. J.; Downs, J. B. and Hodges, M.

Rampton A. J., Griffin, R. M.; Stuart, C. S.; Durcan, J. J., Huddy, N. D. and Abbott, M. A. (1989). Comparison of electrical measurements on constant voltage and constant current ECT machines. British Journal of Psychiatry, 151, 241-247.

Rajendra, P. N. (1989). An investigation into post-ECT cognitive dysfunction using electrophysiological and neurochemical parameters. M. D. Thesis, Bangalore: Bangalore University.

Rampton A. J., Griffin, R. M.; Stuart, C. S.; Durcan, J. J., Huddy, N. D. and Abbott, M. A. (1989). Comparison of methohexital and propofol for electroconvulsive therapy. Journal of Affective Disorders, 16, 59-64.

Rajlion, R.; Fisher, J., Sinclair, A. and Shrigmankar, J. M. (1997). Comparison of electrical measurements on current and voltage of ECT. British Journal of Psychiatry, 5, 180-183.

Rifkin A. (1988). ECT versus tricyclic antidepressants in depression: a review of the evidence. Journal of Clinical Psychiatry, 49, 3-7.

Robin, A. A. (1981). ECT, current status. In: Palmer, R. L. (Ed.): ECT: An Appraisal. Oxford: Oxford University Press, 66-78.

Robin, A. A. (1989). Energy and therapeutic response. In: Malkin, J. C. and Brandon, S. (Eds.): Current Approaches: ECT. Southampton: Duphar Medical Relations, 1-7.

Robins, A. and deTissere, S. (1980). A double-blind controlled comparison of the therapeutic effects of low and high energy electroconvulsive therapies. British Journal of Psychiatry, 141, 357-366.

Robin, A.; Binnie, C. D. and Copas, J. B. (1983). Electrophysiological and hormonal responses to three types of electroconvulsive therapy. British Journal of Psychiatry, 147, 707-712.

Rasch, G. S., Pollack, M. H.; Brown, A. W.; Farhadi, A. M. and Geleberg, A. J. (1986). Enhancement of ECT benefit by yohimbine. Journal of Clinical Psychiatry, 47, 508-510.

Rasch, G. S.; Geleberg, A. J. Bellinghausen, B.; Wojcik, J. Falk, W. E., Farhadi, A. M. and Jenike, M. (1989). Ergoloid mesylates and ECT. Journal of Clinical Psychiatry, 50, 87-99.

Sackeim, H. A. (1981). ECT, current status. In: Malkin, J. C. and Brandon, S. (Eds.): Current Approaches: ECT. Southampton: Duphar Medical Relations, 1-7.

Sackeim, H. A.; Decina, P.; Kander, M., Kerr; B. and Malitz, S. (1987a). Effects of electrode placement on the efficacy of tridate, low-dose ECT. American Journal of Psychiatry, 144, 1449-1455.

Sackeim, H. A.; Decina, P.; Portroy, S.; Neesley, P. and Malitz, S. (1987b). Studies of dosage, seizure threshold and seizure duration in ECT. Biological Psychiatry, 22, 249-268.

Sackeim, H. A., Decina, P.; Prohovnik, I. and Malitz, S. (1987d). Seizure threshold in electroconvulsive therapy. Archives of General Psychiatry, 44, 355-364.

Scott, A. I. F. (1988). Which depressed patients will respond to electroconvulsive therapy? The search for biological predictors of recovery. British Journal of Psychiatry, 154, 8-17.

Scott, A. I. F.; Shering, P. A. and Dykes, S. (1989). Would monitoring of electroencephalogram improve the practice of electroconvulsive therapy? British Journal of Psychiatry, 154, 839-837.
Suedfeld, P., Ramirez, C. E., Remick, R. A. and Flemming, J. A. (1987). Optimum frequency of electroconvulsive therapy. Convulsive Therapy, 3, 75.

Suedfeld, P., Ramirez, C. E., Remick, R. A. and Flemming, J. A. (1987). Memory effects of restricted environmental stimulation therapy (REST) and possible applications to ECT. Progress in Neuropsychopharmacology and Biological Psychiatry, 11, 179-181.

Suedfeld, P., Ramirez, C. E., Remick, R. A. and Flemming, J. A. (1989). Reduction of post-ECT memory complaints through brief, partial restricted environmental stimulation (REST). Progress in Neuropsychopharmacology and Biological Psychiatry, 13, 693-700.

Swartz, C. M. (1989a). Safety and ECT stimulus electrodes: I. Heat liberation at the electrode-skin interface. Convulsive Therapy, 5, 171-175.

Swartz, C. M. (1989b). Safety and ECT stimulus electrodes: II. Clinical Procedures. Convulsive Therapy, 5, 175-179.

Swartz, C. M. and Larson, G. (1986). Generalization of the effects of unilateral and bilateral ECT. American Journal of Psychiatry, 1040-1041.

Swartz, C. M. and Larson, G. (1989). ECT stimulus duration and its efficacy. 1989 AACP Clinical Research Award Paper, Annals of Clinical Psychiatry, 1, 147-152.

Tandon, R., Grunhaus, L., Hackett, R. F., Kugler, T. and Oreden, J. F. (1988). Relative efficacy of unilateral and bilateral electroconvulsive therapy in melancholia. Convulsive Therapy, 4, 133-159.

Tepper, J. M., Nakamura, S., Spanis, C. W., Squire, L. A., Young, S. J. and Groves, P. M. (1982). Sensitivity of catecholaminergic neurons to direct acting agonists after single or repeated electroconvulsive shock. Biological Psychiatry, 17, 1059-1070.

Weaver, L. A., Jr. and Williams, R. W. (1982). The electroconvulsive therapy stimulus. In: Abrams, R. and Esman, W. B. (Eds.). Electroconvulsive Therapy: Biological Foundations and Clinical Applications. Lancaster: MTP Press Limited, 129-156.

Weaver, L. A. and Williams, R. W. (1987). ECT: Second generation instruments. Biological Psychiatry, 22, 1181-1182.

Weaver, L. A. Jr., Ives, J. and Williams, R. (1985). Total energy and rate of application as measures of the electroconvulsive therapy stimulus. Convulsive Therapy, 1, 22-31.

Weiner, R. D. (1984). Does electroconvulsive therapy cause brain damage? The Behavioural and Brain Sciences, 7, 1-51.

Weiner, R. D. (1986a). Minimizing therapeutic differences between bilateral and unilateral nondominant ECT. Convulsive Therapy, 2, 261-265.

Weiner, R. D. (1986b). Electrical dosage, stimulus parameters, and electrode placement. Psychopharmacology Bulletin, 22, 499-502.

Weiner, R. D. and Coffey, C. E. (1988a). Indications for use of electroconvulsive therapy. In: Francis, A. J. and Hales, R. E. (Eds.): Review of Psychiatry, Vol. 7, Washington, D. C. : American Psychiatric Press, 438-481.

Weiner, R. D. and Coffey, C. E. (1988b). Current contrast vs. constant voltage ECT devices. British Journal of Psychiatry, 152, 292-293.

Weiner, R. D. and Coffey, C. E. (1989). Comparison
of brief-pulse and sine wave ECT stimuli. Convulsive Therapy, 5, 181-185.
Weiner, R. D., Rogers, H. J., Davidson, J. R. and Kalm, E. M. (1986a). Effects of electroconvulsive therapy upon brain electrical activity. Annals of the New York Academy of Sciences, 462, 270-281.
Weiner, R. D., Rogers, H. J., Davidson, J. R. and Squire, L. R. (1986b). Effects of stimulus parameters on cognitive side effects. Annals of the New York Academy of Sciences, 462, 313-325.
Welch, C. A. (1982). The relative efficacy of unilateral nondominant and bilateral stimulation. Psychopharmacology Bulletin, 18, 68-70.
Widopalm, K. (1987). Comparison of frontofrontal and temporoparietal unilateral nondominant ECT: A retrograde memory study. Acta Psychiatrica Scandinavica, 75, 441-444.
Zimmerman, M.; Coryell, W.; Pfohl, B.; Corenthal, C. and Stangl, D. (1986). ECT response in depressed patients with and without a DSM III personality disorder. American Journal of Psychiatry, 143, 1030-1032.