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PREDICTING RESPONSE TO METHYLPHENIDATE (RITALIN) IN HYPERACTIVE BOYS

by
Terry Joyce Kathleen Brandts

Thesis presented to the School of Graduate Studies of the University of Ottawa as partial fulfillment of the requirements for the degree of Master of Arts

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CURRICULUM STUDIORUM

Terry Joyce Kathleen Brandts was born on February 25, 1955, in Ottawa, Ontario. She received the Bachelor of Science degree with Great Distinction from McGill University in 1977.

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ABSTRACT

The goal of this study was to explore the utility of a number of variables in the prediction of response to methylphenidate treatment in hyperactive boys. A double-blind crossover design was employed. The 96 boys (aged 6 to 14 years) received methylphenidate and placebo in one of two orders: Drug-Placebo-Drug or Placebo-Drug-Placebo. Response to methylphenidate was evaluated employing the Continuous Performance Test (errors of omissions and errors of commission), the Matching Familiar Figures Test (latency and number of errors), Conners' Parent Symptom Questionnaire Impulsive-Hyperactive scale, and Conners' Teacher Rating Scale Hyperactivity scale. Fourteen definitions of response were derived from these measures, and ten of them were employed as dependent variables in the subsequent analyses. Two sets of independent variables were employed to predict response to treatment. These were (1) diagnosis on a binary classification scheme of brain dysfunction - no brain dysfunction and learning difficulty - no learning difficulty, and (2) neuropsychological test factor scores.

There was a higher percentage of responders in the brain dysfunction group than in the no brain dysfunction group, and in the learning difficulty group than the no learning difficulty group. However, Chi-squared (χ^2) analysis of these variables failed to reach significance. Discriminant

function analyses utilizing neuropsychological test factor scores as predictors of response, and subsequent one-way analyses of variance of the factor scores, and t-test analyses of the actual test variables involved provided evidence of a significant relationship between neuropsychological test scores and response defined in terms of certain measures of attention. Responders were found to perform more poorly on neuropsychological tests than nonresponders. These results were interpreted as reflecting a relationship between neuropsychological impairment and response to methylphenidate.

CHAPTER I

INTRODUCTION

The present study was concerned with the prediction of response of hyperactive boys to treatment with methylphenidate. It has been recognized in the literature that not all hyperactive children respond to stimulant drugs sufficiently well to warrant the continuance of this particular method of treatment for them. A number of studies have attempted to predict response to stimulant drugs, in an effort to provide information that would lead to drug treatment only for those children who would be most likely to benefit from it. Two of the problems involved in studies of this nature are arriving at a suitable definition of response to treatment, and finding appropriate predictors of that response. These two issues have been addressed in the present study, the goal of which was to explore the utility of the following variables in predicting response to methylphenidate: diagnosis of presence or absence of brain dysfunction and learning difficulty and neuropsychological tests.

Chapter I of this thesis reviews the following background information about hyperactivity: terminology involved and clinical picture presented; prevalence; history and prognosis; treatment intervention; pharmacology, dosage, and drug effects of methylphenidate; and methodology of treatment intervention studies. This is followed by a

review of the different ways response to treatment has been defined in the literature and a review of studies employing various predictors of response. Chapter I concludes with a statement of the issues under investigation in the present study.

The methodology of the present study, including description of subjects, the assessment measures employed as independent and dependent variables, the procedure, and the data preparation is presented in Chapter II. Chapter III presents the analyses employed and the results of this study. These results are discussed in Chapter IV, which concludes with comments on the present study and suggestions for future research.

Background Information

Terminology/Clinical Picture

Hyperactivity is a common presenting problem seen among children referred to child guidance clinics and related facilities (Cantwell, 1977; Coleman, 1976, pp. 535-538; Trites, 1979a). A satisfactory definition of hyperactivity appears to be lacking at present (Kinsbourne & Swanson, 1979; Lahey, Stempniak, Robinson & Tyroler, 1978; Trites, 1979a), making criteria for diagnosis and/or inclusion of subjects in research studies vary with different clinicians and experimenters (Barkley, 1976; Douglas, 1972; Rie, Rie, Stewart & Ambuel, 1976; Trites, 1979b; Wolraich, 1977).

The terms "minimal brain damage", "minimal brain dysfunction", "hyperactivity" and "hyperkinesis" have often been used interchangeably, leading to much confusion in the literature. These terms have been used in different ways by different investigators. As a result, "the same children end up being described in different terms, and different children by the same terms" (Cantwell, 1977, p. 524). Because brain damaged children are often hyperactive, brain injury of some sort was often assumed to underlie the behavior of hyperactive children (Douglas, 1972; Dubey, 1976; Millichap & Johnson, 1974; Sroufe & Stewart, 1973; Trites, 1979a). Hence the origin of terms such as minimal brain dysfunction (MBD). Clements and Peters (1962) provided a list of a number of characteristics associated with what they termed "MBD", which proved to have considerable influence on subsequent studies involving hyperactive children. These characteristics were: (1) specific learning deficits, (2) perceptual-motor deficits, (3) general coordination deficits, (4) hyperkinesis, (5) impulsivity, (6) emotional lability, (7) short attention span and/or motor distractibility, (8) equivocal neurological signs and (9) borderline abnormal or abnormal EEG.

The term MBD carries with it a number of implications, the first being that cerebral dysfunction is present and presumably plays a causative role in the behavioral manifestations of so-called MBD. This is held to be the case

even though present methods of investigation may not be able to demonstrate this brain dysfunction (Benton, 1973; Cantwell, 1977). Subtle manifestations of brain dysfunction are thus believed to be involved in the hyperactivity of many more of these children than has currently been demonstrated. Dubey (1976), addressing this issue, suggests that "an assumption of organicity in the absence of clear indicators is unwarranted" (p. 365). He concludes from his review of organic factors in hyperactivity that "the evidence taken as a whole does not strongly support the notion that organic factors play a significant role in the behavior problems of most hyperactive children" (p. 362). That is not to say that organicity does not play a significant role in the problems of some hyperactive children, a point Dubey readily concedes. However, due to the present uncertainty about the role of brain dysfunction in hyperactivity, the term MBD does not appear to be particularly appropriate.

The second implication of the term MBD stems from the adjective "minimal". This adjective reflects the assumption that the more severe the behavioral manifestation, the more severe the underlying brain pathology. Hence, since the behavioral manifestations of MBD are relatively mild (for instance, as compared to those involved in mental retardation of cerebral palsy), the underlying brain dysfunction must also be mild (Benton, 1973). Benton (1973), after reviewing the role of brain damage on behavior (e.g., in ablation

studies in animals, cases of aphasia, and hemispherectomy patients) concluded:

> This mass of evidence points to the fact that cerebral lesions in children must either be quite extensive, or have specific disorganizing functional properties in order to produce important behavioral abnormalities. It follows, I think, that if the behavioral deviations defining MBD are to be ascribed to brain damage or dysfunction, then that damage or dysfunction can hardly be minimal in character (p. 30).

Further problems with the term MBD emerge with the issue of learning disabilities. To illustrate: Knights and Hinton (1969) studied the effects of methylphenidate on behavior and motor skills in 40 children diagnosed as MBD. Four chief presenting complaints were used as criteria for MBD and hence inclusion in the study. These were: (1) "hyperactive, poor attention span, distractible", (2) "reading, spelling, arithmetic problems", (3) "generally slow progress, failure" and (4) "clumsy, poor coordination" (p. 644). The term MBD seems to serve as a catch-all for what are potentially four separate and distinct groups of difficulties. Hyperactivity, school difficulty, and clumsiness are all grouped together under one term. Of relevance here is Rie et al's (1976) conclusion: "Children selected on the basis of both hyperactivity and learning disabilities may be unjustifiably regarded as representative of either population" (p. 259). To this could be added, that children selected on the basis of any one of the four presenting complaints above, could be

unjustifiably regarded as representative of the others, under the term MBD. Hence studies employing the criteria of MBD for subject selection, may have such a diverse group of children so as to mask any systematic results that may apply to the different groups of children. Rie et al (1976) found little to support "the presumed coexistance of hyperactivity, organicity, and learning disorders" in their sample of underachieving children (p. 259). This finding supports the suggestion that finer distinctions of symptoms than those offered under the diagnosis of MBD are needed when choosing subjects for research. Clinical implications are present as well. If the best treatment for each child is to be found, the clinician must be able to recommend a treatment that has been found useful for other children with the same kinds of problems. The treatment interventions for a hyperactive child and a child with learning disabilities are not necessarily the same, as might be implied were both these types of problems viewed as variants of MBD.

To recapitulate: (1) Available indices of brain dysfunction have not found it to play a significant role in the behavior problems of <u>most</u> hyperactive children. (2) If brain dysfunction, detectable by current methods, or not, is an important factor, whether this brain dysfunction is minimal or more severe, as Benton (1973) suggests, remains unanswered as yet. (3) Hyperactivity and learning disability are often independent of each other, and to

include both under the same rubric has presented subject selection problems in research and diagnostic tangles in clinical practise. This list by no means exhausts the problems encountered with the term MBD, but considerations like the preceding have led to a move away from the MBD terminology to that of simply "hyperactivity", (which is not without problems of its own, however; i.e., confusing the term "hyperactivity" with the single symptom of motor over-activity).

The symptoms of motor over-activity, distractibility and short attention span, impulsivity and excitability have been consistently reported in the literature (Conners, 1970; Conners & Webb, 1979; Kløve & Hole, 1979; Stewart, Pitts, Craig & Dieruf, 1966; Werry, Minde, Guzman, Weiss, Dogan & Hoy, 1972) and may be considered to be the "cardinal symptoms" of hyperactivity (Cantwell, 1977). Other symptoms that are often, but not necessarily associated with hyperactivity are aggression and antisocial behavior, cognitive and learning disabilities, depression and low self-esteem (Cantwell, 1977). According to Klein and Gittelman-Klein (1971) hyperactivity is characterized by the relatively high intercorrelation between the different symptoms described above, but each symptom in itself is neither sufficient nor necessary for establishing the diagnosis of hyperactivity. Loney, Langhorne and Paternité (1978) speak on similar terms to Cantwell's (1977) when they describe primary or core symptoms (e.g. motor overactivity

and inattention) and secondary symptoms (e.g. self-esteem deficit and delinquent behavior). Douglas (1972) has argued for attention deficits and impulsivity, i.e. the inability to "stop, look and listen" as the identifying characteristics of hyperactivity, with other symptoms as adjuncts, present in some, but not all hyperactive children.

Clearly, hyperactivity is not a unitary disorder in terms of symptoms, or in terms of etiology. The view of hyperactivity as being the result of different causative agents in different children (Dubey, 1976; Lambert, Windmiller, Sandoval & Moore, 1976), the "final common pathway for a wide variety of possible etiologies" (Ferguson & Pappas, 1979, p. 62), has become widely accepted. With this view of diverse symptomotology and etiology have come a number of approaches to subgrouping hyperactive children. For example: Fish's (1971) diagnostic categories; Rutter, Shaffer and Shepard's (1977, p. 530) four subcategories, as presented to the World Health Organization; Conners' (1971, 1972a) profile types; Loney, Langhorne and Paternite's (1978) two binary dimensions of hyperactivity and aggression; Lahey et al's (1978) separation of hyperactive from learning disability groups; and Ferguson and Trites' (1979) two binary dimensions of learning difficulty and brain dysfunction. Many factors are undoubtedly involved in the overall picture of hyperactivity for different children, i.e., personality variables, family variables, organicity, learning difficulty, conduct disorder etc. and subgrouping can take into account

different combinations of these variables. The utility of these subgroupings rests with their treatment implications, which provides the rationale for the present study.

Prevalence

The estimates of the prevalence of hyperactivity vary widely with the criteria for diagnosis, methods of investigation and population studied. Studies using rating scales tend to give higher prevalence estimates than those using direct observation (Cantwell, 1977). It has been estimated that perhaps 4 to 6% of all school-aged children are hyperactive and 50% of all childhood behavior problem referrals are for MBD or hyperactivity (Sandoval, 1977; Stewart, et al, 1966; Wender, 1971). Using a criterion of 1.5 or more on the Conners' Teacher Rating Scale (TRS) Hyperactivity factor, 22% of boys attending regular school were identified as being hyperactive, and a criterion of 1.8 or more identified 11% of boys attending regular school as being hyperactive (Trites, 1979b). Although these estimates may vary considerably, there is no question that a significant proportion of school-aged children, especially boys, are affected.

History and Prognosis

Whereas early investigators believed that the hyperactive child outgrew his symptoms, it now appears that

although the symptom of overactivity may diminish with age, the prognosis for untreated hyperactive children may be quite poor (Cantwell, 1977). Follow-up studies of children treated with stimulant drugs have not been encouraging so far, either (Barkley, 1977; Wolraich, 1977). Hyperactive children often encounter social and educational difficulties (Rie et al, 1976) which seem to persist. Low self esteem, poor self-image, depression and a sense of failure are common, according to Cantwell (1977). Hyperactive children may be at risk for alcohol abuse as well as other behavioral difficulties (Blouin, Bornstein & Trites, 1978a,b). Perhaps such discouraging results can be explained by limited treatment approaches, and poor matching of individual children to the treatment program best suited to each child.

Treatment

Treatment approaches to hyperactivity include drug intervention (Barkley, 1977; Wolraich, 1977), diet control (Tryphonas, 1979), behavior modification techniques (Mash & Dalby, 1979), and individual psychotherapy (Cantwell, 1977), among others. The present review will focus on stimulant drugs as a treatment approach.

Since Bradley's (1938-1939) report on the effectiveness of stimulant drugs in the treatment of children's behavior disorders, much effort has been directed at furthering this investigation, especially with children described as MBD or

hyperactive. Drug treatment is the easiest, least time consuming, and for the previous two reasons, the most frequently used intervention technique with hyperactive children (Cantwell, 1977). Millichap (1973) suggested that:

> The ideal drug for treatment of children with MBD should control hyperactivity, increase the span of attention, reduce impulsive and aggressive behavior, and have measurable beneficial effects on visual and auditory perception, reading ability, and coordination, without inducing insomnia, anorexia, drowsiness or other more serious toxic effects (p. 321).

Millichap (1973) concluded that methylphenidate is the treatment of choice (although, even so, it does not do all that his "ideal drug" should do). For those children who develop tolerance to methylphenidate or show no improvement, dextroamphetamine (d-amphetamine) would be the second choice. Anorexia, insomnia, headache, stomachache, nausea, tearfulness, and pallor are common side effects of both these stimulant drugs (i.e., methylphenidate and d-amphetamine), but anorexia and insomnia seem to be more frequent and more severe with d-amphetamine than with methylphenidate (Cantwell, 1977). D-amphetamine is also reported to inhibit weight gain more than methylphenidate (Safer, Allen & Barr, 1972) and to suppress height gain (Safer & Allen, 1973). The choice of methylphenidate over d-amphetamine is reflected in the number of recent studies employing the former.

A thorough, recent review of the literature on stimulant

drug therapy with hyperactive children (110 studies) (Barkley, 1977) supports the claims of a high degree of effectiveness of stimulant medication in improving attention span, reducing distractibility, restlessness and overactivity, and reducing impulsivity. Although it seems to follow that this kind of behavioral improvement should facilitate academic performance, a review of academic outcome studies has not supported this contention (Barkley & Cunningham, 1978). These authors concluded that the major effects of stimulants appears to be an improvement in classroom manageability, rather than an improvement in academic performance. Rie and co-workers (1976) suggested that with drug treatment, there is a reduction not only of the behaviors that interfere with learning, but also of the desirable behaviors that facilitate it (spontaneity, curiosity, initiative and interest). Children with learning disabilities only, would not appear to benefit from drug treatment, and for those hyperactive children with learning problems whose behavior improves on drugs, but whose academic work is still behind, remedial help is needed.

The response of hyperactive children to stimulant drugs has been called "paradoxical" since these children appear to become more quiet rather than stimulated when treated with these drugs. It was widely believed that amphetamines and methylphenidate served to stimulate adults, or normal children, but that these drugs somehow worked in the opposite

way for hyperactives. These views have been questionned recently as having no scientific data to support them (Axelrod & Bailey, 1979; Cantwell & Carlson, 1978; Kløve & Hole, 1979; Werry, 1976). The hypothesis of equivalent drug effects for adults, normal and clinical groups of children, including hyperactivity, is gaining support in the literature. The pharmacological effect of stimulant drugs seen in hyperactive children is largely one of heightened efficiency and alertness, which is seen in normal adults given comparable doses of stimulants, as well (Cantwell & Carlson, 1978; Rapoport, Buchsbaum, Zahn, Weingartner, Ludlow, & Mikkelsen, 1978; Werry, 1976). Safer and Allen (1976) state that whereas stimulants can produce euphoria in adults, this does not occur in children. Cantwell and Carlson (1978) criticize this opinion, stating that little research has been conducted on this aspect of drug effects, and that what research has been done does suggest, if not euphoria, some positive mood change in some children taking stimulant drugs. (Tearfulness, sadness, and irritability are other mood changes reported for some children.) "Mood effects" are likely related to dosage.

The view that stimulants do not effect hyperactive children in a unique manner compared to other pediatric populations is suggested by the fact that children selected for treatment on the basis of teacher recommendation alone, delinquent behavior without motor restlessness or attentional

deficit, and learning disorder without behavioral disturbance, all show similar short-term improvement in attention, and decrease in restless-impulsive behavior when taking stimulants (Rapoport et al, 1978). Positive response to stimulants in hyperactive children who respond to stimulants is directly dose related; a "responder" that is overdosed or underdosed will show less than optimal improvement (Kinsbourne & Swanson, 1980). Presumably, children in other clinical groups and normal children who are responders would have an optimal dose, as well.

In a study of 44 normal prepubertal boys, Rapoport et al (1978) reported that d-amphetamine decreased motor activity and improved attentional performance (faster reaction time, superior memory, and improved vigilance). There was also an increase in task-related descriptive speech, and a decrease in speech that was not task-related. These results are consistent with those reported for hyperactive children receiving stimulant drugs. Neither self-rated nor observer rated mood effects were significant. They concluded: "These results indicate that models of MBD which assume that patients have an altered behavioral response to stimulants compared to normal children are not appropriate for the hyperactive child syndrome" (p. 562). A study of the effects of d-amphetamine on language performance in hyperactive and normal boys (Ludlow, Rapoport, Bassich, & Mikkelsen; 1980) found that d-amphetamine had a beneficial effect on their

language performance and improved the linguistic complexity of their speech, as well. D-amphetamine reduced impulsive speech in both groups. Normal subjects also improved in speech fluency, and task-directed speech. They concluded that "the greater enhancement of performance in the normal subjects implies that stimulant administration can benefit the cognitive performance of subjects who are without deficits in selective attention, inhibition, or cognition" (p. 204).

In contrast to the above, Swanson & Kinsbourne (1976) found that while their 32 hyperactive subjects being treated with methylphenidate did perform better on a paired associate learning task, their 16 non-hyperactive subjects, who were also being treated with methylphenidate, did not demonstrate this facilitated performance.

The fact that some normal children have been shown to respond favourably to stimulants raises a number of questions relevant to the study of response in hyperactive children, For instance, would the percentage of responders and nonresponders to stimulants in normal children be comparable to the data for hyperactive children? Would extended treatment maintain the behavioral and attentional changes shown, or would normal children return to their pre-drug levels? Could response be predicted for normal children, and would the same kinds of predictors apply to the hyperactive population? How would the "optimal" dose for normals compare

to that of hyperactives? Given that some normal children do respond to stimulants makes it perhaps more surprising that some hyperactives do not. Very little research has been done with normal children and stimulant drugs for obvious ethical reasons. It seems that answers regarding who responds and why will most likely be coming from continued study of children whose everyday life may be benefitted from drugs, that is, hyperactive children or perhaps other "problem" children.

Methylphenidate: Pharmacology

> "Methylphenidate is a piperidine derivitive with a structural relationship to amphetamine ... It is a mild central nervous system stimulant with mental effects more prominent than motor effects. The pharmacologic properties are essentially those of amphetamine. It produces central nervous stimulation, an increase in arousal level, stimulation of smooth muscle and cardiovascular responses, and stimulation of the central reticular formation and the respiratory center (White, 1977, p. 8).

Almost all of the drug is metabolized with little appearing unchanged in the urine. Methylphenidate disappears so rapidly from plasma after oral administration that the plasma half-life is difficult to determine. Measuring a 20 mg dose of C^{14} methylphenidate revealed peak levels in adults at about two hours, with a half-life of two to seven hours. The C^{14} consisted of metabolites, almost all of which appeared in the urine by 72 hours (Faraj, Isreali, Perel,

Jenkins, Holtzman, Cocinill, & Dayton, 1974).

Methylphenidate: Dose Response and Time Action Relationships

Werry and Sprague (1974) found that hyperactive children's performance on a picture recognition test was best at a daily dosage of .3 mg/kg, but that long term behavioral changes measured by the Conners' Parent Symptom Questionnaire (PSQ) required .7 to 1 mg/kg daily for optimal response. Sprague and Sleator (1977) showed that for hyperactive children, a peak enhancement of learning occurred with a dose of .3 mg/kg daily, and that a decrement in learning occurred with a higher dose. Social behavior showed the greatest improvement when the dose was 1 mg/kg daily.

In a study measuring the effect of methylphenidate on hyperactive children's performance on a paired associate learning task, Swanson, Kinsbourne, Roberts, and Zucker (1978) found that responders reached their peak of accuracy between one and two hours after drug administration, and that the effect was almost completely over after four hours.

Methylphenidate: Recommended Dosage

The recommended dosage of methylphenidate varies considerably. Safer and Allen (1976) state that the average daily dose of methylphenidate is 20 to 30 mg. The dose cited in American papers and which is recommended by the 1975 report of the American Academy of Pediatrics (Council on

Child Health) is 2 mg/kg daily (Werry, 1976). This can mean a dose of as much as 80 mg a day for the larger child. Werry (1976) commented that this dose "is mis-stated to appear essential when in fact it should be regarded as highly exceptional" (p. 83). The Compendium of Pharmaceuticals and Specialties (1980), published by the Canadian Pharmaceutical Association, gives the following dosage recommendations:

> "In children with MBD, start with small doses (e.g. 5 to 10 mg, three times daily), with weekly increments of 5 to 10 mg in the daily dosage. Dosage should be individualized on the basis of factors such as age, body weight, and individual response. Daily dosage above 60 mg is not recommended" (p. 500).

The work of Sprague and Sleator (1977) mentioned above, suggests that on a group basis, a daily dose of .5 mg/kg should show positive effects for both cognitive ability and behavior. Due to the fact that individual response is so very idiosyncratic (Cantwell & Carlson, 1978; Kinsbourne & Swanson, 1979) the optimal dose for an individual cannot be worked out on a mg/kg basis, and careful individual titration is necessary (Kinsbourne & Swanson, 1979). (However, for research studies of groups of children, standardized dosages (i.e., mg/kg) are necessary to avoid the confounding of dosage with individual subject variation. Further discussion of this issue follows in the next section.) With research showing that in many cases smaller doses are sufficient, recommended doses appear to be becoming more conservative.

Methodology of Treatment Intervention Studies

Before one can draw inferences and conclusions from research, it is necessary to insure that the methodology of the research under consideration is acceptable. Sprague and Werry (1971) and Sprague (1979) presented what they considered to be minimal requirements for sound research into treatment intervention. Much of the research in the area of stimulant drug treatment for hyperactive children has fallen short of these requirements, limiting the conclusiveness of these efforts. Sprague and Werry's requirements are the following: (1) placebo control, (2) random assignment of subjects, (3) double-blind conditions, (4) standardized dosages, (5) standardized evaluations, (6) appropriate statistical analysis and (7) comparitive efficacy. Placebo control and double-blind conditions are essential to control for expectancy effects. Random assignment of subjects is necessary to eliminate bias in the sample, and if a matched pair design is used, the member of each pair should be assigned randomly to the sequences of treatment to control for order effects. Standardized dosages, a condition that few of the studies reviewed met, are necessary, because without standardized dosages there is a confounding of dosage with individual subject variation, and it is impossible to separate the two. The work of Sprague and Sleator (1977) suggests that on a group basis a daily dosage of .5 mg per kg of body weight should lead to improvements in cognitive

abilities and social behavior. Even if this is not the optimal dose for a particular subject, it should still be sufficient to produce a detectable improvement in those subjects who are responders (Ferguson & Trites, 1980). Standardized evaluations require that the measure used must have been used before and/or empirical information on basic reliability and validity must be available. With regard to statistics, the statistics chosen should be appropriate to the study and the basic assumptions of any particular statistical test must be respected. In studies on treatment evaluation Sprague (1979) requires that any new treatment being assessed must be compared to current accepted treatments in terms of efficacy and cost/benefit.

Werry and Sprague (1974) have pointed out the advantages of using a crossover design. Not only does it control for differences between subjects, it allows for fewer subjects, and since each child receives each condition, useful clinical information is available for the treatment of each child.

The Need for Prediction

Although stimulant drugs are most frequently the treatment of choice for hyperactive children, it is acknowledged in the literature that not all hyperactive children respond, or respond favourably to stimulant medication (Barcai, 1971; Barkley, 1977; Rapoport, Quinn,

Bradbard, Riddle & Brooks, 1974; Safer & Allen, 1976; Weiss, Minde, Douglas, Werry & Sykes, 1971). Identifying the variables which discriminate responders from nonresponders would allow the clinician to better decide who should or should not be treated with stimulants, and would provide the scientist with information that may help explain the etiology and pathophysiology underlying the behavior in different groups of hyperactive children. Before discussing prediction of response, however, the question of how response to medication is defined must be addressed. This review will first cover dependent or criterion variables, that is, how response has been defined in the literature. Following this discussion will be a review of studies predicting response to stimulant drug treatment, using a variety of predictor variables.

Defining Response to Stimulant Drug Treatment

Whereas many earlier studies (e.g. Conrad & Insel, 1967; Levy, 1966) simply employed an investigator's judgment of response, the subjectivity of this kind of criteria is not acceptable in present day research studies. Standardized evaluation measures are clearly required. Even with more objective, or at least quantifiable measures, for example, parent and teacher rating scales, single measures can be misleading, because the behavior of hyperactive children (or any children, for that matter) differs in different

environments (Langhorne, Loney, Paternite & Bechtoldt, 1976). It is necessary to measure objectively a variety of specific variables to determine how the hyperactive child's behavior is or is not affected by stimulants (Barkley, 1976).

So far, the majority of drug research with hyperactive children has used some type of rating scale completed by parents, teachers, clinicians, or independent raters (Barkley, 1977; Wolraich, 1977). Reviews of outcome studies by Barkley (1977) and Wolraich (1977) vouch for the sensitivity of behavior rating scales to drug treatment effects. The Conners' Parent Symptom Questionnaire (PSQ) (Conners, 1970) and the Conners' Teacher Rating Scale (TRS) (Conners, 1969) have been used frequently in recent studies.

Conners, Taylor, Meo, Kurtz and Fournier (1972) in a double-blind study of 81 children grouped into pemoline, d-amphetamine, and placebo groups, found that both the PSQ and TRS hyperactivity scales were sensitive to drug effect. Arnold, Wender, McCloskey and Snyder (1972) in a double-blind crossover study of 11 subjects who received levo-amphetamine, d-amphetamine and placebo, found both the PSQ and TRS hyperactivity scale results significantly different for drug compared to placebo. Rapoport et al (1974) compared (double-blind) 76 subjects grouped into imipramine, methylphenidate and placebo groups, and found a significant drug effect using both PSQ and TRS hyperactivity scales. Conners (1972a) in a double-blind uncrossed study of 75

subjects receiving either methylphenidate, d-amphetamine, or placebo, found a significant drug effect on the hyperactivity scale of both the TRS and PSQ. Finnerty, Soltys and Cole (1971) in a double-blind uncrossed study of 20 subjects found no significant drug effect for d-amphetamine on the PSQ hyperactivity scale. Werry and Sprague (1974) in a double-blind crossover study of 37 subjects receiving placebo and three different dosages of methylphenidate found a significant drug effect on the TRS hyperactivity scale but not on the PSQ hyperactivity scale. Huestis, Arnold and Smeltzer (1975) in a double-blind crossover study of 18 subjects receiving placebo, caffeine, methylphenidate and d-amphetamine found a significant drug effect for methylphenidate and d-amphetamine and a significant caffeine vs. drug effect using the TRS hyperactivity scale. The less successful rate found for the parent scale in these and other studies, as compared to the teacher scale, can probably be explained by several factors. The home situation is usually less task demanding and has a lower adult/child ratio compared to the classroom environment (Wolfaich, 1977). Thus situations in which the child's hyperactive symptoms usually manifest themselves, e.g. when he has to sit still and work on an assignment, when he has to wait his turn and share an adult's attention with many other children, etc., occur with greater frequency in the school than the home situation. When medication is given only in a morning dose and not on

weekends, as in the studies above by Finnerty et al (1971) and Werry and Sprague (1974), the drug effect may be worn off by the time the child comes home from school.

Werry and Sprague (1974) concluded that teacher ratings were "stable, sensitive, and informative, and were the best source of information for the assessing drug effect" (p. 17). Behavior rating scales have the advantage of giving a global impression, in contrast to direct behavioral observation, which can only look at a small segment of behavior at a time (Wolraich, 1977). Their ease of administration give them a practical value above many other measures. However, they are subjective, and their reliability depends on who is doing the rating. Barkley (1977) criticized the rating scales on three grounds. First, there are simply too many rating scales in use with little regard to their construction and relationship to other scales already in use. The trend towards using Conners' scales is encouraging in reference to this first problem. Conners (1970) has shown high congruence between his rating scale symptom clusters and psychiatric diagnosis based on more extensive data. As more studies employ the same measures, more meaningful comparisons and conclusions can be drawn from the literature. Barkley's second (1977) criticism concerns the lack of information with regard to reliability of these ratings scales, either test-retest or inter-rater. A recent report by Trites (1979b) sheds some light on this issue. One thousand, one hundred and

fifty-four school children were each rated by two of their teachers who knew them well. The two teachers were asked not to consult with each other regarding their ratings of a particular child. High inter-rater agreement for the hyperactivity scale of the TRS was achieved. In addition, for 747 cases, ratings were obtained from the child's teacher and a trained independent observer who spent half a day in the child's classroom. The results here showed substantial differences between the ratings made by the teacher and the external rater. Wolraich's (1976) comment, above, about behavior rating scales is relevent here. He applauded rating scales for giving a global impression, in contrast to direct behavioral observation, which can only look at a small sample of behavior at a time. The teacher's rating of a pupil she deals with every day would appear to be of a global nature, whereas the rating scale completed by an external observer would appear to more closely resemble direct behavioral observation. Barkley's (1977) third issue involves validity. There is little information available on the behavior rating scales' relationship to the constructs they purport to measure e.g. aggression, attention, impulsivity. Thus, Barkley (1977) recommends that future drug studies use objective measures of the constructs under investigation in addition to the rating scales in order to clarify the relationships among these measures.

A number of tests and measures have been used to assess

a variety of behavioral and psychological constructs. For instance: intelligence tests, achievement tests, measures of impulsivity and attention, measures of drawing and copying ability, and measures of activity level. Barkley (1977) has presented a thorough review of these measures, hence the present review will focus on measures of impulsivity and attention span, which have particular relevance to the present study. Before reviewing some of these studies, however, a few comments will be presented regarding these other measures. Given the inconsistency of findings in the area of intelligence tests, achievement tests, and tests of drawing and copying ability, it is most likely that the positive results reported by a few studies were due to increased concentration or attentiveness rather than to changes in the various abilities during drug treatment (Barkley, 1977; Conners, 1971b; Conners, 1972b; Douglas, 1972; Weiss et al, 1971). While stimulant drugs appear to reduce activity level, such findings are less predictable than those of studies employing measures of attention. The changes in activity level observed appear to depend on a number of factors such as the type of setting (e.g., free play, or structured setting), type of activity measured (e.g., wrist, ankle, locomotor, etc.), and the type of instrument used to assess the type of activity (e.g., wrist actometers, pedometers, stabilemetric cushions, grid-marked playrooms, etc.) (Barkley, 1977; Barkley & Ullman, 1975;

Shaffer, McNamara & Pincus, 1974).

Attention span and impulsivity have been assessed by a number of tests and measures. These include the Matching Familiar Figures test (MFF) (Kagan, Rosman, Day, Albert & Phillips, 1964) and the Continuous Performance Test (CPT) (Rosvold, Mirsky, Sarason, Bransome & Beck, 1956). While these tests may measure more than just attention span, it has been suggested that concentration or attention span form a common source of variance for these tests (Barkley, 1977; Douglas, 1972).

The CPT has proved informative in studies with hyperactive children. Sykes, Douglas, Weiss and Minde (1971) studied the performance of 40 hyperactive and 19 control children on the CPT. The hyperactive children demonstrated impaired performance when compared to the control group. Subsequently, the hyperactive group were assigned randomly to either methylphenidate or placebo, and a double-blind procedure was used to assess drug effects. The methylphenidate group showed significant improvement in performance compared to the placebo group. The results of this study were replicated by Sykes, Douglas and Morgenstern (1972) using 24 hyperactive and 20 control children. For the drug part of the study, each of the 24 hyperactive subjects acted as his own control in a double-blind crossover design with methylphenidate and placebo. Weiss et al (1971) in a double-blind study with 26 hyperactive children receiving

methylphenidate and 26 hyperactive children receiving placebo, found that the methylphenidate group increased in correct responses and decreased in errors on the CPT. Conners (1972a) in a double-blind uncrossed study of 75 subjects receiving either methylphenidate, d-amphetamine, or placebo, found the CPT to be sensitive to drug effects. However, Conners et al (1972), in a double-blind noncrossed study of 81 subjects receiving either magnesium pemoline, d-amphetamine, or placebo, did not find a significant drug effect on the CPT. Werry and Aman (1975) found drug to improve CPT scores in a double-blind crossover study of 24 subjects receiving methylphenidate, haloperidol, and placebo.

Kagan (1965) has demonstrated that one factor contributing to differences in cognitive functioning is the child's "cognitive tempo, his habitual speed of decision making in situations of high response uncertainty" (Campbell, Douglas & Morgenstern, 1971). Kagan has called this dimension "reflection-impulsivity". Campbell et al (1971) compared 19 hyperactive and 19 matched control subjects and found that the hyperactives were more impulsive (i.e., had shorter latencies and more errors on the Matching Familiar Figures test (MFF) than the normal subjects. In a second study (Campbell et al, 1971), 22 hyperactive children each served as their own control in a double-blind crossover methylphenidate-placebo design. They found a significant

drug effect (i.e., increased latency, decreased errors) on the MFF. Rapaport et al (1974) in a double-blind noncrossed study of 76 subjects receiving either methylphenidate, imipramine, or placebo, found a significant methylphenidate vs. placebo and methylphenidate vs. imipramine effect on the MFF, and nonsignificant differences between imipramine and placebo. In a double-blind crossover study of eight subjects, Garfinkel, Webster and Sloman (1975) found that subjects performed significantly better on the MFF when on methylphenidate as compared to caffeine or placebo.

Gittelman-Klein and Klein (1975) investigated the issue of whether behavioral and psychometric changes were related in hyperactive children treated with methylphenidate. Eighty-six hyperactive children were assigned randomly to either methylphenidate or placebo group. The measures employed included mother's, teacher's and psychiatrist's global ratings of improvement, Conners' TRS and PSQ hyperactivity scales, psychologist's rating of cooperation and distractibility, WISC and WRAT, and CPT, among others. They did not find any meaningful patterns of related change between behavioral and cognitive indices used. It is not surprising that some of their measures, e.g., WISC and WRAT did not parallel behavior change, as this has been demonstrated by others, as discussed. Parents, teacher, and psychiatrist reports agreed on some measures, but not on others. Again the question is raised whether the child is

behaving differently in different situations, whether the three different raters are rating the same behaviors in the same way, or whether the scales are asking the same questions of the three raters.

In summary, a number of studies have found behavior rating scales and measures of attention to consistently discriminate between hyperactive and normal children, and to be sensitive to drug treatment. Effects on other tests and measures of cognition, intelligence, achievement, sensory or motor abilities, when observed, are likely to be due to increased attentiveness or concentration, rather than to significant changes in these various abilities (Barkley, 1977; Conners, 1971; Conners, 1972b, Douglas, 1972; Weiss et al, 1971). As far as behavior rating scales can tap into empirically demonstrable changes in attentional measures (which awaits confirmation) by giving a global impression of the child's functioning, they have clinical utility. Further study employing behavior rating scales and more objective measures of attention, as described above, would appear to be productive in assessing stimulant drug effects.

Predicting Response to Stumulant Drug Treatment

Much research has been involved with attempting to predict response to stimulant drug treatment. A variety of potential predictors have been investigated. Barkley (1976) reviewed studies employing the following types of predictor

variables: psychophysiological, neurological, familial, demographic/sociological, diagnostic category (e.g. Fish, 1971) parent/teacher/clinician behavior rating scales, cognitive, intelligence and achievement measures, and profile types (e.g. (Conners, 1971, 1972a)). The aim of the following review is to be selective and illustrative, rather than exhaustive, due to the voluminous amount of relevant literature. Certain predictor variables are of special interest to the present study, hence will receive more notice in the present review. The reader is referred to Barkley's (1976) thorough review of predictor variables for studies not reviewed here.

Psychophysiological studies of drug response gain their rationale from hypotheses regarding the arousal state of the hyperactive child and the effects of stimulant drugs on arousal. Electroencephalogram (EEG), evoked potentials, heart rate, Galvanic Skin Response etc., have been used in these studies as indices of Central Nervous System arousal. Regarding psychophysiological predictors, Barkley (1976) concluded:

> In summary, in the category of psychophysiological predictors, EEG, average evoked potentials, other EEG parameters, heart rate, heart rate variability, Electropupillogram, and free amphetamine recovery from urine, have been reported to discriminate good from poor drug responders. Of these variables, all but urine recovery of amphetamine probably bear some relationship to attention span (p. 337).

Conners' (1976) suggestion that any effects stimulant drugs have on arousal level are secondary to their main effect on attention would appear to offer support to Barkley's conclusions.

The relationship between familial variables and drug response has been investigated in a number of studies (Loney, Comly & Simon, 1975; Loney, Prinz, Mishalow & Joad, 1978; Weiss et al, 1971; Conrad & Insel, 1967; Schleifer, Weiss, Cohen, Elman, Cvejic & Kruger, 1975). Loney, Prinz, Mishalow & Joad (1978) did not find sufficient evidence to conclude that a relationship exists between parenting styles and response to stimulants. However, the authors of three of the earlier studies (Loney et al, 1975; Conrad & Insel, 1967; and Weiss et al, 1971) interpreted their results as indicating that responders to stimulant medication were more likely to come from homes where parents were competent, good managers of their children, and that the parents were more likely to have a good positive relationship with their children than were the parents of nonresponders. Perhaps at variance with this conclusion is the finding of Schleifer et al (1975) that mothers of hyperactive pre-schoolers who were good responders, were more "frustrated" and used more physical punishment. However the responders were also rated as more hyperactive at pre-testing than were the nonresponders, making the interpretation of these results less clear-cut. A problem with this kind of study is that familial predictors

are not as straightforward as more objective predictors. Another problem is the lack of standard measures, making comparison across studies difficult. Information on inter-judge reliability would appear to be essential in this kind of study, yet it was omitted in Loney et al's (1975) study. The direction of causality raises questions for interpretation, as well. Do drug responders create better parent-child relationships, or do children experiencing positive parent-child relationships respond more favourably to drug treatment? Certainly, there is room for additional study of familial predictors, and studies combining drug treatment and home management techniques would be a direction for further study.

Barkley (1976) concluded from his review of demographic/sociological predictors that race, sex and socioeconomic status do not appear to have predictive utility for drug response.

Fish (1971) in her article "The 'One Child, One Drug' Myth of Stimulants in Hyperkinesis", concluded that there are many types of hyperactive children and that stimulants are the drugs of choice for only some of them. Studies examining differences in response to stimulant drugs using children diagnosed according to Fish's classification scheme have not consistently found differences in stimulant response (Arnold, Huestis, Smeltzer, Schieb, Wemmer & Colner 1976; Werry & Aman, 1975).

Conners (1971, 1972a) correlated and factor analyzed a large number of psychological tests, rating scales, physiological measures and objective behavioral measures. This analysis yielded seven distinct profile patterns that accounted for a significant amount of drug treatment effects. Cross-validation of these profiles is necessary before their predictive utility can be ascertained (Barkley, 1976).

Several studies (e.g., Hoffman et al, 1974; Steinberg, Troshinsky & Steinberg, 1971; Werry & Sprague, 1974; Rapoport et al, 1974) have used behavior rating scale predictors in an effort to discriminate responders from nonresponders on such variables as impulsivity, hyperactivity, aggression, etc. These rating scale predictors do not appear to be consistent in predicting drug response (Barkley, 1976).

Considerable effort has been directed to using a variety of psychological tests to predict response to drugs in hyperactive children (e.g., WISC, Bender Gestalt, ITPA, Goodenough Draw-A-Man Test, the Primary Mental Abilities Test, etc. (Barkley, 1976). Most of these measures have not proven useful. Rie et al (1976) in a double-blind crossover study of 28 children treated with methylphenidate and placebo found WISC Full Scale and Performance I.Q.s to be predictive of improvement in parental ratings of attention. However, many other investigators have not found WISC scores to be useful predictors of drug response (e.g., Hoffman et al, 1974; Knights & Hinton, 1969; Rapoport et al, 1974;

Satterfield, Cantwell, Lesser & Podosin, 1972). The psychological measures that appear to have some predictive utility in discriminating responders from nonresponders all seem to have some relation to attention span (Barkley, 1976). For example, the following variables were seen to discriminate responders from nonresponders: reaction time (Porges, Walter, Korb & Sprague, 1975; Zahn, Abate, Little & Wender, 1975); Porteus Mazes (Epstein, Lasagna, Conners & Rodriguez, 1968), Kagan Matching Familiar Figures Test (Rapoport et al, 1974).

Neurological predictors, used to indicate presence and degree of organicity are of special interest to the present study and will be discussed in more detail. Werry et al (1972) from their review of a number of studies concluded that although many of the studies reviewed had methodological deficiencies "there is, nevertheless, a high degree of agreement that EEG abnormalities and certain neurological signs are more frequent amongst emotionally disturbed children in general, and hyperactive children, in particular" (p. 442). In their study of 20 hyperactive children compared to 20 neurotic controls and 20 normal controls, Werry et al (1972) found that the hyperactive children showed significantly more neurological abnormalities, principally minor neurological signs indicative of sensory-motor incoordination, but no differences in major neurological signs, EEG abnormalities, or medical history.

A brief review of studies that have used various criteria to investigate the predictive utility of organic factors in response to stimulant drugs follows. Conrad and Insel (1967) in a retrospective study (no placebo, or control group) of thirty-one children who had been placed on amphetamine therapy, concluded that children who responded positively to drug therapy were those who showed an "organic" background, positive parent child relationships, and absence of severe psychiatric problems in the parents. "Organic" classification was based on the presence of three or more of the following "hypertension or infection during pregnancy, premature or abnormal delivery; cyanosis or related problems at birth; childhood head injuries, convulsions; poor motor coordination, visual perceptual impairment; marked scatter on intelligence tests, positive neurological findings; abnormal EEG; diagnosis of chronic brain syndrome" (p. 96).

Epstein et al (1968) in a double-blind crossed study of ten children found that "organics" showed greater improvement on stimulant drugs (d-amphetamine) than nonorganics, and concluded that the "data strongly suggest that the group of hyperactive children is not a homogeneous one. Rather there are some with CNS damage whose response to d-amphetamine is one of dramatic improvement" (p. 146). "Organic" subjects in this study were so judged on the basis of "a detailed psychiatric and medical history, psychiatric interview with the child, psychologist's evaluation, diagnostic

questionnaire, and brief neurological examination" (p. 136).

Steinberg et al (1971) from their double-blind crossover study of 54 children concluded that two or more neurological soft signs or one or more hard neurological signs and a clearly manifest hyperactive syndrome "may be strongly predictive of a dramatic response to d-amphetamine" (p. 178). The neurological soft signs included "failure of the eyes to converge; spooning; awkward alternating movements of the upper extremities or tongue; head circumference 1.5 cm. above the standard deviation; motor overflow; mild pronator sign; head 1 cm. above two standard deviations with prowing and wide parietes; café au lait spots (5 cm. at largest); mild assymetry of the perioral musculature, diminished auditory acuity in right ear, mah pes cavus with mild hammer toeing" (p. 176). The hard signs included "bilateral esotropia; extensor response of the right toes; ptosis of the right eye; visual field defect in the right eye; different perception of colours by the right and left eyes" (p. 176).

Millichap and Johnson (1974) evaluated the response to methylphenidate in 28 children in a double-blind uncrossed (i.e. a drug and a placebo group) study and concluded that the beneficial effect of methylphenidate on hyperactivity was related to the level of motor activity before treatment, and the incidence of abnormal neurological signs. Patients with the greatest number of neurological signs tended to be the most active and showed the best response to the drug. The

neurological signs employed in this study were: "impairment of rapid alternating movement of forearms; impaired finger tapping; dyspraxic tandem gait; cortical sensory loss, mainly graphanathesia; impaired hopping; finger-to-nose incoordination; Babinski signs; speech disorder; involuntary movements, mainly choreiform, when arm held in outstretched position" (p. 131).

Satterfield, Cantwell, Saul, Lesser and Podosin (1973) in a study (no placebo) of 57 hyperactive boys found that the probability of a good response to stimulant drugs (methylphenidate) was correlated with the degree of evidence of brain dysfunction (obtained from EEG and neurological examination). Neurological abnormalities included "upper extremity fine motor incoordination, altered tonus or weakness; synkinesis or motor impersistence; hyperactive or asymetrical reflexes; choreiform movements or abnormal posturing of the hands and fingers; lower extremity nonequilabratory incoordination; altered tonus or weakness; dysarthria or infantile speech; equivocal plantar response; gait or equilibrium disorder; deviant hand preference; discriminitive sensory loss or perceptual disorder" (p. 39).

In contrast to the above studies, Knights and Hinton (1969) in an uncrossed double-blind study of 40 children found no differences in response to stimulant drugs (methylphenidate) between children with "physical findings or histories of probable damage" and those who had very little

evidence of impairment (p. 652).

Rie et al (1976) investigated response to stimulant drugs (methylphenidate) in 28 children in a double-blind crossover design. They found that drug induced behavioral changes occurred somewhat more often in children who were viewed as less organic. "Organic" here was defined on an "organicity scale" that included measures of"integrative synthesizing skills"; "perseveration"; "conceptual shifts"; "concrete thinking"; "word recall"; and "word misuse" (pp. 253-254).

It is difficult to compare these studies with each other for a number of reasons. One of the greatest problems arises due to the variety of ways in which "organicity" was defined. The criteria used to define organicity in these studies can be seen to originate from the following sources of information: (1) pregnancy and birth complications, (2) medical history (e.g. encephalitis, convulsions, head injuries, etc.), (3) EEG findings, (4) neurological examination findings (e.g. "soft" and "hard" signs) and (5) other (e.g. visual-perceptual impairment, Rie et al's (1976) "organicity scale"). Not only has organicity been based on different criteria in different studies, but information on the validity of any of these criteria, and comparison of hyperactives to other deviant groups and normal controls appears to be lacking for most of them. A fundamental criticism of these predictors concerns construct validity.

The relationship between any one of these predictors and brain dysfunction has not been delineated (Dubey, 1976; Satterfield et al, 1973).

Other problems with these studies include the different criteria used to define improvement (e.g., teacher ratings, clinical global judgment, psychological test scores); differences in drug types and dosages, and time on drug; differences in experimental design; and varying criteria for subject selection (Barkley, 1976; Wolraich, 1976). The problems arising from differences in subject selection procedures deserve special note. Studies using the criteria of MBD to select their subjects included a much broader range of patient symptoms than did those that used subjects selected on the basis of hyperactivity alone. Hyperactive children with clear evidence of brain damage are not held to be representative of hyperactive children in general, and recent studies have excluded them from their subject pool. Whereas some of the studies reviewed here did limit their subjects to those who showed no evidence of frank brain damage (other than the symptoms associated with MBD), other studies (e.g., Conrad & Insel, 1967; Epstein et al, 1968; Steinberg et al, 1971) have included children with evidence of probable brain damage (e.g., history of probable damage, head injury, encephalitis, convulsions, and diagnosis of chronic brain syndrome). As a result, comparisons among these studies are of limited value.

The studies employing "soft" neurological signs have not been consistent in the choice of signs to be used as criteria for brain dysfunction. Werry et al (1974) in a search of the literature in pediatric neurology and psychiatry, found reports on 140 neurological signs. This presents quite a variety of criteria to choose from. Had some consensus across studies been reached with regards to which neurological signs to employ, the results would have been greatly clarified. As they stand, each study reviewed has employed its own collection of neurological signs. Other problems with studies employing these neurological signs include the lack of efforts to establish inter-rater reliability, and the non-blind assessment of subjects (i.e., evaluating a child's neurological status without knowledge of his diagnostic status (hyperactive), Dubey, 1976)

The criticisms of lack of inter-rater reliability and construct validity apply to the study by Rie et al (1976) reviewed in this paper, as well. They quoted .80 as test-retest reliability, but provided little information on the rationale behind their "organicity scale", and the assessment measure employed in each category of the scale.

Although no definite conclusions can be drawn from the preceding studies, they have been important in demonstrating that organic factors may play a role in hyperactivity, and that prediction of treatment response from knowledge of a child's neurological status may be possible. Further

research with more attention to methodological concerns is required to clarify the findings in this area.

The hypothesis advanced by many of these investigators (Dubey, 1976; Epstein et al, 1968; Lambert et al, 1976; Satterfield et al, 1973) that hyperactivity not be viewed as a unitary disorder, but as being composed of a number of different factors, has important implications. Some, but not all, hyperactive children may have an organic basis to their problem. This presents a realistic compromise to the all-or-none arguments advanced by earlier investigators. The acknowledgement of the existence of different subgroups of hyperactive children has promoted the search for optimal treatment for different groups of children. The notion of one treatment for the hyperactive child has become more and more untenable. In particular, the medically oriented treatment approach (i.e., drug intervention), has come under closer strutiny and other treatment efforts of a more psychological nature (e.g., behavior management) are gaining in legitimacy and popularity.

Another important change in viewpoint with respect to hyperactivity that has important treatment implications concerns learning problems. Learning disabilities are often assumed to be part of the clinical entity of hyperactivity, probably because both were seen to be manifestations of MBD (Clements, 1974; Douglas, 1972; Lahey et al, 1978; Rie et al, 1976). Since a clinically significant degree of

hyperactivity often leads to academic difficulties, a high proportion of individuals diagnosed as hyperactive would also be diagnosed as learning disabled (Lahey et al, 1978). Douglas (1972) and her associates found that hyperactive children had significantly lower grades than controls on almost all academic subjects, and that hyperactives performed more poorly than controls on standardized achievement tests. They found that the performance of hyperactives was typified by much variability, i.e., from test to test, and subtests within a single test. Douglas (1972) emphasizes, though, that on a large proportion of the tests, including an individually administered reading test, language tests, and tests tapping auditory discrimination, right/left discrimination and short-term memory, no differences were found between hyperactives and controls. Rie et al (1976) found that correlations between achievement test scores and measures of activity and behavior rating scales were inconsistent, and of a low order, leading to the conclusion that "more active and otherwise behaviorally difficult children are not poorer students in this sample of underachieving children". To be noted, of course, is the fact that even though the "most hyperactive" children were not necessarily the "most learning disabled", the subjects in this study were all underachievers, which is consistent with the findings of others (Douglas, 1972; Lahey et al, 1978; Cantwell, 1977; Safer & Allen, 1976).

It seems then, that hyperactive children as a group show poorer academic performance than their normal classmate controls. However, a distinction may be drawn between being behind in academic achievement and learning disability. A hyperactive child may be doing poorly in school because for a great amount of time he is not attending, is responding impulsively to the teacher's questions and responding impulsively on tests, without considering alternatives, or checking his work, etc. A child with learning disability may not be exhibiting any of the above behaviors, but still does poorly in school, perhaps, (for example) because he has difficulty in auditory discrimination. He is attending, but not processing the information correctly. (And, of course, a child may be both hyperactive and learning disabled.) The term Specific Learning Disability encompasses a number of learning problems and as many diagnostic confusions exist in the literature with this term as with MBD and hyperactivity, as discussed. A lengthy discussion of the term "Specific Learning Disability", what it entails, how to diagnose, etc. would present a major digression from the topic at hand, hence comments are limited to a brief discussion of Specific Learning Disability in its relation to hyperactivity. For some hyperactive children, their poor academic performance is secondary to their hyperactivity - they are behind in school because of the characteristic problems associated with hyperactivity (e.g., poor attention span, distractibility,

impulsivity, etc.). Other children, most likely further behind in school, have the problems associated with hyperactivity compounded by those associated with Specific Learning Disability (e.g., problems with auditory and visual discrimination, figure-ground, and memory, etc.). Using achievement test scores can only tell us that a child is behind his peers in school. One has to go beyond the test scores to determine the nature of the child's learning difficulty. Diagnosing Specific Learning Disability cannot be accomplished solely by achievement tests. In addition, problems arise when making the decision just how far behind academically a child must be before being diagnosed as learning disabled. Intellectual potential, which skills appear to show deficiency, comparison of the child's achievement to that of his own ethnic group, his opportunities for learning, his response to corrective measures, all contribute important information that should be considered when making the diagnosis (Spache, 1976). Achievement test measures, however, are objective, and invaluable in research where standardized measures are required to permit for comparability across studies. For the present paper, the term "learning difficulty" will be employed to indicate that the subjects are behind in school, so as not to be confused with the diagnostic term Specific Learning Disability.

How far behind then, is the child to be before he is to

be defined as having learning difficulty? Ullman (1969) has shown, for reading, that the use of a constant criterion of one year behind would result in classifying an increasing number of pupils as behind in each higher grade. This artificial increase is due to the decelerating nature of the reading curve and to the decreasing differences between successive grades. Hence a single fixed cut-off point would produce more and more children defined as being behind. Ullman (1969) considers that approximately 15% of each grade may be considered to be severely behind in reading. Spache's (1976) criteria of one year behind at primary (i.e., grades 1 to 3), two years behind from grades 4 to 8, and three years behind at secondary, produces a similar figure to Ullman's (1969) for those defined as having significant reading problems.

It appears then, that learning difficulties often accompany hyperactivity. Children with learning difficulties alone, are not likely to profit from drug treatment (Barkley & Cunningham, 1978; Rie et al, 1976). It is possible that differential response to stimulant drugs may occur in hyperactive children with and without learning difficulties. Ferguson and Trites (1980) addressed this issue and that of brain dysfunction by identifying these factors in their subjects, and using them to predict response to methylphenidate. They grouped 79 subjects on the two binary dimensions of brain dysfunction/no brain dysfunction, and

learning difficulty/no learning difficulty (yielding four subgroups). The diagnosis of brain dysfunction was made by neuropsychologist, based on the results of an extensive neuropsychological test battery. Learning difficulty was defined by scores of at least one year behind the level of academic achievement expected for the child's age. A double-blind crossover design with placebo control was employed. Responders and nonresponders to methylphenidate were classified on a multiple criteria basis: attention measures, parent and teacher global ratings of improvement, and Conners' TRS and PSQ hyperactivity scales. Their results showed that on all dependent variables, individuals diagnosed as having evidence of brain dysfunction had better response to methylphenidate than those individuals diagnosed as having no evidence of brain dysfunction. However, only when response was defined in terms of improvement on the attentional measures were the results significant. There appeared to be no systematic effect on the learning difficulty/no learning difficulty dimension. The inclusion of a number of different dependent variables as measures of response to stimulants demonstrated that response rates declined as the variables became less subjective and/or more complex. The wide range of response rates achieved with different dependent variables and combinations of dependent variables offers an explanation for the differences in response rates cited in the literature.

Many questions regarding the prediction of response to stimulant medication remain, despite the numerous investigations in this area. Barkley (1976), keeping in mind the limitations inherent in attempting to draw conclusions from such a medley of studies, nevertheless came to the following conclusion: "In general, those variables which have been consistently found to predict improvement during stimulant drug treatment appear to be those related to attention span or concentration" (p. 345).

Summary

The postulation of different subgroups of hyperactive children has been well received in the literature, and there appears to be a consensus that different hyperactive children may respond positively to different treatments or combinations of treatments (Dubey, 1976; Epstein et al, 1968; Ferguson & Trites, 1980; Lambert et al, 1976; Satterfield et al, 1973). Trial and error often has been the clinician's guide in selecting treatment for his patient. However, could response to treatment be predicted by pre-treatment measures, much time and effort on the part of the clinician, parent and child could be saved. The foregoing review dealt first with how to define response to treatment. The need for standardized and objective measures which determine how the hyperactive child's behavior is affected by drugs in various situations was discussed. Various predictor variables were

reviewed. The results of these studies were inconsistent, although it appeared that measures of attention offered the greatest predictive utility. The methodological concerns that have plagued psychopharmacological research, have made it difficult to draw any firm conclusions regarding prediction of response in general, and for organic predictors, in particular.

In concluding his review of predictor variables, Barkley (1976, p. 345) made the following suggestions for further research: (1) "future study of the extent to which the presence or absence of organic impairment or emotional pathology contributes to drug responsiveness", (2) "determination of empirical correlates of commonly used rating scales", (3) "cross-validation of the profile types of Conners (1971, 1972a) or diagnostic categories of Fish (1971)", (4) "further research on the ability of measures of attention span to predict the response of hyperactive children to stimulant drugs".

Goals of this Study

A number of issues have been raised in the preceding review. The question of response to drug treatment is an issue in itself that calls for investigation. That is, how should response to treatment be defined? Barkley (1976) suggested that future research investigate the role of

organic impairment as a contributing factor to drug response. The possibility of a differential response to stimulant drugs in hyperactive children with and without learning difficulties was raised. The present paper proposes to address these issues as follows: (1) multiple response criteria, (2) predicting response from subgrouping along the binary dimensions of brain dysfunction/no brain dysfunction and learning difficulty/no learning difficulty, and (3) predicting response from neuropsychological test scores.

(1) The considerable variation in response rate reported by different investigators is due in part to the fact that how response is defined has not been standard across studies. Ferguson and Trites (1980) have shown that as the definition for response becomes more objective and more complex, the number of subjects designated as responders decreases. That no completely satisfactory criteria for response have yet emerged from the literature provides a rationale for the utilization of multiple definitions of response. Multiple definitions of response serve to permit comparison with studies using one or more of the same criteria for response, and contribute to the endeavor to produce consistent, reliable, and valid criteria. The first issue investigated in this study was that of multiple criteria for response. Attention measures were investigated in more detail in the present study than in the study of Ferguson and Trites, and different criteria of response employing these measures

singly, and in combination with each other and with the PSQ hyperactivity scale were constructed. These various definitions of response were employed as dependent variables in the subsequent analyses.

(2) As reviewed, Ferguson and Trites (1980) did some preliminary work with subgrouping hyperactive children on the basis of presence or absence of brain dysfunction (based on an interpretation of neuropsychological test results) and learning difficulty. The present study repeated this analysis with 96 subjects (i.e., with the original 79 subjects of Ferguson and Trites' study, plus 17 new subjects. In light of this common subject pool, the present study should be viewed as an extension, rather than a replication of their work.) Ferguson and Trites did not find any systematic relationship between response and their learning difficulty dimension. The present study has changed the criteria used by these previous investigators, in an effort to provide a more realistic definition of learning difficulty. (They employed the criteria of one year behind in academic achievement for all subjects, regardless of grade). It was believed that the revised criteria used in the present study would enhance the predictive utility of this dimension.

Ferguson and Trites found that when response was defined in terms of improvement on certain attention measures, there was a significant relationship between brain dysfunction and

response. In the present study, attention measures were investigated in more detail, and different criteria for response based on them were employed in χ^2 analyses testing for a relationship between response and brain dysfunction, as in Ferguson and Trites' study.

(3) Previous studies employing the neuropsychological test battery have found this battery capable of differentiating a number of clinical and non-clinical groups from each other. For example, Trites and Price (1978-79) found that a unique pattern of deficits on the neuropsychological test battery characterized their group of English children who experienced difficulty in French immersion. These children could be successfully discriminated from three other groups where language was a factor, and from four "traditional" problem groups, including hyperactivity. Reitan and Boll (1973) compared the neuropsychological test results of MBD children with both normal children and children with firm and independent evidence of brain damage. The brain damaged group were consistently and significantly inferior on a wide range of abilities. The performance of the MBD groups on the neuropsychological tests was more similar to control children than to those with brain damage. Clinical evaluation of the neuropsychological test results for number of deficits per subject showed that the brain damaged group had significantly more deficits than the MBD group, which in turn had

significantly more deficits than the control group.

To further the investigation of organic factors as predictors of response, the present study employed the neuropsychological tests as predictors of response to methylphenidate. Discriminant function analyses, followed by univariate analyses were carried out. The goal was to discover whether responders and nonresponders could be successfully discriminated on the basis of their neuropsychological test scores. If responders to methylphenidate do in fact have more organic involvement than nonresponders, as suggested by some authors (e.g., Conrad & Insel, 1967; Epstein et al, 1968; Millichap & Johnson, 1974; Steinberg et al, 1971) this would be reflected in poorer neuropsychological test scores for responders.

CHAPTER II

METHODOLOGY

Subjects

The subjects for this study were 96 boys between the ages of 6 and 14 years old, who were referred to the Neuropsychology Laboratory of the Royal Ottawa Hospital for neuropsychological assessment. All subjects were diagnosed as hyperactive. The diagnoses of hyperactivity and of presence or absence of brain dysfunction were made by a senior psychologist specializing in neuropsychology, on staff at this institution. The diagnosis of hyperactivity was a clinical decision made by this psychologist, based on a detailed history of the child, the referring pediatrician and/or team psychiatrist's diagnosis, school record information, mother and/or teacher ratings of the child's behavior obtained at the time of initial assessment (i.e., not at "Baseline"), neuropsychological test results, and observation of the child during assessment. A child's score on the Conners' mother or teacher rating of hyperactivity had to be 1.5 or greater for the child to be included in the study.

The diagnosis of brain dysfunction was a clinical decision made on the basis of an interpretation of the child's neuropsychological test results. Brain dysfunction

was defined as follows. An indication of brain dysfunction may be supported by consistently poor levels of test results, but in most cases must be substantiated by evidence of lateralized sensory and motor dysfunction. In most cases, the actual level of performance would not be the sole criterion, but should be supported by evidence of dysfunction in simple sensory and motor functions on one or both sides of the body. The diagnosis of no brain dysfunction included children whose variations in levels of ability were within the normal range. Subjects with only mild indications that might be suggestive of brain dysfunction were diagnosed as no brain dysfunction. Pronounced intra-individual variations on lateralized sensory or motor performance were not acceptable for subjects diagnosed as no brain dysfunction.

A child was considered to be having learning difficulties if he was behind on either the reading or spelling subtest of the Wide Range Achievement Test (WRAT) (Jastak & Jastak, 1976). The criteria employed were: performance at least one year behind the level of achievement expected for grade placement at primary (grades 1 to 3); at least two years behind for grades 4 to 8; and at least 3 years behind for grades 9 and up. For children in special education classes, or who had repeated a grade or grades, learning difficulty was defined by WRAT scores at least one year behind the child's age-expected grade placement for primary; at least two years behind the child's age-expected

grade placement for grades 4 to 8, and at least three years behind the child's age-expected grade level for grades 9 and up. These criteria were suggested by Spache (1976) as discussed previously in this paper.

All children had a full-scale IQ on the WISC of at least 80. No subjects in the present study showed evidence of gross psychopathology or neurological disease (other than what has been labelled "minimal brain dysfunction" in the literature). Complete data on the defining criteria were available for all 96 subjects. Descriptive data on the subjects are presented in Table 1. (Data for the other scales of the TRS and PSQ given at time of initial assessment are presented in Table B-1, Appendix B.)

Apparatus

Test Battery

Initial Testing

All subjects were administered a standardized and validated neuropsychological test battery (Boll, 1974; Kløve, 1974; Reitan, 1974; Reitan & Boll, 1973; Trites, 1977). This battery assesses a wide range of functions that have been shown to be related to the organic integrity of the brain (Reitan & Boll, 1973). These functions include the so-called "higher brain functions" (intelligence, cognition, and complex perceptual skills) and the lower order skills

Table 1

DESCRIPTIVE STATISTICS ON SUBJECTS

N=96

Variable	X	SD	Range
Age at Initial Testing (years)	8.9	1.97	6 to 14
WISC FSIQ	99.3	10.36	80 to 130
PSQ Hyperactivity at Initial Testing	1.46	.64	0 to 2.88
TRS Hyperactivity at Initial Testing	2.03	.65	0 to 3
Age at Treatment (years)	9.6	1.77	6.8 to 14
Weight at Treatment (kgs)	31.9	8.55	16.5 to 59

(simple motor, sensory, and perceptual skills). The tests in the battery included the WISC-R, Raven's Matrices, Peabody Picture Vocabulary Test, Halstead Category Test, Tactual Performance Test, and tests of motor speed and coordination, dexterity, tremor, strength, and sensory tests. Behavior rating scales (Conners' Parent Symptom Questionnaire (PSQ), Conners' 1970; and Conners' Teacher Rating Scale (TRS), Conners' 1969) were also included. A complete list of the tests employed in this study can be found in Appendix A.

Response Measures

In order to assess responsivity to drug, the following measures were administered at baseline and at each successive stage of the study: The Continuous Performance Test (CPT) (Rosvold et al, 1956); the Matching Familiar Figures Test (MFF) (Kagan, 1964); and the Conners' PSQ and TRS. A brief description of these measures follows. How these measures were employed to define response is described in the Procedure section.

The Continuous Performance Test (CPT) (Rosvold et al, 1956)

The CPT is sensitive to momentary lapses of attention (Sykes et al, 1971). Studies using this measure have been reviewed already. The CPT requires the subject to respond to an experimenter-paced stimulus array presented on a television monitor by correctly identifying a pre-determined

signal stimulus from irrelevent stimuli. In this study, a series of letters was flashed on the screen and each time the letter "X" was immediately preceded by the letter "A", the subject was expected to respond by pressing a button. Two error scores are used: omissions - the number of times the subject neglects to respond to a presented A-X combination; and commissions - the number of times the subject responds to an erroneous letter combination.

The Matching Familiar Figures Test (MFF) (Kagan, 1964)

Studies using the MFF test were presented in the Introduction. In the MFF test, the subject is presented with a booklet on each page of which are printed one standard drawing and six similar comparison drawings. One of the comparison drawings is actually identical to the standard; the other five comparison drawings are strikingly similar, but not identical to the standard. The subject must identify the correct drawing. The test is scored for latency to first response, and for total number of errors.

The Conners' Parent Symptom Questionnaire (PSQ) (Conners, 1970), and the Conners' Teacher Rating Scale (TRS) (Conners, 1969) (See Appendix A for a Copy of These Scales)

These two questionnaires list a series of behaviors (e.g., restless or overactive, disturbs other children) which are to be checked of as "not at all", "just a little", "pretty much", or "very much" by parent or teacher. The

items of these questionnaires have been factor analyzed, yielding a number of symptom clusters which are employed as individual scales. The subject receives a score for each individual scale, in addition to an overall score. The eight individual scales for the PSQ are: Conduct Problem, Anxiety, Impulsive-Hyperactive, Learning Problem, Psychosomatic, Perfectionism, Antisocial, and Muscular Tension. The four individual scales for the TRS are: Conduct Problem, Inattentive-Passive, Tension-Anxiety, and Hyperactivity. The present study was concerned only with the PSQ Impulsive-Hyperactive (i.e., hyperactivity) scale and the TRS Hyperactivity scale as dependent variables. Each item on the individual scales is scored 0, 1, 2, or 3 for "not at all", "just a little", "pretty much", and "very much", respectively. The subjects score on each individual scale was expressed as the average of his scores on that scale. For example, if his total was 16 for the eight items on the PSQ hyperactivity scale, this would be recorded as 2 (i.e., 18/8).

Procedure

The participation and cooperation of the parents and children in this study were very good. Only children whose parents appeared to be well motivated were considered for inclusion in the study. This was done in an effort to keep

the drop-out rate at a minimum, and to optimize compliance with respect to the treatment regimen. Poorly motivated parents would not be expected to reliably adhere to the treatment plan, nor to bring their children in for testing. Of the original 116 subjects selected for participation, three were withdrawn from the study before treatment began, by their parents who had "second thoughts" about drug treatment. The data of three other subjects were not included because it became apparent that they were not taking their pills. Five subjects were withdrawn by their parents due to side effects. These included: "aggression", "teary", "couldn't sleep", "too overactive", "shortness of breath". The data of nine subjects were excluded because either their files were unavailable, or there were too many missing data for a particular case. This left a subject pool of 96 subjects.

As an indication of compliance, Table 2 summarizes parents' and teachers' cooperation; i.e., bringing the child in for testing (parents) and returning the questionnaires (parents and teachers).

All subjects had been tested on an extensive neuropsychological test battery, as described. Testing was conducted by a team of psychotechnicians who rescored each other's test results to insure accuracy. The teacher of each subject was requested to fill out the TRS. The mother was interviewed regarding the child's history and was requested

Table 2

COMPLIANCE WITH TESTING REGIMEN

Variable	Baseline		T1		T2		T3	
	N	%	N	%	N	%	N	%
Attendance at testing	96	100	96	100	96	100	93	97
*PSQs returned	89(7)	100	87(7)	98	84(5)	93	81(9)	94
TRSs returned	82	85	74	77	68	71	65	68

* PSQs were completed by mothers for most children. The number in brackets () indicates that the PSQ was completed by the father. For all analyses employing the PSQ to define response, only those completed by mothers were employed in order to maintain consistency.

to fill out the PSQ. The test results, along with other information, were employed by the senior psychologist to diagnose each child, as described. The parents of the subjects all received feedback regarding their son's assessment results.

As children were brought to the laboratory for assessment, if they were found to be potential candidates for the study, their parents were interviewed to inform them of the study and to determine whether they wished their child to participate. All parents received both oral and written information about the study. After parental consent had been obtained and the referring physician notified, all subjects were tested on the dependent measures (Baseline). Each child was then assigned at random to one of the two treatment conditions. Initially, a goal of 208 subjects had been set for this study. Half of the subjects were to be assigned to each treatment order. When the number of referrals levelled off, only 116 boys had been through the study, and there was not an equal number of subjects in each group.

A double-blind (i.e., subjects, parents, teachers (participants), and examiners were unaware of whether the child was on active drug or inert placebo) crossover design consisting of three treatment periods each three weeks long was employed. Three weeks was chosen as the length for each treatment interval because it provided sufficient time for the child to settle into the treatment regimen, for the drug

to take effect, and for the mothers and teachers to observe any change; yet was brief enough to insure continued participation in the project. To control for order effects, methylphenidate and placebo were administered in two randomly assigned orders; that is, Drug-Placebo-Drug (DPD) or Placebo-Drug-Placebo (PDP). There were 66 subjects in DPD group and 30 subjects in PDP. In that each child was in effect the subject of a single-subject study, and that decisions regarding future treatment of a particular child were to be based on his results from the treatment trials, a Baseline A-B-A design was employed. A Baseline session insures that subjects are familiar with the experimental procedures and at ease in the laboratory setting (Rapoport et al, 1978). The additional treatment phase allows for a better assessment of consistent effects, compared to the traditional Baseline-A-B or simple A-B design.

A standard daily dosage of .5 mg of methylphenidate per 1 kg of body weight was administered to all subjects. The dosage was divided over two periods; one-half hour before breakfast and one-half hour before lunch. The boys' average weight was 31.9 kg. This made the average daily dose around 16 mg. As mentioned, the work of Sprague and Sleator (1977) suggests .5 mg/kg daily as the most appropriate dosage to be employed on a group basis. Although this dosage may not be optimal for each subject, it should be sufficient to produce a detectable improvement for most responders, yet be low

enough to prevent the occurrence of side effects for most subjects. The methylphenidate and placebo were dispensed in small green-blue pills that were indistinguishable from each other. Each methylphenidate pill contained 10 mg of methylphenidate. The psychiatrist involved in the study had access to the information of which treatment each child was receiving, so that in case of emergencies he could be consulted. Parents had been forewarned of possible side effects, e.g., nausea, insomnia. If a child was not feeling well, e.g., had a cold or the flu, and experienced the same kinds of symptoms as drug side effects, parents were advised to keep the child off treatment (drug or placebo) for two days, and then to resume treatment again. (As mentioned, only 5 subjects were withdrawn from the study because of side effects.) In this way, the double-blind was not broken. Methylphenidate is compatible with most other medication, so would not have to be discontinued if the child required another prescription drug during the treatment period.

The child's parent was given the child's first envelope of pills after baseline testing, and every three weeks thereafter, when the child came in for re-testing after each treatment period. When the parent brought the child in for testing, information regarding compliance with respect to pill-taking was gathered. If there was any doubt regarding the regularity of pill-taking, the parent was requested to bring in the child's envelope with any remaining pills, after

the next treatment phase. (As mentioned, three subjects were not complying with the treatment regimen, and their data were not included in the study.) Children were supervised for their pill-taking by parents in the morning, and by teachers and/or principals at lunch time.

The child was tested on the dependent measures at baseline and at the end of each three week treatment period, usually about two hours (at the most three hours) after last taking his pill. One child from out of town was tested late in the afternoon, so his parents were instructed to give him a third pill, which had been supplied in the envelope, on the testing day. Each individual child tended to come at the same time of day for each subsequent testing because testing times were chosen to coincide best with each individual's schedule at school. The child's mother and teacher were requested to fill in the PSQ and TRS, respectively, at baseline and at the end of each three week treatment period.

The order of testing was the MFF test followed by the CPT.

Data Preparation

This study can be divided into three main areas of investigation. The first concerned the dependent variables employed to define response; i.e., a) the actual number of responders and nonresponders as defined by different

dependent variables, b) testing the differences between responders and nonresponders (as defined) on the dependent variables, c) Baseline, Drug, and Placebo comparisons of the dependent variables, d) testing for order effects (DPD vs. PDP) on the dependent variables. The second area of study was concerned with the prediction of response employing diagnosis of brain dysfunction and learning difficulty as the independent variables. Thirdly, this study investigated neuropsychological test scores as predictors of response (as defined).

Before these investigations could be undertaken, the following data preparation was needed: 1) Drug and Placebo scores on the dependent variables had to be determined and response defined. 2) The neuropsychological test results had to be organized into workable independent variables.

This section describes the procedures involved in the preparation of these data.

Defining Response

To determine whether or not a subject was a responder on the different dependent variables, his performance on drug was compared to his performance on placebo. If he performed better on drug than on placebo, he was a responder. Since there were three treatment sessions for each subject (i.e., DPD or PDP), and comparisons were to be made between drug and

placebo, a simple weighting procedure which weighted the two "same" treatments (i.e., drug for DPD, placebo for PDP) by half the weight of the single treatment (i.e., placebo for DPD, drug for PDP) was employed. (This weighting procedure is, of course, equivalent to averaging the two "same" treatments.) Hence, each subject would have a Baseline, Drug and Placebo score for each dependent variable. This procedure is described in more detail for each of the dependent variables in the following sections. The computer program employed for defining response is included in Appendix C.

Response Defined in Terms of Performance on CPT Omissions, CPT Commissions, and MFF Errors

On the measures of CPT omissions, CPT commissions and MFF errors, the lower a subject's score, the better his performance. Response on these measures was defined as follows. In order to equally weight drug (D) and placebo (P) conditions, weights of +1, -2, +1 were assigned respectively to D1, P, and D2 for the D-P-D order. For P-D-P order, weights of -1, +2, -1 were assigned respectively to P1, D, and P2. If a negative total resulted by adding up the three conditions, i.e., D1+P+D2, or P1+D+P2, the individual was designated a responder. If the total was zero or positive, the individual was a nonresponder. For example: if a subject scores 5, 6 and 4 on D1, P, D2 for MFF errors, he is designated a responder, since his total is negative.

	D1	P	D2	Total
MFF Errors	5	6	4	
Weight	(+1)x5	(-2)x6	(+1)x4 =	-3

Response Defined in Terms of Performance on MFF Latency

For the MFF latency measure, a long latency, that is, a larger score, is considered to be indicative of good performance. For the D-P-D order, weights of +1, -2, +1 were assigned respectively to D1, P, and D2. For the P-D-P order, weights of -1, +2, -1 were assigned to P1, D, and P2, respectively. If the sum of the three conditions, i.e., D1+P+D2 or P1+D+P2, was positive, the individual was a responder. If the total was zero or negative, the individual was a nonresponder.

Response Defined in Terms of Conners' PSQ Impulsive-Hyperactive Scale

For the Impulsive-Hyperactive (hyperactivity) scale of the PSQ, a responder was defined if he showed 10% improvement, i.e., a drug score lower than placebo by 10% of placebo. This was calculated by subtracting 10% of placebo from itself, and comparing it to drug. For the D-P-D order, weights of +1, -2, +1 were assigned to D1, [P-(.1xP)], and D2, respectively. For the P-D-P order, weights of -1, + 2, -1 were assigned to [P1-(.1xP1)], D, and [P2-(.1xP2)], respectively. A negative total denoted a responder; a zero

or positive total a nonresponder. For example: if a subject in the D-P-D order received scores of 1.5, 2.0, 1.25 respectively on D1, P, and D2, response would be calculated as follows.

	D1	P	D2	Total
PSQ Hyper-activity	1.5	2.0	1.25	
10% P		[2.0-(.1x2.0)]		
Weight	(+1)x1.5	(-2)x1.8	(+1)x1.25	= -.85

The total score is negative, hence this subject would be a responder on PSQ hyperactivity.

Missing Values

In order to denote each subject as a responder or a nonresponder on each dependent variable, data for each case on each treatment condition of each dependent variable (i.e., D1, P, D2 or P1, D, P2) were needed. If data were missing for any one subject on any one or more conditions, whether that subject was a responder or a nonresponder could not be determined. Hence missing values had to be dealt with. For any case with missing values on CPT omissions, CPT commissions, MFF errors, MFF latency, and PSQ hyperactivity, on any of the conditions, the group mean (i.e., with respect to treatment order and condition) was assigned. For example: if the subject was in the D-P-D order and was missing CPT

commissions from the D2 condition, he would be assigned the mean of the D-P-D group on the D2 condition of CPT commissions. Tables C-1, C-2, C-3, and C-4 in Appendix C present the number of cases, means and standard deviations for the different groups for each condition, before and after substitution of means for missing values. As can be seen, the standard deviations changed very little. It should be noted that the number of cases with missing values for the above dependent variables was small. Excepting the PSQ hyperactivity scale, the mean percentage of missing data for all orders and conditions was only 1.6% (range 0 to 4.2%). The largest amount of missing data was for the PSQ hyperactivity scale, ranging from 6.7% to 16.7% (X=11.6%).

Response Defined Using a Combination of Measures

The attentional measures CPT omissions, CPT commissions, MFF errors and MFF latency were used to define four new categories of response: RSP1, if the subject was a responder on one of the four attentional measures; RSP2, a responder on two of the four attentional measures; RSP3, a responder on three of the four attentional measures; RSP4, a responder on all of the attentional measures. Combining the results of the PSQ hyperactivity scale with the four attentional measures yielded four additional categories of response: BEHATT1, a responder on the PSQ hyperactivity scale (i.e., 10% improvement on drug as compared to placebo) and on one of

the four attentional measures; BEHATT2, BEHATT3, and BEHATT4, a responder on the PSQ hyperactivity scale and on two, three, and four, respectively, of the attentional measures.

Response Defined in Terms of Conners' TRS Hyperactivity Scale

Data for the four (i.e., Baseline and the three treatment conditions) TRS hyperactivity scales were missing for a number of cases in one or more of the conditions. The amount of missing data was much greater than for the other dependent variables, which necessitated a different approach to dealing with the problem of missing data. It was felt that the TRS hyperactivity scale could offer valuable information (as discussed previously) and should be retained, if at all possible. The number, out of 96, of TRSs returned were 82, 74, 68, and 65, respectively for Baseline and the three treatment phases of the study (i.e., D1, P, D2 or P1, D, P2). This did not mean, however, that all data was available for 65 subjects, because data were missing for different subjects on different conditions, in many cases. Complete data (i.e., for Baseline and the three treatment conditions) were available only for 44 subjects. It was felt that replacing missing data with group and treatment condition means, a conservative method suitable when the amount of missing data is not great, as for the other dependent variables, would "average out" or mask individual differences. The solution arrived at instead follows. (The

computer program for this solution is included in the program for defining response in terms of the other dependent variables, and can be found in Appendix C).

D-P-D order: If both D1 and D2 were present, they were averaged to yield the subject's DRUG score. If either D1 or D2, but not both was available, the available score was used as the DRUG score. DRUG was compared to [Placebo - (.1xPlacebo)] to determine whether the subject improved at least 10% on drug compared to placebo. DRUG was weighted by +1, [Placebo - (.1xPlacebo)] by -1. Since a lower score indicates improvement, if the total was negative, the subject was designated as a responder. If the total was zero or positive, the subject was designated as a nonresponder. For example: Subject A on D1, P, D2 receives scores of 1.25, 2.0, 1.0, respectively, on the TRS hyperactivity scale. Subject B receives 1.25, 1.5, and missing for D1, P, D2 respectively.

	DRUG	Placebo	Total
Subject A			
TRS Hyperactivity Score	$\frac{(1.25+1.0)}{2}$	[2.0-(.1x2.0)]	
Weight	(+1)x1.125	(-1)x1.8	= -.675
Subject B			
TRS Hyperactivity Score	1.25	[1.5-(.1x1.5)]	
Weight	(+1)x1.25	(-1)x1.35	= -.10

Both subjects A and B receive negative scores, so both are designated as responders.

P-D-P order: If both P1 and P2 were present, they were averaged to yield the subject's PLACEBO score. If P1 or P2 but not both, was available, the available score was used as the PLACEBO score. [PLACEBO - (.1xPLACEBO)] was then compared to drug. Weights of +1 for drug, and -1 for [PLACEBO - (.1xPLACEBO)], were employed. As before, a negative total designated a responder; a zero or positive total, a nonresponder.

This method of dealing with missing data allowed 67 subjects to be designated as responders or nonresponders on the TRS hyperactivity scale. The modified procedure for defining responders and nonresponders used for the TRS hyperactivity scale, and the smaller number of subjects that would be included in any analysis involving the TRS hyperactivity scale as a dependent variable, should be kept in mind when examining the results of this study.

Baseline, Drug, and Placebo Comparisons on the Dependent Variables

For comparisons made among Baseline, Drug, and Placebo conditions on MFF, CPT, and PSQ hyperactivity variables, the same procedures were employed to arrive at Drug and Placebo scores. That is, the two "same" treatments (i.e., drug in DPD, and placebo in PDP) were weighted by half the weight of the single treatment (i.e., placebo in DPD, and drug in PDP).

Any missing data was treated as described. Tables C-5 and C-6 in Appendix C present the number of subjects, means, and standard deviations before and after replacing missing values. Again, inspection of these tables indicates little change after replacing missing values.

For the TRS hyperactivity scale, if Baseline was missing for a particular case, the hyperactivity score on the TRS completed by the child's teacher at the time of neuropsychological testing was employed as a substitute. Drug and Placebo scores were calculated as described in the section on defining response for the TRS hyperactivity scale.

Factor Analysis of the Neuropsychological Tests

Factor analysis and the creation of factor scores for each subject were employed to reduce a large amount of data to a more manageable number of variables. The neuropsychological tests were divided into three groups of tests and three separate factor analyses were performed, which produced a total of eight new independent variables.

The neuropsychological test battery contains various motor and sensory tests in which developmental factors play a role. Age differences were controlled for these tests that did not have built-in scales permitting comparison across age levels, by calculating T-scores. The T-scores were calculated using norms developed in the Neuropsychology

Laboratory of the Royal Ottawa Hospital on over 2,000 children referred to the laboratory for assessment for a variety of reasons (Trites, 1977).

The neuropsychological test variables were grouped into the following classes of variables based on logical considerations about the nature of the tests, and on previous research (Blouin, Bornstein, & Trites, 1978b; Trites & Price, 1976): (1) general cognitive and intellectual tests, (2) motor tests, (3) sensory tests. Before factor analyses, Pearson product moment correlations (SPSS subprogram PEARSON CORR, Nie, Hull, Jenkins, Steinbrenner & Bent, 1975) were computed for each pair of variables in each class. Variable pairs that correlated greater than .75 were considered to be redundant, hence only one of the variables was retained to be entered into the subsequent factor analysis. Missing values for variables in the correlation calculations were treated in the customary pair-wise deletion fashion (Nie et al, 1975). The data entered into each Pearson correlation are listed in Table D-1 in Appendix D. The results of each Pearson correlation are presented in Tables D-2, D-3, and D-4 in Appendix D.

A separate factor analysis was computed for each class of variables. The method of principal factoring with iteration was employed and in each case a varimax rotation was carried out (SPSS Subprogram PA2, Nie et al, 1975). The conventional method of common variance retained was employed

(i.e., only those factors with an eigenvalue greater than 1 were retained. This criterion insures that only factors accounting for at least the variance of a single variable will be retained as significant (Amick & Walberg, 1975; Cooley & Lohnes, 1966; Nie et al, 1975; Rummel, 1970)). Varimax rotation was carried out for each factor analysis. Pair-wise deletion of missing data was employed. Factor scores were generated for each subject from the factor score coefficients (SPSS subprogram FACSCORE, Nie et al, 1975). For missing data encountered in the construction of factor scores, weighted factor scores were produced based on the existing data. For any case with 50% or greater of the data missing, the output factor score was assigned a missing value of 999 (SPSS subprogram FACTOR OPTION 10, Nie et al, 1975).

The variables included in each factor analysis and the results of each analysis are presented in Appendix D.

1. General Cognitive and Intellectual Variables

The factor analysis of the general cognitive and intellectual abilities variables (listed in Table D-5) yielded two factors with Eigenvalues greater than 1, which together accounted for 53.2% of the variance (Table D-6). The rotated varimax factor matrix is presented in Table D-7. Based on the factor loadings (Table D-7), the first factor was interpreted as a measure of performance or non-verbal abilities. The WISC Performance IQ, Raven's Matrices, TPT

and Category test scores loaded highly on this factor. The second factor was interpreted as a verbal abilities measure. WISC Verbal IQ and Peabody IQ loaded most highly on this factor.

2. Motor Test Variables

The Motor test variables (listed in Table D-8) yielded three factors with Eigenvalues greater than 1, accounting for 61% of the variance (Table D-9). Factor 1 was interpreted as reflecting motor speed and strength. Finger Tapping, Dynomometer Grip Strength and Foot Tapping loaded most heavily on this factor. The second factor received the highest loadings from the Holes Steadiness measures, hence was interpreted as reflecting motor steadiness. The Maze Coordination Test and the Groove Pegboard test variables loaded highly on the third factor, defining this factor as a measure of motor coordination and dexterity. Table D-10 presents these factor loadings.

3. Sensory Test Variables

The factor analysis of the sensory test variables (Table D-11) gave three factors with Eigenvalues greater than 1 accounting for 76.4% of the total variance (Table D-12). The first factor was very highly weighted by the Tactile Forms Test time variables and was thus seen to measure form perception speed. The Finger Agnosia variables essentially

made up the second factor. The third factor was defined by errors on the Tactile Forms measure. Table D-13 presents these results.

Summary

Table 3 lists the eight new independent variables created from the three factor analyses of the neuropsychological tests.

Table 3

INDEPENDENT VARIABLES

Performance Abilities
Verbal Abilities
Motor Speed and Strength
Motor Steadiness
Motor Coordination and Dexterity
Form Perception Time
Finger Agnosia
Form Perception Errors

CHAPTER III

ANALYSIS AND RESULTS

The analyses employed to investigate the issues raised previously, and the results obtained from these analyses are presented here. Discussion of these results follows in the next chapter.

Number of Responders and Nonresponders

MFF Errors and Latency, CPT Omissions and Commissions, PSQ Hyperactivity Scale, and Combined Measures

The frequency and percentage of responders and nonresponders on each of the dependent measures listed above, are presented in Table 4.

The more complex the measure used, i.e., combined measures RSP1 to RSP4, BEHATT1 to BEHATT4, the fewer children were found to be responders. The response rate on the attentional measures ranged from 36.5% (CPT commissions) to 60.4% (MFF errors). The criterion of 10% improvement on the PSQ hyperactivity scale yielded a response rate of 50%.

Responders Vs. Nonresponders on Dependent Variables

T-tests (SPSS subprogram T-TEST, Nie et al, 1975) of the difference in means of the contrast scores of the responders and the nonresponders, are presented in Table 5. The contrast score for D-P-D used the weights +1, -2, +1 for D1,

Table 4

NUMBER OF RESPONDERS AND NONRESPONDERS
(all missing values of raw data replaced by group mean)(N=96)

Variable	Nonresponders		Responders	
	N	Freq. %	N	Freq. %
CPT Omissions	58	(60.4)	38	(39.6)
CPT Commissions	61	(63.5)	35	(36.5)
MFF Errors	38	(39.6)	58	(60.4)
MFF Latency	47	(49.0)	49	(51.0)
PSQ Hyperactivity (10% improvement)	48	(50.0)	48	(50.0)
RSP1	6	(6.3)	90	(93.7)
RSP2	38	(39.6)	58	(60.4)
RSP3	69	(71.9)	27	(28.1)
RSP4	91	(94.8)	5	(5.2)
BEHATT1	49	(51.0)	47	(49.0)
BEHATT2	66	(68.8)	30	(31.3)
BEHATT3	82	(85.4)	14	(14.6)
BEHATT4	94	(97.9)	2	(2.1)

Table 5

t-TESTS OF CONTRAST SCORES (N=96)

Variable	Non-responders N	Non-responders X	Responders N	Responders X	t-value	p
CPT Omissions	58	2.70	38	- 4.59	5.97	.000***
CPT Commissions	61	1.89	35	- 3.22	6.19	.000***
MFF Errors	38	6.92	58	- 7.92	14.70	.000***
MFF Latency	47	-14.15	49	9.37	-3.31	.001***
PSQ Hyperactivity (10%)	48	.54	48	- .65	11.60	.000***

*** p ≤ .001

Table 6

THE HYPERACTIVITY SCALE

Number of Responders (i.e., 10% Improvement) and t-Test of Contrast Scores (N=67)

Nonresponders N	Nonresponders Freq. %	Nonresponders X	Responders N	Responders Freq. %	Responders X	t-value	p
43	(64.2)	.30	24	(35.8)	- .53	6.35	.000***

*** p ≤ .001

P, and D2, respectively; and the weights -1, +2, -1 for P1, D, P2, respectively, for P-D-P, as described previously. T-tests for responders vs. nonresponders on CPT omissions and commissions, MFF errors and latency, and the PSQ hyperactivity scale were all significant ($p \leq .001$). This indicates real (i.e., significant) differences between responders and nonresponders on each of the dependent measures above.

TRS Hyperactivity Scale

The criteria of 10% improvement on drug over placebo on the TRS hyperactivity scale yielded a response rate of 35.8% (based on 67 subjects, as described). A t-test for differences on the TRS hyperactivity scale between responders and nonresponders was significant ($p < .001$), indicating significant differences between the mean of responders and nonresponders on this measure. These results are presented in Table 6.

Definitions of Response Selected for Subsequent Analyses

Ten definitions of response were selected to form responder/nonresponder groups for the subsequent analyses. These were: CPT omissions, CPT commissions, MFF errors, MFF latency, PSQ hyperactivity, TRS hyperactivity, RSP2, RSP3, BEHATT2, and BEHATT3. The response criteria of RSP1, RSP4, BEHATT1, and BEHATT4, which defined 93.7%, 5.2%, 49.0%, and

2.1% of subjets as responders, respectively, were not included in the subsequent analyses. These four dependent variables are of interest only for descriptive, not predictive purposes.[2]

Baseline, Drug, and Placebo Comparisons

MFF Errors and Latency, CPT Omissions and Commissions, and PSQ Hyperactivity Scale

All subjects were compared for baseline, drug, and placebo conditions. T-tests of Baseline vs. Drug, Baseline vs. Placebo, and Drug vs. Placebo are presented in Table 7. Significant results were found for Baseline vs. Drug and Baseline vs. Placebo for CPT commissions, MFF errors, and the PSQ hyperactivity scale. Significant Drug vs. Placebo differences were found for MFF errors and the PSQ hyperactivity scale. The significant results for Drug vs. Placebo differences found for MFF errors and the PSQ hyperactivity scale are consistent with the high number of responders (i.e., improvement on drug vs. placebo) defined by these two measures. The nonsignificant Drug vs. Placebo

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2. For example, it is of interest that 97.9% of subjects do not improve on all four of the attention measures, but meaningless to attempt to correctly predict this. One has only to say that no subjects will respond on all four attention measures, and one's prediction would be wrong only 2.1% of the time. BEHATT1 would not appear to add information to that provided by PSQ hyperactivity, since 93.7% of subjects are responders to one attentional measure.

Table 7

t-TESTS BASELINE VS. DRUG, BASELINE VS. PLACEBO, DRUG VS. PLACEBO

Variable	N	Baseline X	Drug X	Placebo X	t	p
CPT Omissions	96	2.49	2.15	-	.97	.335
	96	2.49	-	2.25	.54	.587
	96	-	2.15	2.25	- .29	.771
CPT Commissions	96	2.49	1.41	-	2.71	.008**
	96	2.49	-	1.40	3.30	.001***
	96	-	1.41	1.40	0.06	.954
MFF Errors	96	13.24	9.17	-	7.86	.000***
	96	13.24	-	10.20	6.67	.000***
	96	-	9.17	10.20	-2.29	.024***
MFF Latency	96	11.84	11.93	-	-0.08	.934
	96	11.84	-	13.01	-0.72	.474
	96	-	11.93	13.01	-0.58	.564
PSQ Hyperactivity	96	1.39	.92	-	10.31	.000***
	96	1.39	-	1.06	7.21	.000***
	96	-	.92	1.06	-3.12	.002**
TRS Hyperactivity	81	1.75	1.25	-	6.88	.000***
	71	1.68	-	.81	3.21	.002**
	67	-	1.25	1.39	-1.88	.065

** $p \leq .01$
*** $p \leq .001$

differences for the other comparisons are reflected in the lower rate of response on these measures. It must be kept in mind that all these comparisons were made between Baseline, Drug and Placebo for all subjects, regardless of whether they were responders or nonresponders. MFF errors and PSQ hyperactivity would appear to be the measures most sensitive to drug effects.

TRS Hyperactivity Scale

T-tests showed significant Baseline vs. Drug and Baseline vs. Placebo results. The Drug vs. Placebo comparison approached significance. These results are presented in Table 7.

Order of Treatment Administration

In order to determine whether the order of drug and placebo administration affected the Drug and Placebo scores employed in the present study to define response to treatment, t-tests of Drug and Placebo were performed for all the dependent variables. Drug and Placebo were determined as before, and missing values dealt with as discussed. Table 8 presents the results of the t-test analyses. (Baseline scores were included for comparison purposes). In only one instance (CPT Omissions, Baseline Score) were the DPD and PDP groups significantly different ($p < .05$), and this would not effect Drug vs. Placebo differences used in defining

Table 8

t-TEST COMPARISONS OF DPD GROUPS WITH PDP GROUP ON DEPENDENT VARIABLES (BASELINE, DRUG, AND PLACEBO)

Variable	Condition	Group: DPD N	DPD X	DPD S.D.	PDP N	PDP X	PDP S.D.	t	p
CPT Omissions	Baseline	66	2.92	4.08	30	1.53	1.66	2.37	.020*
	Drug	66	2.15	2.51	30	2.17	2.90	- .03	.975
	Placebo	66	2.27	3.51	30	2.19	2.56	.12	.906
CPC Commissions	Baseline	66	2.82	3.77	30	1.77	3.40	1.31	.195
	Drug	66	1.59	1.97	30	1.03	1.16	1.72	.088
	Placebo	66	1.40	1.53	30	1.40	2.28	.01	.988
MFF Errors	Baseline	66	12.83	6.64	30	14.13	6.60	- .89	.375
	Drug	66	8.78	5.65	30	10.03	7.37	- .91	.363
	Placebo	66	9.67	6.55	30	11.35	4.71	-1.27	.209
MFF-Latency	Baseline	66	11.92	5.77	30	11.67	5.00	.21	.833
	Drug	66	11.23	4.48	30	13.47	17.85	- .68	.504
	Placebo	66	13.89	17.93	30	11.05	6.70	1.13	.263
PSQ Hyperactivity	Baseline	66	1.43	.60	30	1.29	.65	1.05	.296
	Drug	66	.96	.41	30	.84	.63	.92	.366
	Placebo	66	1.08	.59	30	1.01	.63	.49	.625
TRS Hyperactivity	Baseline	64	1.83	.72	30	1.57	.80	1.55	.124
	Drug	63	1.28	.66	20	1.16	.84	.66	.512
	Placebo	48	1.44	.73	25	1.29	.95	.74	.459

* $p < .05$

response. In all other cases, DPD and PDP groups did not differ significantly on the dependent variables. These results suggest that the order of drug and placebo administration did not significantly affect the Drug and Placebo scores which were employed to define response.

Brain Dysfunction (BD), Learning Difficulty (LD) and Response

The frequency of the classification of brain dysfunction and learning difficulty are presented in Table 9. The cell frequencies were not significantly different from chance expectation (χ^2=.423, p=.515) (SPSS subprogram CROSSTABS, Nié et al, 1975).

Two by two (2x2) crosstabulations of brain dysfunction (no brain dysfunction (NBD), brain dysfunction (BD)) and response (nonresponder, responder) using various dependent variables to define response, as discussed, did not yield any significant results between brain dysfunction and response to treatment. However, in 9 out of 10 comparisons, there was a higher percentage of responders in the BD group than in the NBD group.

Two by two crosstabulations of learning difficulty (no learning difficulty (NLD), learning difficulty (LD)) and response, using various dependent variables to define response, as above, did not yield any significant results. However, in 8 out of 10 comparisons, there was a higher percentage of responders in the LD group than the NLD group,

Table 9

FREQUENCY AND PERCENT FREQUENCY OF BRAIN DYSFUNCTION (BD) AND LEARNING DIFFICULTY (LD)

		Learning Difficulty		
		NLD	LD	Total
Brain Dysfunction	NBD	35 (36.8%)	19 (20.0%)	54 (56.8%)
	BD	23 (24.2%)	18 (18.9%)	41 (43.2%)
	Total	58 (61.1%)	37 (38.9%)	95 (100.0%)

$\chi^2 = .423$ $p = .515$

although these differences were not as marked as for BD vs. NDB.

The results of these 2x2 crosstabulations of brain dysfunction and response, and learning difficulty and response are presented in Table 10.

Discriminant Function Analyses

In order to investigate whether neuropsychological test variables were predictive of response to methylphenidate, ten discriminant function analyses were performed.

The independent variables (i.e., the eight neuropsychological test factor scores) were used as predictors in ten discriminant function analyses, the dependent variable being response/nonresponse defined in ten different ways.

The direct method of discriminant function analysis (SPSS subprogram DISCRIMINANT, Nie et al, 1975), which enters all independent variables into the analysis concurrently was employed. Excluding the analyses which employed TRS hyperactivity to define responders, out of 96 cases, 90 were included in the nine discriminant function analyses using neuropsychological test variables as predictors. The remaining 6 cases had at least one missing discriminating variable, so were not included in the analyses. for TRS hyperactivity as the dependent variable used to define

Table 10

NUMBER OF RESPONDERS AND NONRESPONDERS CLASSIFIED IN TERMS OF BRAIN DYSFUNCTION (BD) AND LEARNING DIFFICULTY (LD)

1. BD By Response 2. LD By Response

Variable Used to Define Response	Classification	Non-responder	Responder	Total	% Responders
CPT Omissions	NBD	36	18	54	33.3
	BD	21	20	41	48.8
		χ^2 = 1.718	p = .190		
	NLD	33	25	58	56.9
	LD	24	13	37	35.1
		χ^2 = .312	p = .577		
CPT Commissions	NBD	37	17	54	31.5
	BD	24	17	41	41.5
		χ^2 = .623	p = .430		
	NLD	38	20	58	34.5
	LD	23	14	37	37.8
		χ^2 = .013	p = .910		
MFF Errors	NBD	23	31	54	57.4
	BD	14	27	41	65.9
		χ^2 = .389	p = .533		
	NLD	23	35	58	60.3
	LD	14	23	37	62.2
		χ^2 = .000	p = 1.000		
MFF Latency	NBD	26	28	54	51.9
	BD	20	21	41	51.2
		χ^2 = .000	p = 1.000		
	NLD	32	26	58	44.8
	LD	14	23	37	62.2
		χ^2 = 2.069	p = .150		

Variable	Classification	Non Responder	Responder	Total	% Responders
RSP2	NBD	23	31	54	57.4
	BD	14	27	41	65.9
		X^2 = .389	p = .533		
	NLD	26	32	58	55.2
	LD	11	26	37	70.3
		X^2 = 1.577	p = .210		
RSP3	NBD	41	13	54	24.1
	BD	27	14	41	34.1
		X^2 = .720	p = .396		
	NLD	39	19	58	32.8
	LD	29	8	37	21.6
		X^2 = .884	p = .347		
PSQ Hyperactivity (10% improvement)	NBD	31	23	54	42.6
	BD	16	25	41	61.0
		X^2 = 2.458	p = .117		
	NLD	29	29	58	50.0
	LD	18	19	37	51.4
		X^2 = .000	p = 1.000		
BEHATT2	NBD	39	15	54	27.8
	BD	26	15	41	36.6
		X^2 = .479	p = .489		
	NLD	41	17	58	29.3
	LD	24	13	37	35.1
		X^2 = .136	p = .712		
BEHATT3	NBD	47	7	54	13.0
	BD	34	7	41	17.1
		X^2 = .072	p = .789		
	NLD	50	8	58	13.8
	LD	31	6	37	16.2
		X^2 = .001	p = .978		

Variable	Classification	Non-Responder	Responder	Total	% Responders
TRS-Hyperactivity (10% improvement)	NBD	24	12	36	33.3
	BD	19	11	30	36.7
		χ^2 = .001	p = .981		
	NLD	27	14	41	34.1
	LD	16	9	25	36.0
		χ^2 = .000	p = 1.000		

response, 66 cases were available for the discriminant function analysis.

In summary, multiple discriminant function analyses were employed to test the hypothesis that there were no multivariate differences on neuropsychological test measures between responders and nonresponders to methylphenidate, as defined.

Table 11 presents a summary of the discriminant function analyses using the neuropsychological test factor scores as predictors. As can be seen from this table, neuropsychological test factor scores predicted significantly ($p=.008$) responders from nonresponders, as defined by RSP2, overall correctly classifying 71.1% of the subjects. Defining response in terms of improvement on MFF errors and RSP3 led to discriminant functions that approached significance at the .05 level, when neuropsychological tests were used as predictors. When response was defined in terms of improvements on MFF errors, 66.7% ($p=.069$) were correctly classified; for RSP3, 64.4% ($p=.063$) were correctly classified as responders or nonresponders. Drug and Placebo scores on all the dependent variables for responders and nonresponders on MFF errors, RSP2, and RSP3 are presented in Appendix E.

The independent variables involved in the three discriminant function analyses that reached, or almost reached, statistical significance (i.e., when response was

Table 11

DISCRIMINANT FUNCTION ANALYSES SUMMARY TABLE
NEUROPSYCHOLOGICAL TEST FACTOR SCORES AS PREDICTORS
OF RESPONSE

Responders vs. Nonresponders	Total N	Wilk's λ	df	p=	% Overall Correctly Classified
CPT Omissions	90	.9380	8	.716	58.9
CPT Commissions	90	.9041	8	.389	67.8
MFF Errors	90	.8413	8	.069	66.7
MFF Latency	90	.9015	8	.367	61.1
RSP2	90	.7805	8	.008**	71.1
RSP3	90	.8383	8	.063	64.4
PSQ Hyperactivity	90	.9538	8	.859	56.7
BEHATT2	90	.8797	8	.216	67.8
BEHATT3	90	.8570	8	.113	77.8
TRS Hyperactivity	66	.8330	8	.204	66.7

** $p \leq .01$

defined by MFF errors, RSP2 and RSP3) were explored further by univariate analysis at two levels. Tables 12, 15, and 18 present more detailed information on the discriminant function analyses of the three above. In order to identify on which factor scores the responders and nonresponders differed, one-way analyses of variance for each variable (factor score) included in each discriminant analysis were carried out. Tables 13, 16, and 19 present the univariate F-ratios for these analyses.

The second univariate analysis identified which actual neuropsychological tests separated the groups. Those tests that loaded highly on each factor that had proved significant in the one-way analysis of variance were selected. T-tests for differences between means on neuropsychological tests between responders and nonresponders were carried out (Tables 14, 17, and 20). The presentation of the results from the above described analyses now follows, in more detail.

1. Response as Defined by Performance on MFF Errors:

The discriminant function analysis employing neuropsychological test factor scores as predictors of response on MFF errors yielded a single discriminant function with a Wilk's Lambda of .8413 (df 8, p=.069). The standardized discriminant function coefficients indicate that the highest loadings were on Performance Abilities and Finger Agnosia. These results are presented in Table 12.

Table 12

RESULTS OF DISCRIMINANT FUNCTION ANALYSIS OF MFF ERRORS
RESPONDERS VERSUS NONRESPONDERS
NEUROPSYCHOLOGICAL TEST FACTOR SCORES AS PREDICTORS
OF RESPONSE

Standardized Canonical Discriminant Function Coefficients	
Performance Abilities	0.69094
Verbal Abilities	0.26643
Motor Speed and Strength	-0.12149
Motor Steadiness	0.25340
Motor Coordination and Dexterity	-0.17414
Form Perception Time	0.13471
Finger Agnosia	-0.45846
Form Perception Errors	0.17318

Discriminant Function	Eigenvalue	Canonical Correlation	Wilk's λ	df	p=
1	.18867	.398	.8413	8	.069

Classification Results

Actual Group	N	Predicted Group Membership: Nonresponders	Responders
Nonresponders	36	27 (75.0%)	9 (25.0%)
Responders	54	21 (38.9%)	33 (61.1%)
	90		

Overall correctly classified: 66.7%

In Table 13, the univariate F-ratios for each factor score variable are presented. The results of the univariate F-tests indicate that responders and nonresponders differed most on Performance Abilities and Finger Agnosia.

In order to determine on which specific tests the two groups differed, univariate t-tests were performed on the actual test data that made up the factor scores variables that were significant. These results are presented in Table 14. The results show that responders performed more poorly than nonresponders on all the actual assessment variables and that this difference was significant for the following variables: WISC Performance IQ, TPT location and TPT memory scores, Category Test, and Finger Agnosia for dominant and nondominant hands.

2. Response as Defined by Performance on RSP2:

Table 15 presents the results of the discriminant function analysis employing neuropsychological test factor scores as predictors of response on RSP2. This analysis yielded a single discriminant function with a Wilk's Lambda of .7805 (df 8, p=.008). The standardized discriminant function coefficients indicate that the highest loadings were on Performance Abilities and Finger Agnosia.

In Table 16, the univariate F-ratios for each factor score variable are presented. The results of the univariate F-tests indicate that responders and nonresponders differed

Table 13

UNIVARIATE F-RATIO FOR EACH VARIABLE INCLUDED IN THE DISCRIMINANT EQUATION OF DIFFERENCES BETWEEN MFF ERRORS RESPONDERS AND NONRESPONDERS (1 AND 88 df) NEUROPSYCHOLOGICAL TEST FACTOR SCORES

Variable	F-Ratio	p=
Performance Abilities	7.814	.006**
Verbal Abilities	2.260	.136
Motor Speed and Strength	.143	.707
Motor Steadiness	2.041	.157
Motor Coordination & Dexterity	2.885	.093
Form Perception Time	.209	.649
Finger Agnosia	6.975	.010**
Form Perception Errors	.115	.915

** $p \leq .01$

TABLE 14

UNIVARIATE t-TESTS OF DIFFERENCES BETWEEN RESPONDERS AND NONRESPONDERS AS DEFINED BY MFF ERRORS NEUROPSYCHOLOGICAL TEST (ACTUAL) SCORES

Test	Mean (X)		t	p=
	Nonresponders	Responders		
WISC Performance IQ	106.1	100.4	2.32	.023*
Raven's Matrices	54.1	51.0	1.71	.090
TPT Total Time T-Score	44.9	47.9	-1.54	.128
TPT Location T-Score	53.9	49.3	2.08	.040*
TPT Memory T-Score	54.9	50.4	2.28	.025*
Category Test Errors T-Score	43.5	48.5	-2.67	.009**
Finger Agnosia Dominant T-Score	48.3	52.6	-2.32	.023*
Finger Agnosia Non-Dominant T-Score	49.5	53.0	-2.07	.042*

* $p \leq .05$
** $p \leq .01$

Table 15

RESULTS OF DISCRIMINANT FUNCTION ANALYSIS OF RSP2 RESPONDERS VERSUS NONRESPONDERS NEUROPSYCHOLOGICAL TEST FACTOR SCORES AS PREDICTORS OF RESPONSE

Standardized Canonical Discriminant Function Coefficients	
Performance Abilities	.87639
Verbal Abilities	-.05595
Motor Speed and Strength	-.17364
Motor Steadiness	-.25431
Motor Coordination and Dexterity	-.26851
Form Perception Time	.32207
Finger Agnosia	.41888
Form Perception Errors	.13040

Discriminant Function	Eigenvalue	Canonical Correlation	Wilk's λ	df	p=
1	.28130	.469	.7805	8	.008**

Classification Results

Actual Group	N	Predicted Group Membership: Nonresponders	Responders
Nonresponders	35	26 (74.3%)	9 (25.7%)
Responders	55	17 (30.9%)	38 (69.1%)
	90		

Overall correctly classified: 71.1%

** $p \leq .01$

Table 16

UNIVARIATE F-RATIO FOR EACH VARIABLE INCLUDED IN THE DISCRIMINANT EQUATION OF DIFFERENCES BETWEEN RSP2 RESPONDERS AND NONRESPONDERS (1 AND 88 df). NEUROPSYCHOLOGICAL TEST FACTOR SCORES

Variable	F-Ratio	p=
Performance Abilities	15.06	.000***
Verbal Abilities	.937	.760
Motor Speed and Strength	.162	.688
Motor Steadiness	.251	.618
Motor Coordination & Dexterity	4.483	.037*
Form Perception Time	.141	.991
Finger Agnosia	6.423	.013*
Form Perception Errors	.589	.445

* $p \leq .05$
*** $p \leq .001$

most on Performance Abilities, Finger Agnosia, and Motor Coordination and Dexterity.

In order to determine on which specific tests responders and nonresponders differed, univariate t-tests were performed on the actual test data that made up the factor scores that were significant in the F-tests. The results of the t-tests are presented in Table 17. The results show that the performance of the responders was more impaired than that of the nonresponders on all the actual assessment variables. For the following variables, this difference was significant: Raven's Matrices; TPT total, location and memory scores, the Maze Coordination test for the nondominant hand, and Finger Agnosia for the dominant hand.

3. Response as Defined by Performance on RSP3:

The results of the discriminant function analysis employing neuropsychological test factor scores as predictors of response on RSP3 are presented in Table 18. This analysis yielded a single discriminant function with a Wilk's Lambda of .8383 (df 8, p=.063). The standardized discriminant function coefficients indicate that the highest loadings were on the Performance Abilities, Motor Steadiness, Finger Agnosia, and Motor Speed and Strength factor score variables.

The results of the univariate F-tests indicate that responders and nonresponders differed most on the factor score variable Performance Abilities. These results are

Table 17

UNIVARIATE t-TESTS OF DIFFERENCES BETWEEN RESPONDERS AND NONRESPONDERS AS DEFINED BY RSP2 NEUROPSYCHOLOGICAL TEST (ACTUAL) SCORES

Test	Mean (X) Nonresponders	Responders	t	p=
WISC Performance IQ	105.4	100.8	1.86	.066
Raven's Matrices	56.6	49.4	4.21	.000***
TPT Total Time T-Score	43.7	48.7	-2.60	.011*
TPT Location T-Score	56.1	47.2	4.05	.000***
TPT Memory T-Score	55.7	49.8	3.02	.003**
Category Test Errors T-Score	45.3	47.2	-1.02	.312
Maze Coordination Dominant Total Time T-Score	44.6	45.6	-1.16	.248
Maze Coordination Nondominant Total Time T-Score	42.6	46.2	-2.66	.009**
Pegs Dominant Total Time T-Score	43.9	45.3	-1.24	.220
Pegs Nondominant Total Time T-Score	44.7	46.9	-1.19	.238
Finger Agnosia Dominant T-Score	48.1	52.8	-2.62	.010**
Finger Agnosia Nondominant T-Score	49.7	53.4	-1.86	.067

* $p \leq .05$
** $p \leq .01$
*** $p \leq .001$

Table 18

RESULTS OF DISCRIMINANT FUNCTION ANALYSIS OF RSP3 RESPONDERS AND NONRESPONDERS NEUROPSYCHOLOGICAL TEST FACTOR SCORES AS PREDICTORS OF RESPONSE

Standardized Canonical Discriminant Function Coefficients	
Performance Abilities	.60832
Verbal Abilities	-.31223
Motor Speed and Strength	-.40572
Motor Steadiness	-.47653
Motor Coordination and Dexterity	-.19291
Form Perception Time	.18894
Finger Agnosia	-.41416
Form Perception Errors	-.30000

Discriminant Function	Eigenvalue	Canonical Correlation	Wilk's λ	df	p=
1	.19290	.402	.8383	8	.063

Classification Results

Actual Group	N	Predicted Group Membership: Nonresponders	Responders
Nonresponders	64	42 (65.6%)	22 (34.4%)
Responders	26	10 (38.5%)	16 (61.5%)
	90		

Overall correctly classified: 64.4%

presented in Table 19.

Univariate t-tests of the actual test data that had gone into the factor score variable Performance Abilities are presented in Table 20. The results show that responders performed equally (Category Test Errors) or more poorly than the nonresponders on all the variables although they differed significantly only on the TPT location score.

Summary

Neuropsychological test factor scores were employed in discriminant function analyses as predictors of response to methylphenidate. The predictor variables involved in the discriminant function analyses that reached or approached statistical significant were explored further by univariate analyses at two levels; i.e., one-way analyses of variance for the neuropsychological test factor scores, followed by t-tests of the variables that loaded heavily on the significant factor scores. These t-tests of the actual neuropsychological test scores were performed in order to determine which tests separated the groups (i.e., responders from nonresponders). For response defined by RSP3, responders and nonresponders did not differ on Category Test Errors T-Score. For all other neuropsychological test variables subjected to t-test analyses, the responders showed more impaired performance than did the nonresponders, and many of these differences were statistically significant.

Table 19

UNIVARIATE F-RATIO FOR EACH VARIABLE INCLUDED IN THE DISCRIMINANT EQUATION OF DIFFERENCES BETWEEN RSP3 RESPONDERS AND NONRESPONDERS (1 AND 88 df) NEUROPSYCHOLOGICAL TEST FACTOR SCORES

Variable	F-Ratio	p=
Performance Abilities	5.067	.027*
Verbal Abilities	.384	.537
Motor Speed and Strength	.488	.487
Motor Steadiness	2.740	.101
Motor Coordination & Dexterity	1.874	.175
Form Perception Time	.948	.923
Finger Agnosia	2.334	.130
Form Perception Errors	3.608	.061

* $p \leq .05$

Table 20

UNIVARIATE t-TESTS OF DIFFERENCES BETWEEN RESPONDERS AND NONRESPONDERS AS DEFINED BY RSP3 NEUROPSYCHOLOGICAL TEST (ACTUAL) SCORES

Test	Mean (X) Nonresponders	Responders	t	p=
WISC Performance IQ	103.8	99.6	1.53	.129
Raven's Matrices	53.0	50.4	1.34	.185
TPT Total Time T-Score	45.9	48.9	-1.37	.174
TPT Location T-Score	52.9	46.3	2.71	.008**
TPT Memory T-Score	53.1	50.0	1.36	.179
Category Test Errors T-Score	46.5	46.4	.05	.962

** $p \leq .01$

CHAPTER IV

DISCUSSION

A number of issues were addressed in the present study and each will be considered in turn. The first concern of this study was to define response to treatment. Ferguson and Trites (1980) demonstrated that using different criteria for response resulted in wide variability of response rate. This finding was cited as a plausible explanation for the varying rates of response reported in the literature. The criteria employed by Ferguson and Trites (1980) were: improvement on 5 out of 7 measures of attention; improvement on parent and teacher global ratings of response; a 10% improvement on Conners' TRS and PSQ hyperactivity scales; and different combinations of the three preceding criteria. The criteria in the present study were somewhat different than those employed by Ferguson and Trites. Response on attention measures was broken down further in the present study, and parent and teacher ratings were not combined. Nevertheless, the results of the present study also show that the more complex the criteria for response (i.e. combined measures), the fewer children were found to be responders.

Barkley (1976) cited 75% as the average response rate in the studies he reviewed. In general, lower levels of response were found in the present study. This may be due to the more stringent criteria for response employed here.

Whereas some studies have defined response as drug condition showing improvement over baseline, the present study contrasted drug to placebo, and only if a subject performed better on drug than on placebo was he considered to be a responder. This comparison was possible because each subject received both drug and placebo. Subjects in this study were also required to show a consistent response, before they were designated as responders or nonresponders. This could be achieved because an A-B-A (i.e., Drug-Placebo-Drug or Placebo-Drug-Placebo) design was employed, as opposed to the traditional A-B (i.e., Drug-Placebo, or Placebo-Drug) design. Another possible reason for the lower response rates reported in the present study, has to do with drug dosage. In this study, drug dosage was not individually titrated for each subject. The daily dosage of methylphenidate was based on a standard mg/kg equation, following the suggestion of Werry and Sprague (1971). Although this method is preferable in research, due to its objectivity, it is possible that the standard daily dosage of .5 mg/kg was too low for some would-be responders. The average daily dosage in this study was around 16 mg, which is low compared to the daily dosage recommendations in the literature.

Responders were significantly different from nonresponders ($p \leq .001$) on all the dependent variables used to define response, indicating that real group differences were present. However, there still remains the problem that

responders and nonresponders who fall in the middle ground between definite improvement and no improvement may differ very little from each other. The average number of responders for the attentional measures taken singly, was 46.8%, which compares favourably to the response rates achieved when response was defined in terms of 10% improvement on the PSQ hyperactivity scale (i.e., 50% of subjects were responders on PSQ hyperactivity). The rate of response was considerably lower when defined in terms of TRS hyperactivity scale (35.8%), however, as discussed, this figure was determined on fewer subjects, and response was defined in a different fashion for this dependent variable. The fact that the different individual criteria for response produced such discrepancy in the reported rate of responders cautions one in interpreting the results of other studies that have used only one criterion for response.

In the recent literature on hyperactivity, it has become more and more apparent that hyperactivity is not a unitary disorder, and that all hyperactive children do not respond equally well to the same kind of treatment. This prompted the postulation of different subgroups of hyperactive children based on certain outstanding features that were felt to differentiate certain hyperactive children from others (Dubey, 1976; Epstein, et al, 1968; Ferguson & Trites, 1980; Lambert et al, 1976; Satterfield et al, 1973). Brain dysfunction was hypothesized to play an important role in the

hyperactivity of some, but not necessarily all hyperactive children. Many of the studies reviewed (Conrad & Insel, 1967; Epstein et al, 1968; Millichap & Johnson, 1974; Steinberg et al, 1971) provided evidence for better response to drug treatment in hyperactive children with evidence of brain dysfunction. However, definitive conclusions could not be drawn from this literature. One of the most frequent difficulties encountered in these studies was in how a subject was diagnosed as having brain dysfunction. Ferguson and Trites (1980) provided a more objective measure of brain dysfunction. Diagnosis of presence of brain dysfunction was based on neuropsychological test scores. They found that when response was defined as improvement on 5 out of 7 attention measures, individuals diagnosed as showing evidence of brain dysfunction demonstrated higher rates of response than those with no evidence of brain dysfunction ($p < .025$). The brain dysfunction group showed a higher response rate when response was defined in terms of the other seven criteria employed, however none of these findings was significant.

Learning difficulties often accompany hyperactivity. Ferguson and Trites (1980) investigated the possibility that differential response to stimulants may occur in hyperactive children with and without learning difficulties. They found no systematic relationship between response to methylphenidate and learning difficulty. The criterion

employed in their study to define learning difficulty was academic achievement at least one year behind expected level (as measured by the WRAT). This criterion is not very stringent and perhaps has resulted in too many false positives (i.e., children labelled as having learning difficulties who do not have them). Hence, in the present study learning difficulty was defined employing different criteria, as discussed.

One goal of the present study was to investigate further the predictive utility of subgrouping children in terms of brain dysfunction and learning difficulty. Although the results of this study showed that in 9 out of 10 comparisons there was a higher percentage of responders in the brain dysfunction than in the no brain dysfunction group, the results of χ^2 analyses of the relationship between brain dysfunction and response to treatment failed to reach significance. For learning difficulty, in 8 out of 10 comparisons the learning difficulty group showed a higher response rate than the no learning difficulty group, but these differences were not as marked as for brain dysfunction/no brain dysfunction, and were in fact not significant. These findings suggest that the dichotomies of brain dysfunction/no brain dysfunction and learning difficulty/no learning difficulty are not significant predictors of drug response. This does not mean however, that brain dysfunction and learning difficulties do not play

a role in response to treatment. The present study simply shows that brain dysfunction and learning difficulty as defined, and as dichotomies, were not predictive of response to treatment. These results are compatible with those of Ferguson and Trites (1980), even though learning difficulty and response criteria were different in their study. Only one of their χ^2 analyses of brain dysfunction and response was significant ($p < .025$). This occurred when response was defined as improvement on 5 and 7 attention measures. This criterion defined 39% of their subjects as responders. The present study has no directly comparable measure of response. RSP2 in the present study defines 60.4% of subjects as responders; RSP3 defines 28.1% of subjects as responders. It appears then, that the distinction of brain dysfunction/no brain dysfunction and learning difficulty/no learning difficulty, although suggestive of a relationship with response, did not have significant predictive utility.

A second approach to the issue of prediction of response to stimulant medication in the present study involved the use of the neuropsychological test scores as predictors of response. A large amount of data was reduced by (1) deleting variables found to be redundant (i.e., having a Pearson correlation of greater than .75 with one or more other variables) and (2) by factor analysis of the remaining variables and the creation of factor scores. The original neuropsychological assessment data were thus reduced to

eight factor score variables.

The results of the discriminant function analyses using the eight neuropsychological test factor scores as predictors showed that neuropsychological test scores were significant predictors of response, when response was defined as improved performance on 2 out of 4 attention measures (RSP2). The discriminant function analyses using neuropsychological test factor scores as predictors approached significance when response was defined as improvement on MFF errors and when performance on 3 out of 4 attention measures (RSP3) was improved. The number of responders defined by improvement on MFF errors and on RSP2 was 58; for RSP3, 27 subjects were responders. It would appear that RSP3 is defining a different group of subjects. Except for Category test errors, where nonresponders and responders on RSP3 scored the same, in all univariate analyses of the actual neuropsychological test scores, responders performed more poorly than nonresponders, and many of these comparisons were significant. The variables that were significantly different for responders and nonresponders (t-test) on MFF errors were WISC Performance IQ, TPT location and memory scores, Category test errors, and Finger Agnosia for both dominant and nondominant hands. For RSP2, the following test variables were significantly different for responders and nonresponders: Raven's Matrices, TPT total, location, and memory scores, Maze Coordination (nondominant), and Finger

Agnosia for the dominant hand. For RSP3, only the TPT location score was significantly different for responders and nonresponders.

One possibility to consider here is that responders were initially more hyperactive (i.e., more impulsive, distractible, and deficient in attention) than nonresponders, and as a result performed more poorly on the pre-treatment neuropsychological assessment. During treatment, these same children may have improved most dramatically on the dependent measures, hence were designated as responders. In this way, initial degree of hyperactivity would be the predictor of drug response. If original degree of hyperactivity was the actual predictor of drug response, one might expect significant differences between responders and nonresponders on the pre-treatment TRS and PSQ hyperactivity scales and on the baseline measures of attention. T-tests of the scores of responders vs. nonresponders (as defined by response on MFF errors, RSP2, and RSP3) on PSQ and TRS hyperactivity scales and the four baseline attentional measures are presented in Tables E-1 and E-2 in Appendix E. The results show that responders in fact scored lower on the PSQ and TRS hyperactivity scales given at pre-treatment than did nonresponders (although only one comparison reached significance). Of the baseline measures of attention, two were significant; one suggesting poorer initial attention for responders (MFF errors for RSP2 responders), the other,

better initial attention for responders (CPT omissions for RSP3 responders). The comparisons that approached significance suggest poorer initial attention span for responders. These findings then, do not suggest that responders to methylphenidate are more hyperactive as viewed by mothers and teachers, although when more objective measures were employed the results suggest that they may initially have more deficits in attention.

What can we conclude from the present study? Single measures of response may be unreliable. As the criteria for response become more stringent, i.e., combined measures, one may feel more certain that a real change is being assessed, and that improvement is less likely to be due to chance. A problem arises when one must decide which criterion to apply. For example: 60.4% of children responded to 2 out of 4 attention measures, and 28.1% responded on 3 out of 4 attention measures in the present study. A criterion of 2 out of 4 may have too many false positives (that is, equivocal responders defined as responders), but a criterion of 3 on 4 may leave out many children who could benefit from stimulant drug treatment. This latter problem appears to have occurred in the present study. An average response rate across studies of 75% has been cited in the literature (Barkley, 1976). RSP3 defines only 28.1% of subjects as responders. Thus the RSP3 nonresponder group likely includes many false negatives (i.e., subjects that are classified as

nonresponders when they really are responding to the treatment). This would explain why neuropsychological differences between responders and nonresponders decrease when going from RSP2 to RSP3. The would-be responders in the nonresponder group presumably have poorer neuropsychological test scores which they bring with them into the nonresponder group, thus minimizing the differences between the two groups. Follow-up studies of those children who continue on a program of stimulant medication, to compare outcome of those who were responders on RSP2 and on RSP3 would provide information necessary in evaluating which criteria proved to be the most useful in the long run. Given what is presently known about response to drug treatment in general, the number of responders defined by RSP2 is more in keeping with what has been reported in the literature. If we take responders as defined by RSP2 as perhaps the most effectual measure in the present study, the results demonstrate that responders and nonresponders can be significantly discriminated by neuropsychological test scores. The factor scores that contributed significantly to the difference between responders and nonresponders were Performance Ability, Motor Coordination and Dexterity, and Finger Agnosia. The actual neuropsychological test scores that achieved significance on t-test comparisons between responders and nonresponders were Raven's Matrices, the three scores from the TPT test, Maze Coordination nondominant hand, and Finger Agnosia dominant

hand. On all these measures, and on those that failed to reach statistical significance as well, responders scored more poorly than nonresponders. On parent and teacher ratings of hyperactivity, responders and nonresponders were not significantly different. On one out of four attention measures given at baseline, responders were seen to perform more poorly than nonresponders. Several conclusions can be drawn from the preceding. Neuropsychological test scores are significant predictors of improvement on attention measures given during methylphenidate treatment. Children with neuropsychological test deficits appear to be better responders to treatment. The pre-treatment behavior of these responders was not rated by mothers and teachers as being more hyperactive on the Conners' scales, than that of nonresponders. However, on the measures of attention, results of baseline performance suggested that initial attentional deficits may be more severe in subjects subsequently found to be responders to methylphenidate.

A few comments about the present study and suggestions for future research may be noted. The use of multiple criteria for response has pointed out the great variability in the number of responders when defined by different criteria. The results of the present study do not suggest that response as measured by improvement on behavior rating scales and on measures of attention are necessarily related. This raises some questions regarding behavior rating scales

and measures of attention. The rating scales contain items pertaining to attention span, as well as to other symptoms of hyperactivity. Changes in attention likely cannot be judged accurately by parents and teachers, or other observers for that matter. Children whose most obvious behavioral symptoms have been attenuated may erroneously be assumed by raters to have improved in all facets of their hyperactivity, including attention span. A child who has become noticeably less disruptive may still maintain his original attentional deficit. The discrepancy between what observers believe to have changed and what actually has changed is apparent in academic outcome studies. In their review Barkley and Cunningham (1978) found that academic outcome studies frequently led to the conclusion that stimulant drugs increased academic achievement, when change in achievement was assessed by teacher opinion. However, when objective achievement tests were employed as measures of academic performance, few positive short-term or long-term drug effects were found. It appears that teachers assumed academic improvement because noticeable positive behavioral change had occurred.

It seems that with treatment, some children who have become more manageable, have not improved in attention; others may have improved attention span, but remain a management problem. Of course some children may improve in both ways, or in neither way as a result of treatment. What

is being suggested here is that different problems associated with hyperactivity may improve as a result of treatment for different children. Gittelman-Klein and Klein (1975) found little evidence to support the notion that cognitive and behavioral change occur together. Sprague and Sleator (1976) found that optimal cognitive change and optimal social change did not occur together, and that this was related to drug dosage. It seems that behavior rating scales and measures of attention are sensitive to different aspects of hyperactivity, and that treatment may effect different aspects of hyperactivity for different children. This being so, perhaps the subsequent school performance of children treated with stimulant drugs who improve on attention measures and children who improve on behavior rating scale measures would differ. The literature has shown that children whose behavior has been rated by their teachers as improved, do not necessarily show significant improvement on academic achievement tests. Perhaps the outcome for responders on attention measures would be more positive. Future long term treatment studies comparing the classroom behavior and academic achievement of responders as measured by behavior rating scales and responders on attention measures would clarify this issue. Neuropsychological test predictors may be linked to this endeavor as well, due to their ability to predict improvement in attention.

Why do some children improve on measures of attention

and others on behavior ratings? It is possible that the nature of their problems was different to begin with. If behavior rating scales and measures of attention could be related to actual classroom performance, this would likely provide information on why children respond to treatment in different ways. It would also provide a test of construct validity for both those types of measures, as suggested by Barkley (1977).

One of the problems encountered in employing dichotomies such as response/no response, brain dysfunction/no brain dysfunction, and learning difficulty/no learning difficulty, is that subjects who fall between these extremes may not differ greatly from each other, yet are classified into the two groups. Response to treatment can be seen as a continuum from adverse to optimal response. This can be demonstrated in a single subject by varying the drug dosage; which in fact, is the principle employed when titrating dosage for a particular child. The medication is increased until an optimal level of behavior change is reached, without accompanying side effects. Perhaps a graded index of response would be more reflective of the actual nature of response. For example: response could be graded as optimal, good, fair, nonresponse, and adverse response. Such a graded scale of response may also be used to make the distinctions between response and nonresponse using multiple criteria less rigid. For example: a responder on 2 out of 4 measures may

be seen as a fair responder; on 3 out of 4, a good responder; and on 4 out of 4, an optimal responder.

The same kind of problem arises with the issue of brain dysfunction. Some cases may not be as clear-cut as others, yet due to the dichotomy of BD/NBD employed in this study, must be assigned to one or the other group. Perhaps if brain dysfunction was subdivided into three groups i.e., evidence of brain dysfunction, equivocal evidence of brain dysfunction, and no evidence of brain dysfunction, such a subgrouping might prove to have significant predictive (and hence clinical) utility.

The nature of learning difficulty may perhaps be better represented by taking degree of difficulty into account. The present study employed different criteria at different grade levels, in order to consistently define the same number of children as having learning difficulty at the different grade levels. This represents an improvement over previous research which employed a single criterion. However, the present criteria were still rough, being based only on achievement test scores. Perhaps subdividing learning difficulty to reflect the degree of the problem would be instructive. Another possibility would be to separate the children who are simply behind in school from those who have problems that fall under the diagnostic category of Specific Learning Disabilities.

To summarize, the present study shows that neuropsychological test scores are predictive of response to methylphenidate when response is defined in terms of improvement on certain measures of attention. However, in terms of clinical practice, it would be difficult to apply results from a group study of neuropsychological scores to an individual child, when recommending treatment. This is where the subgroups would have been useful.

When children were simply grouped according to presence or absence of brain dysfunction, based on clinical interpretation of neuropsychological test scores, responders and nonresponders could not significantly be predicted from each other. It was suggested that this may be due to subjects with equivocal evidence of brain dysfunction, and that would they be classified as such, the subgroupings may prove more productive. Suggestions regarding the defining of response and learning difficulty were discussed.

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APPENDIX A

TEST BATTERY, CONNERS' PSQ, CONNERS' TRS

TEST BATTERY

(in order of administration)

Dynamometer Grip Strength (Dominant & Nondominant) 1st trial

Finger Agnosia (Dominant and Nondominant)

Tactile Forms (Dominant and Nondominant)

Dynamometer Grip Strength (Dominant & Nondominant) 2nd trial

Grooved Pegboard (Dominant and Nondominant)

Wechsler Intelligence Scale for Children Revised (WISC)

Holes Steadiness Test (Dominant and Nondominant)

Peabody Picture Vocabulary Test

Developmental Drawings Test

Finger Tapping (Dominant and Nondominant)

Foot Tapping (Dominant and Nondominant)

Maze Coordination Test (Dominant and Nondominant)

Raven's Coloured Progressive Matrices

Category Test

Tactual Performance Test (TPT)

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Conners' Parent Symptom Questionnaire (PSQ)

Conners' Teacher Rating Scale (TRS)

CONNERS PARENT'S QUESTIONNAIRE

Name of Child _____ Date _____

Your Name _____ Relationship _____

Instructions: Listed below are items concerning children's behaviour or the problems they sometimes have. Read each item carefully and decide how much you think your child has been bothered by this problem *during the past month* –

NOT AT ALL, JUST A LITTLE, PRETTY MUCH or VERY MUCH

Indicate your choice by placing a check mark (√) in the appropriate column to the right of each item.

ANSWER ALL ITEMS

Observation	Not at All	Just a little	Pretty Much	Very much
PROBLEMS OF EATING				
1. Picky and finicky				
2. Will not eat enough				
3. Overweight				
PROBLEMS OF SLEEP				
4. Restless				
5. Nightmares				
6. Awakens at night				
7. Cannot fall asleep				
FEAR AND WORRIES				
8. Afraid of new situations				
9. Afraid of people				
10. Afraid of being alone				
11. Worries about illness and death				
MUSCULAR TENSION				
12. Gets stiff and rigid				
13. Twitches, jerks, etc.				
14. Shakes				
SPEECH PROBLEMS				
15. Stuttering				
16. Hard to understand				
WETTING				
17. Bed wetting				
18. Runs to bathroom constantly				
BOWEL PROBLEMS				
19. Soiling self				
20. Holds back bowel movements				
COMPLAINS OF FOLLOWING SYMPTOMS EVEN THOUGH DOCTOR CAN FIND NOTHING WRONG				
21. Headaches				
22. Stomach aches				
23. Vomiting				
24. Aches and pains				
25. Loose bowels				
PROBLEMS OF SUCKING, CHEWING or PICKING				
26. Sucks thumb				
27. Bites or picks nails				
28. Chews on clothes, blankets, or others				
29. Picks at things such as hair, clothing, etc.				
CHILDISH OR IMMATURE				
30. Does not act his age				
31. Cries easily				
32. Wants help doing things he should do alone				
33. Clings to parents or other adults				
34. Baby talk				
TROUBLE WITH FEELINGS				
35. Keeps anger to himself				
36. Lets himself get pushed around by other children				
37. Unhappy				
38. Carries a chip on his shoulder				

ANSWER ALL ITEMS

Observation	Not at All	Just a little	Pretty much	Very much
OVER-ASSERTS HIMSELF				
39. Bullying				
40. Bragging and boasting				
41. Sassy to grown-ups				
PROBLEMS MAKING FRIENDS				
42. Shy				
43. Afraid they do not like him				
44. Feelings easily hurt				
45. Has no friends				
PROBLEMS WITH BROTHERS AND SISTERS				
46. Feels cheated				
47. Mean				
48. Fights constantly				
PROBLEMS KEEPING FRIENDS				
49. Disturbs other children				
50. Wants to run things				
51. Picks on other children				
RESTLESS				
52. Restless or over active				
53. Excitable, impulsive				
54. Fails to finish things he starts – short attention span				
TEMPER				
55. Temper outbursts, explosive and unpredictable behaviour				
56. Throws himself around				
57. Throws and breaks things				
58. Pouts and sulks				
SEX				
59. Plays with own sex organs				
60. Involved in sex play with others				
61. Modest about his body				
PROBLEMS IN SCHOOL				
62. Is not learning				
63. Does not like to go to school				
64. Is afraid to go to school				
65. Daydreams				
66. Truancy				
67. Will not obey school rules				
LYING				
68. Denies having done wrong				
69. Blames others for his mistakes				
70. Tells stories which did not happen				
STEALING				
71. From parents				
72. At school				
73. From stores and other places				
FIRE-SETTING				
74. Sets fires				
TROUBLE WITH POLICE				
75. Gets into trouble with the police				
Why?				
PERFECTIONISM				
76. Everything must be just so				
77. Things must be done same way every time				
78. Sets goals too high				
ADDITIONAL PROBLEMS				
79. Inattentive, easily distracted				
80. Constantly fidgeting				
81. Cannot be left alone				
82. Always climbing				
83. A very early riser				
84. Will run around between mouthfuls at meals				

TRITES, OTTAWA

85. Demands must be met immediately – easily frustrated				
86. Cannot stand too much excitement				
87. Laces and zippers are always open				
88. Cries often and easily				
89. Unable to stop a repetitive activity				
90. Acts as if driven by a motor				
91. Mood changes quickly and drastically				
92. Poorly aware of surroundings or time of day				
93. Still cannot tie his shoelaces				

Conners' Teacher Rating Scale

V. Listed below are descriptive terms of behaviour. Place a check mark in the column which best describes this child. ANSWER ALL ITEMS.

Observation	Degree of Activity			
	Not at all	Just a little	Pretty much	Very much
CLASSROOM BEHAVIOUR				
1. Constantly fidgeting				
2. Hums and makes other odd noises				
3. Demands must be met immediately-easily frustrated				
4. Coordination poor				
5. Restless or overactive				
6. Excitable, impulsive				
7. Inattentive, easily distracted				
8. Fails to finish things he starts-short attention span				
9. Overly sensitive				
10. Overly serious or sad				
11. Daydreams				
12. Sullen or sulky				
13. Cries often and easily				
14. Disturbs other children				
15. Quarrelsome				
16. Mood changes quickly and drastically				
17. Acts "smart"				
18. Destructive				
19. Steals				
20. Lies				
21. Temper outbursts, explosive and unpredictable behaviour				
GROUP PARTICIPATION				
22. Isolates himself from other children				
23. Appears to be unaccepted by group				
24. Appears to be easily led				
25. No sense of fair play				
26. Appears to lack leadership				
27. Does not get along with opposite sex				
28. Does not get along with same sex				
29. Teases other children or interferes with their activities				
ATTITUDE TOWARD AUTHORITY				
30. Submissive				
31. Defiant				
32. Impudent				
33. Shy				
34. Fearful				
35. Excessive demands for teacher's attention				
36. Stubborn				
37. Overly anxious to please				
38. Uncooperative				
39. Attendance problem				

How would you rate this child's behaviour compared to other children the same age?

much worse ☐ worse ☐ about the same ☐ better ☐ much better ☐

Do you think this child needs special help?

yes ☐ no ☐

Signature _____ Title _____ Date Signed _____

NAME _____ DATE _____ EX _____ TEST # _____

CONNERS PARENT SYMPTOM QUESTIONNAIRE

Factor	Title	Items to be Summed	Total Sum	Total Possible	%
I	Conduct Problem	39 40 41 47 48 51 69		21	
II	Anxiety	8 9 10 11 42 64 43		21	
III	Impulsive – Hyperactive	79 80 81 82 83 84 89 90		24	
IV	Learning Problem	45 62 63 67		12	
V	Psychosomatic	6 21 22 23 24		15	
VI	Perfectionism	76 77 78		9	
VII	Antisocial	71 72 73 75		12	
VIII	Muscular Tension	12 13 14 36		12	

Total Score _____ Total Possible 279 % _____

CONNERS TEACHER SYMPTOM QUESTIONNAIRE

Factor	Title	Items to be Summed	Total Sum	Total Possible	%
I	Conduct Problem	12 15 17 18 19 20 21		36	
		-30* 25 31 32 36 38			
II	Inattentive – Passive	-4 7 8 11 24 26		18	
III	Tension – Anxiety	9 10 30 33 34 -39*		15	
IV	Hyperactivity	1 2 5 6 14 29		18	

Total Score _____ Total Possible 111 % _____

* NOTE that these scores are *subtracted* from the sum.

TRITES, OTT

APPENDIX B

PARENT (MOTHER) AND TEACHER RATING SCALE SCORES AT TIME OF INITIAL TESTING

Table B-1

PSQ AND TRS AT TIME OF INITIAL TESTING

Scale	X	S.D.	Range
PSQ			
Conduct Problem	1.06	.75	0 to 3.00
Anxiety	.68	.49	0 to 2.14
Impulsive-Hyperactive	1.46	.64	0 to 2.88
Learning Problem	.97	.57	0 to 2.50
Psychosomatic	.44	.44	0 to 1.60
Perfectionism	.66	.83	0 to 3.00
Antisocial	.09	.20	0 to 1.00
Muscular Tension	.41	.52	0 to 2.25
TOTAL	.83	.35	.09 to 1.89
TRS			
Conduct Problem	.83	.68	0 to 2.17
Inattentive-Passive	1.71	.64	0 to 3.00
Tension-Anxiety	.79	.57	0 to 2.61
Hyperactivity	2.03	.65	0 to 3.00
TOTAL	1.19	.46	.15 to 2.00

APPENDIX C

DEFINING RESPONSE:

COMPUTER PROGRAM

TABLES OF NUMBER OF SUBJECTS, MEANS AND STANDARD DEVIATIONS BEFORE AND AFTER REPLACING MISSING VALUES WITH GROUP MEAN

Defining Response

```
 5 IF          (BDP2 EQ 3 AND CPTOM1     EQ 999)   CPTOM1=1.533
 6 IF          (BDP2 EQ 3 AND CPTCO1     EQ 999)   CPTCO1=1.767
 7 IF          (BDP2 EQ 3 AND MFFERR1    EQ 999)  MFFERR1=14.133
 8 IF          (BDP2 EQ 3 AND MFFLAT1    EQ 999)   MFFLAT1=11.667
 9 IF          (BDP2 EQ 3 AND CONMIMP1   EQ 999)   CONMIMP1=43.000
10 IF          (BDP2 EQ 3 AND CPTOM2     EQ 999)   CPTOM2=1.966
11 IF          (BDP2 EQ 3 AND CPTCO2     EQ 999)   CPTCO2=1.517
12 IF          (BDP2 EQ 3 AND MFFERR2    EQ 999)   MFFERR2=11.667
13 IF          (BDP2 EQ 3 AND MFFLAT2    EQ 999)   MFFLAT2=12.000
14 IF          (BDP2 EQ 3 AND CONMIMP2   EQ 999)   CONMIMP2=35.269
15 IF          (BDP2 EQ 3 AND CPTOM3     EQ 999)   CPTOM3=2.167
16 IF          (BDP2 EQ 3 AND CPTCO3     EQ 999)    CPTCO3=1.033
17 IF          (BDP2 EQ 3 AND MFFERR3    EQ 999)   MFFERR3=10.033
18 IF          (BDP2 EQ 3 AND MFFLAT3    EQ 999)   MFFLAT3=13.467
19 IF          (BDP2 EQ 3 AND CONMIMP3   EQ 999)   CONMIMP3=28.120

20 IF          (BDP2 EQ 3 AND CPTOM4     EQ 999)   CPTOM4=2.414
21 IF          (BDP2 EQ 3 AND CPTCO4     EQ 999)   CPTCO4=1.276
22 IF          (BDP2 EQ 3 AND MFFERR4    EQ 999)   MFFERR4=11.034
23 IF          (BDP2 EQ 3 AND MFFLAT4 EQ 999) MFFLAT4=10.103
24 IF          (BDP2 EQ 3 AND CONMIMP4 EQ 999) CONMIMP4=32.231
25 IF          (BDP2 EQ 2 AND CPTOM1     EQ 999)   CPTOM1=2.924
26 IF          (BDP2 EQ 2 AND CPTCO1     EQ 999)   CPTCO1=2.818
27 IF          (BDP2 EQ 2 AND MFFERR1    EQ 999)   MFFERR1=12.818
28 IF          (BDP2 EQ 2 AND MFFLAT1    EQ 999)   MFFLAT1=11.924
29 IF          (BDP2 EQ 2 AND CONMIMP1   EQ 999)   CONMIMP1=47.754
30 IF          (BDP2 EQ 2 AND CPTOM2     EQ 999)   CPTOM2=2.046
31 IF          (BDP2 EQ 2 AND CPTCO2     EQ 999)   CPTCO2=1.877
32 IF          (BDP2 EQ 2 AND MFFLAT2    EQ 999)   MFFLAT2=11.985
33 IF          (BDP2 EQ 2 AND MFFERR2    EQ 999)   MFFERR2=10.258
34 IF          (BDP2 EQ 2 AND CONMIMP2   EQ 999)   CONMIMP2=35.393
35 IF          (BDP2 EQ 2 AND CPTOM3     EQ 999)   CPTOM3=2.274
36 IF          (BDP2 EQ 2 AND CPTCO3 EQ 999) CPTCO3=1.403
37 IF          (BDP2 EQ 2 AND MFFERR3 EQ 999) MFFERR3=9.667
38 IF          (BDP2 EQ 2 AND MFFLAT3 EQ 999) MFFLAT3=13.894
39 IF          (BDP2 EQ 2 AND CONMIMP3 EQ 999) CONMIMP3=35.915
40 IF          (BDP2 EQ 2 AND CPTOM4 EQ 999) CPTOM4=2.250
41 IF          (BDP2 EQ 2 AND CPTCO4 EQ 999) CPTCO4=1.297
42 IF          (BDP2 EQ 2 AND MFFERR4 EQ 999) MFFERR4=7.297
43 IF          (BDP2 EQ 2 AND MFFLAT4 EQ 999) MFFLAT4=10.484
44 IF          (BDP2 EQ 2 AND CONMIMP4 EQ 999) CONMIMP4=28.509
45 IF          (BDP2 EQ 2)CONMP3=(CONMIMP3) - (.1 * CONMIMP3)
46 IF          (BDP2 EQ 3)CONMP2=(CONMIMP2) - (.1 * CONMIMP2)
47 IF          (BDP2 EQ 3)CONMP4=(CONMIMP4) - (.1 * CONMIMP4)
48 IF          (BDP2 EQ 2)MIMPC=(CONMIMP2 * 1) + (CONMP3 * -2) +
49             (CONMIMP4 * 1)
50 IF          (BDP2 EQ 3)MIMPC=(CONMP2 * -1) + (CONMIMP3 * 2) +
51             (CONMP4 * -1)
52 IF          (MIMPC LT 0 AND NE 999) RSPMIMPX=1
53 IF          (MIMPC GE 0 AND NE 999)RSPMIMPX=0
54 ASSIGN MISSING CONMP3 TO RSPMIMPX(999)
55 DO REPEAT   TEST1=CPTOM1,CPTCO1,
56             MFFERR1,CONMIMP1,CONTHYP/
57             TEST2=CPTOM2,CPTCO2,
58             MFFERR2,CONMIMP2,CONTHYP2/
59             TEST3=CPTOM3,CPTCO3,
60             MFFERR3,CONMIMP3,CONTHYP3/
61             TEST4=CPTOM4,CPTCO4,
62             MFFERR4,CONMIMP4,CONTHYP4/
63             CONTX=CPTOMC,CPTCOC,
64             MFFERRC,CONMIMPC,CONTHYPC/
65             RESPX=CPTOMR,CPTCOR,
66             MFFERRR,CONMIMPR,CONTHYPR/
67 IF          (BDP2 EQ 2) CONTX=(TEST2*1) + (TEST3*-2) + (TEST4*1)
68 IF          (BDP2 EQ 3)CONTX=(TEST2*-1) + (TEST3*2) + (TEST4*-1)
69 IF          (CONTX LT 0 AND NE 999)RESPX=1
70 IF          (CONTX GE 0 AND NE 999)RESPX=0
71 ASSIGN MISSING CONTX TO RESPX(999)
72 END REPEAT
```

```
  73 IF              (BDP2 EQ 2) MFFLATC=(MFFLAT2*1) + (MFFLAT3*-2) + (MFFLAT4*1)
  74 IF              (BDP2 EQ 3) MFFLATC= (MFFLAT2*-1) + (MFFLAT3*2) + (MFFLAT4*-
  75 IF              (MFFLATC GT 0 AND NE 999) MFFLATR=1
  76 IF              (MFFLATC LE 0 AND NE 999) MFFLATR=0
  77 ASSIGN MISSING  MFFLATC TO MFFLATR(999)
  78 DO REPEAT       TEST1=CPTOM1,CPTCO1,
  79                 MFFERR1,MFFLAT1,CONMIMP1,CONTHYP/
  80                 TEST2=CPTOM2,CPTCO2,
  81                 MFFERR2,MFFLAT2,CONMIMP2,CONTHYP2/
  82                 TEST3=CPTOM3,CPTCO3,
  83                 MFFERR3,MFFLAT3,CONMIMP3,CONTHYP3/
  84                 TEST4=CPTOM4,CPTCO4,
  85                 MFFERR4,MFFLAT4,CONMIMP4,CONTHYP4/
  86                 DRUGX=CPTOMD,CPTCOD,
  87                 MFFERRD,MFFLATD,CONMIMPD,CONTHYPD/
  88                 PLACX=CPTOMP,CPTCOP,
  89                 MFFERRP,MFFLATP,CONMIMPP,CONTHYPP/
  90 IF              (BDP2 EQ 2 AND NE 999) DRUGX=(TEST2*.5) + (TEST4*.5)
  91 IF              (BDP2 EQ 3 AND NE 999) DRUGX=(TEST3*1)
  92 IF              (BDP2 EQ 2 AND NE 999)PLACX=(TEST3*1)
  93 IF              (BDP2 EQ 3 AND NE 999)PLACX=(TEST2*.5) + (TEST4*.5)
  94 ASSIGN MISSING  DRUGX TO PLACX(999)
  95 END REPEAT

LIRED    1096 BYTES OF WORKSPACE.

  96 COMPUTE         NUMT=CPTOMR + CPTCOR + MFFERRR + MFFLATR
  97 IF              (NUMT GE 1 AND NE 999)RSP1=1
  98 IF              (NUMT LT 1 AND NE 999)RSP1=0
  99 IF              (NUMT GE 2 AND NE 999)RSP2=1
 100 IF              (NUMT LT 2 AND NE 999)RSP2=0
 101 IF              (NUMT GE 3 AND NE 999)RSP3=1
 102 IF              (NUMT LT 3 AND NE 999)RSP3=0
 103 IF              (NUMT GE 4 AND NE 999)RSP4=1
 104 IF              (NUMT LT 4 AND NE 999)RSP4=0
 105 IF              (RSPMIMPX EQ 1 AND RSP1 EQ 1) BEHATT1=1
 106 IF              (RSPMIMPX EQ 0 OR RSP1 EQ 0) BEHATT1=0
 107 IF              (RSPMIMPX EQ 1 AND RSP2 EQ 1) BEHATT2=1
 108 IF              (RSPMIMPX EQ 0 OR RSP2 EQ 0) BEHATT2=0
 109 IF              (RSPMIMPX EQ 1 AND RSP3 EQ 1) BEHATT3=1
 110 IF              (RSPMIMPX EQ 0 OR RSP3 EQ 0) BEHATT3=0
 111 IF              (RSPMIMPX EQ 1 AND RSP4 EQ 1) BEHATT4=1
 112 IF              (RSPMIMPX EQ 0 OR RSP4 EQ 0) BEHATT4=0
 113 ASSIGN MISSING  NUMT TO BEHATT4(999)
 114 IF              (CONTHYP EQ 999) CONTHYP=HYPER
 115 COMPUTE         CONTHYDR = 0
 116 IF              (BDP2 EQ 2 AND CONTHYP2 NE 999 AND CONTHYP4 NE 999)
 117                 CONTHYDR =
 118                 (CONTHYP2 *.5) + (CONTHYP4 * .5)
 119 IF              (BDP2 EQ 2 AND CONTHYP2 EQ 999)CONTHYDR=CONTHYP4
 120 IF              (BDP2 EQ 2 AND CONTHYP4 EQ 999)CONTHYDR=CONTHYP2
 121 IF              (BDP2 EQ 3)CONTHYDR=CONTHYP3
 122 MISSING VALUES  CONTHYDR(999)
 123 COMPUTE         CONTHYPL = 0
 124 IF              (BDP2 EQ 3 AND CONTHYP2 NE 999 AND CONTHYP4 NE 999)
 125                 CONTHYPL= (CONTHYP2 *.5) + (CONTHYP4 * .5)
 126 IF              (BDP2 EQ 3 AND CONTHYP2 EQ 999)CONTHYPL=CONTHYP4
 127 IF              (BDP2 EQ 3 AND CONTHYP4 EQ 999)CONTHYPL=CONTHYP2
 128 IF              (BDP2 EQ 2)CONTHYPL=CONTHYP3
 129 MISSING VALUES  CONTHYPL(999)
 130 COMPUTE         TRSPL10= CONTHYPL - (.1 * CONTHYPL)
 131 COMPUTE         TRSC= CONTHYDR - TRSPL10
 132 IF              (TRSC LT 0 AND NE 999) RSPTHYPX = 1
 133 IF              (TRSC GE 0 AND NE 999) RSPTHYPX = 0
 134 ASSIGN MISSING  TRSPL10 TO RSPTHYPX(999)
 135 IF              (BDLD EQ 1)BD=1
 136 IF              (BDLD EQ 2)BD=1
 137 IF              (BDLD EQ 3)BD=0
 138 IF              (BDLD EQ 4)BD=0
 139 IF              (BDLD EQ 1)LD=1
 140 IF              (BDLD EQ 2)LD=0
 141 IF              (BDLD EQ 3)LD=1
 142 IF              (BDLD EQ 4)LD=0
 143 ASSIGN MISSING  BD TO LD(999)
 144 SAVE FILE       COMPLETE.FILE
```

Table C-1

NUMBER OF SUBJECTS, MEANS AND STANDARD DEVIATIONS,
MISSING VALUES EXCLUDED
DRUG-PLACEBO-DRUG GROUP (N=66)

Variable	Baseline	Drug	Placebo	Drug
CPT Omissions	N=66 X= 2.9 SD= 4.1	N=65 X= 2.0 SD= 2.5	N=62 X= 2.3 SD= 3.6	N=64 X= 2.3 SD= 3.5
CPT Commissions	N=66 X= 2.8 SD= 3.8	N=65 X= 1.9 SD= 2.6	N=62 X= 1.4 SD= 1.6	N=64 X= 1.3 SD= 2.7
MFF Errors	N=66 X=12.8 SD= 6.6	N=66 X=10.3 SD= 6.9	N=66 X= 9.7 SD= 6.6	N=64 X= 7.3 SD= 6.1
MFF Latency	N=66 X=11.9 SD= 5.8	N=66 X=12.0 SD= 5.0	N=66 X=13.9 SD=17.9	N=64 X=10.5 SD= 5.1
PSQ Hyperactivity	N=61 X= 1.43 SD= .62	N=61 X= 1.06 SD= .54	N=59 X= 1.08 SD= .63	N=55 X= .86 SD= .53

Table C-2

MEANS AND STANDARD DEVIATIONS
MISSING VALUES REPLACED BY GROUP MEAN
DRUG-PLACEBO-DRUG (N=66)

Variable	Baseline	Drug	Placebo	N=66 Drug
CPT Omissions	X= 2.9 SD= 4.1	X= 2.0 SD= 2.5	X= 2.3 SD= 3.5	X= 2.3 SD= 3.4
CPT Commissions	X= 2.8 SD= 3.8	X= 1.9 SD= 2.6	X= 1.4 SD= 1.5	X= 1.3 SD= 2.7
MFF Errors	X=12.8 SD= 6.6	X=10.3 SD= 6.9	X= 9.7 SD= 6.6	X= 7.3 SD= 6.0
MFF Latency	X=11.9 SD= 5.8	X=12.0 SD= 5.0	X=13.9 SD=17.9	X=10.5 SD= 5.0
PSQ Hyperactivity	X= 1.43 SD= .60	X= 1.06 SD= .52	X= 1.08 SD= .59	X= .86 SD= .48

Table C-3

NUMBER OF SUBJECTS, MEANS AND STANDARD DEVIATIONS,
MISSING VALUES EXCLUDED
PLACEBO-DRUG-PLACEBO GROUP (N=30)

Variable	Baseline	Placebo	Drug	Placebo
CPT Omissions	N=30 X= 1.5 SD= 1.7	N=29 X= 2.0 SD= 2.2	N=30 X= 2.2 SD= 2.9	N=29 X= 2.4 SD= 3.3
CPT Commissions	N=30 X= 1.8 SD= 3.4	N=29 X= 1.5 SD= 3.4	N=30 X= 1.0 SD= 1.2	N=29 X= 1.3 SD= 1.5
MFF Errors	N=30 X=14.1 SD= 6.6	N=30 X=11.7 SD= 6.4	N=30 X=10.0 SD= 7.4	N=29 X=11.0 SD= 6.5
MFF Latency	N=30 X=11.7 SD= 5.0	N=30 X=12.0 SD=12.5	N=30 X=13.5 SD=17.8	N=29 X=10.1 SD= 4.6
PSQ Hyperactivity	N=28 X= 1.29 SD= .68	N=26 X= 1.06 SD= .65	N=25 X= .84 SD= .69	N=26 X= .97 SD= .75

Table C-4

MEANS AND STANDARD DEVIATIONS
MISSING VALUES REPLACED BY GROUP MEAN
PLACEBO-DRUG-PLACEBO (N=30)

Variable	Baseline	Placebo	Drug	N=30 Placebo
CPT Omissions	X= 1.5 SD= 1.7	X= 2.0 SD= 2.2	X= 2.2 SD= 3.0	X= 2.4 SD= 3.3
CPT Commissions	X= 1.8 SD= 3.4	X= 1.5 SD= 3.3	X= 1.0 SD= 1.2	X= 1.3 SD= 1.5
MFF Errors	X=14.1 SD= 6.6	X=11.7 SD= 6.4	X=10.0 SD= 7.4	X=11.0 SD= 6.4
MFF Latency	X=11.7 SD= 5.0	X=12.0 SD=12.5	X=13.5 SD=17.8	X=10.1 SD= 4.5
PSQ Hyperactivity	X= 1.29 SD= .66	X= 1.06 SD= .60	X= .84 SD= .63	X= .97 SD= .69

Table C-5

NUMBER OF SUBJECTS, MEANS AND STANDARD DEVIATIONS,
MISSING VALUES EXCLUDED
DRUG VS. PLACEBO ALL SUBJECTS (N=96)

Variable	Baseline	Drug	Placebo
CPT Omissions	N=96 X= 2.5 SD= 3.6	N=93 X= 2.1 SD= 2.6	N=90 X= 2.3 SD= 3.3
CPT Commissions	N=96 X= 2.5 SD= 3.7	N=93 X= 1.4 SD= 1.8	N=90 X= 1.4 SD= 1.8
MFF Errors	N=96 X=13.2 SD= 6.2	N=94 X= 9.1 SD= 6.3	N=95 X=10.2 SD= 6.1
MFF Latency	N=96 X=11.8 SD= 5.5	N=94 X=12.0 SD=10.7	N=95 X=13.0 SD=15.4
PSQ Hyperactivity	N=89 X= 1.39 SD= .64	N=79 X= .90 SD= .53	N=84 X= 1.06 SD= .64

Table C-6

MEANS AND STANDARD DEVIATIONS
MISSING VALUES REPLACED BY GROUP MEAN
DRUG VS. PLACEBO ALL SUBJECTS (N=96)

N=96

Variable	Baseline	Drug	Placebo
CPT Omissions	X= 2.5 SD= 3.6	X= 2.2 SD= 2.6	X= 2.2 SD= 3.2
CPT Commissions	X= 2.5 SD= 3.7	X= 1.4 SD= 1.8	X= 1.4 SD= 1.8
MFF Errors	X=13.2 SD= 6.6	X= 9.2 SD= 6.2	X=10.2 SD= 6.1
MFF Latency	X=11.8 SD= 5.5	X=12.0 SD=10.6	X=13.0 SD=15.3
PSQ Hyperactivity	X= 1.39 SD= .62	X= .92 SD= .49	X= 1.06 SD= .60

APPENDIX D

PEARSON PRODUCT MOMENT CORRELATION OF NEUROPSYCHOLOGICAL TEST VARIABLES

FACTOR ANALYSES OF THE NEUROPSYCHOLOGICAL TEST VARIABLES

Table D-1

ORIGINAL DATA GROUPED FOR PEARSON CORRELATION

1. General Cognitive and Intellectual Tests

WISC Verbal IQ (WISCVIQ)

WISC Performance IQ (WISCPIQ)

Peabody IQ (PEABIQ)

Raven's Matrices T-Score (MATRST)

Developmental Drawings T-Score (DEVDRAWT)

TPT Total Time T-Score (TPTOTT)

TPT Location of Blocks T-Score (TPTLOCT)

TPT Memory T-Score (TPTMEMT)

Category Test Errors T-Score (CATOTT)

2. Motor Tests

Finger Tapping Dominant Speed T-Score (FINTAPDT)

Finger Tapping Nondominant Speed T-Score (FINTAPNT)

Foot Tapping Dominant Speed T-Score (FOOTAPDT)

Foot Tapping Nondominant Speed T-Score (FOOTAPNT)

Maze Coordination Test Dominant Total Time T-Score (MAZEDTTT)

Maze Coordination Test Nondominant Total Time T-Score (MAZENTTT)

Maze Coordination Test Dominant Counter Time T-Score (MAZEDCT)

Maze Coordination Test Nondominant Counter Time T-Score (MAZENCT)

Holes Steadiness Dominant Total Time T-Score (STEADDTT)

Holes Steadiness Nondominant Total Time T-Score (STEADNTT)

Holes Steadiness Dominant Counter Time T-Score (STEADDCT)

Holes Steadiness Nondominant Counter Time T-Score (STEADNCT)

Grooved Pegboard Dominant Total Time T-Score (PEGDT)

Grooved Pegboard Nondominant Total Time T-Score (PEGNT)

Dynamometer Grip Strength Dominant T-Score (LDOMDYDM)

Dynamometer Grip Strength Nondominant T-Score (LDOMDYNM)

3. Sensory Tests

Tactile Forms Dominant Total Time T-Score (TACTFDT)

Tactile Forms Nondominant Total Time T-Score (TACTFNT)

Tactile Forms Dominant Error T-Score (TACTFDET)

Tactile Forms Nondominant Error T-Score (TACTFNET)

Finger Agnosia Dominant T-Score (FINGAGDT)

Finger Agnosia Nondominant T-Score (FINGAGNT)

Table D-2

PEARSON CORRELATION
GENERAL COGNITIVE AND INTELLECTUAL TESTS

	WISCVIQ	WISCPIQ	PEABIQ	MATRST	DEVDRAWT	TPTOTT	TPTLOCT	TPTMEMT	CATOTT
WISCVIQ	1.0000								
WISCPIQ	.2483 **	1.0000							
PEABIQ	.6104 ***	.1766	1.0000						
MATRST	.2719 **	.4954 ***	.3245 **	1.0000					
DEVDRAWT	.2353 **	.2609 **	.1452	.2142 *	1.0000				
TPTOTT	-.1160	-.3246 ***	.0290	-.2198 *	-.0608	1.0000			
TPTLOCT	.1592	.2992 **	.1361	.3802 ***	.2213 *	-.4691 ***	1.0000		
TPTMEMT	.4031 ***	.4391 ***	.1667	.3507 ***	.2713 **	-.2957 **	.5292 ***	1.0000	
CATOTT	-.3313 ***	-.3730 ***	-.0779	-.3456 ***	-.1593	.3098 **	-.1968 *	-.3974 ***	1.0000

* $p \leq .05$
** $p \leq .01$
*** $p \leq .001$

Table D-3

PEARSON CORRELATION MOTOR TESTS

	FINTAPDT	FINTAPNT	FOOTAPDT	FOOTAPNT	MAZEDITT	MAZENTTT	MAZEDCT	MAZENCT	STEADDTT	STEADNTT	STEADDCT	STEADNCT	PEGDT	PEGNT	LDOMDYDM	LDOMDYNM
FINTAPDT	1.0000															
FINTAPNT	.6529 ***	1.0000														
FOOTAPDT	.2250 *	.2890 *	1.0000													
FOOTAPNT	.2390 *	.4924 ***	.8017 ***	1.0000												
MAZEDITT	-.2002 *	-.0715	-.1274	-.1339	1.0000											
MAZENTTT	-.1817 *	-.1954 *	-.1961 *	-.2988 **	.6429 ***	1.0000										
MAZEDCT	-.2737 **	-.1535	-.2167 *	-.2320 *	.7978 ***	.6381 ***	1.0000									
MAZENCT	-.2247 *	-.2151 *	-.2669 **	-.3739 ***	.5761 ***	.8794 ***	.7165 ***	1.0000								
STEADDTT	-.0715	-.0244	-.2359 *	-.1618	.2552 **	.1979 *	.2490 **	.1673 *	1.0000							
STEADNTT	-.0504	-.1455	-.1911 *	-.2277 *	.1603	.3079 ***	.1282	.2633 **	.7550 ***	1.0000						
STEADDCT	-.0672	-.0451	-.2178 *	-.1323	.2236 *	.1855 *	.2873 **	.2754 **	.8108 ***	.6528 ***	1.0000					
STEADNCT	-.0879	-.1133	-.2076 *	-.1589	.1211	.1726 *	.1421	.2196 *	.6332 ***	.7975 ***	.7904 ***	1.0000				
PEGDT	-.0859	-.0544	-.0051	-.0707	.3536 ***	.3034 **	.4572 ***	.2950 **	.1107	.0426	.0423	.0183	1.0000			
PEGNT	-.0096	-.3306 ***	.0115	-.2287 *	.1577	.3827 ***	.2317 *	.3763 ***	-.0875	-.0191	-.0095	-.0876	.2801 **	1.0000		
LDOMDYDM	.3364 ***	.3230 ***	.2508 *	.2238 *	-.1618	-.2207 *	-.1850 *	-.1535	-.1883 *	-.0983	-.1905 *	-.1142	-.0489	-.0203	1.0000	
LDOMDYNM	.3304 ***	.4364 ***	.2909 **	.3103 **	-.0838	-.1801 *	-.1198	-.1030	.1409	-.0986	-.1550	-.1418	-.0483	-.0886	.8801 ***	1.0000

* $p \leq .05$
** $p \leq .01$
*** $p \leq .001$

Table D-4

PEARSON CORRELATION
SENSORY TESTS

	TACTFDT	TACTFNT	TACTFDET	TACTFNET	FINGAGDT	FINGAGNT
TACTFDT	1.0000					
TACTFNT	.5480 ***	1.0000				
TACTFDET	.4094 ***	.0840	1.0000			
TACTFNET	.0158	.0602	.3814 ***	1.0000		
FINGAGDT	.0477	.1461	-.0083	.1282	1.0000	
FINGAGNT	.1088	.1263	.0829	.2139 *	.5122 ***	1.0000

* $p \leq .05$
*** $p \leq .001$

Table D-5

GENERAL COGNITIVE AND INTELLECTUAL TESTS
ASSESSMENT VARIABLES GROUPED FOR FACTOR ANALYSIS

WISC Verbal IQ
WISC Performance IQ
Peabody IQ
Raven's Matrices T-Score
Developmental Drawings T-Score
Tactual Performance Test (TPT) Total Time T-Score
Tactual Performance Test (TPT) Location of Blocks T-Score
Tactual Performance Test (TPT) Memory T-Score
Category Test Errors T-Score

Table D-6

EIGENVALUES AND PERCENT OF VARIANCE ACCOUNTED FOR BY THE TWO GENERAL COGNITIVE AND INTELLECTUAL TEST FACTORS

Factor	Eigenvalue	Percent of Variance
1. Performance Abilities	3.337	37.4
2. Verbal Abilities	1.419	15.8
		53.2

Table D-7

GENERAL COGNITIVE AND INTELLECTUAL TESTS
VARIMAX ROTATED FACTOR MATRIX

Variable	Factor 1	Factor 2
WISC Verbal I.Q.	.21201	.77212
WISC Performance I.Q.	.60537	.22325
Peabody I.Q.	.03524	.76314
Raven's Matrices T-Score	.51627	.31554
Developmental Drawing T-Score	.28030	.29080
TPT Total Time T-Score	-.57684	.06596
TPT Location T-Score	.68754	.09593
TPT Memory T-Score	.64815	.24019
Category Test Errors T-Score	-.47828	-.22918

Table D-8

MOTOR TESTS
ASSESSMENT VARIABLES GROUPED FOR FACTOR ANALYSIS

Finger Tapping Dominant Speed T-Score
Finger Tapping Nondominant Speed T-Score
Foot Tapping Dominant Speed T-Score
Maze Coordination Dominant Total Time T-Score
Maze Coordination Nondominant Total Time T-Score
Holes Steadiness Dominant Total Time T-Score
Holes Steadiness Nondominant Total Time T-Score
Grooved Pegboard Dominant Total Time T-Score
Grooved Pegboard Nondominant Total Time T-Score
Dynamometer Grip Strength Dominant T-Score

Table D-9

EIGENVALUES AND PERCENT OF VARIANCE ACCOUNTED FOR BY THE THREE MOTOR TEST FACTORS

Factor	Eigenvalues	Percent of Variance
1. Motor Speed and Strength	2.848	28.5
2. Motor Steadiness	1.672	16.7
3. Motor Coordination and Dexterity	1.584	15.8
		61.0

Table D-10

MOTOR TESTS
VARIMAX ROTATED FACTOR MATRIX

Variable (T-Score)	Factor 1	Factor 2	Factor 3
Finger Tapping Dominant	.68957	-.00940	-.09291
Finger Tapping Nondominant	.92408	.05795	-.09141
Foot Tapping Dominant	.33611	-.22154	-.06945
Maze Coordination Dominant Total Time	-.08200	.19884	.66939
Maze Coordination Nondominant Total Time	-.16667	.19397	.84641
Holes Steadiness Dominant Total Time	-.08148	.99398	.05358
Holes Steadiness Nondominant Total Time	-.12452	.72212	.10280
Grooved Pegboard Dominant Total Time	-.02284	.03218	.44410
Grooved Pegboard Nondominant Total Time	-.15203	-.14665	.41193
Dynamometer Dominant	.40110	-.14165	-.11795

Table D-11

SENSORY TESTS
ASSESSMENT VARIABLES GROUPED FOR FACTOR ANALYSIS

Tactile Forms Dominant Total Time T-Score
Tactile Forms Nondominant Total Time T-Score
Tactile Forms Dominant Errors T-Score
Tactile Forms Nondominant Errors T-Score
Finger Agnosia Dominant T-Score
Finger Agnosia Nondominant T-Score

Table D-12

EIGENVALUES AND PERCENT OF VARIANCE ACCOUNTED FOR BY THE THREE SENSORY TEST FACTORS

Factor	Eigenvalues	Percent of Variance
1. Form Perception Time	1.958	32.6
2. Finger Agnosia	1.418	23.6
3. Form Perception Errors	1.206	20.1
		76.4

Table D-13

SENSORY TESTS
VARIMAX ROTATED FACTOR MATRIX

Variable (T-Score)	Factor 1	Factor 2	Factor 3
Tactile Forms Dominant Total Time	.97849	-.03298	.19562
Tactile Forms Nondominant Time Total Time	.54541	.15186	-.01411
Tactile Forms Dominant Errors	.23124	-.08757	.83989
Tactile Forms Nondominant Errors	-.04458	.18796	.45850
Finger Agnosia Dominant	.07093	.71371,	-.01908
Finger Agnosia Nondominant	.09377	.74241	.19109

APPENDIX E

RESPONSE DEFINED BY MFF ERRORS, RSP2 AND RSP3:

DRUG AND PLACEBO SCORES ON DEPENDENT VARIABLES FOR RESPONDERS AND NONRESPONDERS

UNIVARIATE t-TESTS OF DIFFERENCES BETWEEN RESPONDERS AND NONRESPONDERS ON PSQ AND TRS HYPERACTIVITY SCALES AND ON BASELINE MEASURES OF ATTENTION

Table E-1

RESPONDERS AND NONRESPONDERS AS DEFINED BY MFF ERRORS, RSP2, AND RSP3

Drug and Placebo Scores on the Dependent Variables (Means and Standard Deviations)*

Variable	Nonresponders N	Nonresponders Drug	Nonresponders Placebo	Responders N	Responders Drug	Responders Placebo
			MFF Errors			
CPT Omissions	38	2.0 (3.0)	1.7 (2.3)	58	2.2 (2.3)	2.6 (3.7)
CPI Commissions	38	1.2 (1.5)	1.6 (2.4)	58	1.6 (1.9)	1.3 (1.3)
MFF Errors	38	11.6 (7.0)	8.2 (6.0)	58	7.5 (5.1)	11.5 (5.8)
MFF Latency	38	13.6 (16.0)	13.9 (21.7)	58	10.8 (4.2)	12.4 (9.2)
PSQ Hyper-activity	38	.9 (.5)	1.1 (.7)	58	.9 (.5)	1.0 (.6)
TRS Hyper-activity	26	1.1 (.7)	1.6 (.8)	41	1.3 (.7)	1.3 (.8)
			RSP2			
CPT Omissions	38	2.3 (3.3)	1.1 (1.8)	58	2.1 (2.1)	3.0 (3.7)
CPT Commissions	38	1.2 (1.3)	.7 (.8)	58	1.5 (2.0)	1.9 (2.1)
MFF Errors	38	8.4 (6.4)	7.3 (5.7)	58	9.7 (6.1)	12.1 (5.6)
MFF Latency	38	11.3 (5.5)	15.7 (21.5)	58	12.3 (12.9)	11.3 (9.2)
PSQ Hyper-activity	38	.8 (.5)	.9 (.6)	58	1.0 (.5)	1.1 (.6)
TRS Hyper-activity	26	1.3 (.7)	1.5 (.9)	41	1.2 (.7)	1.3 (.8)

Variable	Nonresponders N	Drug	Placebo	Responders N	Drug	Placebo
			RSP3			
CPT Omissions	69	2.3 (2.8)	1.5 (1.9)	27	1.7 (1.9)	4.2 (4.8)
CPI Commissions	69	1.5 (1.8)	1.3 (1.9)	27	1.2 (1.6)	1.7 (1.3)
MFF Errors	69	8.8 (6.4)	9.3 (5.8)	27	10.0 (5.7)	12.5 (6.2)
MFF Latency	69	12.6 (12.3)	13.8 (17.5)	27	10.3 (3.6)	10.9 (7.0)
PSQ Hyper-activity	69	.9 (.4)	1.0 (.6)	27	1.0 (.6)	1.2 (.7)
TRS Hyper-activity	49	1.3 (.7)	1.5 (.9)	18	1.1 (.6)	1.1 (.7)

* The standard deviations appear in brackets ().

Table E-2

UNIVARIATE t-TESTS OF DIFFERENCES BETWEEN RESPONDERS AND NONRESPONDERS ON PSQ AND TRS HYPERACTIVITY SCALES AT BASELINE

Response Defined by	Scale	Mean (X) Non-Responders	Responders	t	p
MFF Errors	PSQ Hyperactivity	1.47	1.36	.83	.409
	TRS Hyperactivity	2.18	1.83	2.15	.035*
RSP2	PSQ Hyperactivity	1.36	1.43	-.51	.608
	TRS Hyperactivity	2.15	1.86	1.76	.083
RSP3	PSQ Hyperactivity	1.41	1.40	.06	.955
	TRS Hyperactivity	2.07	1.79	1.59	.115

* $p \leq .05$

Table E-3

UNIVARIATE t-TESTS OF DIFFERENCES BETWEEN RESPONDERS AND NONRESPONDERS ON BASELINE MEASURES OF ATTENTION

Response Defined by	Test	Mean (X) Non-Responders	Mean (X) Responders	t	p
MFF Errors	CPT Omissions	2.0	2.8	-1.18	.242
	CPT Commissions	3.1	2.1	1.12	.269
	MFF Latency	13.3	10.9	1.99	.052
	MFF Errors	12.3	13.9	-1.14	.257
RSP2	CPT Omissions	2.7	2.4	.34	.734
	CPT Commissions	2.3	2.6	- .32	.752
	MFF Latency	13.3	10.9	1.94	.057
	MFF Errors	11.6	14.3	-2.05	.043*
RSP3	CPT Omissions	2.9	1.3	2.62	.010**
	CPT Commissions	2.6	2.1	.57	.571
	MFF Latency	12.4	10.3	1.69	.094
	MFF Errors	12.4	15.3	-1.97	.052

* $p \leq .05$
** $p \leq .01$