A clinical investigation of the withdrawal emergent syndrome in children with Gilles de la Tourette's disease

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A CLINICAL INVESTIGATION OF THE WITHDRAWAL EMERGENT SYNDROME IN CHILDREN WITH GILLES DE LA TOURETTE'S DISEASE

BY

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A thesis submitted to the Faculty of Graduate Studies of the University of Manitoba in partial fulfillment of the requirements of the degree of

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ABSTRACT

An investigation was conducted to examine the clinical symptoms of withdrawal from haloperidol in children with Gilles de la Tourette's Syndrome (TS). Six young male TS patients participated in the 6 month study. Four of these subjects underwent a withdrawal from haloperidol for a 2 month period during the middle phase of the experiment. The other 2 subjects remained on medication throughout the experiment and served as experimental controls. Daily, weekly, and monthly measures were gathered including data from the patients, the patient's parents, the experimenter, and 2 independent observers. The data were examined to determine the differences in TS symptomatology while patients were on and off medication and also to monitor symptoms associated with haloperidol withdrawal.

Results indicated that withdrawal from haloperidol was likely to precipitate an increase in some, but not all, TS symptoms. Simple motor tics were found to increase with medication withdrawal while less consistent findings were reported for other TS symptoms. Complex phonic tics were actually observed to decrease in association with haloperidol cessation. All symptoms that were exacerbated by medication withdrawal were observed to return to baseline, or near baseline, levels within a 4 week period despite the fact that the experimental subjects were not on medication at that point.

A number of more subtle behavioural and somatic symptoms were also reported to result from haloperidol cessation. These symptoms are thought

to be associated features of the withdrawal emergent syndrome and should be considered for inclusion in its definition. Results also indicated that experimental subjects were less depressed, less hyperactive, and experienced fewer obsessive-compulsive symptoms when they were medication free as compared to on haloperidol. This finding draws into question the effectiveness of haloperidol in controlling the obsessive-compulsive symptoms of the TS disorder.

I. INTRODUCTION AND THEORETICAL HISTORY OF TOURETTE'S SYNDROME

The literature on Tourette's Syndrome (TS) spans nearly 500 years. It was not, however, until 1885 that Gilles de la Tourette described the symptoms of the syndrome that now bears his name. At that time TS symptoms were described as being characterized by recurrent, involuntary, repetitive, rapid, purposeless motor movements and multiple vocal tics. The motor tics typically involved the head, although other body parts such as the upper limbs and torso could be involved. Occasionally the lower limbs were also affected. The vocal tics included various complicated sounds, words often scatological in nature, echolalia, and coprolalia. Movements could also be voluntarily suppressed for minutes to hours, an important feature as far as psychology is concerned, and the intensity of the symptoms could vary over weeks and months.

In the early 1800's all movement disorders were diagnosed as chorea, a Greek word meaning dance. Bouteille (1810) characterized chorea and also specified a separate movement disorder which he called a psuedo or false chorea. This catagory may have included TS. Itard (1825) provided the first description of a woman with TS. This woman was subsequently seen by Charcot, discussed by Tourette, and has become a famous historical case. The symptoms of TS are such that they easily lend themselves to psychological as well as physiological interpretation. Over the period of time when Tourette's has been a separate and identifiable syndrome, the relative importance of psychological vs. physiological factors has waxed

and waned in parallel with the popularity of psychological approaches at any given time.

Although the disorder was not identified and named until the late 1800's it is probably safe to assume that people have suffered from these symptoms throughout history. Speculation as to how Tourette's was perceived and treated in pre-enlightenment times leads to guesswork about the notion of being cursed, under a witch's spell, or in the throes of demonological possession with treatment consisting of horrors such as blood letting, any one of an array of "ordeals", exorcism, perhaps banishment or even death. In a sense, this kind of understanding is more closely related to psychology than physiology in that what is viewed as being the cause of the disorder is, for all intents and purposes intangible, as in many psychological disorders. The treatments, however, could be regarded as more physiological in nature in that they usually attempted to physically remove what was thought to be the causal agent.

The period from the late 1700's to the late 1800's could be characterized as a time when all mental illness was believed to be hereditary (Shapiro, Shapiro, Bruun, and Sweet, 1978). Exactly what was inherited is not clear. It seems, however, that most investigators at the time looked for various kinds of "neuropathic" antecedents such as other family members with some form of mental instability. Patients were then characterized as "higher degenerates". Although the mechanics of heredity were poorly understood during this period, it remained the focus for understanding the etiology of TS throughout the 1800's. Psychological factors were not considered to be of much importance during these times and even though Tourette had initially commented on the remarkable mental

stability of his patients he later amended this, possibly in response to the work of Charcot (1888-1889) and Guinon, (1887), to concern about their mental instability. His main objective at that time was with differentiation of TS from hysteria. As a result, psychological factors were not considered to be worthy of much serious investigation as long as the cause of the disorder was viewed to be hereditary antecedents.

This began to change around the turn of the century. A highly influential treatise by Meige and Feindel (1902) translated by Wilson (1907), redefined a tic as a "purposive act which had been provoked by a cause or idea". The book became a classic on the subject and had the effect of shifting the focus on not only TS but on all sorts of tic disorders, from physiological to psychological. Meige and Feindel credit Charcot with "demonstrating the pathogenic significance of the psychic factors in ticquers" and quote him as saying that tics are "physical only in appearance" In all other respects, they should be considered a mental disease, a sort of "hereditary aberration". Psychological factors were sought, found, and cited as being crucial components to the etiology of all tic disorders. Patrick (1905), Prince (1906), and Fleischner (1911) were early among many who followed the ideas of Meige and Feindel and promoted the notions that tics were psychic in origin. As part of a changing zeitgeist at that time, there was a sharp increase in interest in the psychology of patients, illnesses, and people in general. As a result, creative, but somewhat wild speculations about the presumed underlying psychological mechanisms determining sickness and personality were generated by physicians, neurologists, and the early psychiatrists. These speculations were based entirely on clinical observations and were without

empirical support. They did, however, enjoy a growing popularity at the time, and were influenced by the thinking of Bernheim, Charcot, Janet, Freud, Breuer, and others of significant prestige and profile.

The trend toward interest in psychological factors continued well into the 1900's. Meige and Feindel's book had a profound effect on the literature for 50 years after its publication. Psychoanalysts became very interested in TS, and research emphasis moved toward becoming exclusively focussed on psycho-etiological factors (Ferenczi, 1921). Tics expressed underlying conflicts. Studies were devoted to identifying specific personality types or dynamic conflicts in TS patients. This research was based on single case studies and conclusions were drawn from records and notes taken during psychiatric treatment or interviews. Although there was little unanimity among psychoanalysts as to what the "underlying conflicts" were or what exactly the illness characterized, the theories remained popular and unchallenged throughout the early to mid 1900's.

A high point of psychoanalytic interest and acceptance was reached in the late 1940's with the presentation of major papers by Ascher (1948) and Mahler (1949). Up until this time, psychoanalytic theories had really had only a small impact on medicine and psychiatry. These studies, however, had a particularly important influence on the subsequent history of Tourette's Syndrome both because the studies looked at large numbers of patients and because of the remarkably uncritical acceptance of the conclusions put forward by the psychoanalytically oriented clinicians despite the poor methodology of their studies. Tourette's Syndrome at this time was viewed almost exclusively as a psychological phenomenom with physical manifestations. Although occasional references were made in the

literature about the possibility of "organic substrate", "constitutional", or physiological factors, clearly psychological concerns were almost unanimously viewed as central to the etiology of TS.

Psychological factors and psychoanalytic theories continued to exert a profound influence on the TS literature throughout the 1950's. This decade was, however, also characterized by the collection and study of large numbers of patients using retrospective information (Zausmer, 1954), a trend which continued into the 1960's. Many studies included reviews of the literature to that point (Kelman, 1965; Fernado, 1967). One result of these more extensive reviews was a revival of interest in organic factors in the etiology of TS. Psychological concerns remained dominant at this point, but a strong case was being built to renew research interest in physiological factors.

The case for organic factors was augmented in the late 1950's with the introduction of psychopharmacological drugs in the treatment of psychiatric illness, tics, and TS. Successful treatment of TS with haloperidol was first reported in Europe (Seignot, 1961; Caprini and Melotti, 1961), then in the United States by Challas and Brauer (1963). This renewed interest in the organic basis for TS was further enhanced by important neurochemical discoveries that began in the 1960's. This research led to highly significant and influential findings regarding the relationship between neurotransmitters such as dopamine and the basal ganglia of the brain, implicating in the process Parkinsonism and other movement disorders including TS. During the 1960's the emphasis of research and treatment shifted from the psychological to the organic. The successful use of haloperidol was illustrated by its increased usage. By 1968, twenty

patients successfully treated with haloperidol had appeared in the literature; and by 1975, success rates ranging from 77 to 91% had been estimated using much larger samples of TS patients (Shapiro et al, 1978). With success rates approaching 90% using pharmacological treatments, it would seem that psychological factors must, in the face of all the organic evidence, retract to a position of relative unimportance in the etiology of TS.

In the early 1970's, however, behavior therapies became a popular mode of treatment. Part of the reason for this sudden change was that attention was refocussed to include an interesting characteristic of the TS disorder. The individual is often able to control the tics for short periods of time, delaying or suppressing them for minutes to hours or making them part of some other more complex behavior. The question was: "if the patient can control the symptoms, how can this be truly a neurological disorder?" A case was made at that time that if control can be exerted over the symptoms, then control can be learned or trained into the patient. Behavior therapies, although often used in tandem with haloperidol or some other TS medication, were essentially grounded in the belief that psychological factors were the most important component in the etiology of TS. These therapies were based on learning theory which was derived experimentally through laboratory studies. As such, behavioral approaches were the most attractive to psychologists and were the major therapies used by young, recently trained clinical psychologists. Questions of treatment effectiveness were soon raised. The American Psychiatric Association developed a task force to evaluate behavior therapies in 1973. Their report was an important summary document that referred to behavior

therapies as being "effective" in reducing the characteristic "tics" of TS and provided four supporting references (Browning and Stover, 1971; Frederick, 1971; Thomas, Abrams, and Johnson, 1971; Yates, 1970). The findings of the task force supported the use of behavior therapies in the treatment of TS. These findings, however, have since been strongly criticized (Shapiro et al, 1978), and a number of other studies have shown behavior therapies or any type of psychotherapy for that matter, to be relatively ineffective (Shapiro, 1976a; Shapiro & Shapiro, 1971; Hersen & Eisley, 1973), especially when compared to the success rates reported with the use of haloperidol or some of the other psychopharmacological treatment approaches.

From about 1975 to the present, it has been a relative rarity to find any kind of psychotherapy or behavioral technique used by itself to alleviate the symptoms of TS. Typically psychotherapies are used in cooperation with or as an adjunct to some kind of chemical control of the symptoms. The research on TS has shifted from a theoretical or conceptual base to an empirical data base. Shapiro et al (1978) have commented on the move in psychiatric research towards "data orientation". They remark on the development of methodologies for the study of clinical phenomena, the double blind procedure, the use of appropriate statistical procedures, and the mulivariate approaches to the analysis of data. Also mentioned are the advances in the use of computer facilities, more reliable and valid measures of subjective states, the power of placebos and many other recent developments in research methods and technology. This orientation, in its initial development in the late seventies, has become an important approach to research in psychiatry, and according to Shapiro and Shapiro (1982) is now the "dominant approach to the study of TS".

II. CURRENT RESEARCH AND TREATMENT OF TS

There currently exists a broad range of clinical studies on TS. Recent epidemiological, genetic, metabolic, pharmacological, neurophysiological, neuropsychological, and phenomenological studies are to be found in the literature. The question of where TS belongs among other neuropsychiatric disorders continues to be raised as new information is gathered. More pragmatic research has concerned itself with different treatment techniques, relief from symptoms, short and long term side effects of medication, psycho-social distress, and specific needs of TS patients. This review reflects the current understanding of the etiology of the disorder and provides a synthesis and summary of the treatment outcome studies of TS.

1) Definition, Prevalence, and Description

Official diagnostic criteria for Tourette Syndrome as set out by Diagnostic and Statistical Manual of Mental Disorders III (DSM III, 1980) are as follows:

1. Age of onset between 2 and 15 years.
2. Presence of recurrent, involuntary, repetitive, rapid, purposeless motor movements involving multiple muscle groups.
3. Multiple vocal tics.
4. Ability to suppress movements voluntarily for minutes to hours.

5. Variations in intensity of the symptoms over weeks or months.
6. Duration of more than one year.

The recently published DSM III-Revised (1987) has altered the diagnostic criteria for Tourette's disorder. Age of onset has been raised to before age 21 and the patient's ability to suppress movements voluntarily has been deleted. The new diagnostic criteria for TS set out by the DSM III-Revised are as follows:

1. Both multiple motor and one or more vocal tics have been present at some time during the illness, although not necessarily concurrently.
2. The tics occur many times a day (usually in bouts), nearly every day or intermittently throughout a period of more than one year.
3. The anatomic location, number, frequency, complexity, and severity of the tics change over time.
4. Onset before age 21.
5. Occurrence not exclusively during Psychoactive Substance Intoxication or known central nervous system disease such as Huntington's chorea and postviral encephalitis.

These new criteria are unlikely to effect the numbers of people now being diagnosed as having TS. The purpose of the changes is more for clarification than revision. Associated features of TS include symptoms such as mental coprolalia, obsessions, and compulsions. Other mental conditions such as Attention-Deficit Hyperactivity Disorder and Obsessive Compulsive Disorder are also frequently reported with TS although it is not clear if this co-morbidity exists outside the clinical sample used in the development of DSM-III-Revised.

Today, TS is accurately diagnosed by many clinicians throughout the world (Bruun, 1984) and the condition is no longer considered a bizarre medical curiosity. Many of the cases now being diagnosed are those with milder symptomatology. Estimates of prevalence are currently in the range of 0.5 per thousand (Bruun, 1984; DSM III-R, 1987) (approximately 11,000 in Canada) to 4.0 per thousand (Messiah & Carlson, 1983) (approximately 88,000 in Canada).

Apart from the clarification of the diagnostic criteria for TS from DSM III (1980) and now the DSM III-R (1987), there are many other reasons for the emergence of this disorder as a much more common clinical syndrome than was once believed. The media has responded to a number of the more spectacular associated symptoms of TS that may or may not be present in any one individual. Focus on these symptoms has had the effect of making TS a much more widely known and recognized disorder than was previously the case.

i) Symptomatology

Features of the disorder such as echokinesis (imitations of other's movements), echolalia (imitations of other's words or phrases), palilalia (repetition of one's own words or phrases), mental coprolalia (intrusive thoughts of offensive words) or obsessive-compulsive behaviors are sometimes present and are difficult to ignore. Coprolalia, an irresistible urge to utter or shout obscenities is present in approximately 33% of TS patients (Shapiro & Shapiro, 1982) and it is perhaps because of this one particular feature that TS has become a much more widely recognized disorder in recent years. Symptoms typically wax and wane on their own

accord. They are thought to be exacerbated by stress and attenuated by absorbing activities (Bruun, 1984). Recent sleep studies have shown that many TS patients have tics during their sleep (Glaze, Jankovic, & Frost, 1982). It was previously believed that tics disappeared during sleep. These findings, however, have not always been replicated and closer examination of differential patterns of sleep stages have been directly contradictory (Glaze, Frost, & Jankovic, 1983: Mandelson, Caine, & Goyer, 1980). Overall, the sleep research has remained relatively unrewarding (Caine, 1986).

Tic onset is generally rostral-caudal in progression (Corbett, Matthews, Connell, & Shaprio, 1969: Jagger, Prusoff, Cohen, Kidd, Carbonari, & John, 1982). Although considerable individual variation exists, the mean age of onset for tics of the eyes, face and head is 7.2 years; for tics of the neck and shoulders, 8.7 years; 9.1 years for arm and hand tics; 9.5 years for tics of the trunk; and 10.1 years for leg tics (Leckman, Detlor & Cohen, 1983). The same study reports a similar pattern for phonic tics. The mean age of onset for simple vocal tics is 10.7 years, and for coprolalia, 11.1 years (Jagger et al., 1982). Related clinical observations are consistent with a rostral-caudal developmental progression. For example, patients with a later age of onset tend to have a more complex symptom presentation as compared to earlier onset patients who tend to more regularly follow the rostral-caudal sequence (Leckman, et al., 1983). Similarly, tics of the eyes, face and head are often severe and remain the most refractory to intervention (Leckman et al., 1983). TS symptoms are likely related to maturational sequences of neuronal systems. There is ample evidence to indicate that brain neurochemical systems

continue to mature during childhood and adolescence (Leckman, Cohen, Shaywitz, Caparulo, Heninger, & Bowers, 1980) and it is thought that the progression of TS symptoms may follow this maturation development.

The most frequently occuring motor tics are those of the facial muscles (eye blinking, facial grimacing, wincing, twitching, etc.) and those of the neck and shoulder muscles (twitching, shrugging, etc.). However, any part of the body may be involved. Complex movements occur in approximately 35% of TS patients (Bruun, 1984). Some typical examples include touching others, hitting oneself, spitting, squatting, and twirling around while walking. Many complex tics strongly resemble, and may be related to, compulsions (Bruun, 1984; Pauls & Leckman, 1986).

Bruun (1984) has described the nature of obsessive-compulsive behaviors of the TS disorder based on her many years of experience with over 300 TS patients. They may be "extremely variable",ranging from the simple repetition of apparently meaningless acts to violent self mutilation. There appears to be no reactive emotion attached to the need to perform compulsive acts other than the frustration from the inconvenience they cause. For example, some TS patients may take hours to get dressed because they must tie their shoes or button their shirts over and over again until they "get it right". Bruun (1984) speaks of one patient who had an irristible urge to file her teeth with a nail file. Others may bite their lips constantly despite the resultant swelling and lacerated sores that develop.

Vocal tics are also variable. They range from meaningless sounds such as barks, grunts, or single syllables, to words, phrases, or even complete

sentences. They can be extremely interruptive to the flow of conversation and are often viewed as intentionally disruptive by educators when they occur in the classroom setting. The phenomenon of coprolalia while receiving much attention from the media and in a sense "popularizing" this disorder, is poorly understood partly because the symptoms seems not be be strictly coprolalic. Outbursts often seem to represent an expression of a thought or impulse which the patient would like to keep concealed. In this sense, coprolalia is sometimes seen as a failure or breakdown in the ability to selectively inhibit certain verbal content or thought processes. This failure of inhibition is also thought to be at the core of some of the more obscene motor behaviors which often involve gestures or movements directed towards the genitals of the TS patient or others in the vicinity. It is not difficult to envision the extreme disruption to the social life and development of the TS patient that these outbursts may cause. It is difficult, however, to comprehend the extent of damage over time of these bizarre aspects of TS symptomatology.

ii) Behavior Problems

In addition to the motor and phonic symptoms, TS patients regularly experience a variety of behavioral symptoms. These include increased motor restlessness, impulsivity, diminished frustration tolerance, argumentativeness, diminished ability to concentrate associated with poor academic performance and disabling compulsive actions (Cohen et al., 1982; Corbett et al., 1969: Jagger et al., 1982; Leckman et al., 1983; Montgomery, Clayton, & Friedhoff, 1982; Nee, Polinsky, & Ebert, 1982; Shapiro, Shapiro, Wayne, & Clarkin, 1973; Wilson, Garron, Tanner, &

Klawans, 1982). Results of a recent Canadian survey indicate that problems with attention, concentration, and difficulty with completing time limited tasks were the most often cited educational difficulties of children with TS (Shady, Fulton, & Champion, 1987).

Impulsivity, concentration deficits, and problems with the ability to attend to stimuli often precede the onset of identifiable TS symptoms. When this occurs individuals are indistinguishable from other children with attention deficit disorder (ADD), hyperactivity, or both, and many TS patients are initially diagnosed as ADD. Unfortunately, stimulant medications such as Ritalin, Methylplenidate, or Pemoline, are used in a high percentage of these cases in an effort to reverse these symptoms. Transient improvements with hyperkinesis and attention span may occur, but research has demonstrated that the development of motor and phonic tics may be accelerated by these medications in vulnerable individuals (Golden, 1974; Golden, 1977; Lowe, Cohen, Detlor, Kremenitzer, & Shaywitz, 1982; Wand, Fulton, Shady, Champion, & Hubka, 1987). In addition, these attention deficit difficulties, which are noted in adults as well as children, may necessitate special placements during the school years.

Many questions have been raised regarding the relationship between TS, ADD, obsessive-compulsive symptoms, and transient and chronic tic disorders. It is possible that the symptoms of these disorders are all on the same continuum, with placement on the continuum in accordance with symptom severity. They may all be genetically related as suggested by Pauls and Leckman (1986), or they may be phenotypically similar but genetically unrelated. Current support falls in favor of the former (Nee, Caine, & Polinsky, 1980; Kidd, Prusoff & Cohen, 1980; Kruger, Caine, & Nee,

1986; Kidd & Pauls, 1982) and genetic research has proved fruitful in the understanding of the etiology of TS (Caine, 1986).

These behavioral symptoms are frequently seen throughout the natural history of TS and are subject to the same waxing and waning pattern of other symptoms. They may disappear entirely or persist after other symptoms have largely disappeared. Obsessive-compulsive behaviors usually appear later in the developmental course of the syndrome (Jagger et al., 1982) and can become extreme and disabling (Cohen et al., 1982). They may make it impossible for a TS patient to make even simple decisions and compulsive rituals such as complex mimicry or copraxic movements may further promote disruption of normal functioning. Elkins, Rapoport, and Lipsky (1980) raise the question of where TS belongs among other neuropsychiatric disorders in terms of its relationship to obsessive-compulsive disorder during childhood.

The "emotional climate" of TS patients, as described by those patients who are old enough and sophisticated enough to do so, speak to a feeling of "inner tension" which is almost continually present. Tics provide a momentary relief of the tension. Many TS sufferers describe a longing for an ability to relax "like other people" (Bruun, 1984), and do not feel that they are successfully medicated until the inner tension they experience has been alleviated. One recent study of the psychological aspects of TS indicates that TS patients are in considerable psychological distress (Grossman, Mostofsky & Harris, 1986). Previous research had indicated that TS patients did not differ significantly from normals on psychological factors (Shapiro et al., 1972; Shapiro et al., 1978) and that they were less disturbed than the general outpatient psychiatric population.

2) Pathogenesis of TS

The pathogenesis of TS remains unknown, but since the successful use of haloperidol in the treatment of TS by Seignot in 1961 the bulk of research has been devoted to the establishment of considerable circumstantial evidence suggesting an organic etiology for TS (Van Woert, Rosenbaum, & Enna, 1982). Despite many efforts to utilize behavior therapies in the 1970's and a recent resurgance of interest in the psychological factors of TS (Grossman et al., 1986), it is now quite clearly "known" and accepted that the cause of TS is neurochemical. A number of models have been generated to assist in the investigation and treatment of TS and these serve as the best and most functionally useful reflections of our current understanding of the disorder.

i) Neurochemical and Pharmacological Findings

Haloperidol was the first medication found to be truly effective in relieving the symptoms of TS (Borison, Ang, Change, Dysken, Comaty, & Davis, 1982; Bruun, 1980, 1981, 1982). Initially, it seemed to be almost a miracle drug and had success rates of up to 90% were reported (Shapiro & Shapiro, 1982). Although the efficacy of haloperidol has been recognized since the early 1960's, the search for alternative medications and treatment methods remains warranted due to the many serious difficulties, both short and long term, associated with the extensive use of haloperidol and other currently available neuropleptics.

Pimoside (Orap), another potent antagonist of the dopamine receptor site, has been reported to decrease TS symptoms as effectively as

haloperidol (Ross & Moldofsky, 1977). Chlorpromazine has also been found to be effective (Devinsky, 1983). In general, however, phenothiazine neuroleptics are reported as being less consistently effective and useful in controlling TS than haloperidol (Abuzzahab & Anderson, 1973: Mesnikoff, 1959: Van Woert,et al., 1982: Walsh, 1962). A precurser of dopamine, Levodopa (L-dopa), has been found to aggravate TS symptoms (Klempel, 1974; Messiha & Knopp, 1976). Interestingly, a dosage of haloperidol that far exceeds the requirements of the patient has also been found to aggravate symptoms (Bruun, 1984). In addition, numerous investigators have observed that the administration of methylphenidate (Fras & Karlavage, 1977; Golden, 1974, 1977; Pollack, Cohen, & Friedhoff, 1977) and amphetamines (Cohen et al., 1978; Feinburg & Carroll, 1979; Golden, 1977; Meyerhoff & Synder, 1973a, 1973b; Singer, 1963) which increase the release of dopamine from nerve terminals have been associated with onset or aggravation of tics in TS patients. "It is now well accepted that drugs that block postsynaptic dopamine receptors ... tend to relieve symptoms, whereas drugs that increase dopaminergic activity ... actively exacerbate symptoms" (Devinsky, 1983).

Haloperidol and pimoside are both potent antagonists of the dopamine receptor site. Since these compounds have been found to be effective in treating TS, dopaminergic hyperactivity has been postulated to be responsible for the tics and vocalizations of this disease. It is also thought that haloperidol and pimoside are effective because they preferentially bind to a different class of dopamine receptors than the phenothiazine drugs. Specifically, they are more potent antagonists at the dopamine-2 (D2) receptor, whereas the other phenothiazine neuroleptics have

a higher affinity for, and antagonist activity at, the dopamine-1 (D1) receptor (Hyttel, 1978). The mechanism of anti-TS action may be the blockade of the D2 receptor and thus it is suspected that it is the D2 rather than the D1 receptor that may be involved in the disease (Van Woert et al., 1982).

The D2 receptor hypothesis is generally supported by the literature. Haloperidol is the most commonly prescribed medication for TS, and patients have rated it as the most effective for TS symptom control (Fulton, Shady, & Champion, 1987). Haloperidol, however, is not always effective, and the D2 receptor model cannot account for all cases of TS. Moreover, there have been reports that apomorphine, a dopamine agonist, can be effective in relieving TS symptoms (Feinberg & Carroll, 1979). Homovanillic acid (HVA), a major dopamine metabolite found in the cerebrospinal fluid (CSF) is often used as an index of dopaminergic activity in the brain (Moir, Asheroft, & Crawford, 1970). Reduced concentrations have been found in selected TS patients (Cohen et al., 1978: Singer, Butler, Tune, 1982: Siner et al., 1982). This observation is consistent with other neurotransmitter models such as those suggesting that there is a primary loss of dopaminergic cells which results in hypersensitive postsynaptic receptors, in turn causing low HVA levels and symptoms of TS. Similarly, the low HVA levels could be due to a primary hypersensitivity of the postsynaptic receptor which may cause feedback inhibition of the dopaminergic cell, again resulting in TS symptoms.

Other neurotransmitters such as seretonin and norepinephrine have been investigated through the observation of levels of 5-hydroxyindoleacetic acid (5-HIAA) and 3-methoxy-4-hydroxy-phenylglycol (MHPG) respectively, in

the CSF. Decreased levels of 5-HIAA have been found (Cohen et al., 1978, 1979; Butler, Doslow, & Seifert, 1979) implicating and associating abnormalities of seretonin (5-HT) with symptoms of TS. This finding is consistent with a loss of seretonergic neurons or a hypersensitivity of 5-HT receptors leading to feedback inhibition, or both. However, the use of drugs affecting 5-HT have generated equivocal results. Marked improvements were produced in two studies (Van Woert, Jutkowitz, & Rosenbaum, 1976; Yariyura-Tobias, 1979) but a third reported no effects (Sweet, Bruun, Shapiro, & Shapiro, 1976).

There has been less direct evidence suggesting that alteration in norepinephrine (NE) levels is involved instrumentally with TS symptoms. Cohen et al. (1978) found normal MHPG levels in 3 patients and markedly elevated levels in a fourth. This patient was treated with clonidine hydrochloride, an active presynaptic and postsynaptic alpha-adrenergic agonist which reduces the turnover of NE in the CSF probably through feedback inhibition (Svensson, Bunney, Aghajanian, 1975; Cedarbaum, Aghajanian, 1977). Clonidine has been used successfully in the treatment of TS (Cohen et al., 1978) and has even produced dramatic results in some patients with normal MHPG levels who were not responsive to haloperidol. Some studies have shown substantial improvements in at least 50% of patients (Bruun, 1982; Borison et al., 1982; Cohen et al., 1979), others found that only 20% of patients benefitted from clonidine administration (Abuzzahab, 1981). The role of NE in TS and the effectiveness of clonidine remains uncertain both because clonidine has been shown to be effective in patients who do not have elevated levels of MHPG and because it also has an inhibiting effect on the 5-HT neurons in the nuclei of the midbrain raphne (Svennson et al., 1975).

In sum, data regarding the pathogenic role of CNS neurotransmitters in TS, is, at best, inferential (Koslow & Cross, 1982). The matter is further complicated by the poorly understood interactions between dopaminergic, serotonergic, noradrenergic, and cholinergic systems (Devinsky, 1983). It is clear, however, that abnormalities of CNS biogenicamines do occur in TS and the neuropharmacologic findings must be addressed in any hypothesis concerning the etiology of the syndrome and must be consistent with the available research data.

ii) Neuroanatomic Models of Tourette's Syndrome

Richardson (1982) has concluded that the neuroanatomic correlates of TS remain unknown. Several models have, however, been put forward that are worthy of discussion.

The most popular model regarding the neuroanatomy of TS involves the basal ganglia. It is generally held that this is the area of the brain that is accountable for the genesis and symptoms of TS. The popularity of the basal ganglia hypothesis seems to be directly linked to the neurochemical dopamine hypothesis. They are dependent upon one another and mutually dependent on pharmacological studies using haloperidol, pimoside, or other available neuroleptics.

It has been suggested that it is the D2 receptors rather than the D1 receptors that are responsible for TS (Van Woert et al., 1982). Most of the D2 receptors in the basal ganglia are located on axons and terminals of the corticostriate neurons (Kebabian & Caine, 1979; Schwarcz, Creese, Cogle, & Snyder, 1978; Snyder & Goodman, 1980) and cell bodies in the

substantia nigra (Quick, Ensonn, & Joyce, 1979). Activation of the dopamine receptors at the level of the basal ganglia inhibits dopamine synthesis, release, and neuronal activity (Roth, 1979). If haloperidol blocks the D2 receptors at this point, then dopaminergic activity would be enhanced and tics, vocalizations, and other symptoms of TS would be aggravated. Since, however, haloperidol has been repeatedly shown to have an anti-TS action, the controversy continues as to exactly how it does this. It has been argued that haloperidol affects the corticostriate neurons, the substantia nigra, or unidentified intrastriatal neurons (Schwarcz et al., 1978). Results from clinical trials of pharmacological agents have yielded inconsistent results (Barbeau, 1980; Polinsky, Ebert, Caine, Ludlow, & Bassich, 1980; Shapiro, Shapiro, & Sweet, 1980; Stahl & Berger, 1981). Thus, support for the proposal that haloperidol affects D2 receptors acting on intrastriatal cholinergic neurons is equivocal (Van Woert et al., 1982). The search continues within the basal ganglia hypothesis for specific actions of haloperidol on specific D2 receptors but the effectiveness of haloperidol in controlling TS symptoms continues to be regarded as indirect support for the basal ganglia hypothesis.

Devinsky (1983) has suggested that the periaqueductal gray (PAG) and midbrain tegmentum may be involved in TS. Data from some neurotransmitter studies, research on the localization of lesions in encephalitis lethargica (EL), and animal studies on the anatomy of vocalizations can be interpreted as supporting his hypothesis.

Although somewhat conflicting, the neurotransmitter studies quite consistently implicate dopaminergic and serotonergic systems in TS. Devinsky contends that these results are consistent with his hypothesis

that tics are caused by the stimulation of supersensitive DA receptors. In short, he proposes that an initial loss of DA neurons results in low levels of DA at the postsynaptic receptor. This is compensated for by the increased activity of the remaining DA neurons and the development of hypersensitive receptors. Eventually, the output of the DA neurons and the sensitivity of the DA receptors reach a plateau. As the level of DA continues to fall, Parkinsonian symptoms and oculogyric crisis (OGC's) develop. Tics then result from the stimulation of the hypersensitive DA receptors. Since almost all central DA is produced in the midbrain, specifically the substantia nigra and the ventral tegmental area, Devinsky proposes that this area is central to the neuroanatomy of TS.

Further support for midbrain involvement, and unique opportunity for insight into the pathophysiologic mechanisms of TS may be provided by encephalitis lethargica (EL). This disorder involves vocal tics, motor tics, and obsessive-compulsive behaviors that develop in the setting of localized neurologic lesions. Other common sequelae to EL include a parkinsonian syndrome, respiratory and oculogyric crisis (OGC). The OGC is a spasm of extraocular muscles lasting from seconds to days that results in the conjugate upward deviation of the eyes. Emotional factors are often thought to precipitate OCG's, such as when the patient is overwhelmed by "forbidden thoughts" (Jellitte, 1929: Sacks, 1976). Emotionally charged thoughts are able to trigger certain symptoms common to both EL and TS.

Interestingly, among those with Parkinson's disease it is only those with the postencephalitic form that develop symptomatology resembling TS (Schwab, Fabing, & Prichard, 1951). With regard to the localization of sites in which a lesion might result in OGC's or other TS symptoms among

postencephalitic Parkinson's disease patients, structures within or adjacent to the midbrain must be held as prime candidates (Devinsky, 1983).

Devinsky cites animal studies on the anatomy of vocalizations as a third source of support for his hypothesis. Vocal tics are perhaps the single most characteristic feature of TS and the fact that TS vocalizations have not been produced by neocortical stimulation in either monkeys or humans seems relevant (Penfield & Jasper, 1954: Robinson, 1967: Jurgens & Ploog, 1970). Of particular interest to TS is the cingulate gyrus which connects to both cortical and limbic structures known to be involved in vocalization (Muller-Preus & Jurgens, 1976; Baleydier & Maugierre, 1980) and also receives a DA projection from the ventral tegmental area. Jurgens & Ploog (1970) systematically studied the evoked vocalizations in the monkey and concluded that the mesencephalic gray served a unique function in vocalization. In short, Devinsky (1983) contends that sufficient circuitry to produce vocalizations exists in the midbrain and lower brain stem and that the PAG and midbrain tegmentum are involved in TS.

Most recently, it has been speculated that other areas of the brain such as the cingulate cortex may be responsible for the symptoms of TS. This is also consistent with the view of Sacks (1986) who believes TS lies in the "old brain", where the instinctual determinants of personality are lodged - a sort of missing link between mind and body. Whatever the neuroanatomy of TS may be, A. R. Luria is likely correct in his assumption that by understanding TS we will also understand much about humaness and our deepest selves.

iii) Genetic studies of TS

Genetic approaches to understanding TS have been rewarding (Caine, 1986), and it is likely that genetic research regarding the specific mode of transmission will eventually prove fruitful.

Tourette recognized the familial nature of the disorder and assumed that there were underlying factors that were responsible for the manifestation of the symptoms of TS. Early studies concluded that the syndrome was familial because many patients had a family history of the disorder (Eldridge, Sweet, Lake, Zeigler, & Shapiro, 1977; Nee et al., 1980; Shapiro et al., 1978). Interest in possible genetic mechanisms has increased over the last decade and recent attempts have been made to understand the mode of transmission of TS.

Most investigations have utilized family-history data and have reported the results of the genetic analysis (Baron, Shapiro, Shapiro, & Rainer, 1981; Comings, Comings, Detlor, & Cloninger, 1984; Devor, 1984; Price, Pauls, & Caine, 1984). All gave evidence for a single major gene contributing to the expression of the syndrome and a single-locus model seems to provide the best statistical fit to the data (Kidd & Pauls, 1982). The specific mode of inheritance, dominant or recessive, has differed from study to study and a wholly satisfactory solution remains to be demonstrated.

The best available information to date shows a correlational relationship between TS, chronic tics, and obsessive-compulsive disorder (Fernando, 1967; Kidd & Pauls, 1982; Montgomery et al., 1982; Nee et al., 1980, 1982; Pauls et al., 1981, 1986; Yaryura-Tobias, Nexiroglu, Howard, &

Fuller, 1981). Recent estimates of penetrance for the genotypes of the abnormal allele for TS are 1.000 for males, 0.709 for females; for chronic tics are 1.000 for males, 0.709 for females; and for obsessive-compulsive disorder are 0.002 for males, 0.000 for females (Pauls & Leckman, 1986). These results predict that approximately 10% of all patients are phenocopies.

In sum, there is strong support for the hypothesis that TS, chronic tics, and obsessive-compulsive disorder are related and that TS is inherited as a highly penetrant, sex-influenced, autosomal dominant trait (Pauls & Leckman, 1986; Pauls, Towbin, Leckman, Zahner, & Cohen, 1986).

3) Pharmaceutical Treatment of TS

Much evidence suggests the critical role of dopaminergic overactivity in TS. Results of a study by Shapiro and Shapiro (1982) indicate that only haloperidol, pimoside, penfluridol and possibly clonidine appear to be clinically useful according to their criteria. Results of a recent nationwide Canadian survey indicate that patients rated haloperidol, pimozide, and clonidine as effective treatments for TS (Fulton et al., 1987). A haloperidol-cogentin combination was also rated as highly effective by most patients.

Unlike Parkinson's disease, where the pharmacotherapeutic treatment breakthrough of L-Dopa grew from the demonstration of reduced dopamine in the substantia nigra of post-mortem brain specimens, or Huntington's disease where investigation of post-mortem brain specimens consistently uncovered a variety of neurochemical abnormalities; there exists for TS, a

failure to define the basic neurochemistry of the disorder (Caine, 1986). Post-mortem brain investigations are few in number and have produced no consistent evidence of CNS abnormalities (Balthasar, 1957; Bing, 1925; Dewulf & Van Bogaert, 1941). Although a number of theoretical models have been generated that purportedly "account" for the symptoms of the disorder and explain its pathogenesis in terms of neurochemistry and anatomy, these models are almost unanimous in the utilization of the pharmacotherapeutic effects of haloperidol as a basis for the model. Van Woert et al. (1982) reviewed the literature regarding pharmacological treatments of TS. In general, they found butyrophenone compounds such as haloperidol and pimoside to be the most effective. Phenothiazine neuroleptics, although known as potent blockers of dopamine receptors, are less consistently effective and useful in the treatment of TS. Noradrenergic autoreceptor agonists, such as clonidine, have also been reported to relieve motor tics, vocalizations, behavioral and psychological symptoms of TS (Cohen et al., 1979; 1980). Similarly, benzodiazepine drugs, such as clonazepam, which enhance presynaptic y-amino butyric acid (GABA) receptors, have been reported as effective agents in the treatment of TS (Gonce & Barbeau, 1977).

A number of other drugs have been recommended for use or experimentation in the treatment of TS. Van Woert suggests that specific D2 receptor antagonists such as sulpride, domperidone, metoclopramide and molindone be investigated. This would provide important theoretical implications for the pathogenesis of TS. It is also suggested that a direct GABA agonist would facilitate the release of glutamate from the corticostriated neurons (Mitchell, 1980). Glutamate release is inhibited by dopamine agonists and

this inhibition is counteracted by haloperidol (Mitchell & Doggett, 1980). Since clonazepam has been found to be an effective agent in the treatment of TS (Gonce & Barbeau 1977), and it is known to enhance glutamate release, direct GABA agonists such as progabide may be of clinical benefit to those with TS.

Ross (1986) has suggested that buspirone, a nonbenzodiazepine anxiolitic compound that has the properties of both a dopamine agonist and antagonist may be useful in the treatment of movement disorders such as TS. It has been demonstrated that buspirone has the properties of post-synaptic dopamine receptor agonist (Taylor, 1982), and an antagonist at both pre and post-synaptic sites (Meltzer, 1983; Taylor, 1982), and acts on the same pre-synaptic D2 autoreceptor as haloperidol (Roth, 1984). As such, it warrants a clinical trial with TS patients especially in light of the fact that it has very few side effects (Ross, 1986).

In sum, haloperidol is seen as the most effective medication for TS. Nevertheless, in light of the fact that haloperidol is known to cause many side effects in up to 75% of patients, clinical trials of new medications are not only warranted but imperative.

4) Psychological aspects of TS

There is little doubt that TS is a neurological disorder. While the precise etiology and pathogenesis is not yet clear, the idea that TS is at base an emotional or personality disorder has essentially been abandoned. Shapiro et al. (1972) concluded "that psychological factors are unrelated to the etiology, useless for diagnosis, and irrelevant to the treatment of

Tourette Syndrome" (p. 434). Recently, an interactionist model that exploits the best features of both neurological/biological and personality/environmental factors has been proposed by Grossman, Mostofsky and Harrison (1986). While it would be surprising if TS had no impact on mood, psychological, or interpersonal functioning, the investigation of psychological factors has produced few consistent findings and seems not to be critical to the genesis of TS.

The search for clinical and neuropsychological markers for TS has continued since such tests were available. From a clinical point of view it is of interest to note that there are nonorganic precipitants of TS symptoms such as emotional stimuli and/or stressful situations. Similarly, it is noteworthy that sleep, relaxation, and involvement in pleasurable activities are thought to result in the attenuation or disappearance of symptoms. These features of TS continue to encourage those who believe that psychological factors are central to the development and maintenance of the syndrome. Despite recent evidence that TS patients are in "considerable psychological distress" (Grossman et al., 1986) as evaluated by traditional MMPI scales, there is virtually no evidence of psychological factors contributing to the actual biological development of the syndrome.

There is no question that psychological factors are important to TS. Alterations in the shape of the dysfunction, and the differentiation of those patients who are successful in coping with their TS symptoms with those less successful in doing so are to a large extent determined by psychological variables such as individual development, maturation, changes in social role and personal identity, stability, defence mechanisms, organizational abilities, and so on. The role of psychology has been

clearly shown to be important to the treatment of TS. Psychological factors, however, cannot logically be held as important to the biological development of the syndrome.

5) Neuropsychological functioning of TS patients

"No definitive neuropsychological pattern of deficits has emerged from the test results obtained from TS children and adolescents studied to date" (Newman, Borth,& Zillman, 1986, p. 182). TS children do, however, manifest a complex array of deficits including problems in speech perception (Moldofsky & Lazar, 1983), nonconstructional visuopractic skills (Borstein, King, & Carroll, 1982; Incagnoli & Kane, 1981), visual-motor coordination (Shapiro et al., 1978), a significant number of patients who are left handed (Sutherland, Kolb, School, Wishaw, & Davies, 1982), and a high frequency of verbal-performance discrepancies on general measures of intellectual functioning (Borstein et al., 1982; Incagnoli & Kane, 1981; Shapiro, Shapiro & Clarkin, 1974). The attribution of these difficulties to TS is confounded by the fact that most of these patients are on haloperidol which has been shown to affect learning and behavior (Campbell, Anderson & Small, 1982; Mikkelson, Detlor, & Cohen, 1981).

Results from the administration of intelligence scales have yielded IQ's from the borderline to superior range of functioning (Izmeth, 1979; Shapiro et al., 1974, 1978; Wagner, 1970) and occasionally greater verbal than Performance IQ scores (Shapiro et al., 1974) particularly in adults. Similarly, Bender-Gestalt and Rorschach protocols have been found to be impaired with many TS individuals (Shapiro et al., 1982, 1974, 1972). Results such as these have heightened interest in the neuropsychological

status of TS patients. Most of the available data reflect the assessment of cognitive and behavioral functioning of children or adolescents with TS in single case, or small group studies.

Sand (1972) tested a 9 year old boy with TS both before and after treatment with haloperidol. She concluded that there was no evidence of cerebral dysfunction, that the child's response times were very quick, that no negative effect on concentration or coordination was evident, and that haloperidol did not significantly impair intellectual efficiency (p. 599). A closer review of her data suggests, however, that on second testing the patient's new problem solving skills were impaired as compared to previous testing. Left sided motor difficulties were also evident and poor arithmetic skills were demonstrated (Newman et al., 1986).

Sand's (1972) conclusions are based on the results of testing with the following instruments: Wechsler Intelligence Scale for Children (WISC); Reitan Indiana Neuropsychological Test Battery (Trails, Halstead Categories, Tactual Performance Test, Seashore Rhythm, Speech Perception, Finger Tapping, Sensory Suppression, Lateral Dominance Test); Wide Range Achievement Test (WRAT); and Bender-Gestalt. Differences between first testing (no medication) and second testing (on haloperidol) are summarily attributed to the effects of haloperidol by both Sand (1972) and Newman et al. (1986). No mention is made of the possible influence of practise effects on test-retest results, personal history or maturational factors, measurement error, motivation, or the fact that this patient's IQ, at 123 and 125 respectively, places him in approximately the 95th percentile of intellectual functioning for children in his age group (Wechsler, 1974), making him "atypical" of both other children and other TS patients his age.

It is therefore difficult to attribute test-retest differences strictly to the effects of haloperidol or to assume that haloperidol has no effects on neuropsychological functioning. Competing variables are not adequately controlled for and it would be unwise to generalize from this single atypical case.

Testing of an 11 year old TS boy indicated "chronic diffuse neurological involvement" (Logue, Platzek, Hutzell, & Robinson, 1973; p. 860). Significant cognitive effects were found in psychometrically measured intelligence, complex motor activities, and some numerical and language skills. Average to above-average performance was obtained where simple motor strength and speed, sensory and perceptual abilities, or spatial relationship skills were measured. An organic etiology for TS was supported (Logue et al., 1973).

Data for the Logue et al. (1973) study was collected using the WISC and Reitan-Indiana Neuropsychological Test Battery (Tactual Performance Test, Tapping Test, Hand Dynamometer, Trails A and B, Category Test, Sensory-Perceptual Exam, Seashore Rhythm Test, Speech Perception). The subject of this study, however, had clear cognitive impairments (FSIQ=80, approximately the 9th percentile for his age group Wechsler, 1974) and it is not clear whether the patient was on haloperidol or not at time of testing. The conclusion that TS has an organic etiology, or that chronic diffuse neurological involvement is necessarily associated with TS, is highly precipitious based on the testing of one 11 year old TS patient who has other cognitive impairments.

Joschko and Rourke (1982) noted slight perseveration problems in the performance of 3 children with TS on neuropsychological testing. These problems were thought to be caused by "problems in disinhibition" (p. 303), and otherwise the test performance of these children was generally quite good. No consistent pattern of neuropsychological abilities or deficits was found in their study of test-retest profiles of these 3 TS children.

A comprehensive neuropsychological test battery was used in the Joschko and Rourke (1982) study. Included in their battery were the following tests: Reitan Neuropsychological Test Battery, Reitan-Klove Tests, WISC, Halstead-Wepman Aphasia Screening Test, Halstead Catagories Test, Color Form Test, Individual Performance Tests, Klove-Matthews Motor Steadiness Battery, Peabody Picture Vocabulary Test, Children's Word Finding Test, Matching Figures and Progressive Figures Test. These test procedures have been used clinically for many years in the assessment of children with learning disabilities and a variety of other developmental impairments (Boll, 1974; Reitan, 1966, 1974; Rourke, 1975, 1976, 1978, 1981). Since a relatively high proportion of children with TS also suffer from some sort of learning disability associated with their TS symptoms (Lucas et al., 1967; Shapiro et al., 1978), considerable merit exists in applying these same procedures to the neuropsychological investigation of children with TS.

Thompson, O'Quinn and Logue (1979) present further neuropsychological test data of 4 cases with TS, suggesting organic dysfunction as the basis for the disorder. They also found that "right hemisphere functions consistently appeared to be selectively decreased on several independent indicators (verbal-performance split, simple motor performance, complex

motor performance, auditory perception, and relative handwriting speed)" (p. 382). These results were equivocal even among their 4 cases and their suggestion of right hemisphere localization seems unwarranted in light of the fact that only 1 of the 4 patients indicated this pattern whereas 2 of the 4 showed dysfunction in the left hemisphere (Golden, 1984). In fact, their most consistent finding was the impairment of motor skills which did not involve a visual perceptual component.

Thompson et al. (1979) used the Reitan-Indiana Neuropsychological Test Battery and the WAIS or WISC-R with their subjects. Specific neuropsychological subtests included in their battery were: Hand Dynamometer Grip Strength Test; Trail Making Test A & B; Category Test; Tactual Performance Test; Finger Tapping Test; Tactile Finger Localization; and Fingertip Symbol Writing Test. Their results are presented as a series of single case studies. The suggestion of right hemisphere impairment seems unwarranted on close review of their reported data (Golden, 1984).

Eventually, the study of cognitive disorders in patients with TS moved from analysis based on global concepts such as "organicity" and hemisphere localization to attempts to define more specific deficits in higher cerebral functions. Research utilizing larger groups of subjects has been more useful in this regard.

All studies of larger groups of TS patients have found IQ scores to fall in the normal range. The single most consistently found difficulty across all studies of neuropsychological functioning of TS patients to date involves visuo-practic deficits (Hagin, Beecher, & Pagano, 1982; Harcherik, Carbonari, Shawitz, Shawitz, & Cohen, 1982; Incagnoli & Kane, 1982; Logue

et al., 1973; Lucas, Kaufmann, & Morris, 1967; Shapiro et al., 1978; Sutherland et al., 1982; Thompson et al., 1979). These are mostly detected by the Bender-Gestalt test or performance on the coding or digit symbol subtest of the Wechsler scales.

Language abilities have been found to be significantly impaired in 3 studies (Joschko & Rourke, 1982; Logue et al., 2973; Sutherland et al., 1982). Language skills in general, however, appear to be largely unimpaired despite the interjections of vocal tics, complex sounds, and coprolalia (Golden, 1984). Interestingly, linguistic studies have determined that vocal tics almost always occur at the end of a clause rather than mid-sentence or within words (Frank, 1978; Martindale, 1977). Motor tics seemingly do not respect word boundaries (Frank, 1978).

Memory functioning has been found to be impaired in one of two studies that investigated this capacity in TS patients. Sutherland et al. (1982) found immediate recall of a verbally presented story to be impaired as measured by the Wechsler Memory Scale (1945). In addition, the near universal problems with coding or digit symbol performance may reflect difficulty with short term memory. TS patients complain frequently about problems with memory and attention (Shady et al., 1987).

Investigations of specific neuropsychological deficits have attempted to comprehend the underlying mechanisms and deficits in overall school performance and academic achievement. Unfortunately, many factors are involved in the complex interactions which eventually result in academic achievement. Arithmetic skills, as measured by the Wide Range Achievement Test (WRAT) have been found to be impaired in most studies that examine

this particular skill (Golden, 1984; Incagnoli & Kane, 1982; Joshkc & Rourke, 1982; Plaisted et al., 1983) but no specific pattern of problems in overall school performance or deficits in academic achievement has been identified for TS patients.

III. PROBLEMS WITH THE CURRENT RESEARCH

In the past 20 years, there has been a virtual revolution in the medical profession's understanding of TS. These dramatic changes are almost exclusively attributable to research endeavors on the part of medicine, psychiatry, and psychology. This research is not without is shortcomings. It is useful to examine the problems with this research that require further study and to propose new methodologies to promote greater insight into the etiology of TS. Much more research is required to gain in our understanding of the clinical features of this perplexing disorder.

1) Identification and diagnosis of TS

Clearly the media has played a significant role in diagnosis and public awareness of TS. Two recent episodes of the popular television series Quincy have been devoted to TS (1983; 1985), as has a recent episode of the series, St. Elsewhere (1986). National and international organizations are now in place, with local chapters often playing an important role in public awareness campaigns and fund raising projects (The Tourette Syndrome Foundation of Canada; The Tourette Syndrome Association; Tourette Syndrome Society of Manitoba). Despite the volume of work by groups such as these and the early pioneering efforts of Drs. Arthur and Elaine Shapiro and their colleagues, many problems remain in the identification and diagnosis of TS.

The DSM III criteria have several weaknesses. Criterion #1 sets the age of onset between 2-15 years. At least three epidemiology studies have found individuals with a later age of onset with no suggestion that these patients were distinctive in any other way (Jagger et al., 1982; Lucas et al., 1982; Wand et al., 1986). With the "popularization" of TS and many new cases currently being diagnosed, the range of the age of onset may have to be expanded upwards to include those with symptoms beginning at a later age (Caine, 1986; Jagger et al., 1982; Lucas et al., 1982; Wand et al., 1987). DSM III-R (1987) has addressed this concern.

Similarly, criterion #4 states that the patient must have the ability to suppress movements voluntarily for minutes to hours. This phenomenon is not only difficult to observe and confounding in its implications toward the neurological basis for the disorder, but is also not a useful criteria for distinguishing TS from other disorders. "The ability to modulate the expression of abnormal movements is not unique to TS patients" (Caine, 1986). Therefore, the descriptive value of this criterion for identifying TS patients and distinguishing them from other movement disorder patients, is very limited and has been deleted from the DSM III-R (1987) criteria for TS.

A significant number of TS patients manifest obsessive-compulsive behaviors (Champion, Fulton & Shady, 1987; Nee et al., 1980) and some experience the impairment of the Obsessive-Compulsive Disorder (Montgomery et al., 1982). It is suggested that this common occurrence is more than just coincidence (Pauls & Leckman, 1986) and it remains a difficult task to draw the line and distinguish between the two syndromes. DSM III-R (1987) identifies the Obsessive Compulsive Disorder as a frequent associated feature of TS.

Variations in the intensity of symptoms over weeks or months is the fifth DSM III criterion for TS. This phenomenon has not been investigated carefully despite the importance it would have for biochemical studies. The waxing and waning of symptoms is always a confounding variable in the research on TS but the systematic documentation of the patient's 'normal' and 'clinical' phases which would contribute to the understanding of TS has not yet been undertaken.

The genetic approach to understanding TS has been comparatively rewarding. A commonality has been demonstrated establishing the occurrence of familial TS, where multiple family members of an affected individual have either the full blown syndrome or motor or vocal tics (Kidd et a., 1980; Nee et al., 1980; Wassman et al., 1978). Positive family history and both the responsiveness to haloperidol and the occurrence of obsessive-compulsive symptoms in the proband have also been suggested (Kruger, Caine, & Nee, 1986; Nee et al., 1980). It has been noted that female TS patients must carry a heavier "genetic dose" before expression is apparent (Kidd et al., 1980; Kidd & Pauls, 1982). Attempts to determine a specific pattern of genetic transmission, however, have been frustrated (Baron et al., 1981; Kidd et al., 1980, 1982; Nee et al., 1980).

Despite the success of genetic studies, research utilizing monozygotic twins have suggested that non-genetic factors are prominent in the final expression of the symptoms (Comings, Gursey, & Hecht, 1982; Caine, Weitkamp, & Chiverton, 1986), and pathogenic variables remain undetermined. Significant obstacles stand in the way of further progress of research on the genetics of TS. Since there is no defined genetic pattern of transmission, simple linkage methods are inadequate for TS. Secondly, the

disorder does not manifest complete genetic penetrance and because of the high rate of background occurrence of single tics in the general population, the potential exists for high false positive rates for diagnosing TS. Finally, a variety of phenocopies may represent a distinct genotype and perhaps differing pathophysiological anomolies. Nevertheless, the payoff from genetic research may prove to be substantial. The possibility exists to identify the altered genes and determine which genetic products are abnormal. This may be the key for designating a specific therapy for TS patients.

2) Neurochemistry

The neurochemical understanding of TS can best be described as "The tics of Gilles de la Tourette's disease can be controlled by dopamine antagonists, but what this means is not known" (Marsden, 1982). Studies in neurochemistry have often used small numbers of subjects making generalization to the larger population difficult. Variable techniques and testing procedures have also been used and no attempt has been made to pre-select patients along meaningful lines such as haloperidol responders and non-responders or positive vs. negative family history.

The dopamine hypothesis has the most support, but whether the involvement of dopamine is primary or secondary is not yet possible to ascertain. The pathogenic role of all neurotransmitters has been referred to as "inferential, at best" (Koslow & Cross, 1982). Haloperidol appears to be effective and stimulant medications appear to exacerbate symptoms, but their actions in more controlled research settings are less predictable (Caine, Ludlow, & Polinsky, 1986). The methodology and meaning of some of

the research on HVA, a major dopamine metabolite, have come into question (Koslow & Cross, 1982). Similarly, the relevance of animal facsimile models to the central dopamine functioning of humans with TS is unknown (Diamond, Reyes, & Borison, 1982; Shaywitz, Wolf, & Shaywitz, 1982).

Chemical probes and brief trials with other pharmacotherapeutic agents have been attempted. The results are generally equivocal (Koslow & Cross, 1982). In addition, the assumptions behind some of these investigations and the calculations used in their studies have been questioned (Koslow & Cross, 1982).

Progress in at least three major areas of research is necessary in order for neurochemical studies to prove more useful. A convincing animal model of TS must be developed. This process, which is paradoxically confounded by the inability to define the basic neurochemistry of TS, presents an inescapable research conundrum. Secondly, a well-formulated neurochemical profile of CNS alterations in TS has to be made available, otherwise investigations will have to rely on the crude similarities between induced motor abnormalities in primates and symptoms of TS. Finally, postmortem neurochemical analysis of TS patients and related neuropsychiatric disorders are crucial (Bloom, 1982).

3) Pharmacotherapeutic agents

A tradition of open, poorly controlled therapeutic investigations was established early and has continued. An array of pharmacological compounds has been investigated in the treatment of TS and these efforts have been recently reviewed (Van Woert et al., 1982). It is interesting to note that

although haloperidol has been the treatment of choice for TS for some 25 years, there has never been a large scale, double blind, and placebo controlled study of haloperidol with TS patients (Caine, 1986).

In general, studies investigating the effectiveness of different pharmacological treatments of TS have been poorly controlled and lack uniformity in the selection of patients, the method of drug administration, the identification of target symptoms to be monitored, and methods or instruments for the assessment of drug-induced symptom change. These criticisms must be addressed in future research on pharmacotherapeutic agents.

"Alternative therapies" have frequently been described by TS patients. Many functionally autonomous TS patients have learned to modulate their symptoms consciously through some variations of behavior therapies, yet behavior therapy is reported as being of limited value to TS patients. Similarly, dietary approaches have yielded significant symptom reduction in some well-informed, intelligent TS patients. These claims have never been systematically investigated.

4) Withdrawal from medications

Following the gradual or sudden withdrawal of a neuroleptic, a possibility exists for developing the withdrawal emergent syndrome (Engelhardt and Polizos, 1978). This syndrome, which may occur after the cessation of neuroleptic medication in up to 50% of children, is of special interest to TS patients because it is twice as likely to occur on withdrawal from low-dose and high-potency drugs such as haloperidol, than from high-dose and low-potency drugs (Engelhardt & Polizos, 1978).

The symptoms of this syndrome, as described by Wiener (1984) include: "nausea, vomiting, diaphoresis, ataxia, various combinations of oral dyskenesias (tongue and lips), and dystonic movements of the extremities, head, and trunk. Symptoms appear within a few days to a few weeks after withdrawal, with spontaneous remission in up to 80% of patients after 8 to 12 weeks. Remission in all cases is reported upon resumption of medication" (p. 839). This syndrome has not been systematically investigated under controlled conditions to date. It is a confounding variable to virtually all pharmacotherapeutic research which employs a "no-medication" condition. It is suggested that this syndrome should be monitored, investigated and accounted for by any treatment study of pharmacotherapeutic agents because of its possible confounding effects on the results of the data collected regarding a specific treatment.

The withdrawal emergent syndrome is the central concern of the present study. Many TS patients use haloperidol for TS. Some of these patients take supervised "drug holidays" from their medication in the belief that this will help to prevent or delay some of the more insidious long term side effects of neuroleptic medication such as tardive dyskenesia. For those TS patients who are of school age, summer vacation is commonly designated as the time for the "drug holiday". Although TS symptomatology may return to previous high levels on the occasion of haloperidol cessation and tics may be frequent and disruptive, many patients regard this as an acceptable price to pay for a medication free period. In general, a "drug holiday" is regarded by many to be a desirable component in the overall treatment of TS providing the patient is able to tolerate the return of their symptoms and other adverse reactions which could be a result of the withdrawal emergent syndrome.

The implementation of a medication free period in the treatment of TS is often not a realistic goal for many TS patients. Some elect to remain on medications continually because of good symptom control with very few side effects (Fulton et al., 1987). Results of a recent Canadian survey indicate that most patients have at least tried a medication free period at some time in their treatment history, but most choose to remain on medications on a relatively continual basis (Fulton et al., 1987). There may be other reasons for this general trend. Withdrawal effects in conjunction with an exacerbation of tic symptomatology may render medication cessation intolerable to many TS patients. Symptoms of the withdrawal emergent syndrome may begin to occur within a very short time of medication cessation (Weiner, 1984). Haloperidol has a half life of 13 to 35 hours (Compendium of Pharmaceucticals and Specialties, 1987) and effects of withdrawal may be felt within a short period of time. If intense, these symptoms may preclude the scheduling of a "drug holiday" and make the prospect of medication cessation highly unpleasant and an unrealistic and undesirable objective. Many parents of school age children with TS, report that their children are unable or unwilling to cease intake of their medication. The problem is not only the return of TS symptoms, but also an array of severe behavior problems which quickly become unmanageable. Because of these difficulties, many parents elect to have their child remain on medications rather than have them suffer through what could well be the results of the withdrawal emergent syndrome as much as the return of their TS symptomatology.

Features of the withdrawal emergent syndrome if present, could meet the DSM III-R (1987) criteria for withdrawal. These criteria, which refer to withdrawal from the intake of a psychoactive substance are as follows:

1. Development of a substance-specific syndrome following the cessation of, or reduction in intake of a psychoactive substance that the person previously used regularly.
2. The clinical picture does not correspond to any of the other specific Organic Mental Syndromes, such as Delirium, Organic Delusional Syndrome, Organic Hallucinosis, Organic Mood Syndrome, or Organic Anxiety Syndrome.

In the case of the withdrawal emergent syndrome, these conditions could be met in a number of patients. The research of Englehardt and Polizos (1978) indicates that withdrawal symptoms may be experienced by as many as 50% of children after the cessation of a neuroleptic medication. Their sample was composed of those children who met the definition of "childhood psychosis". Medication dosages used in the treatment of "childhood psychosis" are considerably higher than those used in the treatment of movement disorders such as TS. Typical dosage of haloperidol in the treatment of childhood schizophrenia is 0.1 mg per kg per day (Weiner, 1984), and may range much higher. The average TS patient requires 2.0 to 3.0 mg's of haloperidol daily regardless of age, body size, or weight (Bruun, 1984; Golden, 1984) and rarely exceeds 5 mg's daily. If medication dosage effects the frequency or severity of the withdrawal emergent syndrome in a positively correlated way, then it would be expected that frequency and severity would be less for TS than for other disorders which require higher medication levels. Some TS researchers, however, such as Bruun (1984) and Weiner (1984) have commented on the presence of the withdrawal emergent syndrome in TS patients. They refer to the need to differentiate between symptoms that are induced by medication cessation and

the remergence of TS symptoms which were previously suppressed by medication. A study by Campbell, Grega, and Green (1983) emphasizes the importance of baseline data taken prior to medication withdrawal in this regard.

5) Problems with neuropsychological testing

Specific problems with neuropsychological studies of TS have been reviewed. Examination of the neuropsychological functioning of TS patients both while on and off medication was thought to be a useful measure to be employed in the current study. There were, however, certain problems in the area of neuropsychological testing and research which were of concern. These included test-retest stability, identification of specific deficits, and "significance" in terms of test-retest differences.

Test-retest stability data is available for most test instruments. The issue of "stability" of test scores over time is somewhat different than the "practice effects" which are a potential confound in studies in which there is more than one testing. Stability data is gathered over a longer period of time. This may allow subjects to "forget" most of the materials and procedures between testings. If the testing sessions are in close temporal proximity, practice effects may be more of a confounding variable. No specific information is currently available on the relationship between test-retest results and the variation of the intermittent time interval.

A second problem involves the measurement and evaluation of specific neuropsychological deficits. TS patients have complained of problems with their concentration, attention, memory, and performance on tasks which are

time-limited. Specific subtests of the neuropsychological battery examine these abilities. Successful completion of these subtests, however, often requires more than just one of these abilities. A poor score may be the result of difficulties in any of the abilities required for a given task. Conversely, a good subtest score may reflect a subject's good compensatory skills rather than the absence of a specific deficit. A close examination of the raw test data and the qualitative content of a subject's responses often yields valuable interpretive information. Identification of specific deficits is also made easier by the inclusion of many tests in the battery rather than just one subtest for each specific ability. Cross-referencing subtest performance may help to clarify a subjects' neuropsychological strengths and weaknesses.

A third shortcoming involved with neuropsychological testing in research application is the question of "significance" regarding differences in test-retest results. Most neuropsychological studies in the TS literature report test-retest results simply in terms of "differences". There is no standardized procedure for determining which differences are statistically or numerically significant and which are not in the context of a short term test-retest schedule. The possibility exists of identifying differences which do not reflect actual improvement or deterioration of neuropsychological functioning. The changes may be due to measurement error, practice effects, motivation, or any one of an array of intrinisic neuropsychological testing confounds. The possibility also exists to fail to identify improvements or deteriorations which are present in a subject's neuropsychological functioning. There may be slight but consistent changes in functioning which are not reflected in neuropsychological subtest scores.

These problems make the interpretation of neuropsychological test results in short interval test-retest administration difficult and render the results unreliable. Test-retest stability, practice effects, and the question of significance combine to make neuropsychological tests unsuitable for use in the context of an A-B-A research design. Therefore, neuropsychological measures will not be reported as data for inclusion in the context of this clinical investigation of the withdrawal emergent syndrome. A unique opportunity exists, however, to examine the neuropsychological functioning of young TS patients at a time when they are on haloperidol and compare it to their functioning when they are medication free. This data will be gathered for discussion purposes. It will be of heuristic and exploratory value in the investigation of the effects of neuroleptic medications on neuropsychological functioning. It is mentioned in the context of this investigation of the withdrawal emergent syndrome for reasons discussed in the rationale for the current study.

IV. PROBLEMS WITH TREATMENT

Despite efforts to investigate a number of pharmacotherapeutic agents (Morison et al., 1982; Shapiro & Shapiro, 1982; Van Woert et al., 1983) and the suggestion that pimozide (Wiener, 1984) or clonidine may be the treatment of choice of TS patients (Borison et al., 1982; Cohen et al., 1980), haloperidol remains the most commonly prescribed and effective medication for TS in the U.S. (Bruun, 1984), and Canada (Fulton et al., 1987). Cohen et al. (1980) has suggested that the side effects of haloperidol are so unacceptable that only 20% of patients continue haloperidol therapy for long periods of time. These estimates however, seem inconsistent with current epidemiological research employing larger and more diverse samples (Fulton et al., 1987), and there does not appear to be a reluctance to prescribe haloperidol therapy for TS patients today. Many side effects continue to plague users of this medication. Shapiro et al. (1978) divided these side effects into 5 categories: dyskenesic, parkinsonian, autonomic nervous system effects, cognitive and akathesis. It is more useful for the purpose of the present study to examine the adverse side effects of haloperidol in terms of physiological, behavioral, and psychological functioning.

1) Physiological Reactions

Dopamine-blocking neuroleptic drugs such as haloperidol are highly potent compounds with a variety of adverse effects ranging from short term irritations to long term dangers. Most TS patients who are treated with haloperidol experience at least one or two of its adverse side effects (Fulton et al., 1987). Recipients of high-potency compounds such as haloperidol are twice as likely to experience a reaction to medication than are patients on low-potency drugs such as thioridazire (Engelhardt & Polizos, 1978). Therefore, a brief review of these side effects is relevant to the present study.

Minor irritations involving the skin, autonomic system, bone marrow, and liver functioning which are thought to be side effects of haloperidol have either been infrequently reported or are not clinically significant (Wiener, 1984). Other effects such as sedation and dramatic weight gain are quite common (Fulton et al., 1987; Weiner, 1984). More serious physiological side effects that require attention include dystonic reactions, parkinson like reactions, tardive dyskinesia and the withdrawal emergent syndrome (Engelhardt & Polizos, 1978; Gualiteri & Hawk, 1980).

i) Dystonic reactions

These reactions which are defined as abnormal tonicity of the musculature, are believed to occur in about 25% of children treated with medication for TS (Wiener, 1984). The rate may be even higher for children treated with haloperidol (Englhardt & Polizos, 1978). These rates however, are based on anecdotal reports and surveys rather than controlled experimental conditions.

Tongue protrusion, drooling, grimacing, and torticollis, (writhing and twisting of the neck and cervical muscles producing an unnatural positioning of the head) are common dystonic reactions. Less commonly seen, but perhaps needing more immediate attention, are oculogyria or oculogryric crisis (OGC) and catatonic or akathesic reactions (an inner sense of restlessness and need to change positions). Treatment consists of lowering medication dosage, discontinuing treatment, or adding an anti-dystonic medication (binzotropine).

ii) Parkinsonlike Reactions

Haloperidol is also more likely than other less potent medications to cause parkinson-like side-effects including visible tremor, muscle rigidity, excessive salivation, mask-like facial expression, and bradykinesia (abnormal slowness of movement and sluggishness of physical and mental responses). These reactions are reported in 20% to 25% of children on medication for TS.

iii) Tardive dyskinesia

Dyskenesia is defined simply as difficulty in performing voluntary movements. Tardive dyskensia is a form marked by involuntary repetitive movements of the facial, buccal (pertaining to the cheeks), oral and collar musculature affecting chiefly the elderly. It is induced by long term administration of neuroleptic (antipsychotic) agents and may persist after the withdrawal of the agent.

Although this disorder is more common in adults than children, it is perhaps the most serious possible side effect of haloperidol both because of its insidious nature and long term duration. Ross (1986) states that "tardive dyskinesia is the most serious and debilitating complication of chronic neuroleptic treatment". It has been found to result from long term treatment with neuroleptic medications such as haloperidol (Brunn, 1984; Shapiro & Shapiro, 1982; Wiener, 1984) and is therefore of critical importance to the treatment of TS. Others (Fog, Pakkenberg, Regeur, & Pakkenberg, 1982; Klawans, Nausieda, Goetz, Tanner, & Weiner, 1982) have found that symptoms resembling both tardive dyskinesia and TS have resulted from long term treatment with neuroleptic medication. The relationship between tardive dyskinesia, TS, and the withdrawal emergent syndrome remains unclear despite their similar characteristics.

Chronic exposure to neuroleptic agents can produce involuntary movements. This disorder is called neuroleptic-induced tardive dyskinesia. The movements are usually choreatic in nature, although they may have occasional dystonic characteristics. Multifocal tics, such as those found in TS, are not usually thought to be characteristic of tardive dyskinesia, yet they have been found to be produced by chronic neuroleptic medication use (Fog et al., 1982; Klawans et al., 1982). Symptoms of tardive dyskinesia such as ataxia, combinations of oral dyskinesias involving the tongue and lips, and dystonic movements of the extremities, head and trunk, are also found to be produced by long term exposure to haloperidol (Wiener, 1984).

iv) Withdrawal emergent syndrome

The withdrawal emergent syndrome may occur in up to 50% of children upon the gradual or sudden withdrawal of a neuroleptic agent. Its symptoms, including nausea, vomiting, diaphoresis (profuse perspiration), ataxia, oral dyskinesias and some dystonic movements which strongly resemble those of tardive dyskinesia and may even overlap onto those of TS. The relationship between these disorders remains unclear, and the problem of defining and diagnosing "tardive" vs "drug-induced" dyskinesia remains with us (Campbell, Grega, & Green, 1981).

2) Behavioral symptoms

A number of cognitive and motor difficulties are seen in children receiving haloperidol therapy for TS. A problem exists, however, in determining which of these difficulties are attributable to TS, and which are attributable to the neuroleptic medication. Few studies have been concerned with this problem which when coupled with the waxing and waning symptomatology of TS often render the results of even well-controlled studies uninterpretable (Bruun, 1984).

i) Cognitive difficulties

Cognitive side effects have been labelled "fogging" or "cognitive obfuscation". They include: impairment in concentration, attention, memory, aquisition and retention of new knowledge. In higher cognitive functions such as reasoning, "slowed mentation", drowsiness, and a feeling of being "spaced out" or "not with it" have been reported along with feelings of depression or paranoia (Bogommolny, Erenberg, & Rothner, 1982, p. 427).

TS patients' self reports most commonly cite problems with concentration, paying attention, and performance on time limited tasks (Shady et al., 1987). Cognitive blunting, depression, and school phobia have also been reported (Brunn, 1982; Shapiro et al., 1978). To date, no exact pattern of cognitive deficits that is attributable directly to treatment with haloperidol has been established in the research literature. While certain impairments in cognitive functioning seem evident (see neuropsychological testing review), the exact pattern and causes of these deficits remains unclear. A common theme, however, that seems to emerge from most studies examining cognitive functioning is a difficulty in obtaining or maintaining a concentrated effort-- a cognitive vigilance deficit.

ii) Difficulties in motor functioning

Level of arousal is a factor generally ignored in drug studies (Aman, 1978). It is, however, a factor of critical importance to haloperidol treatment research because side effects such as weight gain, lethargy, drowsiness, apathy, and listlessness are often cited (Fulton et al., 1987). Similarly, sleep disturbances such as insomnia, problems staying awake, nightmares, somnambulism and enuresis have also been reported by TS patients (Champion et al., 1987). Haloperidol withdrawal symptoms may include increased irritability, tension, and insomnia (Bruun, 1984). Bogomolny et al. (1982) have found that patients have greater grip strength off haloperidol than when they are on haloperidol. This effect may be due to a kind of vigilance toward task completion, or motivation, rather than to actual changes in overall physical strength. The final conclusion of

Bognomolny et al. (1982) states "we found no reliable effects of haloperidol on higher cognitive processes involving planning, attention, or memory, simple sensory and motor functions, visual-motor integration, speech, or affect" (p. 431). This conclusion is contrary to that of a number of other studies examining the cognitive and motor functioning of children with TS and the precise pattern of deficits remains unclear.

3) Psychological symptoms

Research has indicated that TS patients are in considerable psychological stress (Grossman et al., 1986). The extent to which this is a result of the Tourette syndrome or side-effects of neuroleptic treatment is not known. Bruun (1984) observed that children on high-dose medication "tended to gain too much weight and to give an overly tranquilized appearance which was often mistaken for stupidity. As a result they were avoided by their peers perhaps as much or more than they would have been had they been exhibiting the now suppressed symptoms of TS" (p. 128). Dysphoria, depression, apathy, moodiness, motivational problems, and lethargy have also been reported (Borison et al., 1982; Bruun, 1982; 1984; Golden, 1984; Shapiro & Shapiro, 1982; Van Woert et al., 1982; Wiener, 1984). Many of these symptoms are thought to be the result of treatment with haloperidol rather than psychological reactions to TS. Sacks (1987) contends that many TS patients prefer their tics to a drug-induced relief which leaves them basically competent "but lacking energy, enthusiasm, extravagence -- and joy".

More than half of TS patients report that having TS has interfered to some extent with the rest of their families' daily activities and many have

sought counselling (Hubka, Fulton, Shady, Champion, & Wand, 1987). Unfortunately, counselling has not generally been found to be effective and much dissatisfaction exists with currently available services (Hubka et al., 1987; Shapiro et al., 1978).

Despite the many difficulties associated with TS and medical treatments, about half of the TS patients in Canada rated their own mental health as good and claimed to be coping fairly well with their symptoms (Champion et al., 1987). Although many TS patients (approximately 40%) choose not to take medication for their symptoms (Fulton et al., 1987), even among those utilizing pharmacotherapeutic agents, mental health was rated as good in about half the cases (Fulton et al., 1987). It can also be argued from the same data that about half of the TS patients in Canada are unsatisfied with available medical treatments and view their own mental health as fair to poor. In short, ratings of satisfaction with currently available treatments is relatively low and it would appear that the physiological, behavioral, and psychological side effects of currently available neuroleptics are many.

4) Rationale for current study

The available research indicates that although currently available neuroleptics are successful in the treatment of TS with a high percentage of patients, the side effects are many, and the price, both short term and long term of using neuroleptic medication may be greater than previously estimated. Side effects of medication withdrawal have also been mentioned but have never been specifically investigated. Research investigating the specific results of medication cessation is warranted.

The withdrawal emergent syndrome is a poorly understood phenomenon. It has not been systematically investigated under controlled conditions to date and remains a largely ignored confounding variable to any research which employs "no medication" as an experimental condition. The main problems encountered with the investigation of the withdrawal emergent syndrome involve its definition and behavioral description, its distinction from symptoms of other disorders, and its etiology in terms of onset, duration and intensity.

Reports and descriptions of the withdrawal emergent syndrome have largely been based on reviews of clinical experiences (Bruun, 1984). There has not been a behavioral investigation of the withdrawal emergent syndrome that followed patients' symptoms closely over a period of time when they were on medication, then off medication, then back on medication. This would provide information about which symptoms actually "emerge" under a medication free condition and then disappear with the resumption of medication. This is a necessary step toward distinguishing withdrawal emergent syndrome symptoms from those that may not be associated with medication or its withdrawal in any way. This information will help in the identification of the syndrome.

A second problem with the withdrawal emergent syndrome is in distinguishing its symptoms from those of other disorders. This is a very difficult task for which there are no easy answers. Campbell et al. (1983), in studies with autistic children on haloperidol, remark on the difficulty in differentiating between withdrawal-induced and disorder-induced symptoms. Tourette's syndrome may be useful in this regard. TS symptoms are qualitatively different than those that are

suggested as resulting from the withdrawal emergent syndrome. Furthermore, specific testing instruments have been developed for reliably measuring, monitoring, and scoring TS symptomatology. These factors help to distinguish TS symptoms from withdrawal symptoms. While some overlap may exist, there are clear advantages to using TS patients to investigate the withdrawal emergent syndrome. The distinction of withdrawal symptoms from those associated with TS is facilitated by these specific testing instruments.

In addition, TS patients have generally been found to be of normal intelligence and in possession of adequate communication skills. This is often not true of populations who use neuroleptic medications such as haloperidol. This factor allows for self-report measures to be gathered from TS patients and permits the usual level of confidence to be placed in measures gathered through self-report procedures.

The third area of difficulty with examining the withdrawal emergent syndrome involves the lack of information regarding its onset, duration, and intensity. Bruun (1984) suggests that withdrawal symptoms may occur quickly but usually disappear within 10 days of onset. Weiner (1984) suggests that symptoms may appear within a few days to a few weeks following medication cessation, with spontaneous remission after 8 to 12 weeks. In order to explore the clinical picture of withdrawal emergent syndrome, patients' symptoms must be closely monitored over a period of time that spans on-medication, off-medication, and back on-medication conditions. The symptoms should be monitored extensively and frequently enough to detect trends in the individual's symptomatology. This will begin to explore the larger questions regarding the etiology of the withdrawal emergent syndrome.

The "drug holiday" provides a format to investigate the withdrawal emergent syndrome. Some TS patients who take haloperidol have regularly scheduled "drug free" periods as part of their treatment regimen. These "withdrawals" have never been clinically investigated. It may be argued that since these patients regularly take drug holidays they are clearly able to tolerate mediation withdrawal and will therefore show no withdrawal symptoms. It is suggested, however, that if the withdrawal symptoms are monitored closely and frequently, patterns of symptoms may emerge that are not associated with TS and which disappear upon resumption of medication.

The drug holiday of some TS patients also provides a unique opportunity to examine the effects of haloperidol on the neuropsychological functioning of an individual at a time when they are on haloperidol and compare it to their functioning when they are medication free. This data, which will be of exploratory value in the investigation of the effects of neuroleptic medication on neuropsychological functioning, will be gathered for discussion purposes of the present paper.

Neuropsychological testing is mentioned in the context of this investigation of the withdrawal emergent syndrome for a number of reasons. First, the study of the neuropsychological functioning of TS patients to date has not resulted in the emergence of a definitive pattern of deficits (Newman et al., 1986). Further, results of such investigations are often confounded by possible medication effects on neuropsychological functioning (Golden, 1984). The current investigation of the withdrawal emergent syndrome not only provides a unique opportunity for on-haloperidol off-haloperidol comparisons, but does so during a time when both TS symptoms and drug effects are being closely monitored. Neuropsychological

test performance can therefore be placed into the perspective of the individual's current level of TS symptomatology and their reactions to medication.

A second reason for monitoring the neuropsychological testing in the context of the current study is that it will provide a forum in which the examiner will be able to gather clinical data about the individual patient. Testing procedures require 5 to 7 hours of the patient's time per assessment. With younger children, a number of intermissions will be scheduled to ensure compliance and optimal performance. Over the course of these evaluations, the examiner will be able to observe the patient's behavior while engaged in a variety of purposeful tasks and also while relaxing. This is an important contribution to the withdrawal emergent syndrome study in terms of inter-rater reliability data regarding the patient's withdrawal symptoms and behaviors.

A third reason for including the neuropsychological test data in the context of the present study is that the use of such specific and objective tests may uncover small but consistent differences in neuropsychological functioning. While these results may lack the reliability necessary for inclusion in the main body of data, they may be useful in the interpretation of the behavioral data taken during the different experimental conditions. A great deal of information is taken in during a neuropsychological assessment. This information may supplement the behavioral observations of the examiner for the purposes of inter-rater reliability.

Finally, the neuropsychological test data may prove interesting in its own right. The difficulties in data interpretation are best addressed by using a large number of tests in the battery for cross-reference purposes in interpretation, by examining the qualitative contents of the test data and by reporting test-retest differences with the appropriate caution. Despite its limitations in the current context, valuable information regarding the neuropsychological functioning of TS patients is attaintable through these test procedures in the context of the present design.

VI. METHOD

1) Subjects

Six voluntary participants for the present study were recruited through the Tourette Syndrome Clinic at the St. Boniface General Hospital. They were contacted directly by the experimenter regarding their participation in the study and were fully informed regarding the nature of the research. All subjects were required to meet the following inclusion criteria:

1. They must have been diagnosed as having TS.
2. They must be on haloperidol and no other medication for TS.
3. They must have been on haloperidol for a minimum period of 2 months and an optimal dosage level must have been established.
4. They must have taken their medication on a regular and consistent basis during the period of time when haloperidol is being administered.
5. They must take a "drug holiday" (i.e. medication free) for a minimum period of 4 weeks during the year (experimental subjects only, controls remained on medications throughout the study).
6. They must sign, or have their parent or guardian sign a consent form for research purposes (see Appendix A).
7. Subjects must be at least 9 years of age.

Participation in the study was completely voluntary. No experimental confederate or deception of subjects was employed. Participants were free

to discontinue testing or drop out of the experiment at any point, although they were encouraged not to do so.

2) Instruments and Measures

Measures for the current study were concerned with two main features of a patient's symptomatology. The first of these was the withdrawal emergent syndrome. Instruments were used which helped to identify and measure various behavioral symptoms of the withdrawal emergent syndrome. Although these instruments are not specifically designed to measure withdrawal symptoms, they are widely used in clinical studies of pharmaceutical agents and are also appropriate for monitoring withdrawal symptoms. A second concern of the present study was the identification and monitoring of TS symptoms during the different medication conditions. Instruments that were specifically designed to measure TS symptoms were used for this purpose. The differentiation of withdrawal emergent and TS symptoms was facilitated by using these specific instruments. Neuropsychological test data was also gathered at certain points during the study. These are considered for discussion purposes.

i) Instruments for monitoring the withdrawal emergent syndrome

a) SCL-90

The Symptom Checklist-90-Revised (SCL-90-R) (Derogatis, 1977) is a self report clinical rating scale developed to monitor the symptomatic behavior of psychiatric outpatients. The scale is comprised of 90 items which reflect a factorial composition of the following 9 primary symptom dimensions:

1. Somatization (N=12)
2. Obsessive-Compulsive (N=10)
3. Interpersonal Sensitivity (N=9)
4. Depression (N=13)
5. Anxiety (N=10)
6. Anger-Hostility (N=6)
7. Phobic-Anxiety (N=7)
8. Paranoid Ideation (N=6)
9. Psychoticism (N=10)

Each of the 90 items is rated on a 5 point scale of distress ranging from "not at all" to "extremely". Typical administration time is 25 minutes and under ordinary conditions the patient is instructed by the technician how to complete the form. It is possible however, under special circumstances for an external observer to rate the SCL-90-R, and it may be easily and effectively administered by a trained technician.

The SCL-90-R has been designed as a general measure of psychiatric outpatient symptomatology for use in both clinical and research settings (Derogatis et al., 1973). Under standard conditions the time context used with this instrument is 7 days. An attempt was made during the development of the SCL-90-R to use the most fundamental phrasing available for each item. Despite the basic vocabulary used, some patients will not have the literacy level needed to validly complete the profile. It is suggested that these profiles be assigned a conditional status (Derogatis et al., 1973).

In the current investigation, it was thought that the literacy level of school age children might not be adequate to validly complete the SCL-90-R. Due to this concern, the SCL-90-R was administered to the patient on a weekly basis by the child's parent and on a monthly basis by the experimenter. Parents had been instructed regarding the administration of this instrument. In addition, the experimenter contacted the parent on a weekly basis to provide procedural advice on any problems encountered with test administration or understanding.

The reliability ratings of the SCL-90-R are very good. Internal consistency coefficients range from .77 to .90. These measure the consistency with which the items selected to measure a particular construct actually reflect the underlying factor. Eight of the nine SCL-90-R dimensions have internal consistency coefficients of .80 or above.

Coefficients of test-retest reliability for the SCL-90-R range from .78 to .90. Again, eight of the nine scales are .80 or above. The somatization scale which is of specific interest to the current study is .86 for both internal consistency and test-retest reliability (Derogatis, 1977).

A number of validation studies have also been conducted with the SCL-90-R. Efforts have been made to determine the degree of equivalence between the SCL-90-R and other measures of similar constructs such as those in the MMPI. Results of a study by Derogatis, Rickels, and Roch (1976) reflect a high degree of convergent validity between the SCL-90-R and the MMPI. Correlations range from .41 to .68 and each SCL-90-R dimension has its highest correlation with its like construct in the MMPI.

Extensive factor analysis studies have also been conducted with the SCL-90-R to examine the hypothesized internal structure of the instrument and its degree of agreement with more empirically-based analysis. In general, the empirical-theoretical match with the SCL-90-R is excellent (Derogatis, 1977), and the empirical analysis matches the theoretical construct on almost all dimensions.

The SCL-90-R has been shown to have very high and consistent sensitivity to change in psychopharmacological studies of medication withdrawal (Winokur, Rickels, Greenblatt, Snyder & Schatz, 1980). It has also been used in studies involving neuroleptic medication (Prusoff, Williams, Weissman, & Astrachan, 1971). It is an appropriate instrument for exploratory research in the clinical investigation of symptoms that result from cessation of neuroleptic medication.

Symptoms of the withdrawal emergent syndrome were expected to inflate the Somatization dimension of the SCL-90-R. This scale is concerned with distress arising from the patient's perception of body dysfunction. Complaints of cardiovascular, gastrointestinal, respiratory and other systems are included. Headaches, backaches, and other pain and discomfort is also represented in this dimension. Some of these types of concerns have been suggested as part of the withdrawal emergent syndrome (see Appendix B for SCL-90-R).

b) CBCL

The Child Behavior Checklist (CBCL) (Achenbach & Edelbrock, 1983) has been designed for both clinical and research purposes. No special

qualifications are needed to administer this test. It is designed to be filled out by parents or parent surrogates and can usually be completed in less than one hour. If this instrument is used in an applied research setting, the time interval between testings can be adjusted to suit the purposes of the research. If the time interval is too short, however, some scales may reflect lower scores on certain items than they would have from a longer time interval (e.g., fire setting, suicide attempt, running away from home). In the current study the CBCL was completed on a monthly basis throughout the scheduled 6 month period.

The CBCL provides the researcher with a Child Behavior Profile. Behavior problems are identified and arranged into clinical scales which are based on extensive factor analysis of checklist items. There are 9 behavior problem scales. These are arranged under three headings, Internalizing Syndromes, Mixed Syndromes, or Externalizing Syndromes. The exact position of each of the 9 scales vis-a-vis the three headings varies with the age and sex of the child. For example, the behavior problem scales are arranged in the following way for boys age 6 to 11:

Internalizing Syndromes

Schizoid or Anxious

Depressed

Uncommunicative

Obsessive-Compulsive

Somatic Complaints

Mixed Syndromes

Social Withdrawal

Externalizing Syndromes

Delinquent

Aggressive

Hyperactive

The CBCL has been found to be a highly reliable instrument. Test-retest reliability, interrater reliability, and longer term stability were assessed and found to be .74, .96, and .60 (6 month period) respectively (Achenbach & Edelbrock, 1983). In general, the stability of the CBCL increases as the time interval decreases. At 3 months, the longer term stability correlation was .74. Individual items were analyzed by computing intraclass correlations (ICC's). These were all found to be .90 or above (Achenbach & Edelbrock, 1983).

Content validity was determined by investigating whether or not the items were related to the clinical concerns of parents. The CBCL was found to be significantly ($p < .01$) associated with clinical status established independently of the CBCL. Construct validity was determined by comparing the total CBCL behavior problem score with scores on other widely used parent rating forms. Correlations were reported to be as high as those typically found between tests of general intelligence. Criterion-related validity was determined by using referral for mental health services as the criterion. The CBCL was able to significantly ($p < .001$) differentiate between referred and nonreferred children with demographically matched groups.

Other related instruments are available to supplement the CBCL. The Direct Observation Form (DOF) allows a structured sample of a child's behavior to be recorded by a more neutral observer. The Youth Self Report (YSR) is designed to be filled out by the youngsters themselves. It

requires a mental age of about 10 years or a Grade 5 reading level to complete. It can also be read aloud to the respondent if necessary. Both the DOF and the YSR were used in the present study to assist the examiner in recording a complete CBCL on a monthly basis for each child in the study. Scales which load on the Internalizing Syndromes heading were expected to be inflated by symptoms of the withdrawal emergent syndrome (see Appendix C for CBCL, Appendix D for DOF, Appendix E for YSR).

c) PQ and ARR

The Physician's Questionnaire (PQ) and Adverse Reactions Report (ARR) were also used in the present study. These forms were developed for research purposes by the Brystol-Myers Co. Pharmaceutical Research and Development Division (1985). They are designed to be used on a weekly basis in studies of different medications, medication dosages, or medication withdrawal.

The PQ consists of a global rating of psychopathology, a rating of symptom changes over a 7 day period, and checks for adverse reactions or other unrelated illnesses. If a concurrent illness is present, the researcher monitors the severity, duration, and concomitant medication use. If an adverse reaction is reported, an ARR is completed by the researcher.

The ARR is a partially open-ended form that allows for side effects to be identified and rated for severity; monitored in terms of onset, cessation, source, and action taken; and related to current treatment or agent withdrawal. The ARR is designed to be used on a weekly basis only if adverse reactions are reported, otherwise it is not completed.

In the present study, both subtle and severe withdrawal emergent symptoms were recorded in the ARR. Similarly, adverse reactions to haloperidol re-administration were also recorded in the ARR. These were distinguishable from each other not only through the treatment condition, but also through the rating of relationship between symptom and causal agent in the ARR (see Appendix F for PQ, Appendix G for ARR).

ii) Monitoring of TS symptomatology

The TS Global Scale (TSGS) (Harcherik, Leckman, Detlor, & Cohen, 1983) is a multidimensional scale for TS which was "specifically designed to permit reliable and valid, across-subject comparisons on several dimensions of TS symptomatology including behavioral symptoms, motor restlessness and school or occupational performance as well as simple and complex motor and phonic tics" (p. 153).

Scores from two major domains contribute equally to the total TSGS score. One domain consists of the motor and phonic tics and accounts for 50% of the global score. Tics are rated according to frequency, complexity, and degree of disruption. Inter-rater reliability regarding this domain is good (0.65 to 0.85;, $p < .001$). The second domain which comprises the other 50% of the global score is a composite score of social functioning. Three areas including behavioral problems, motor restlessness, and level of school or occupational functioning are monitored and scored on a scale of 0 to 25. The sum of these three areas is then multiplied by 2/3 to yield the overall social functioning score. Good inter-rater reliability was observed for behavior problems (0.87; $p < 0.001$), and school performance (0.93; $p < 0.001$). Motor restlessness

however, did not achieve the same high ratings of inter-rater reliability (0.32; p=N.S.).

The TSGS comprehensively scores and examines both TS symptomatology and social functioning. It is described by Harcherik et al. (1984) as being "comprised of 8 individually rated dimensions summed into an overall global score. The scale ranges from "0", which represents no symptoms, to "100", representing the worst possible TS symptoms, consisting of constant and debilitating motor and phonic symptoms, unacceptable social behavior, nonstop motor restlessness, and an inability to function in school or work settings" (p. 154).

The scores for the TSGS range from 0 to 100. They are distributed normally with a mean of 40.2 and standard deviation of 15.2. A clinical typology of TS involving 4 subgroups as identified by TSGS score is suggested by Harcherik et al. (1984): Mild (TSGS score 0-24); Moderate (TSGS score 25-39); Severe (TSGS score 40-59); Extreme (TSGS score 69-100).

Construct validity of the scale was measured by having 6 TS patients rank ordered in terms of overall severity of TS symptomatology under baseline conditions by 4 different raters. This measure agreed reasonably well with the consensus global score of the TSGS (0.46 to 0.99; $p < 0.05$). Concurrent validity was measured in a similar way during a second phase of the study by comparing the Children's Global Assessment Scale (C-GAS) to the TSGS (0.76 to 0.89; $p < 0.001$). The overall strength of the instrument is indicated by the high inter-rater reliability for the TSGS global score (0.89; $p < 0.001$). The TSGS has been used successfully in pharmacological trials (Leckman, Harcherick, Young, Anderson, Shawitz & Cohen, 1983;

Leckman, Cohen, Gertner, Ort, & Harcherik, 1984), and in ongoing studies of the natural history of TS (see Appendix H for a copy of the TSGS).

An individual training session was held with each parent prior to the beginning of the study. The purpose of this session was to train parents in the appropriate use of the TSGS, ARR, SCL-90-R, and the other measures used in the present study. This was necessary in order to apply consistent standards of measurement across all subjects and all phases of the experiment. Detailed written instructions regarding the appropriate use of the instruments and the data collection procedures were left with each parent (see Appendix I, Questionnaire Instructions).

iii) Neuropsychological testing

As previously indicated, the most common cognitive complaints of TS patients, whether they are on medication or not, involve problems with paying attention, concentrating, and memory. Research regarding the neuropsychological functioning of TS patients while not yielding a common pattern of deficits, has suggested that there may be some widespread difficulty with visuopractic tasks and also with sustaining an effort or "vigilance". The present study will utilize the following instruments to assess the neuropsychological functioning of TS patients under different experimental conditions. These findings will be reported for discussion purposes.

a) WISC-R or WAIS-R

Dependent upon the age of the subject either the Wechsler Intelligence Scale for Children-Revised (Wechsler, 1974) or the Wechsler Adult Intelligence Scale-Revised (Wechsler, 1981), WISC-R or WAIS-R respectively, was used in the present study. All experimental subtests of the appropriate scale was administered to each subject at two different times; once while on haloperidol and once while medication free.

b) Reitan-Indiana or Halstead Intermediate Tests

The selection of neuropsychological tests was based on the criterion that they should be capable of reflecting a fairly broad spectrum of abilities, including those that are expected to be impaired when various brain systems are dysfunctional (Boll, 1974; Reitan, 1974; Rourke, 1981). For the most part, the following tests and procedures were developed and standardized by Ward Halstead (1947) or Ralph Reitan (1974). The procedures are described by Reitan and Wolfson (1985) and Reitan and Davidson (1974) respectively. They have been used in other studies investigating the neuropsychological functioning of children with TS and were employed with age appropriate subjects in the present study.

Trail Making Test (for children) Part A and Part B

This is basically a visual-perceptual task (Part A), but also involves elements of concentration, attention, and short term memory.

Bender-Gestalt Test (Bender, 1946) or Beery-Buktenica Test of Visual Motor Integration (Beery & Buktenica, 1967)

These tests were used to investigate visual-perceptual and visual-motor integration skills in TS patients. The Koppitz (1963) scoring system was used for the Bender-Gestalt test because it provided a chronological age equivalent score as does the Berry-Buktenica Test of Visual Motor Integration.

Reitan-Klove Tactile-Perceptual and Tactile Form Recognition Test

These tests were used to examine performance in tactile perceptual tasks.

Tactual Performance Test

This test was included to investigate tactual performance, tactual-spatial skills, attention, concentration and memory. It is also a timed task.

Reitan-Klove Lateral Dominance Examination Dynamometer Grip Strength Finger Tapping Test

These tests were used to assess motor and psychomotor functioning.

Seashore Rhythm Test

Speech Sounds Perception Test

These tests were used to examine auditory-perceptual and language-related discriminatory and activity skills.

Halstead Category Test

This test were used to assess cognitive flexibility, problem solving skills, and higher cognitive functioning.

3) Design and procedures

The design for the current study made use of a subject's regularly scheduled "drug holiday" as an experimental condition to explore the withdrawal emergent syndrome. It employed what Hersen and Barlow (1976) call an A-B-A withdrawal design. This design is well suited for investigations that do not emanate from the operant (reinforcement) framework, such as the current study. The following phases constituted the A-B-A design: baseline - treatment - return to baseline. In the present study, the phases A-B-A corresponded to the following conditions: (A)-on haloperidol; (B)-medication free; (A)-on haloperidol. The main general concerns over use of this type of design involve the length of phases, carryover effects, and cyclic variations. In the present study, the length of phases is equal. The carryover and cyclic effects were closely monitored, visually graphed, and considered in the final interpretation of the results. A more specific concern of the design for the present study was that all experimental subjects were medication free at the same time as they were on vacation from school. They were on haloperidol while school was in session. School and medication with haloperidol therefore occured together for each experimental subject. There was no period of time when a subject was on haloperidol during the summer vacation, or off haloperidol while school was in session. Therefore, two control subjects who remained on medications for the entire experimental period were monitored to serve as a kind of control for these confounding factors of the current design.

Symptoms of the withdrawal emergent syndrome were expected to appear during condition B when the experimental subjects were medication free. There is no research to indicate that a vacation from school should have any effects on the withdrawal emergent syndrome. TS symptoms however, are more unpredictable and may or may not be altered by summer holidays. In any event, symptoms of both the withdrawal emergent syndrome and TS were monitored closely throughout the study using the SCL-90-R, CBCL, PQ, ARR, and TSGS (see figure 1 for design).

FIGURE 1
DESIGN

	BASELINE	WITHDRAWAL	RETURN TO BASELINE
	'A'	'B'	'A'
CONDITION:	ON HALOPERIDOL	MEDICATION FREE	ON HALOPERIDOL
MEASURES:	SCL-90 ARR TSGS Weekly by patient CBCL Monthly by parent PQ ARR Weekly by experimenter SCL-90 TSGS CBCL Monthly by experimenter	SCL-90 ARR TSGS Weekly by patient CBCL Monthly by parent PQ ARR Weekly by experimenter SCL-90 TSGS CBCL Monthly by experimenter	SCL-90 ARR TSGS Weekly by patient CBCL Monthly by parent PQ ARR Weekly by experimenter SCL-90 TSGS CBCL Monthly by experimenter
TIME LINE:	8 weeks	8 weeks	8 weeks
ADDITIONAL TESTING PROCEDURES:	Neuropsychological testing with 2 of 4 subjects	Neuropsychological testing with all 4 subjects	Neuropsychological testing with 2 subjects not tested at first Condition 'A' -

N=4

ARR = Adverse Reaction Report
CBCL = Child Behaviour Checklist
PQ = Physician's Questionnaire
SCL-90 = Symptom Checklist - 90
TSGS = Tourette Syndrome Global Scale

i) Condition A (baseline)

All subjects continued on their regular dose of haloperidol. The inclusion criterion specified that each individual's dose of medication had been stabilized for at least a period of two months prior to the beginning of the baseline phase. Therefore, no major changes were expected to occur with the patient's symptomatology during this phase of the study although some slight variations were anticipated.

All symptoms were closely monitored throughout the study. The SCL-90-R, ARR, and TSGS were completed on a weekly basis by the individual patients with help from their parents. The CBCL was filled out on a monthly basis by the child's parents. In addition, the experimenter had weekly contact with the child's parents to help to resolve difficulties with the data collection process and completed the PQ and ARR on a weekly basis for each subject. The experimenter also completed a CBCL on a monthly basis with the patient using the YSR to assist in the collection of this data. The time line for Condition A was 8 weeks which made it comparable in length to the other experimental conditions.

ii) Condition B (withdrawal)

In this condition the four experimental subjects were taken off active medication for TS. The two control subjects remained on their medications. Changes in TS symptomatology were monitored by the TSGS. The effects of withdrawal from haloperidol were monitored by the SCL-90-R, ARR and the CBCL. Withdrawal symptoms were expected to emerge during this phase. TS symptoms were expected to be either exacerbated by the removal of

medication or attenuated in conjunction with the summer holidays. Tic symptomatology is unpredictable in this regard. Withdrawal symptoms were expected to occur during the first few days after medication cessation and to decrease over the duration of this phase. The time line for Condition B was 8 weeks.

iii) Condition A (return to baseline)

All subjects were returned to their regular dose of haloperidol. Changes in TS symptomatology were monitored by the TSGS. Withdrawal symptoms were expected to disappear with the resumption of medication. This change was monitored by the SCL-90-R, ARR, and the CBCL. In addition, adverse reactions to haloperidol which might have disappeared during Condition B were expected to reemerge with the resumption of medication. Instruments used in the present study were designed to be able to detect these changes. The time line for Condition A was 8 weeks.

Additional Measures

Neuropsychological testing was conducted within the framework of the current investigation. Each experimental subject was tested twice, once while on haloperidol and once while medication free. The order of testing was alternated between subjects to help to control for practice effects (see figure 1 - additional testing procedures). These results are included for discussion purposes in the current investigation. They are also useful in the interpretation of the data gathered for the clinical investigation of the withdrawal emergent syndrome.

iv) Inter-rater reliability checks

The procedures used to collect the data for this investigation required a certain level of cooperation and communication between subjects, parents, and the experimenter. This collaborative effort posed some threat to inter-observer independence and also provided an avenue for the introduction of experimenter bias. An additional problem was that no one involved in the data collection process was blind to the experimental procedures or conditions. It was thought that this knowledge might influence the data collection process in unpredictable ways and contribute to data contamination. Inter-rater reliability checks were necessary to address these difficulties in the current study.

A number of reliability checks were included in the present design. First, subjects were required to provide information regarding their symptoms through the experimental questionnaires. Parents were asked to assist in this process. At the end of each month of data collection, parents completed the CBCL on an independent basis. This provided some inter-rater reliability checks between parent and child. The actual 'independence' however, of these measures is suspect due to the weekly data collection process which required a cooperative effort between parent and child. A second measure was therefore necessary to check the reliability of the parent collected data. To do this, the experimenter conducted monthly interviews and observation sessions. As part of these in-home visits a comprehensive set of questionnaires including the SCL-90, CBCL, TSGS, and YSR were completed. This information provided inter-rater reliability data between the parent and experimenter.

A third reliability check was also required. The subjects, parents, and experimenter were not blind to the experimental conditions or data collection procedures. This could have influenced the data collection process. Ratings from a blind and independent third party were needed to establish inter-rater reliability in the current study. In order to do this it was necessary to video tape segments of the monthly visits to be used as a sample of the subject's behavior during a given experimental condition. The segment of the monthly visit that was recorded was that which the experimenter used to complete the TSGS and SCL-90-R. These recordings were viewed by two experimentally blind and independent third parties who rated the behaviors using the TSGS. This provided reliability data among the independent raters, the experimenter, and the parent. This reliability check was completed once for each subject. The recordings were conducted randomly throughout the experimental conditions and efforts were made to complete this aspect of data collection as unobtrusively as possible. To help to control for "novelty" effects of video taping procedures, a number of recordings of each subject were conducted. The first video tape recording was not used for reliability check purposes for any subject. The third party ratings were completed after all experimental data had been gathered. This precluded the possibility that the third party could deduce the experimental condition of the subject through temporal proximity of the rating.

v) Internal validity checks

Although there are no specific research findings which indicate that a summer vacation is likely to have an effect on symptoms of the withdrawal

emergent syndrome, this possibility certainly exists. A confound to the current study is that summer vacation from school is concurrent with medication cessation for all experimental subjects. Resumption of medication use coincides with a return to school in September. This confound posed a threat to the internal validity of the study and measures were required which addressed this issue.

Experimental data were gathered on two control subjects who were matched for sex, age, and level of medication use to the experimental subjects. These patients did not take a drug holiday during the summer months. Their medication levels remained constant throughout the six month duration of the experiment and they also met the inclusion criteria for the study as specified on the experimental consent form (Appendix A). In all ways, these subjects were treated in a manner identical to those who took a drug holiday. All dependent measures, data collection procedures, and in home interviewers and observations were conducted. Video taped sessions and other inter-rater reliability check data was also gathered.

Although the small number of subjects in the study precluded the utilization of statistical techniques for between group comparisons, useful information was obtained through a visual analysis of this additional data. Symptoms were expected to emerge among those patients who underwent a withdrawal from haloperidol but not among those who remained on medication. Some confidence could then be placed in attributing these symptoms to the effects of medication withdrawal. Some symptoms, however, may have emerged among all subjects over the course of the experiment regardless of medication use. These symptoms would not necessarily be attributable to summer vacation, but they will not be identified as part of the withdrawal

emergent syndrome. It was important to note the differences and consistencies between subjects who remained on medications and those who took a drug holiday. In this way, the confound of summer vacation was at least partially addressed by the measures taken in the current study. As in any clinical research, efforts were made to address identified confounds and make results attributable to a certain causal agent. In the case of the withdrawal emergent syndrome, the more subtle symptoms had not yet been identified. Any additional information that could be gathered for the purpose of clarification was gathered in the context of the research design.

The control subjects helped to address concerns regarding internal validity. Although the numbers were very small due to the overall prevalence of the disorder and the inclusion criteria for the study, useful information was gathered through these additional measures. These control subjects were used to reduce the possibility of wrongly attributing symptoms to the withdrawal emergent syndrome. They were also useful in assisting with the identification of small but consistent differences between those who withdrew from medication and those who did not in areas not specifically being presently investigated. Used in this way, these additional measures were useful in the clinical exploration of the withdrawal emergent syndrome.

vi) Comparisons, analysis, and interpretations

The main area of comparison for the current study is the clinical investigation of the withdrawal emergent syndrome. Symptoms of TS and the withdrawal emergent syndrome were extensively monitored on a weekly basis

over a 6 month period. During this time patients were on medication, medication free, and back on medication. Results of the weekly data collection were compiled and displayed graphically. Comparisons were made between the three experimental conditions A-B-A through a visual analysis of the data.

Martin and Pear (1978) have suggested a number of scientific considerations that should be kept in mind when conducting a visual data inspection. It is necessary to use these in order to judge whether or not a significant effect has occurred. Specifically, they assert that one has greater confidence that an effect has occurred "the greater number of times that it is replicated; the fewer the overlapping points between baseline and treatment phases; the sooner the effect is observed following the introduction of the treatment; the larger the effect in comparison to baseline; the more precisely the treatment procedures and response measures are specified; and the more consistent the findings with existing data and accepted behavioural theory" (p. 315). In the present study data analysis focussed on the magnitude and duration of changes in symptoms, the direction of change, and the association between symptom change and medication withdrawal and resumption. Comparisons were also made between experimental and control subjects to examine symptom changes that may be associated with summer holidays as opposed to medication withdrawal.

It was expected that withdrawal symptoms as measured by the SCL-90, CBCL, and ARR would emerge during Condition B in the present study. Symptoms were expected to emerge within a few days of medication cessation and to dissipate over the duration of Condition B. All withdrawal emergent syndrome symptoms were expected to disappear with the resumption of medication intake (Condition A - return to baseline).

Adverse reactions to haloperidol were thought to be detected by the instruments used in the present study. Reactions to medication that were present in Condition A (baseline) and Condition A (return to baseline) but disappeared during Condition B were thought to be attributable to medication with haloperidol. These reactions were difficult to parcel out from the effects of the summer vacation which occurred in concert with the experimental conditions. The control subjects were critical regarding this matter.

Neuropsychological testing results are included as additional data for discussion purposes in the present study. These results are useful in the interpretation of the clinical data gathered for the investigation of the withdrawal emergent syndrome.

VII. RESULTS

1) TS Symptomatology

The TS Global Scale (TSGS) was used to monitor TS symptoms for all subjects throughout the study. Differences emerged between "experimental" subjects (1 to 4) and "control" subjects (5 and 6). These differences are generally seen as being attributable to the change in medication intake over the six month period. Individual variability in TS symptoms is quite high and it is very important to note that the total number of subjects in the present study was quite small. Therefore the generalizability of these results to the overall population of TS patients is limited. In addition, it should be noted that experimental subject #2 in the present study did not return to medication use in phase 3 of the experiment. This subject found that his symptoms were no worse when not medicated and therfore elected not to return to medication use. The experimental data for this subject were however, collected throughout the entire study. The fact that subject #2 did not return to medication use in phase 3 of the study was kept in mind in the interpretation of the data.

In general, results indicate that withdrawal from medication is likely to result in an overall increase in TS symptoms. This increase can be severe but does not appear to last beyond the midpoint of phase 2 of the study (i.e. 4 weeks) before returning to baseline or sub-baseline levels. Specifically, simple motor tics were observed to increase dramatically with

haloperidol cessation. Less consistent results were recorded with measures of complex motor and simple phonic tics. Complex phonic tics, which often resemble and may be genetically related to compulsions, were actually observed to decrease with the withdrawal of haloperidol. The present results indicate that haloperidol withdrawal may result in a sharp increase in some, but not necessarily all, aspects of TS and that certain symptoms may actually decrease with medication cessation.

i) Motor and phonic tics

The TSGS global score is reported to be an excellent indicator of overall TS symptom severity and life adjustment. The global score is, however, a summed total of tic scores and social functioning scores. Therefore large differences in tic symptomatology may be somewhat obscurred by low scores on other scales which are also included in the TSGS global score. Reference to the individual subscales is necessary to detect the nature of changes recorded by the global score. In the present study, 3 of the 4 experimental subjects reported an increase in TS symptoms which was concurrent with the withdrawal of medications (see Figure 2). Both control subjects also reported increases in TSGS global scores during phase 2 of the study. The changes in the control subjects were not necessarily associated with the beginning of the phase, but do indicate that a slight increase in the TSGS global score may be associated with phase 2 of the study (i.e., summer holiday months) rather than being solely attributable to medication withdrawal. Experimental subjects tended to experience more variability in their symptoms during phase 2 than did the control subjects. This variability tended to be associated with the early stages of phase 2

FIGURE 2
TSGS: GLOBAL SCORES

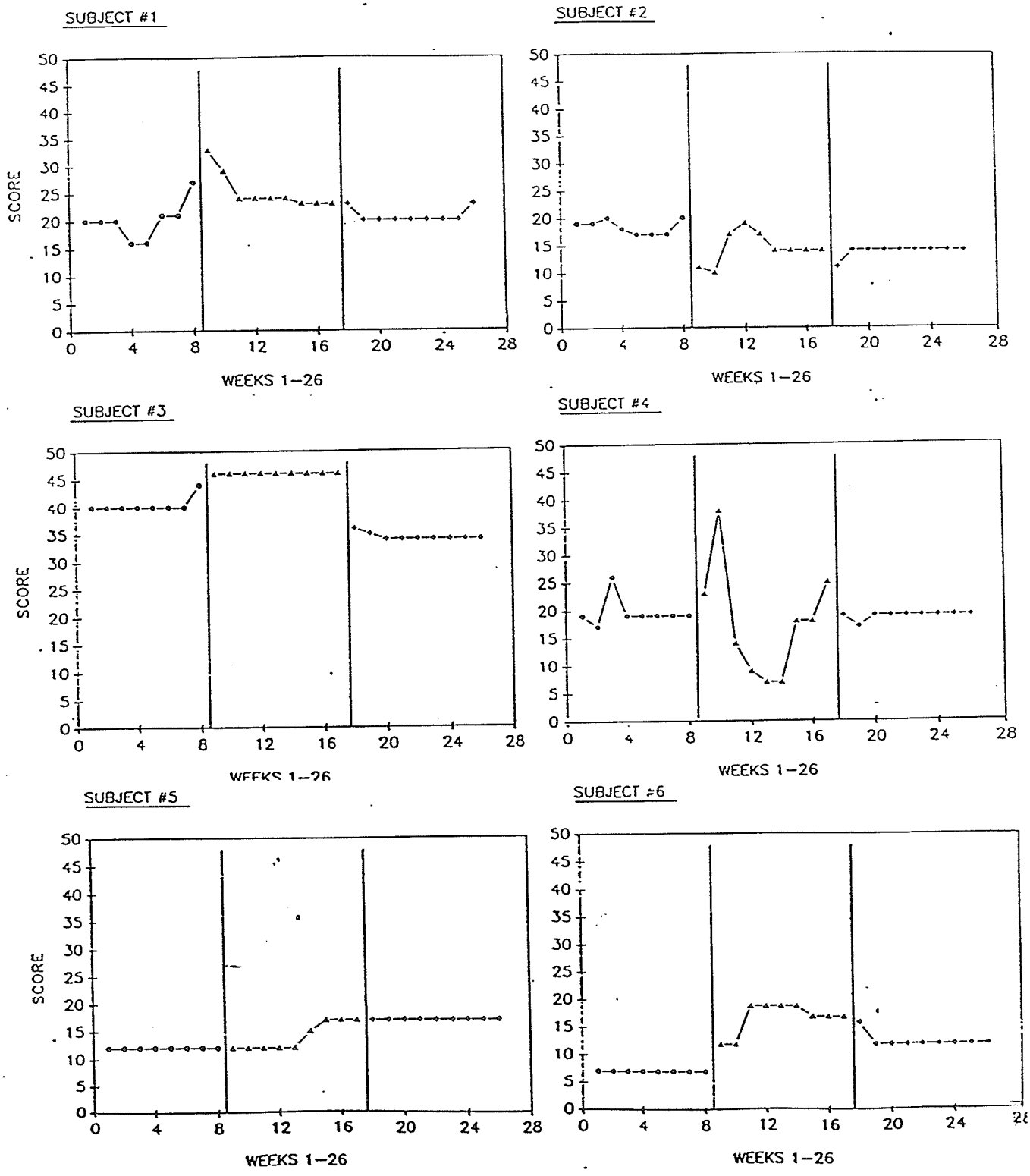
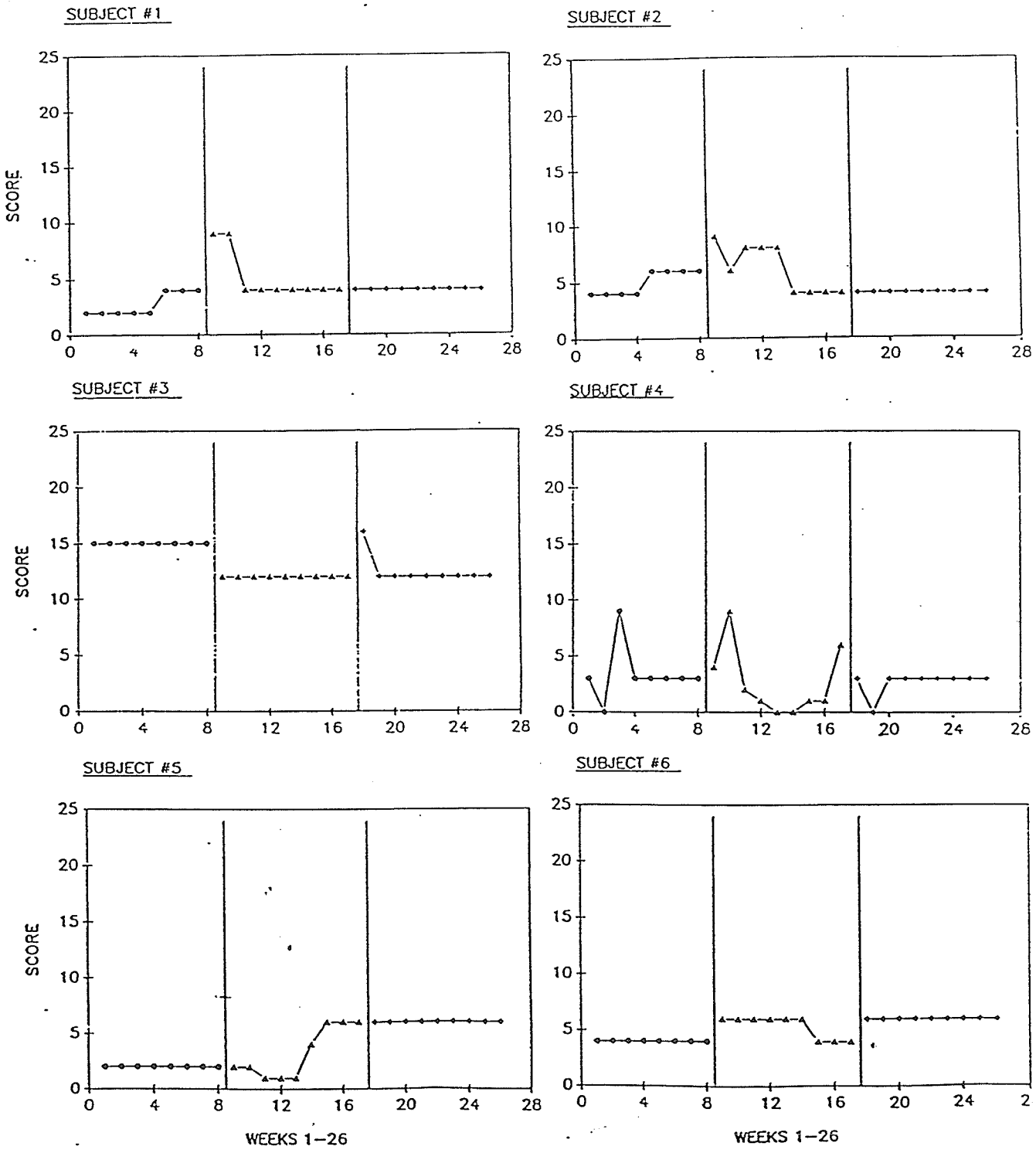


FIGURE 3
TSGS: SIMPLE MOTOR TICS



and symptoms appeared to stabilize toward the end of the medication free period near baseline levels 3 of the 4 experimental subjects.

Tic symptomatology was more closely monitored by the specific subscales of the TSGS. Subject 1 reported a sharp increase, and subjects 2 and 4 reported a slight increase in simple motor tics when haloperidol was withdrawn. One of the control subjects also reported a slight increase in simple motor tics at the beginning of phase 2. Although this increase was not as dramatic as that reported by subject 1, it suggests that an increase in simple motor tics is not necessarily associated strictly with medication cessation.

An consistent increase in the severity of complex motor tics was reported by 1 experimental subject (#3). A temporary increase was reported by experimental subject 4, and also by control subject 6. This is also true of the simple phonic tics. No experimental or control subjects reported an increase in complex phonic tics at the beginning of phase 2. In one experimental subject (#2), a temporary decrease in the frequency and severity of complex motor tics was found. This seems to be associated with the withdrawal of haloperidol.

A sharp increase in simple phonic tics was reported with medication cessation by 2 of the 4 experimental subjects. The other 2 experimental subjects did not report this increase. Both control subjects also reported an increase in simple phonic tics during phase 2 of the study. For one of the control subjects the increase was reported at the beginning of phase 2 while the other did not report this increase until near the end of the phase (see figure 5). The magnitude of the increases reported in simple

FIGURE 4
TSGS: COMPLEX MOTOR TICS

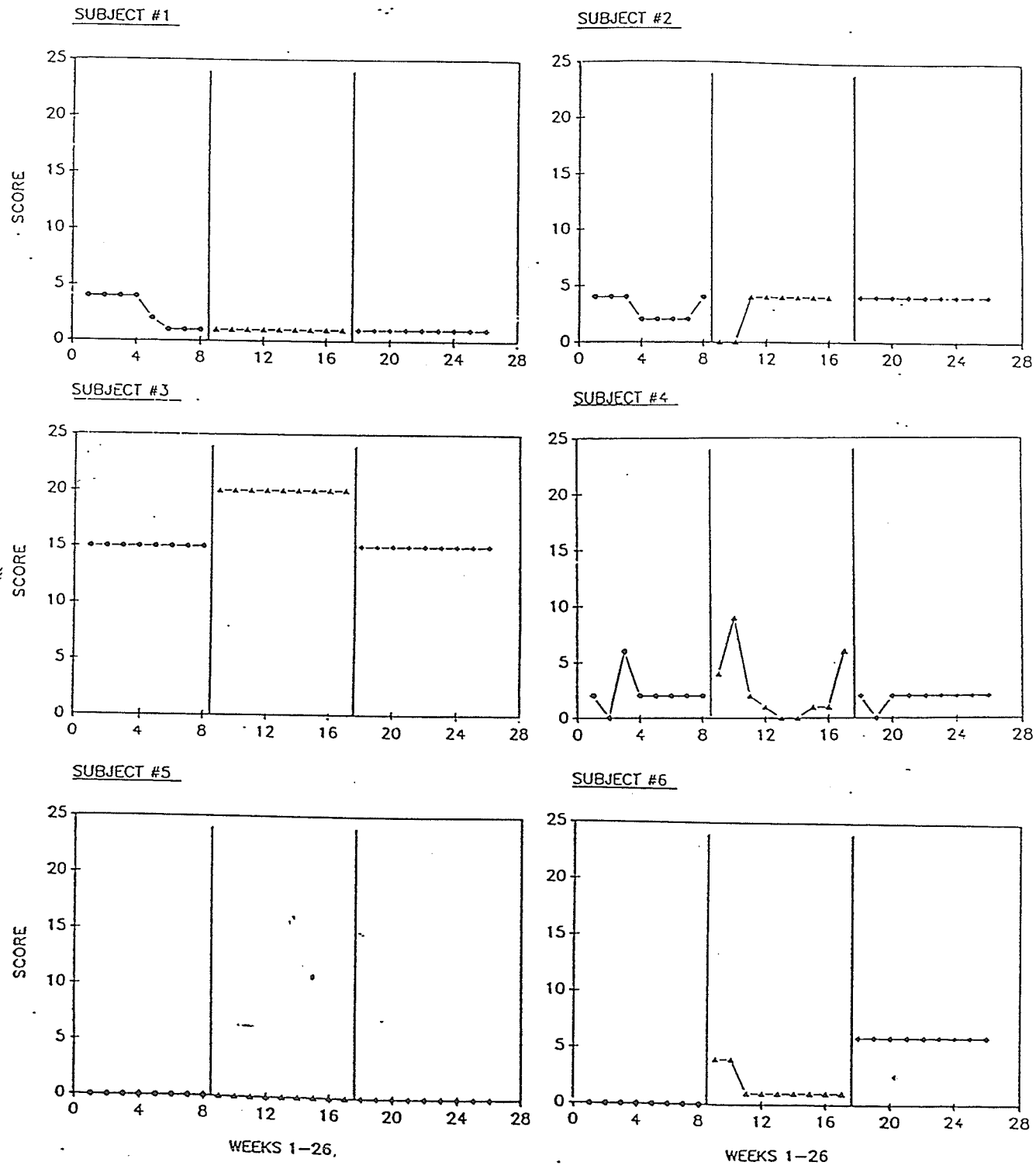


FIGURE 5
TSGS: SIMPLE PHONIC TICS

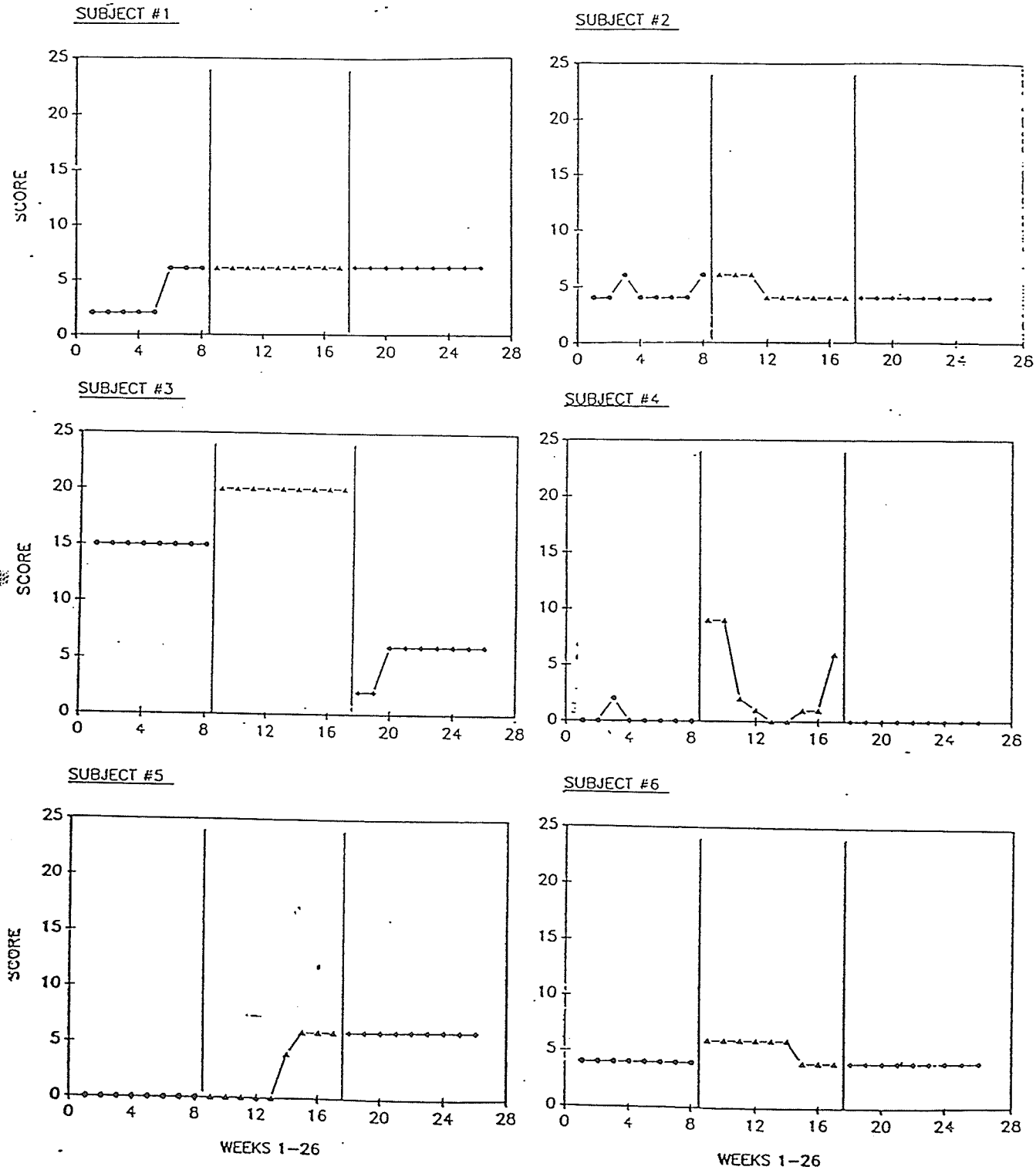
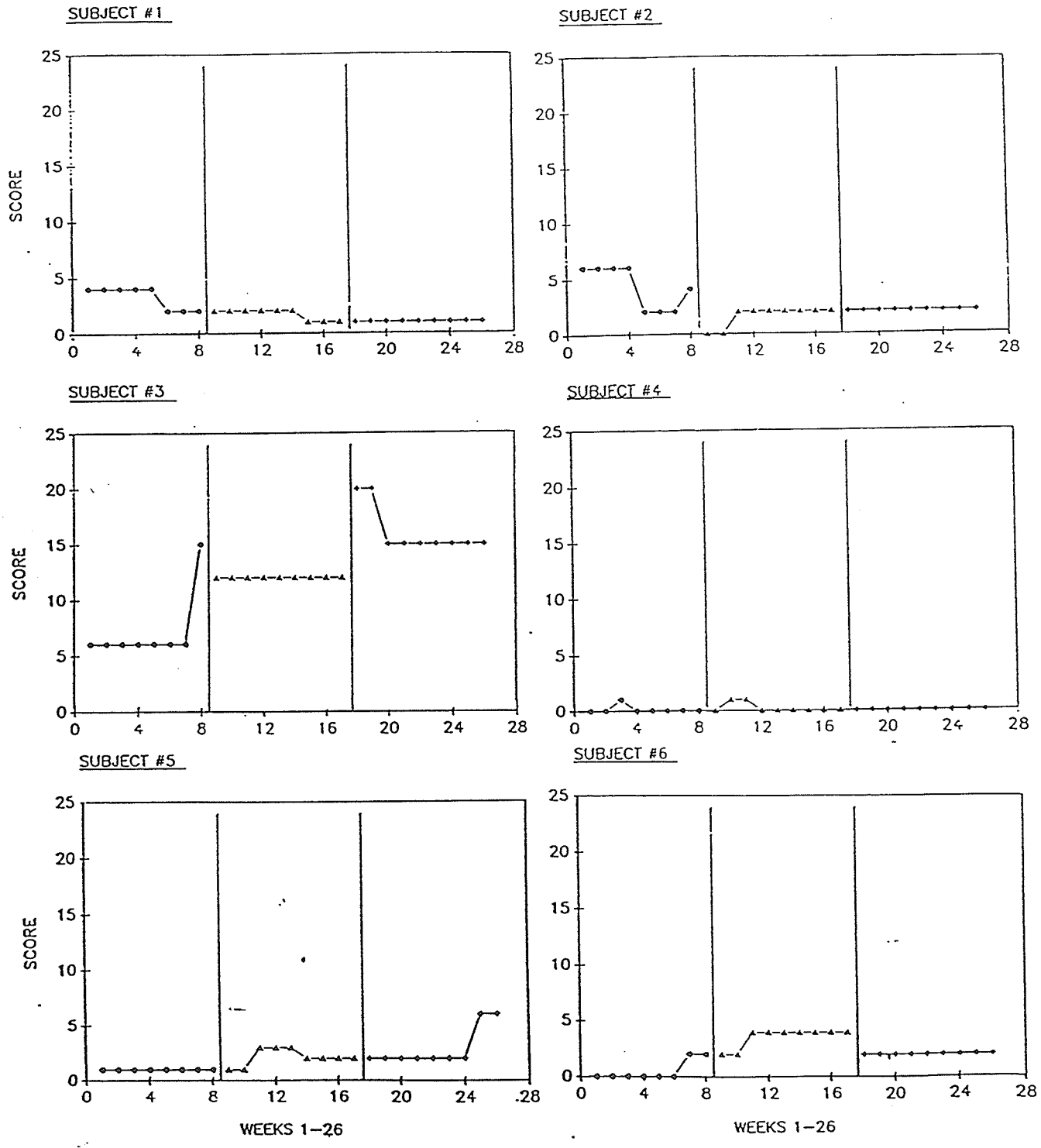


FIGURE 6
TSGS: COMPLEX PHONIC TICS



phonic tics is greater for the two experimental subjects that showed an effect than the control subjects, and both experimental subjects reported a sharp decrease in these symptoms with the resumption of medication use in phase 3. Simple phonic tics remained constant from phase 2 to phase 3 in the control subjects. This suggests that medication cessation is likely to result in an increase in simple phonic tics for some TS patients and that resumption of medication use controls this increase in symptoms.

Medication cessation did not appear to have the same effect on levels of complex phonic tics. Only 1 experimental subject (#3), reported a slight increase in complex phonic tics with medication cessation, two subjects reported no change, and 1 subject reported a temporary decrease concomitant with medication cessation. Both control subjects recorded an increase in complex phonic tics during phase 2 of the study. Interestingly, one experimental subject who had indicated that cessation of haloperidol was associated with a decrease in complex phonic tics reported an increase in symptoms concomitant with the resumption of medication use in phase 3 of the study. The relative lack of complaints by experimental subjects suggests that for some TS patients the use of haloperidol may possibly be associated with an increase in complex phonic tics (see figure 6).

ii) Social functioning

Overall results of the psychometric assessment of social functioning was somewhat surprising in that the severe behaviour problems and difficulties in socializing that were recorded elsewhere did not seem to be reflected to the same degree in the TSGS measures. There were, however, some reported difficulties and complaints in these areas.

Social functioning was evaluated by scale ratings of behaviour problems, motor restlessness, and school and learning problems. Two of the 4 experimental subjects reported a temporary increase in behaviour problems (#1 & #4). Subjects 2 and 3 reported no change (see figure 7). One control subject (#6), reported an increase in behaviour problems during phase 2 of the study, the other indicated that there was no change. Some changes were also reported in levels of motor restlessness. Experimental subject 2 and 4 show a decrease in phase 2 of the study. Control subject 6 shows a delayed increase and experimental subject 3 shows a decrease in phase 3 (see figure 8). The motor restlessness scale, however, has poor reliability ratings as compared to the other TSGS subscales and the current results are difficult to interpret. There were no consistent changes reported with school and learning problems by any of the subjects. The fact that they were not in school during phase 2 of the study likely affected these ratings (see figure 9).

FIGURE 7
TSGS: BEHAVIOUR PROBLEMS

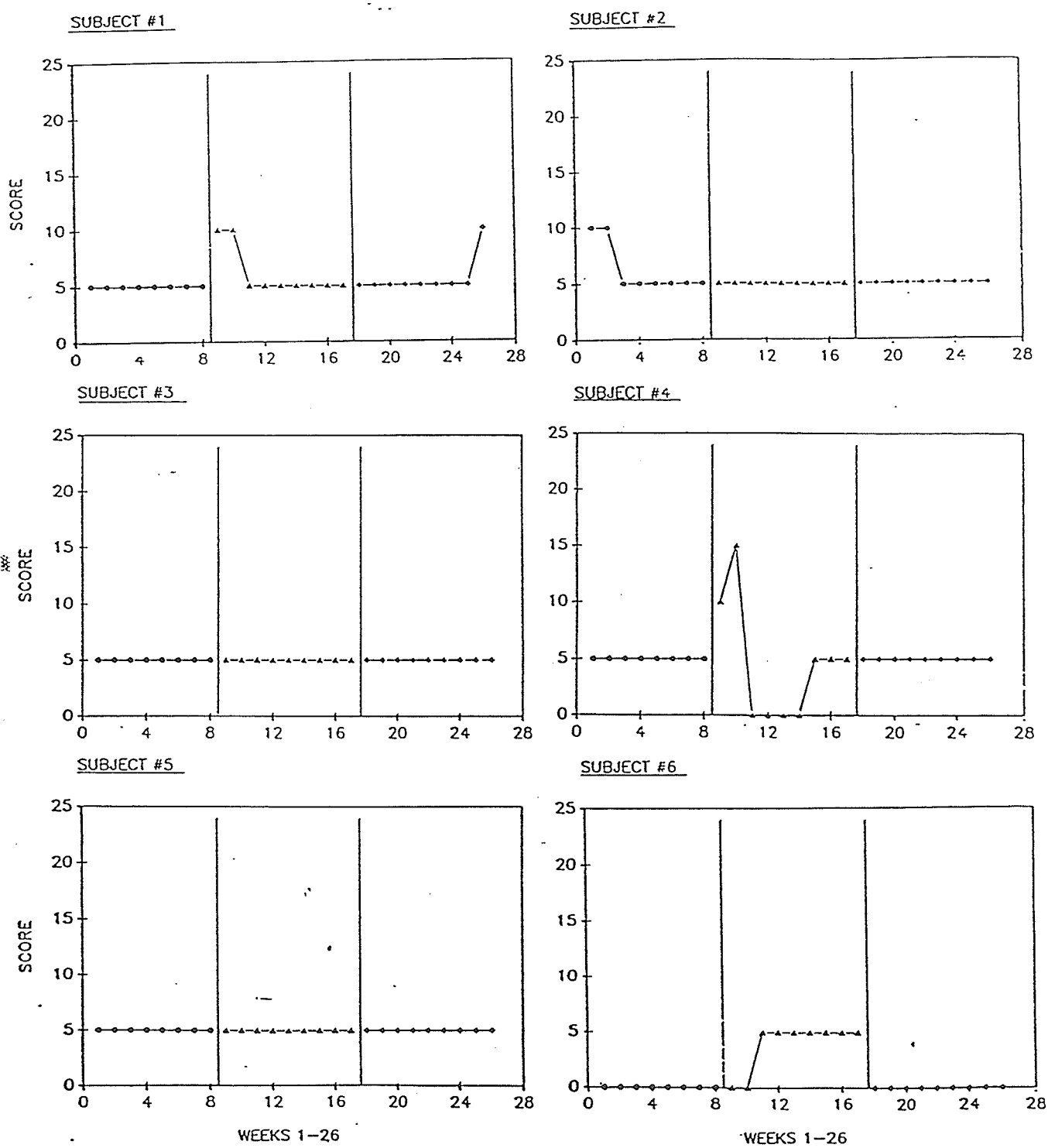


FIGURE 8
TSGS: MOTOR RESTLESSNESS

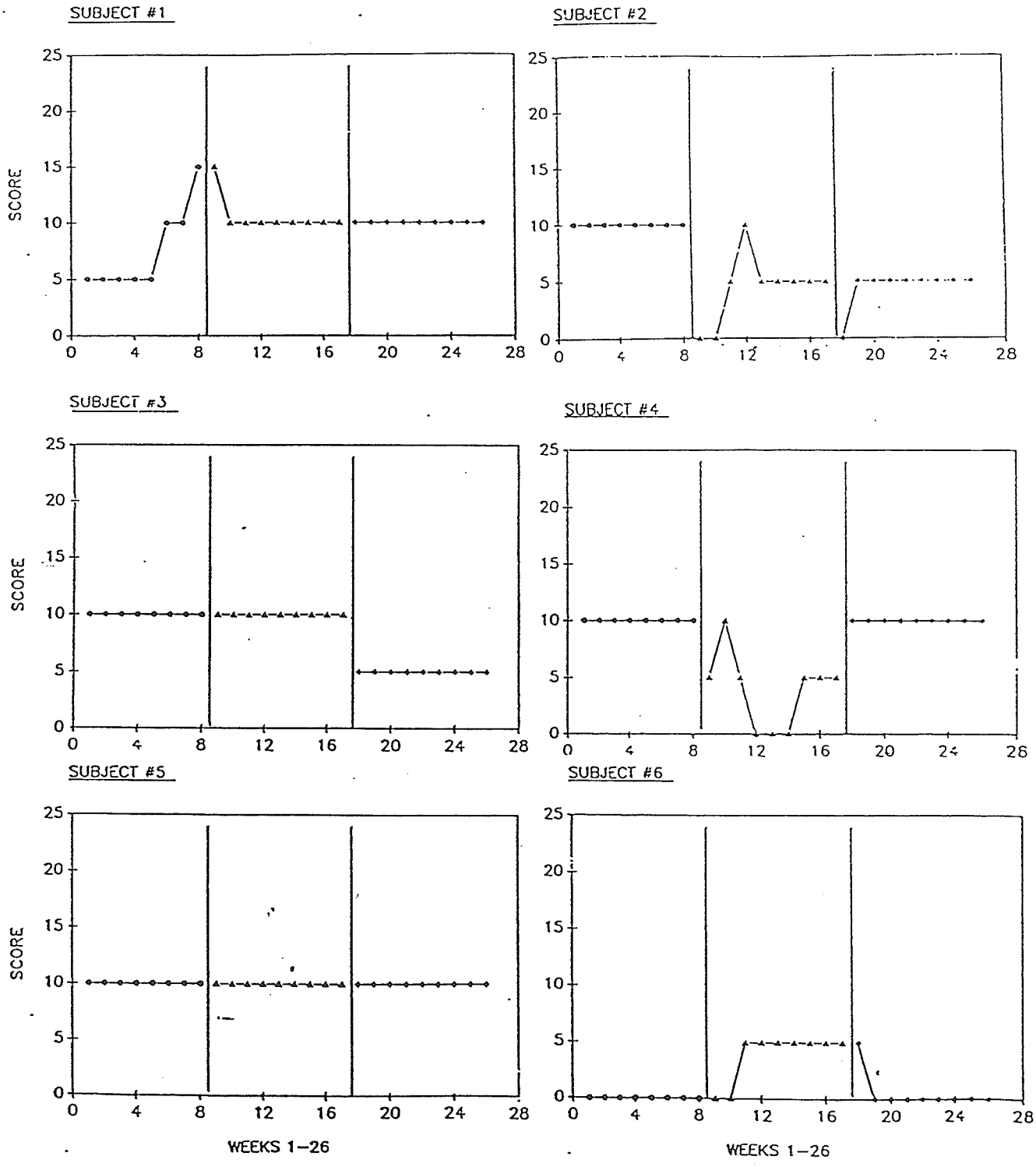


FIGURE 9
TSGS: SCHOOL AND LEARNING PROBLEMS

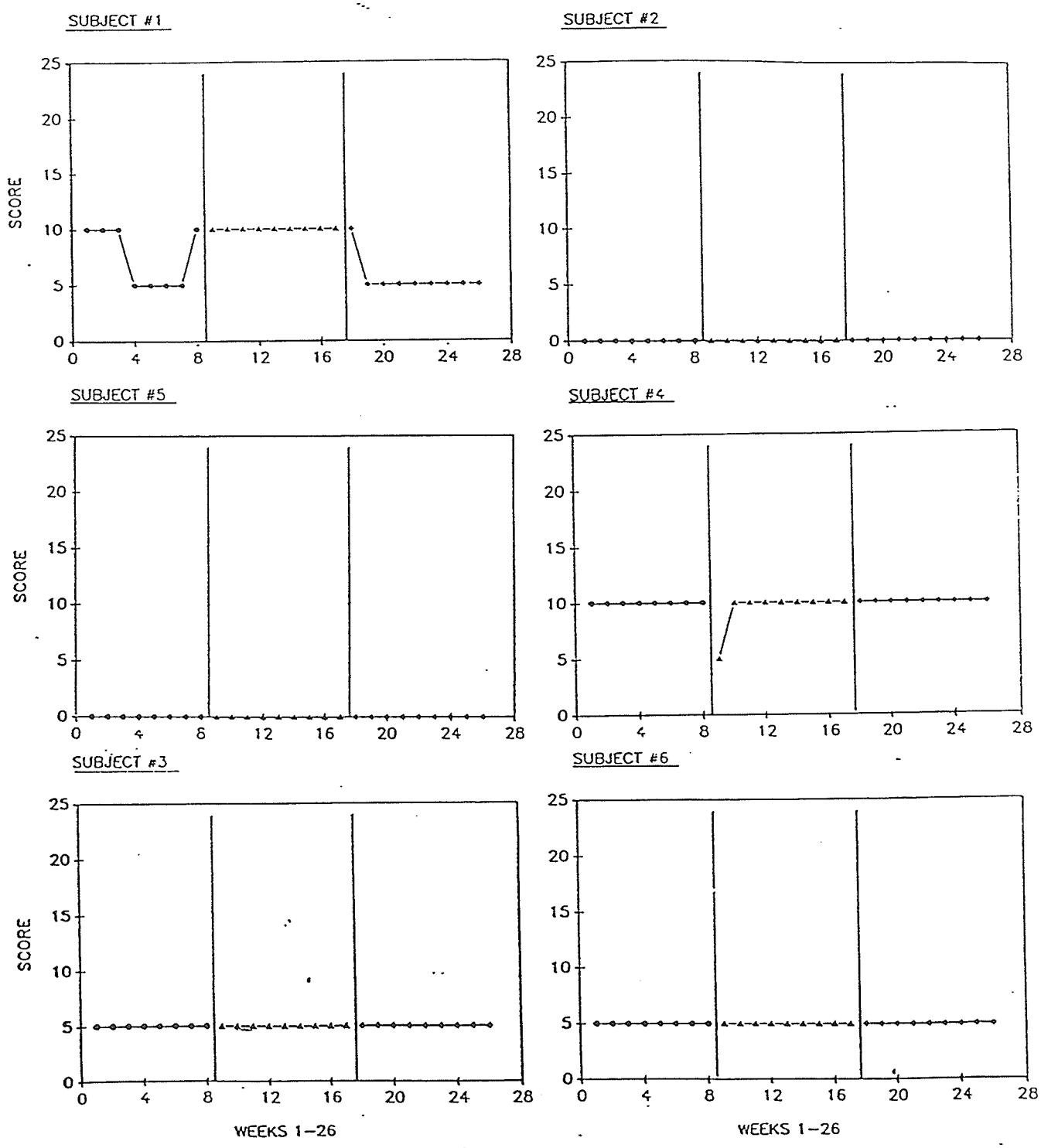


TABLE 1
TSGS: Summary of Visual Analysis

Subscale	Phase	Subject #1	Subject #2	Subject #3	Subject #4	Subject #5	Subject #6
Global Scores	1 - 2	temp.inc.	temp.dec.	cons.inc.	dram.temp. inc.	del.inc.	mod.inc.
	2 - 3	sl.dec.	temp.dec.	cons.dec.	ret'n.to BL	N/C	sl.dec.
Simple Motor	1 - 2	temp.inc.	temp.inc.	cons.dec.	temp.inc.	del.inc.	sl.temp.inc.
	2 - 3	N/C	N/C	temp.inc.; N/C	temp.dec.	N/C	sl.inc.
Complex Motor	1 - 2	N/C	temp.dec.	cons.inc.	temp.inc.	N/C	temp.inc.
	2 - 3	N/C	N/C	ret'n.toBL	ret'n.toBL	N/C	cons.inc.
Simple Phonic	1 - 2	N/C	N/C; del.dec.	cons.inc.	dram.temp. inc.	del.inc.	sl.cons.inc; ret'n.to BL
	2 - 3	N/C	N/C	dram.dec.	ret'n.to BL	N/C	N/C
Complex	1 - 2	N/C; sl. del.dec.	temp.dec.	cons.inc.	sl.temp.inc.	del.sl.inc.	del.sl.inc.
Phonic	2 - 3	N/C	N/C	dram.temp. inc.; over-all inc.level	N/C	N/C	ret'n.to BL
Behaviour	1 - 2	temp.inc.	N/C	N/C	dram.temp. inc.	N/C	del.inc.
Problems	2 - 3	N/C	N/C	N/C	N/C	N/C	ret'n.to BL
Motor	1 - 2	del.dec.; overall inc.	dram. temp. dec.	N/C	del.dec.	N/C	del.inc.
Restless-ness	2 - 3	N/C	N/C	dec.	ret'n.to BL	N/C	ret'n.to BL
School and	1 - 2	N/C	N/C	N/C	temp.dec.; N/C	N/C	N/C
Learning Problems	2 - 3	del.dec.	N/C	N/C	N/C	N/C	N/C

Key: increase = inc. temporary = temp. slight = sl.
decrease = dec. consistent = cons. moderate = mod.
No Change = N/C delayed = del. dramatic = dram.
return to baseline levels = ret'n. to BL

iii) Summary of TSGS results

It was expected that TS symptoms would be exacerbated by medication withdrawal, and that the TSGS scores would reflect this symptom increase. The results, however, are generally equivocal. Haloperidol cessation did not appear to cause a dramatic or sustained increase in TS symptoms, and some of the symptoms may actually decrease in some patients. In general experimental subjects reported a greater increase in TS symptomatology and more variability of symptoms during phase 2 of the study than did the control subjects. The greatest differences between experimental and control subjects were found in the tic symptomatology rather than social functioning domain. Specifically, experimental subjects reported greater difficulties with simple motor tics, complex motor tics, and simple phonic tics than did the control subjects. These differences are thought to be attributable to the withdrawal of the haloperidol. Results also suggest that levels of complex phonic tics may be decreased with medication cessation. It is interesting to note, however, that all TS symptomatology tended to stabilize toward the latter half of the no medication phase. One experimental subject, (#2), did not return to haloperidol in phase 3 of the study because symptoms were stable and at a manageable level with no medication.

2) Withdrawal Symptoms

Physical symptoms of withdrawal were measured on a weekly basis by the SCL-90-R and on monthly basis by the CBCL. A less structured monitoring and recording of daily events was carried out with the PQ and ARR. In general, the structured weekly and monthly measures did not support the

hypothesized increase in physical discomforts and somatic complaints. There were, however, some indications that these symptoms were more variable for the experimental subjects than for the control subjects and that the experimental subjects were less depressed, less hyperactive, and experienced a decrease in obsessive-compulsive behaviour during the medication free period. In addition, the iess formal daily observations recorded by the PQ and ARR indicated that experimental subjects experienced a number of physical symptoms and complaints that were not detected and recorded with the weekly and monthly measures. These results suggest that there are a number of subtle withdrawal symptoms that are not included in the current definition of the withdrawal emergent syndrome.

i) Weekly measures: The SCL-90-R

Results from the SCL-90-R do not indicate consistent or clear differences between experimental and control subjects. Although a much greater degree of variability was reported by experimental subjects on virtually all of the SCL-90-R scales, no consistent directions or tendencies were observed and no clear differences between experimental and control subjects were observed.

Experimental subject #4 showed a dramatic decrease in somatic complaints with the cessation of haloperidol (see Figure 10). Subjects 2 and 3 showed smaller decreases which may have been the continuation of Phase 1 trends. The other experimental subject reported no change. One control subject, however, also reported a decrease in somatic complaints at the onset of phase 2 while the other reported no change. Somatic complaints, therefore, decreased or remained the same for all subjects during phase 2 of the study and therefore cannot be attributed solely to medication withdrawal.

Clear decreases in obsessive-compulsive behaviours were reported for 3 of the 4 experimental subjects (#2,3,& 4). Subject 1 reported no change. One of the control subjects (#5), reported a slight temporary decrease while no change was indicated by control subject 6 (see figure 11). Obsessive-compulsive symptoms are often part of TS symptomatology and a decrease would not be expected with the withdrawal of haloperidol. The reported decrease in obsessive-compulsive symptoms is thus thought to be associated with medication withdrawal rather than the summer holiday months. This interpretation is supported by phase 3 data which indicates that an increase in obsessive-compulsive behaviours occurred in 2 of the 4 experimental subjects with the end of summer vacation and the return to medication use.

Ratings of interpersonal sensitivity, depression, anxiety, and hostility were not associated with any clear differences between experimental and control subjects (see figures 12, 13, 14, & 15). Two of the 4 experimental subjects, however, indicated some changes in phobic responses during medication cessation while all other subjects indicated no change throughout the study. One subject (#2), reported a dramatic temporary increase in phobic responses while experimental subject 4 recorded a dramatic decrease (see figure 16). While these reactions are likely in response to medication withdrawal, as they both disappeared with medication resumption, they are difficult to generalize from and are regarded as idiosyncratic to these individuals. Some general differences were also evident in the paranoia and psychoticism scales. Experimental subjects reported decreases or no change in levels of paranoia wheras the controls reported increases or no change (see figure 17). Similarly, experimental

FIGURE 10
SCL-90-R: SOMATIZATION

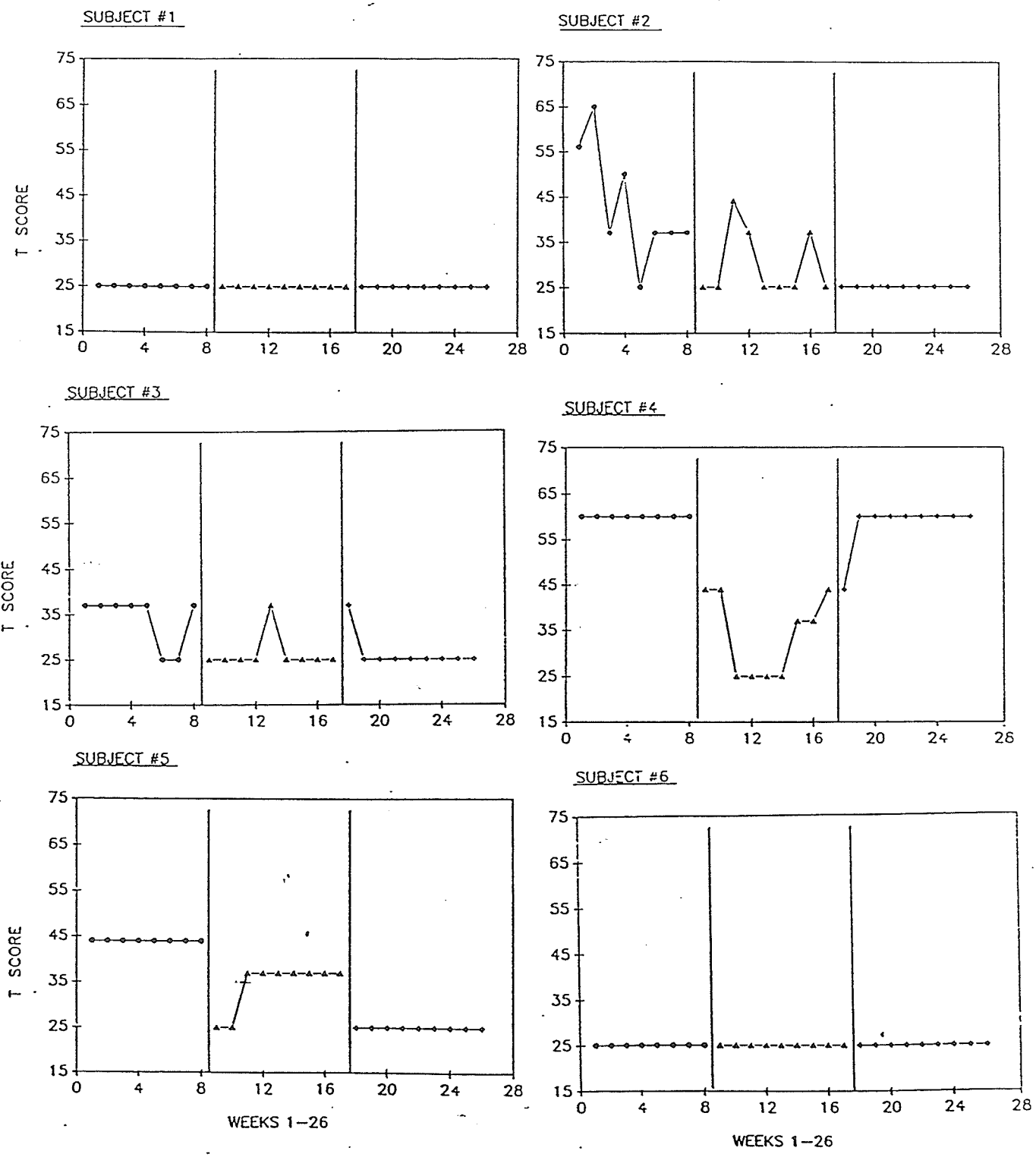
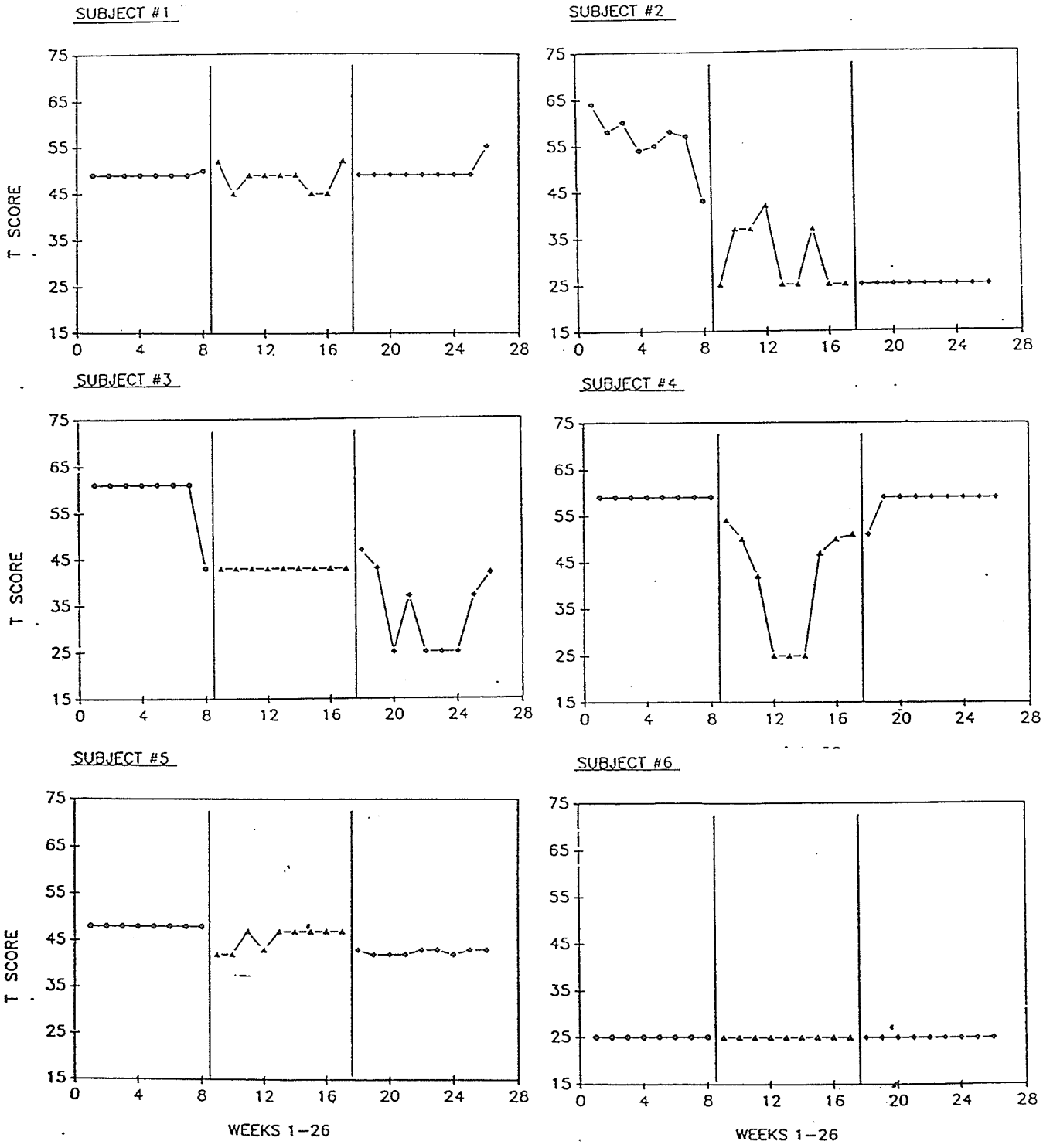


FIGURE 11
SCL-90-R: OBSESSIVE COMPULSIVE



subjects showed either a decrease (#4) or no change in levls of psychoticism. The control subjects showed no change (see figure 18). These reactions are also difficult to interpret and seem to be most likely attributable to individual differences between subjects.

The global indices of the SCL-90-R which include a global severity index and a positive symptom distress index did not indicate any consistent symptom differences between experimental and control subjects. More variability was reported by experimental subjects than control and may reflect general lack of symptom stability for these subjects during medication withdrawal. The exact nature of this instability, however, would be difficult to predict from the current study (see figures 19 and 20).

FIGURE 12
SCL-90-R: INTERPERSONAL SENSITIVITY

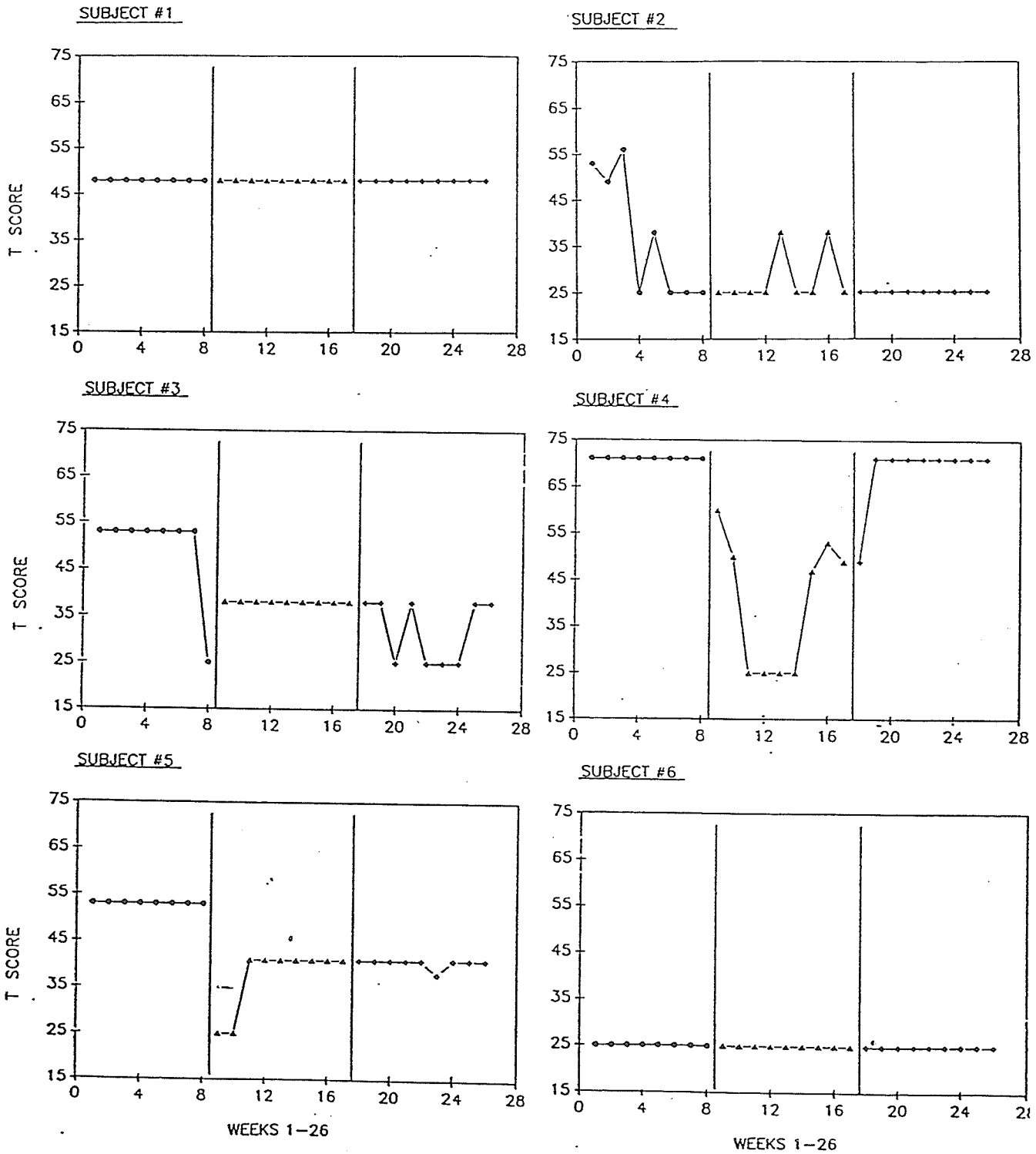


FIGURE 13
SCL-90-R: DEPRESSION

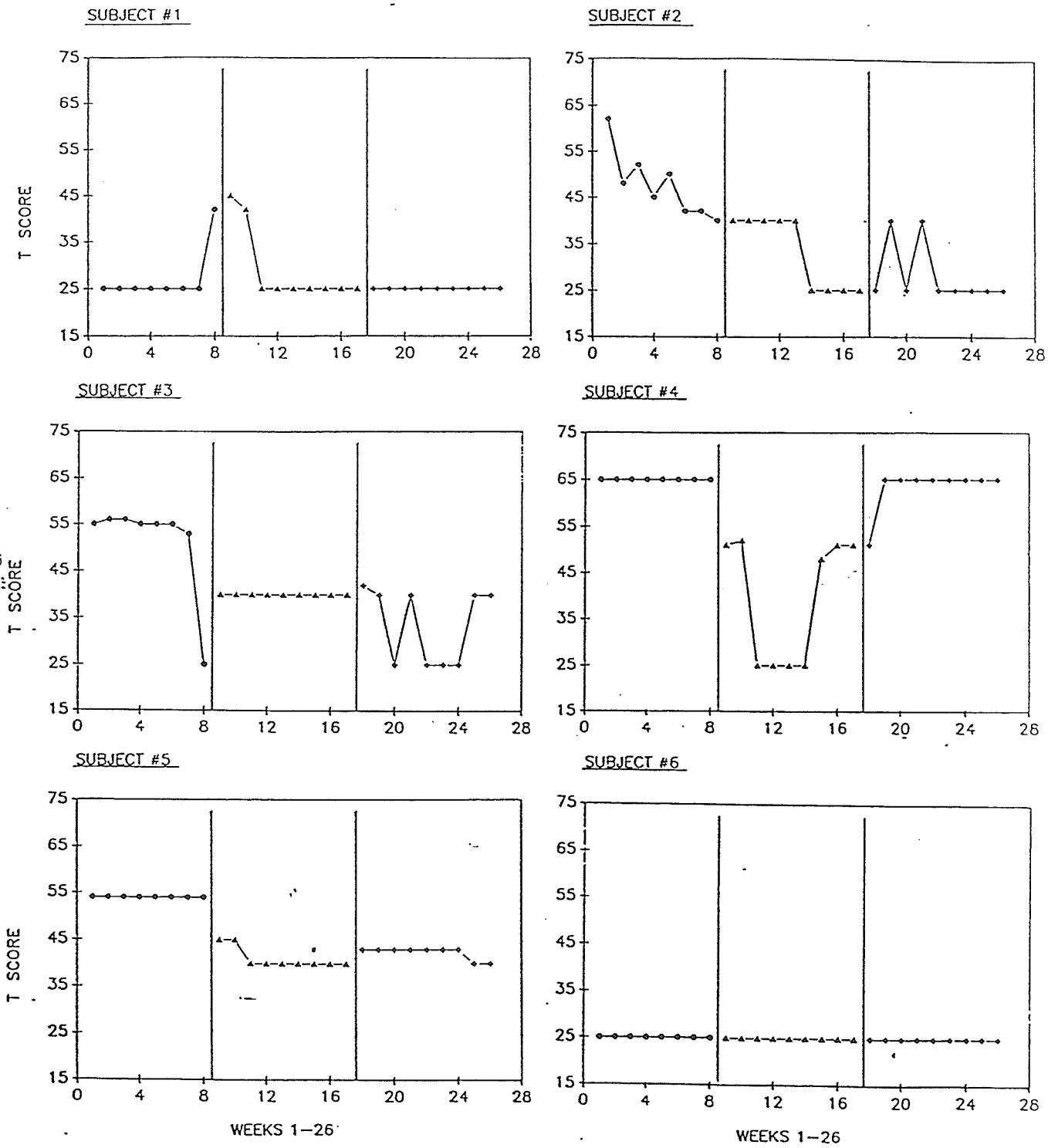


FIGURE 14
SCL-90-R: ANXIETY

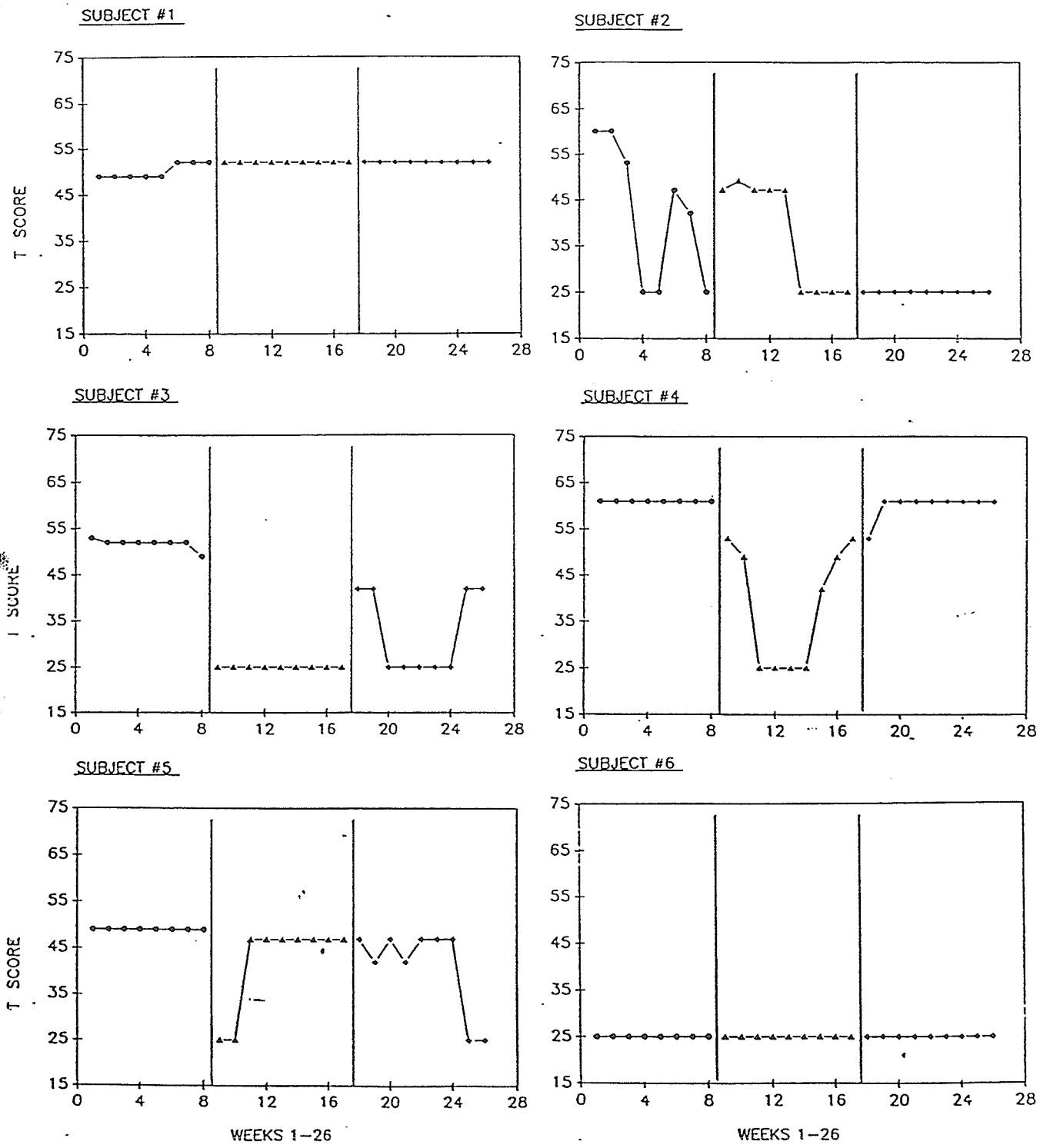


FIGURE 15
SCL-90-R: HOSTILITY

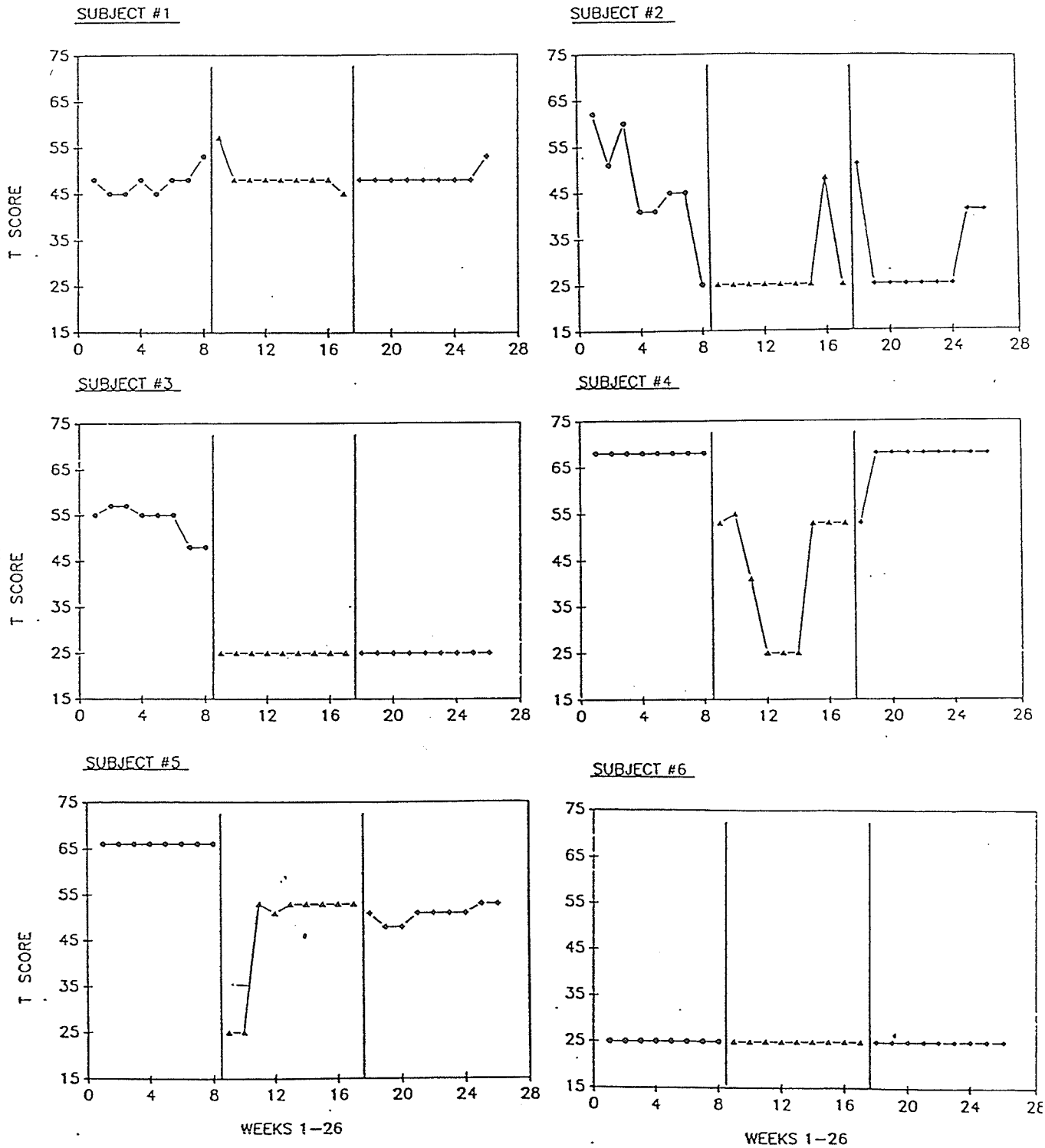


FIGURE 16
SCL-90-R: PHOBIC

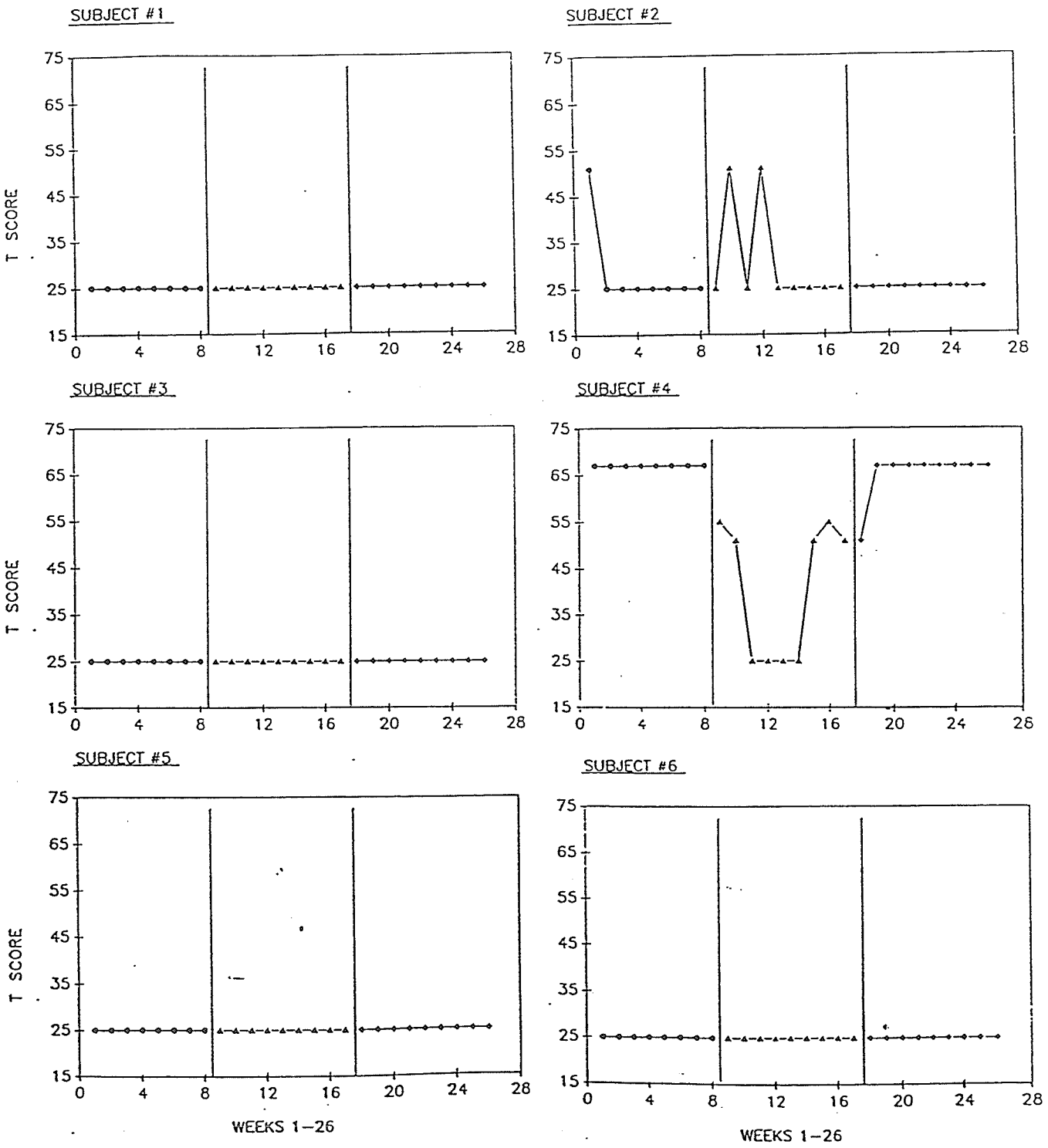


FIGURE 17
SCL-90-R: PARANOIA

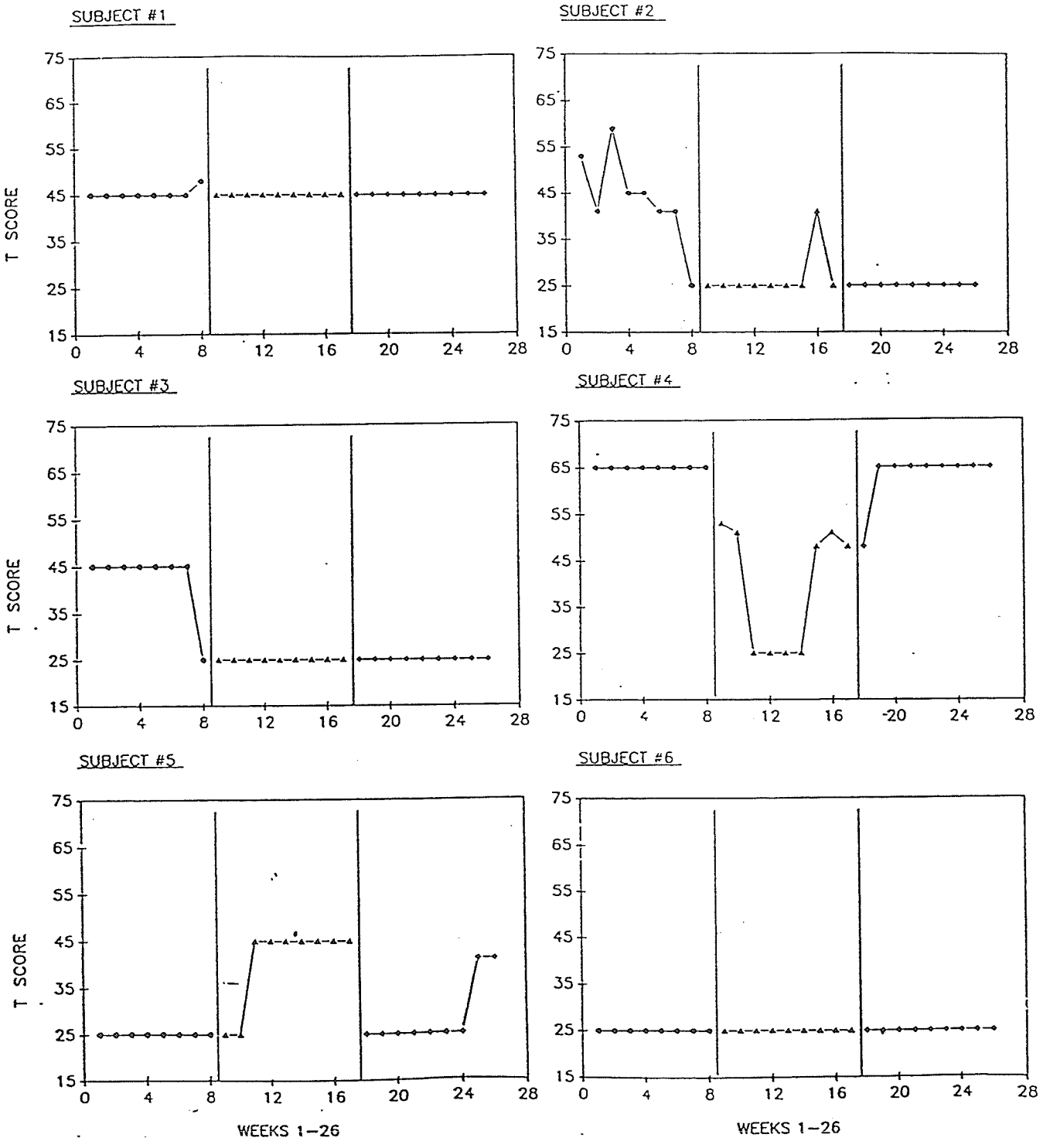


FIGURE 18
SCL-90-R: PSYCHOTICISM

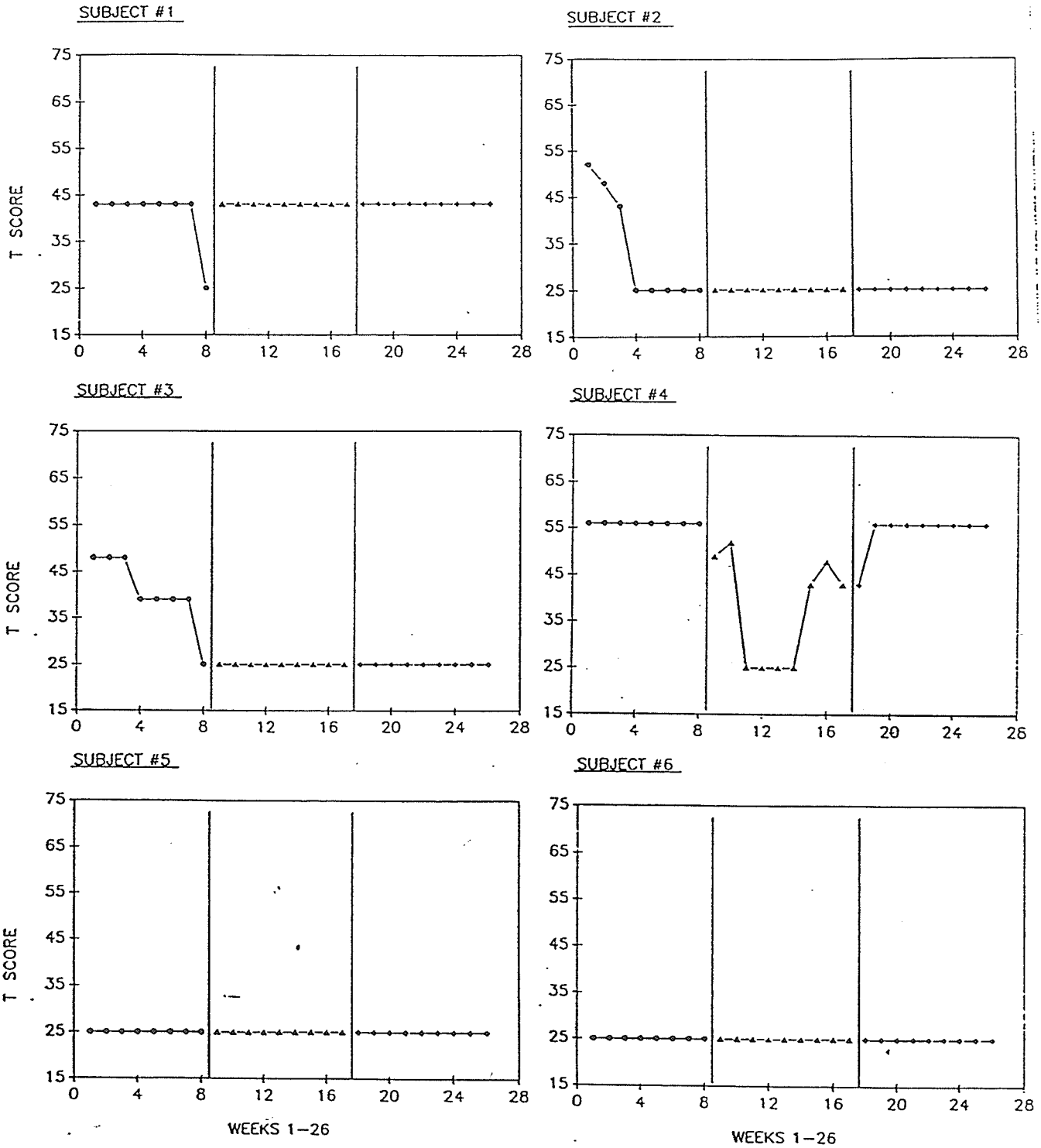


FIGURE 19
SCL-90-R: GLOBAL SEVERITY INDEX (GSI)

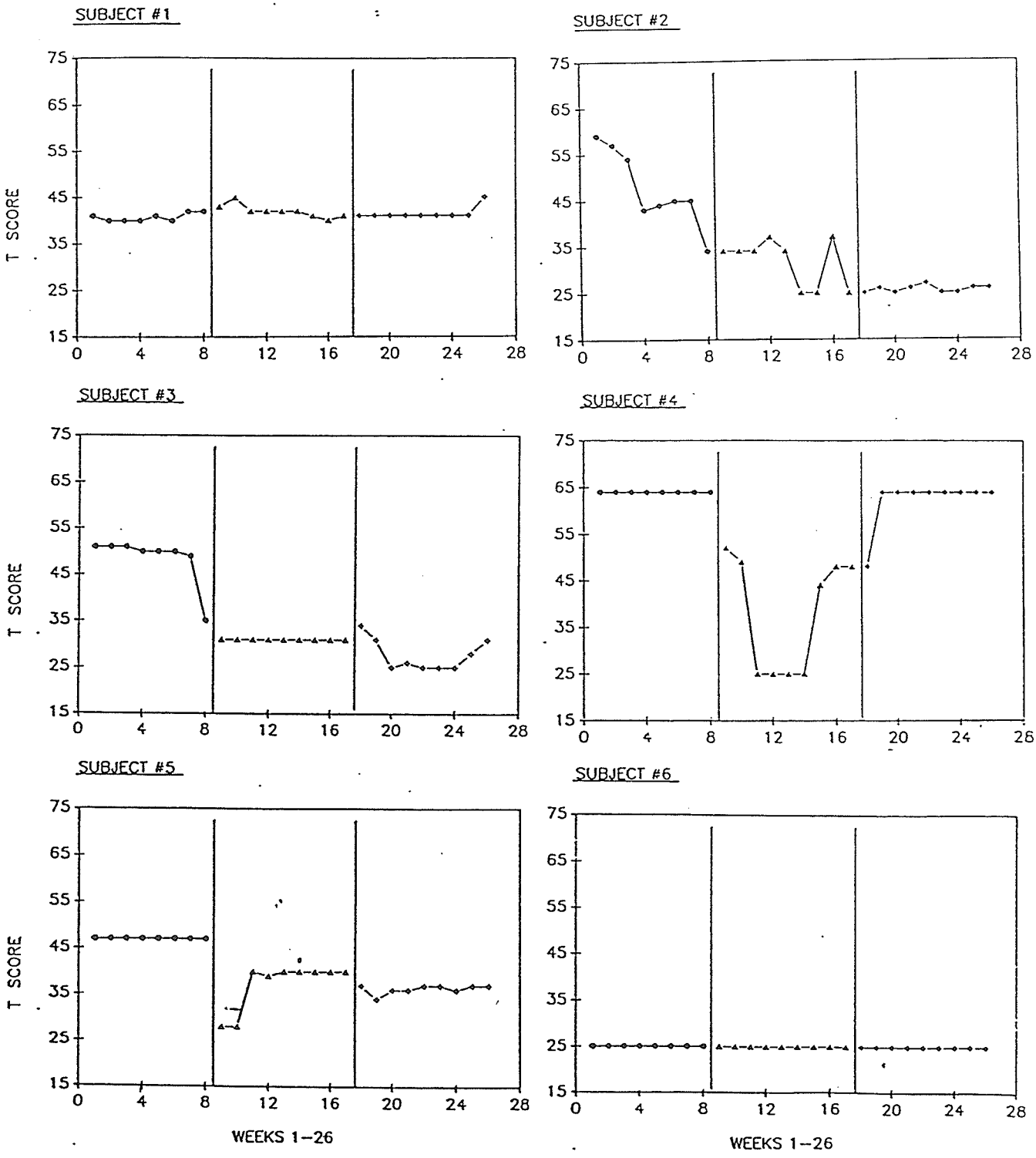


FIGURE 20
SCL-90-R: POSITIVE SYMPTOM DISTRESS INDEX (PSDI)

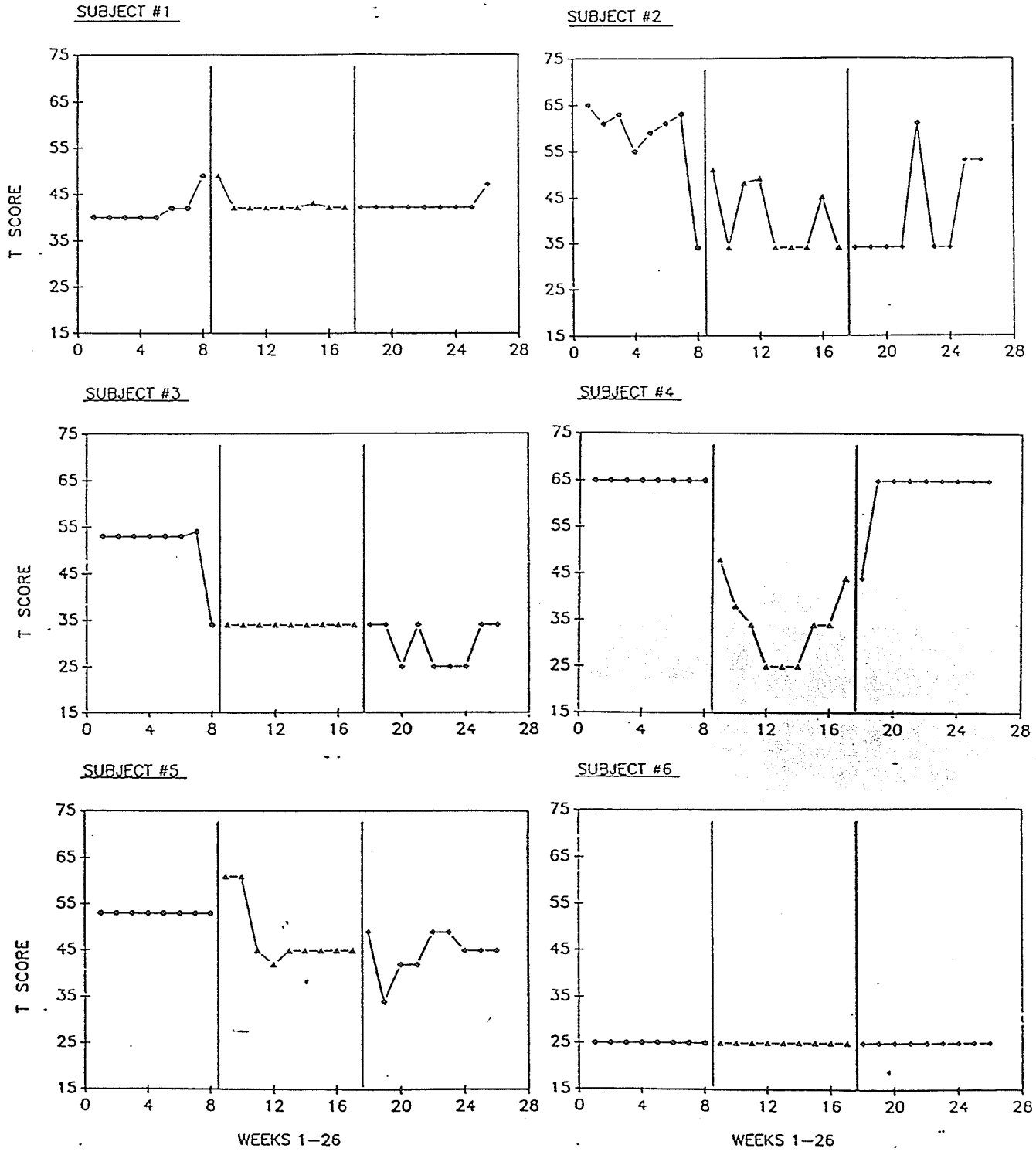


TABLE 2
SCL-90-R: Summary of Visual Analysis

Subscale	Phase	Subject #1	Subject #2	Subject #3	Subject #4	Subject #5	Subject #6
Somatization	1 - 2	N/C	var.dec.	dec.	dram.dec.	dec.	N/C
	2 - 3	N/C	N/C	temp.inc;N/C	ret'n.to BL	dec.	N/C
Obsessive-	1 - 2	N/C	dec.	cons.dec.	dram.dec.	sl.temp.dec.	N/C
Compulsive	2 - 3	N/C	N/C	var.dec.	ret'n.to BL	sl.dec.	N/C
Inter-personal	1 - 2	N/C	del.temp.inc.	cons.dec.	dram.dec.	dram. temp.dec.	N/C
Sensitivity	2-3	N/C	N/C	N/C;var.dec.	retn.toBL	N/C	N/C
Depression	1 - 2	temp.inc.; N/C	del.dec.	overall cons.dec.	dram.dec.	dec.	N/C
	2 - 3	N/C	temp.inc.	del.var.dec.	ret'n.to BL	sl.inc.	N/C
Anxiety	1 - 2	N/C	temp.inc.; dec.	cons.dec.	dram.dec.	dram. temp.dec.	N/C
	2 - 3	N/C	N/C	temp.inc.; N/C	ret'n.toBL	del.dec.	N/C
Hostility	1 - 2	temp.inc.; N/C	overall dec.	cons.dec.	dram.dec.	dram.temp. dec.	N/C
	2 - 3	N/C	temp.inc.; N/C	N/C	ret'n.toBL	N/C	N/C
Phobic	1 - 2	N/C	temp.inc.	N/C	dram.temp. dec.	N/C	N/C
	2 - 3	N/C	N/C	N/C	ret'n.to BL	N/C	N/C
Paranoia	1 - 2	N/C	dec.	cons.dec.	dram.temp. dec.	del.inc.	N/C
	2 - 3	N/C	N/C	N/C	ret'n.to BL	ret'n.to BL	N/C
Psycho-ticism	1 - 2	N/C	N/C	overall dec.	dram.dec.	N/C	N/C
	2 - 3	N/C	N/C	N/C	ret'n.to BL	N/C	N/C
G.S.I.	1 - 2	sl.temp.inc.	overall dec.	cons.dec.	dram.dec.	overall dec.	N/C
	2 - 3	N/C	N/C	temp.inc.; further sl. dec.	ret'n.to BL	sl.dec.	N/C
P.S.D.I.	1 - 2	N/C	var.dec.	cons.dec.	dram.dec.	temp.inc.; overall dec.	N/C
	2 - 3	N/C	del.temp.inc.	del.var. dec.	ret'n.to BL	temp.dec.; N/C	N/C

Key: increase = inc. temporary = temp. slight = sl.
decrease = dec. consistent = cons. dramatic = dram.
No Change = N/C delayed = del. variable = var.
return to baseline levels = ret'n.to BL moderate = mod.

ii) Monthly measures: The CBCL

The CBCL was used to gather parents' ratings of each subjects's functioning on a monthly basis. Results reflect parents' perceptions of each subject's behaviour problems and social competence during the study as scored through the summation of the CBCL scales.

Behaviour problems were rated on nine different scales which were then summed to provide a behaviour problem total score. All 4 experimental subjects reported an average decrease in total behaviour problems from phase 1 to phase 2 while both controls reported an average increase (see Figure 30). One of the 4 experimental subjects (#3) reported a further decrease in behaviour problems during phase 3 of the study. Experimental subjects1 and 2 also reported a slight decrease while subject 4 and both of the controls returned to baseline or near baseline levels in phase 3. From this data it appears that an increase in behaviour problems might be expected during the summer months if medication levels remain constant. Medication cessation, however, seems to be associated with a decrease in behaviour problems which persists for some time even after medication intake has been resumed.

Experimental subject 4 reported a decrease in levels of depression which was associated with haloperidol withdrawal. Subject 2 reported a lower overall level of depression during phase 2 as compared with phase 1. Control subjects reported no change in levels of depression during phase 2 of the study (see figure 22). Similarly, all 4 experimental subjects reported either a decrease or a decreasing trend in obsessive-compulsive behaviour which was associated with medication cessation while controls

reported no difference on this scale during phase 2 (see figure 24). One experimental subject, (#4), reported a decreasing trend in levels of hyperactivity during phase 2. Subjects 2 and 3 reported lower overall levels, while both controls indicated a slight increase in hyperactivity during the summer months (see figure 27). Three of the 4 experimental subjects, (#2,3,&4) indicated a slight overall decrease in social withdrawal during the medication free period, the fourth (#1) indicated no change. Both control subjects, however, reported a slight average increase of social withdrawal during the summer months (see figure 26). No consistent differences were found between experimental and control subjects regarding levels of aggression, delinquency, uncommunicativity, or schizoid/anxious behaviours (see figures 21, 23, 28, and 29). More variability regarding somatic complaints was indicated by experimental subjects than controls. Two experimental subjects recorded an overall decrease in somatic complaints while the others indicated no difference between phases 1 and 2 on average. Control subjects reported no change in somatic complaints throughout the study (see figure 25).

Social competence was evaluated using scales examining school behaviour, social interactions, and overall levels of activity (see figures 32, 33, and 34). These were summed into an overall social competency score (see figure 31). No consistent differences were observed between experimental and control subjects regarding social competency scores. Both control subjects and 3 of the 4 experimental subjects reported an increase in social competence across all scales during the summer months. The current data suggests that medication withdrawal has no effect on social competency within the present sample of TS patients.

FIGURE 21
CBCL: AGGRESSIVE

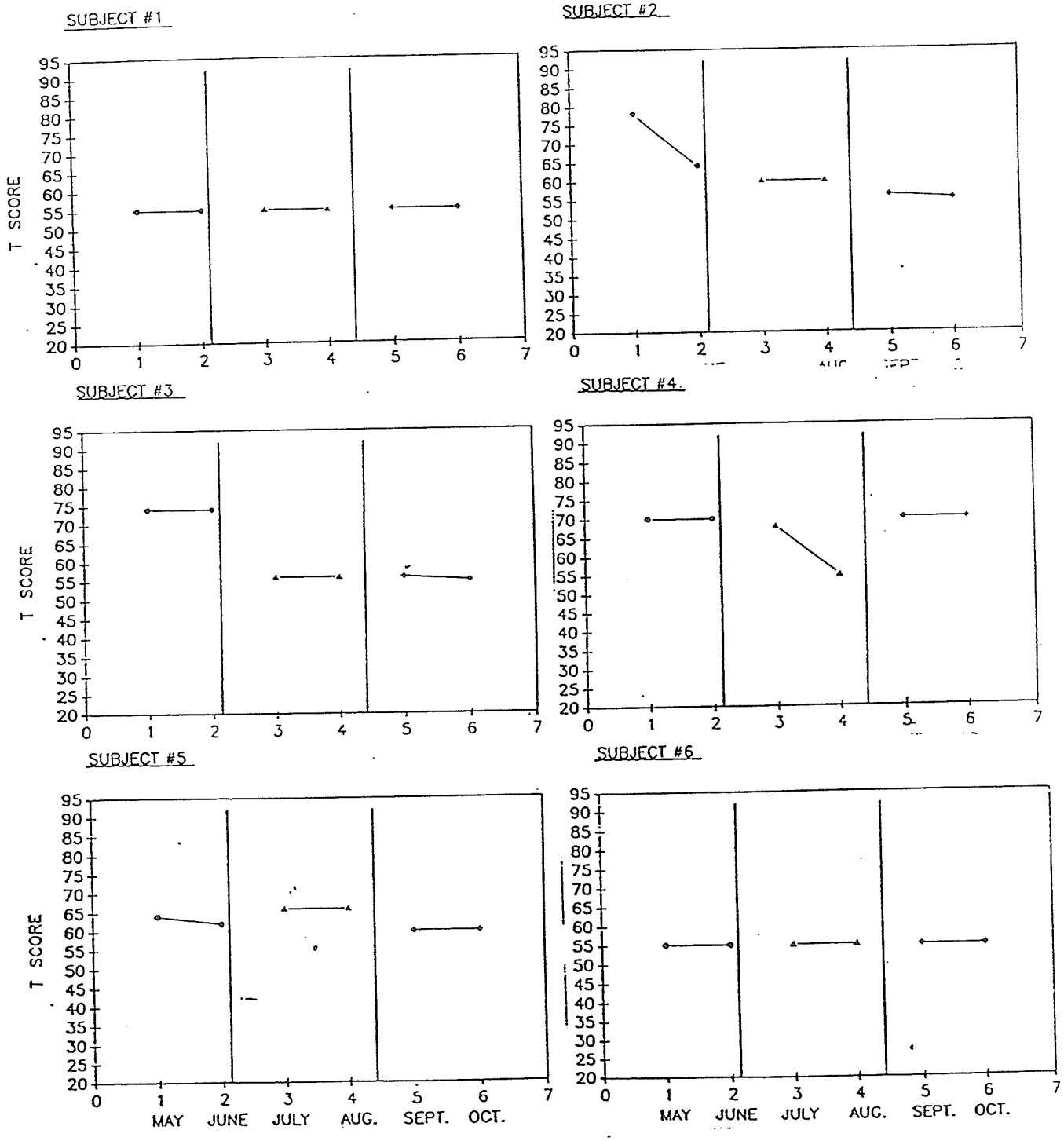


FIGURE 22
CBCL: DEPRESSED

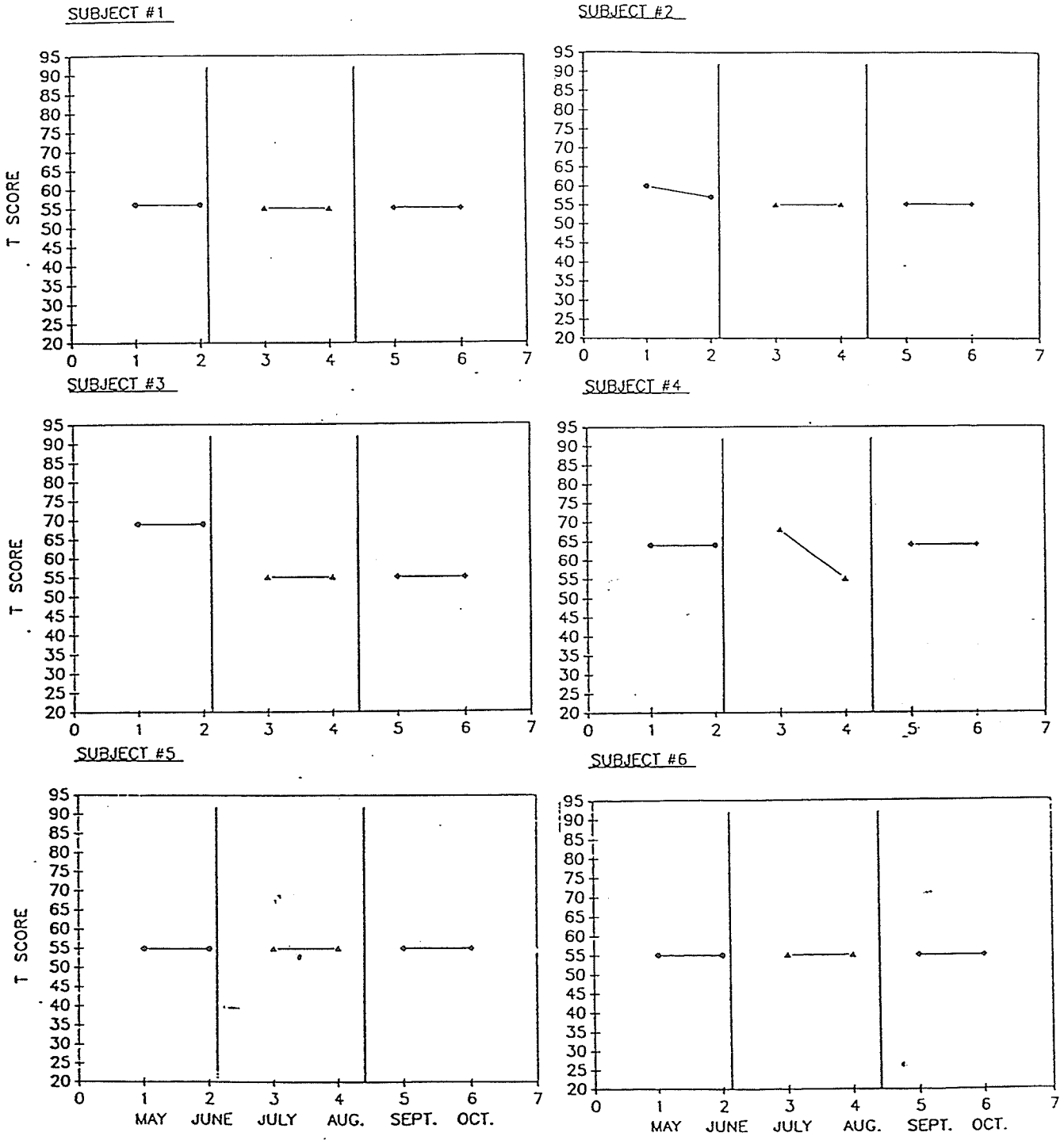


FIGURE 23
CBCL: DELINQUENT

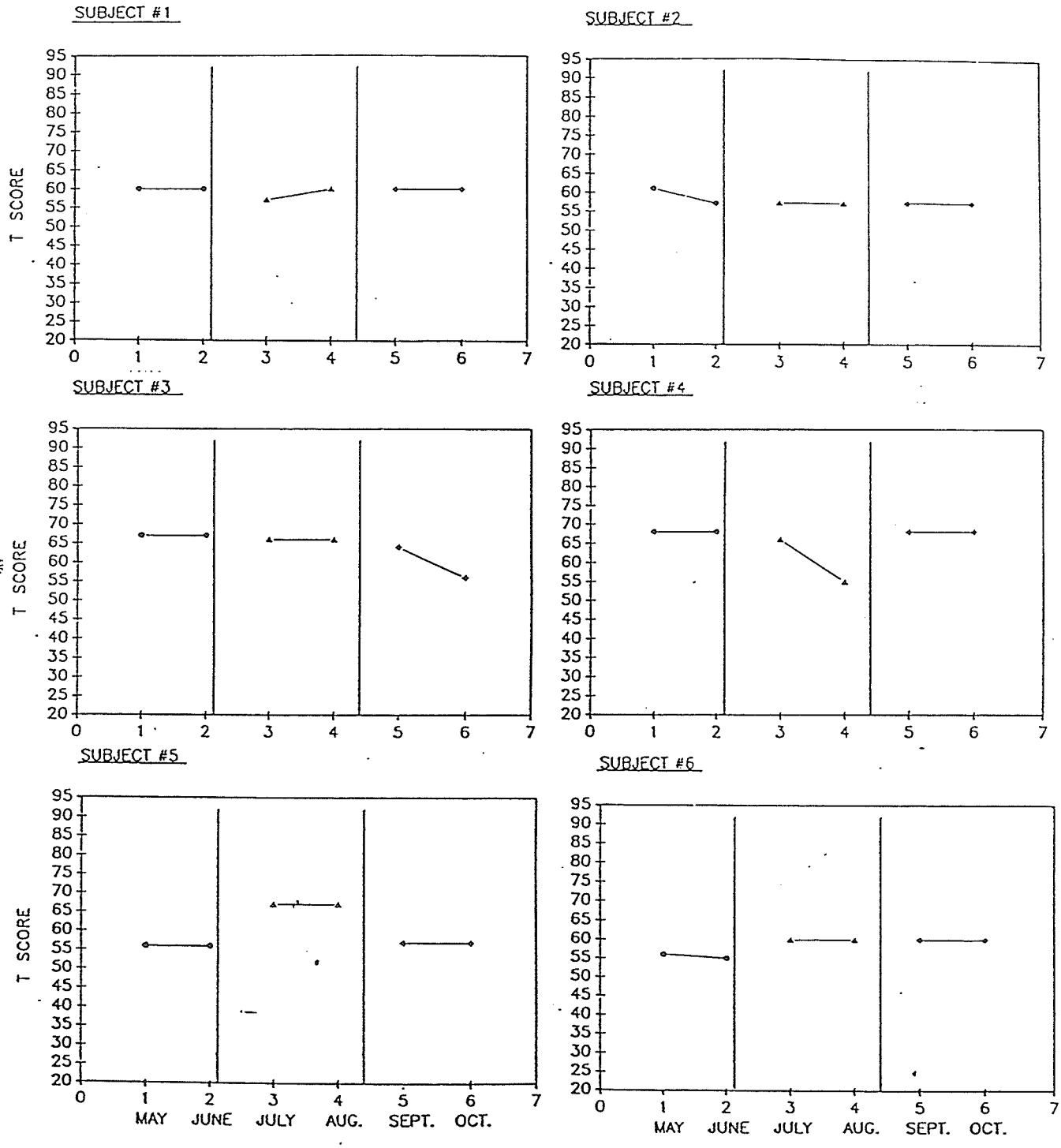


FIGURE 24
CBCL: OBSESSIVE COMPULSIVE

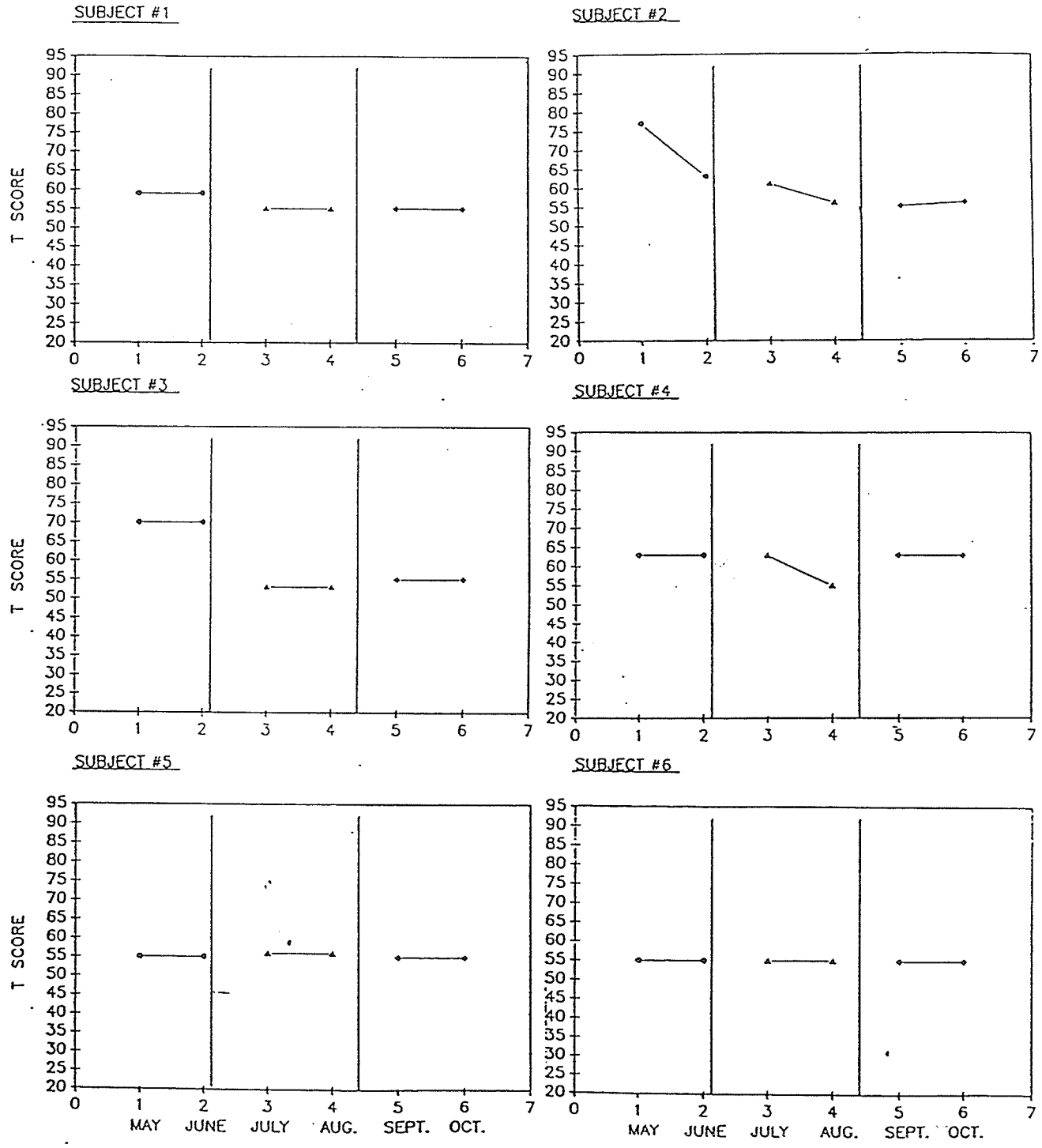


FIGURE 25
CBCL: SOMATIC COMPLAINTS

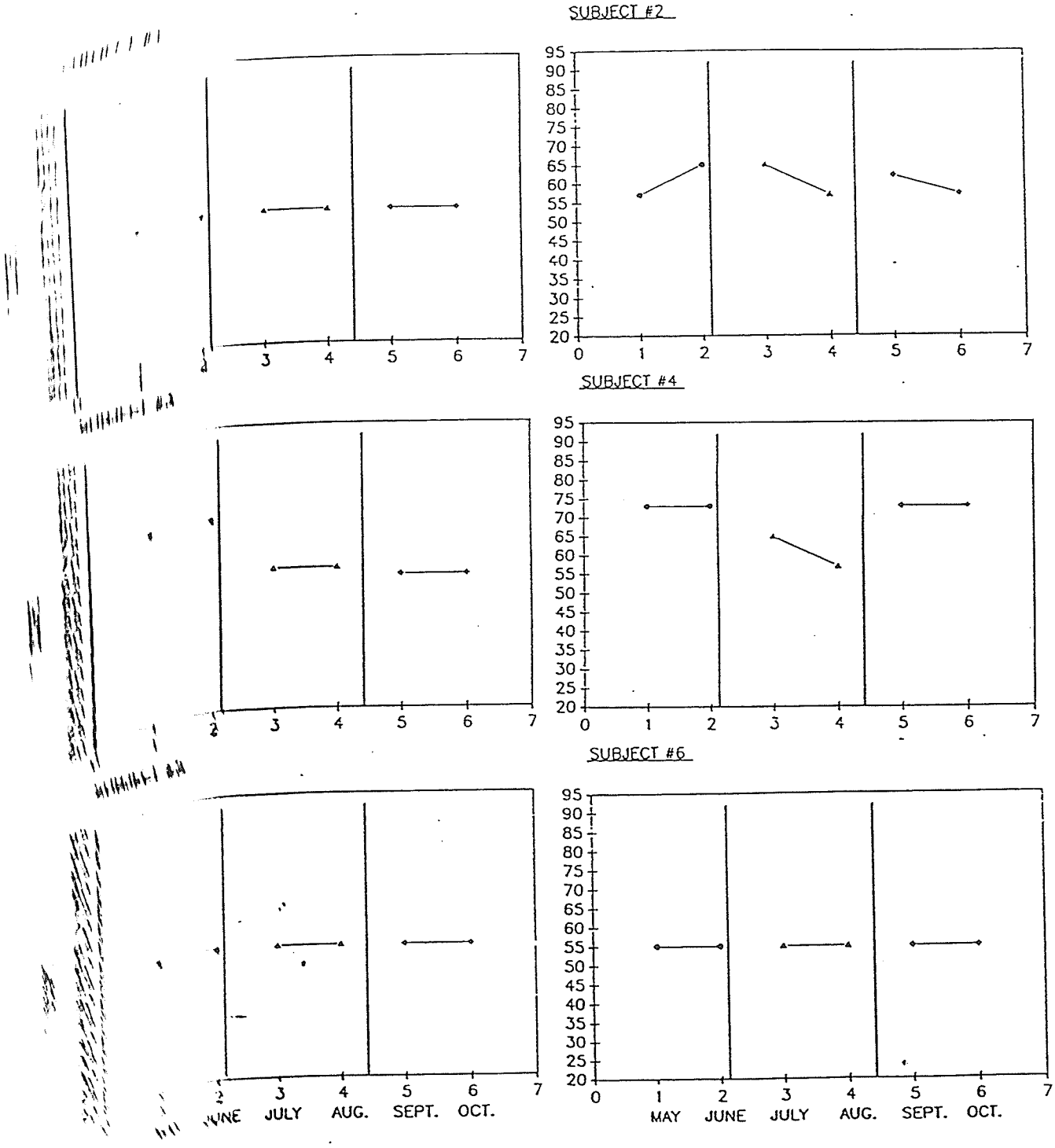


FIGURE 26
CBCL: SOCIAL WITHDRAWAL

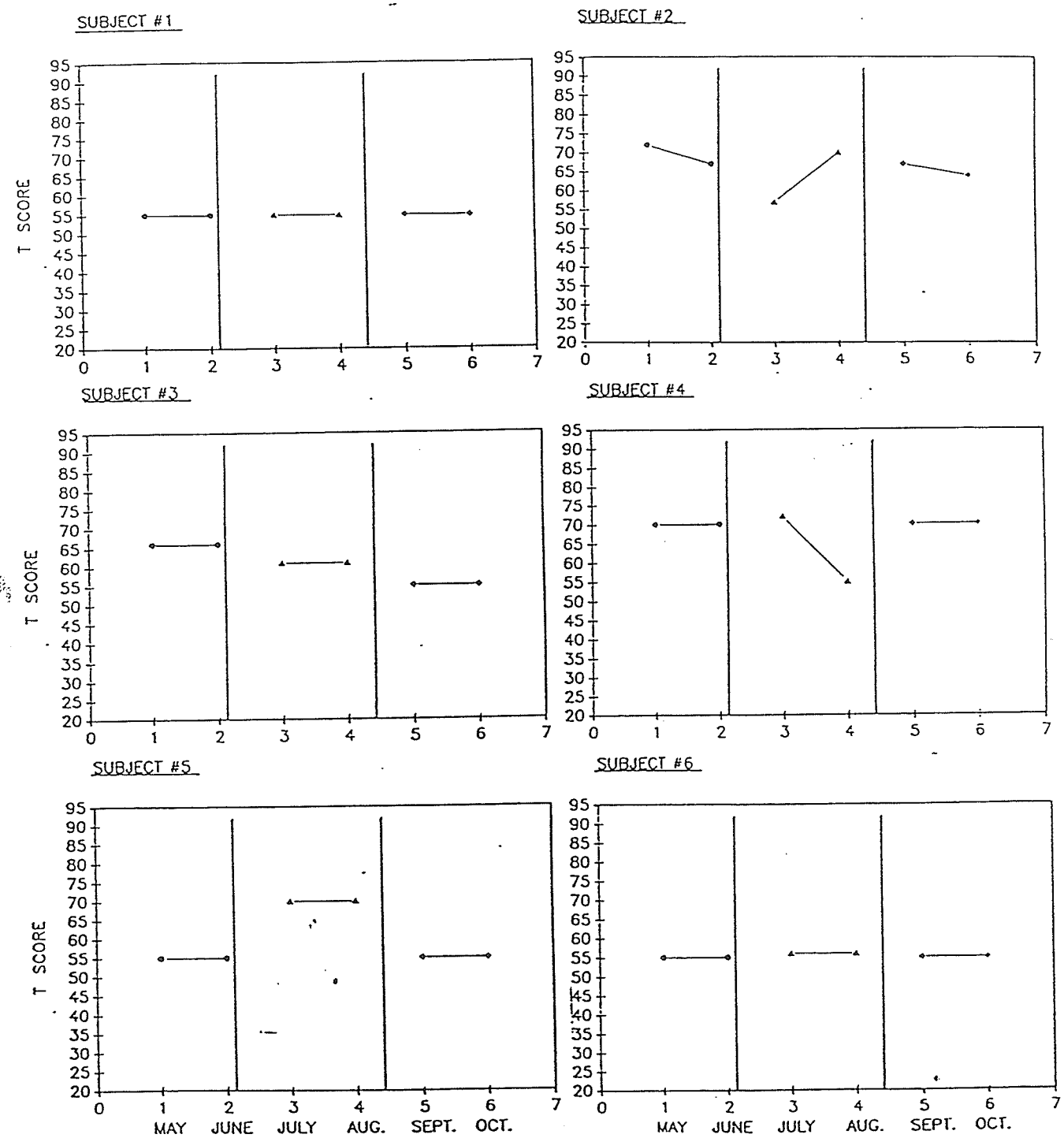


FIGURE 27
CBCL: HYPERACTIVE

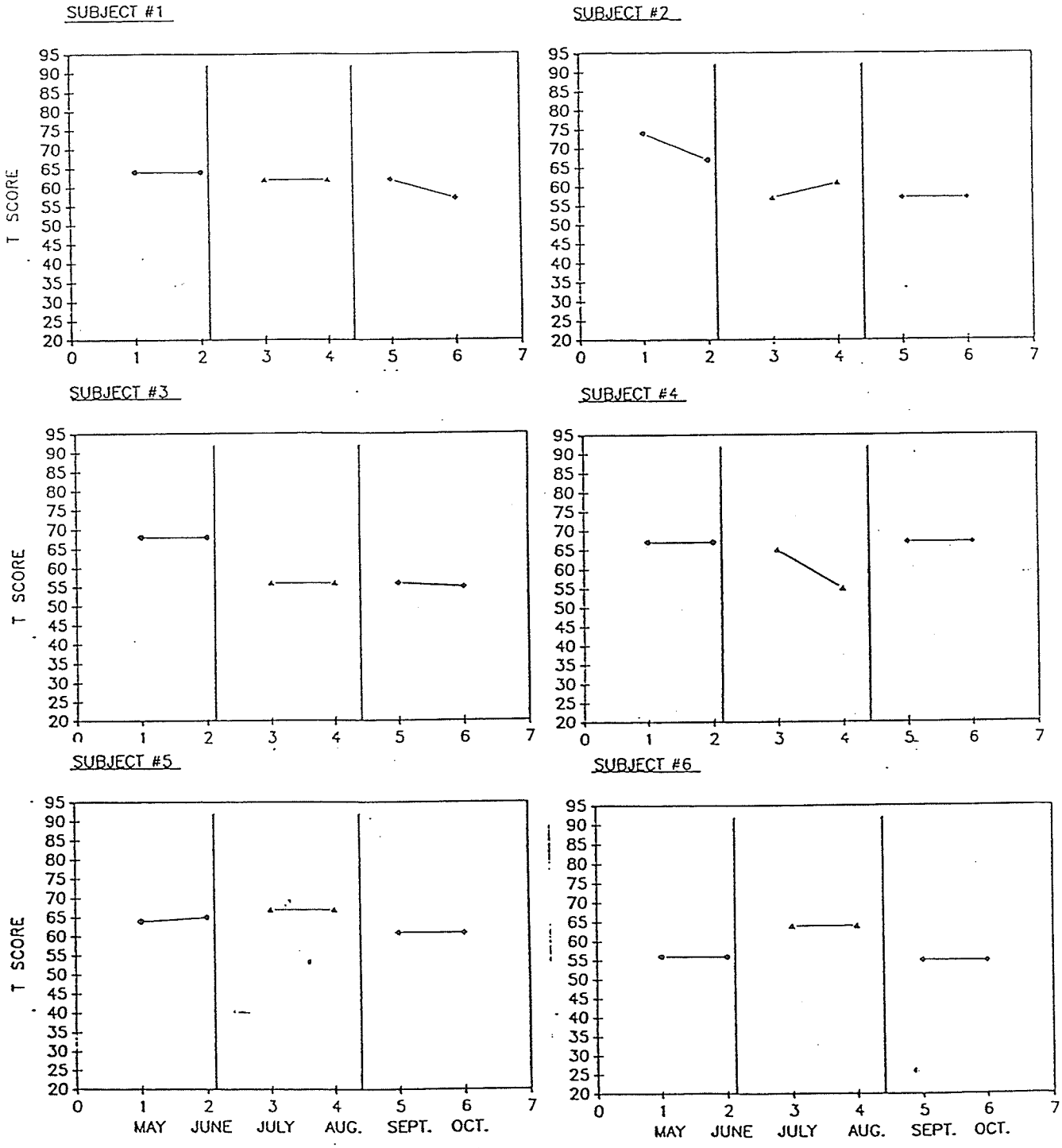


FIGURE 28
CBCL: UNCOMMUNICATIVE

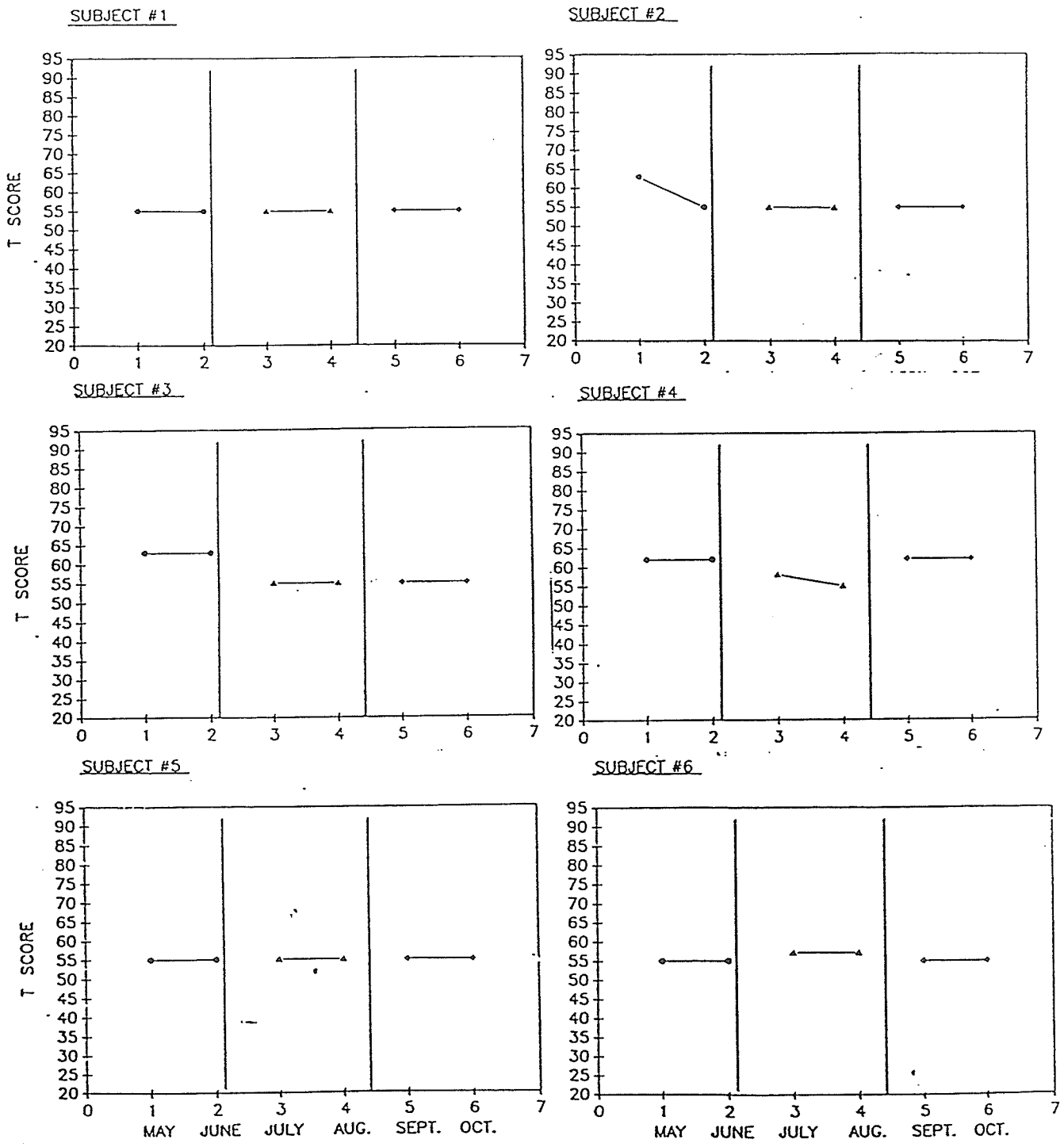


FIGURE 29
CBCL: SCHIZOID/ANXIOUS

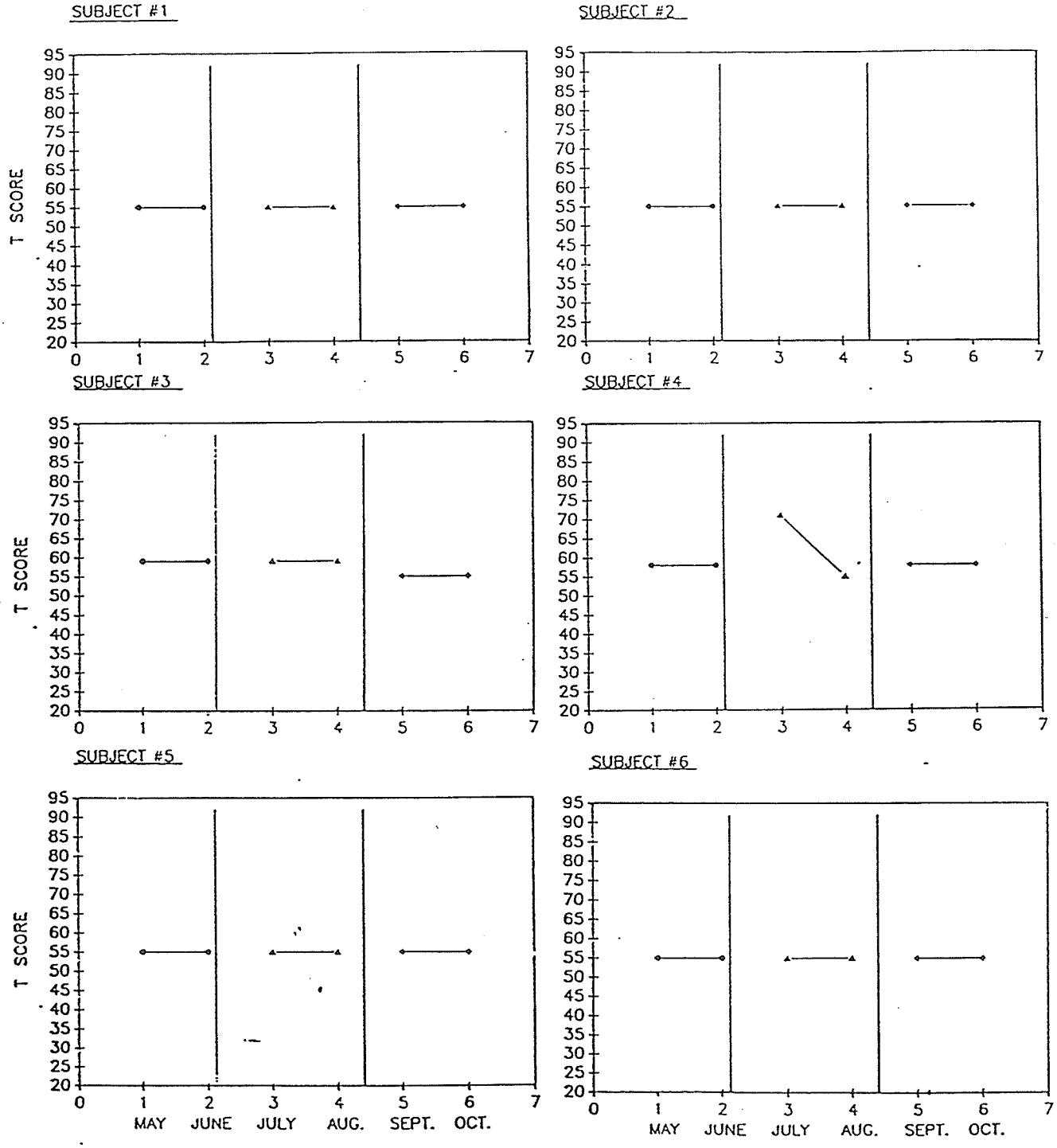


FIGURE 30
CBCL: BEHAVIOUR PROBLEMS TOTAL

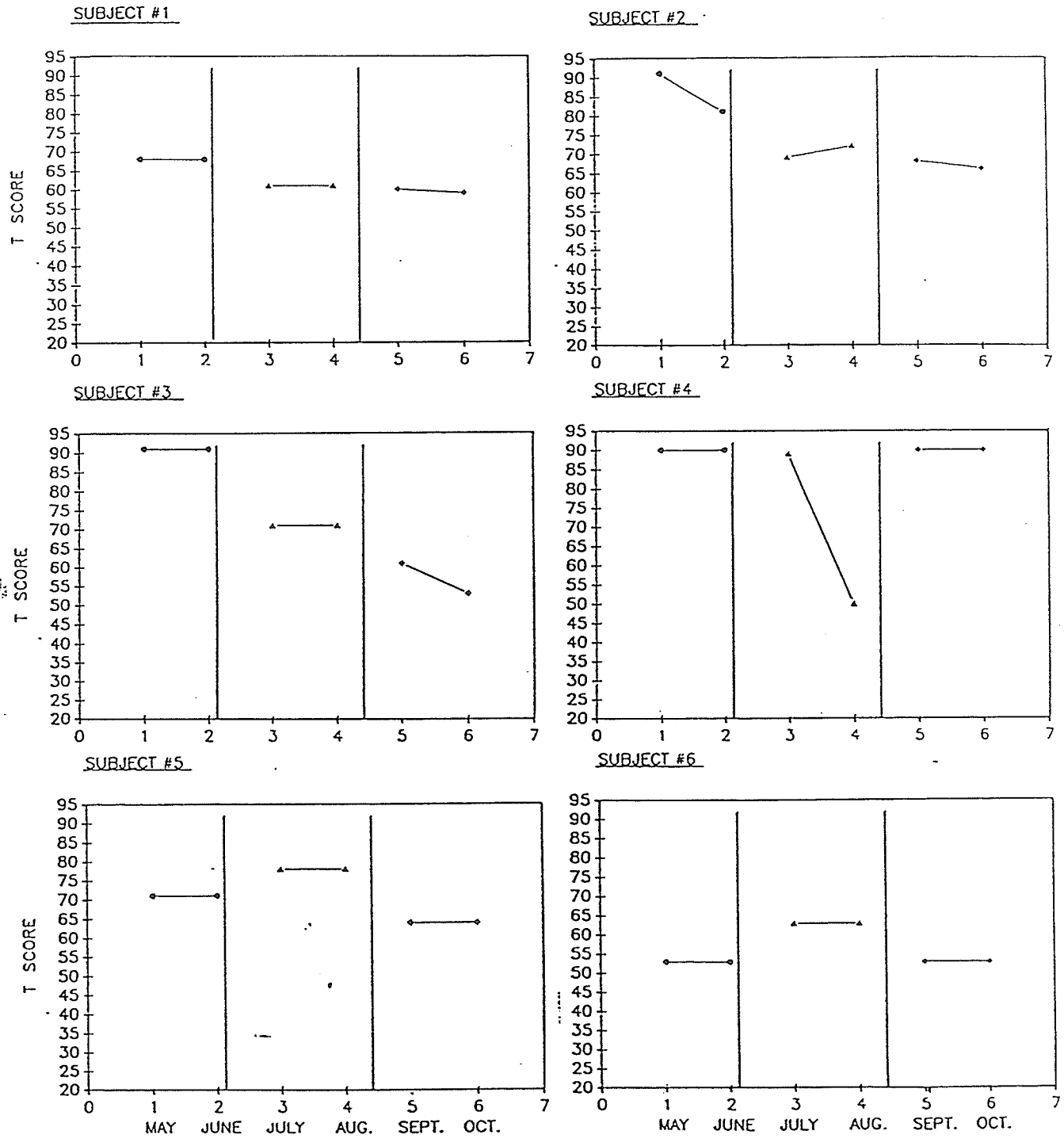


FIGURE 31
CBCL: SOCIAL COMPETENCE SCALE

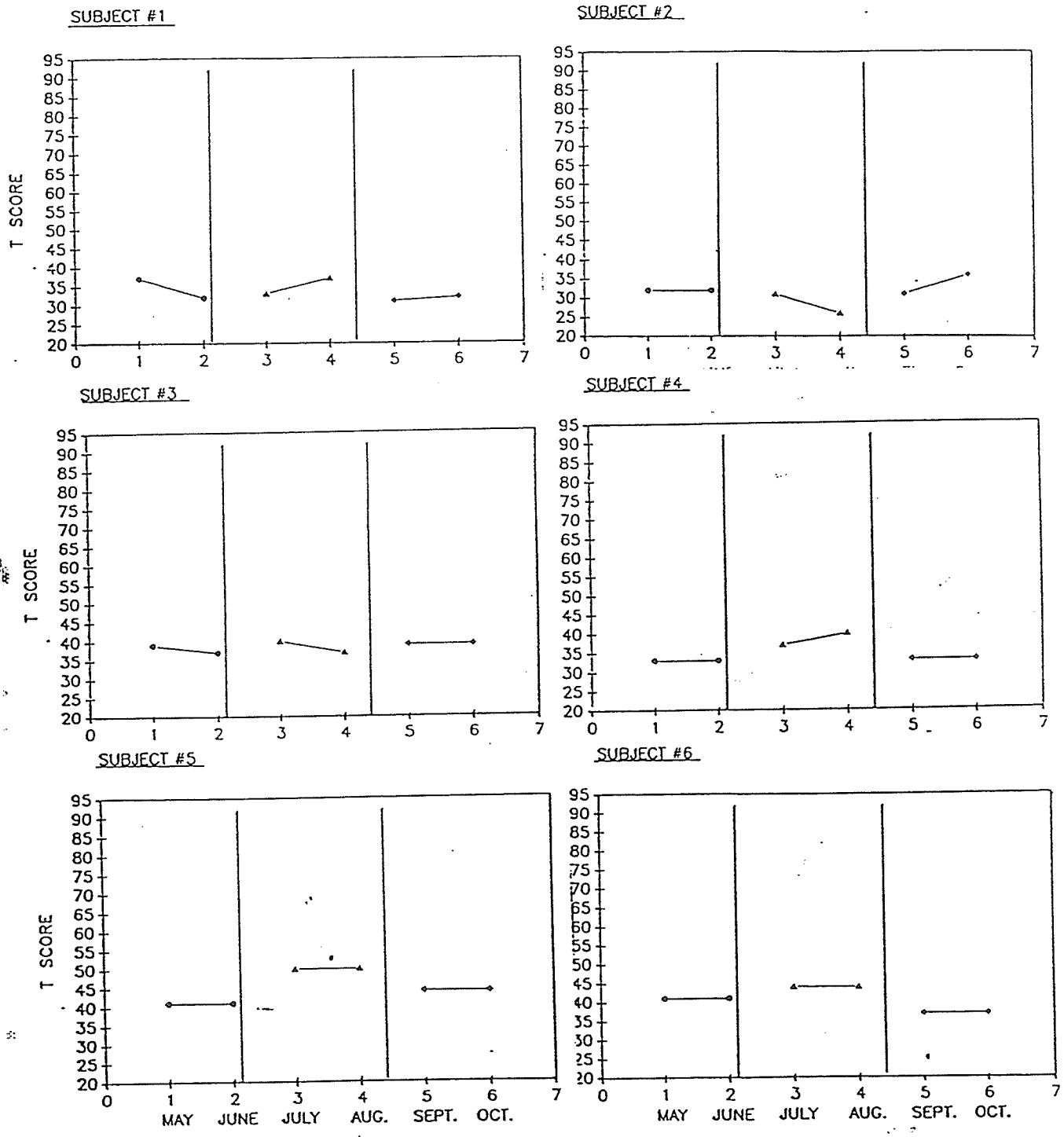


FIGURE 32
CBCL: SCHOOL

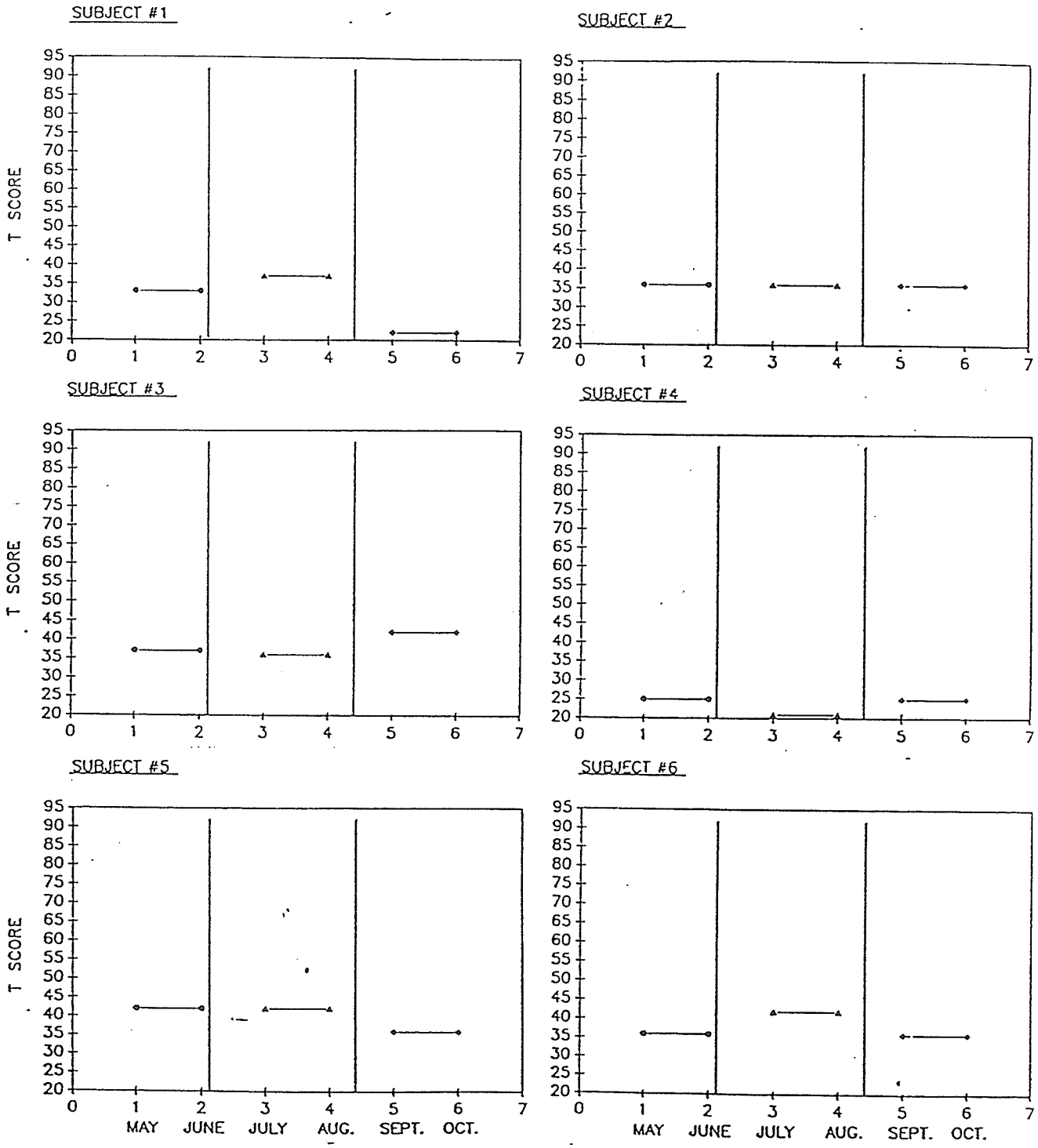


FIGURE 33
CBCL: SOCIAL

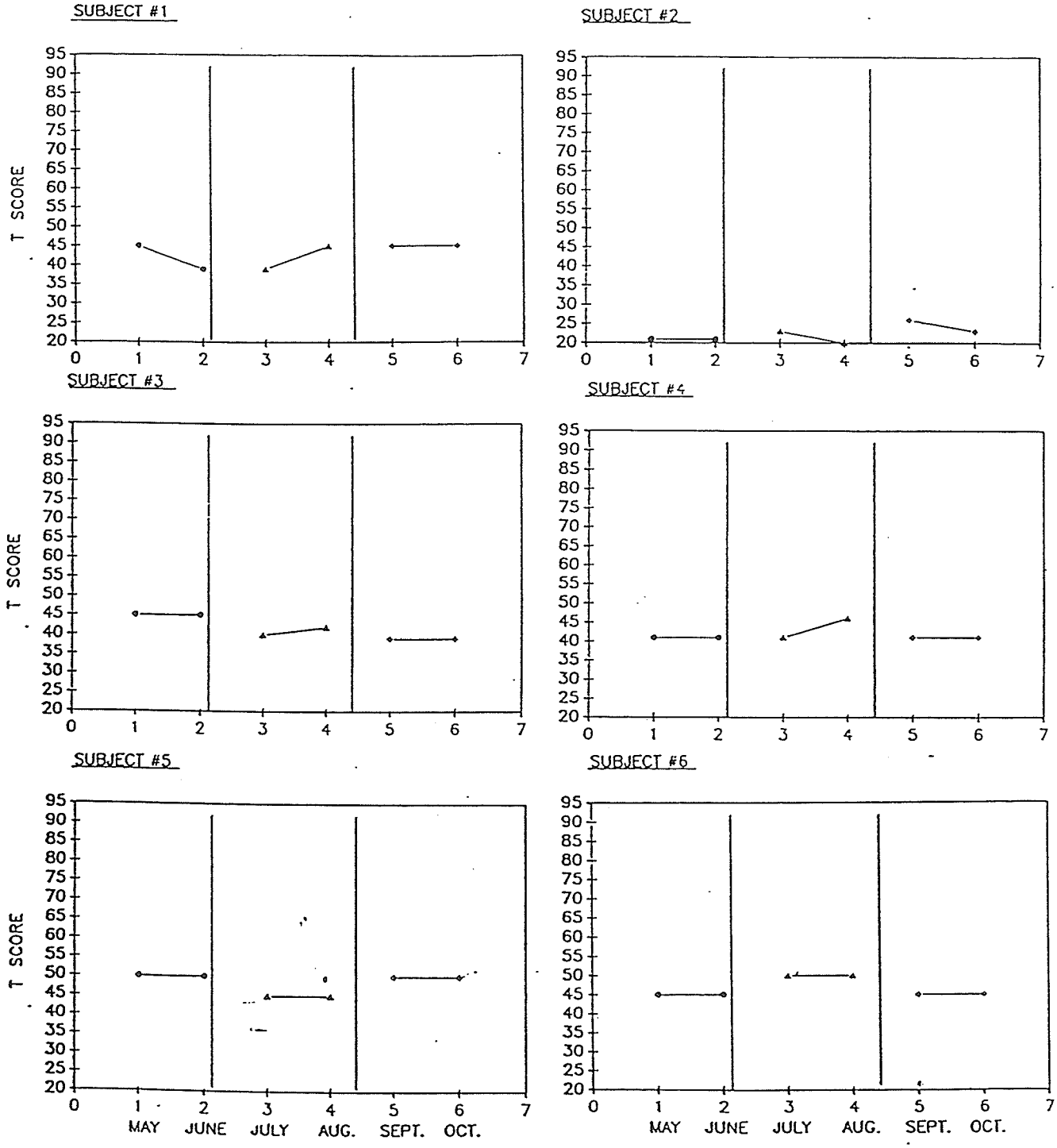


FIGURE 34
CBCL: ACTIVITIES

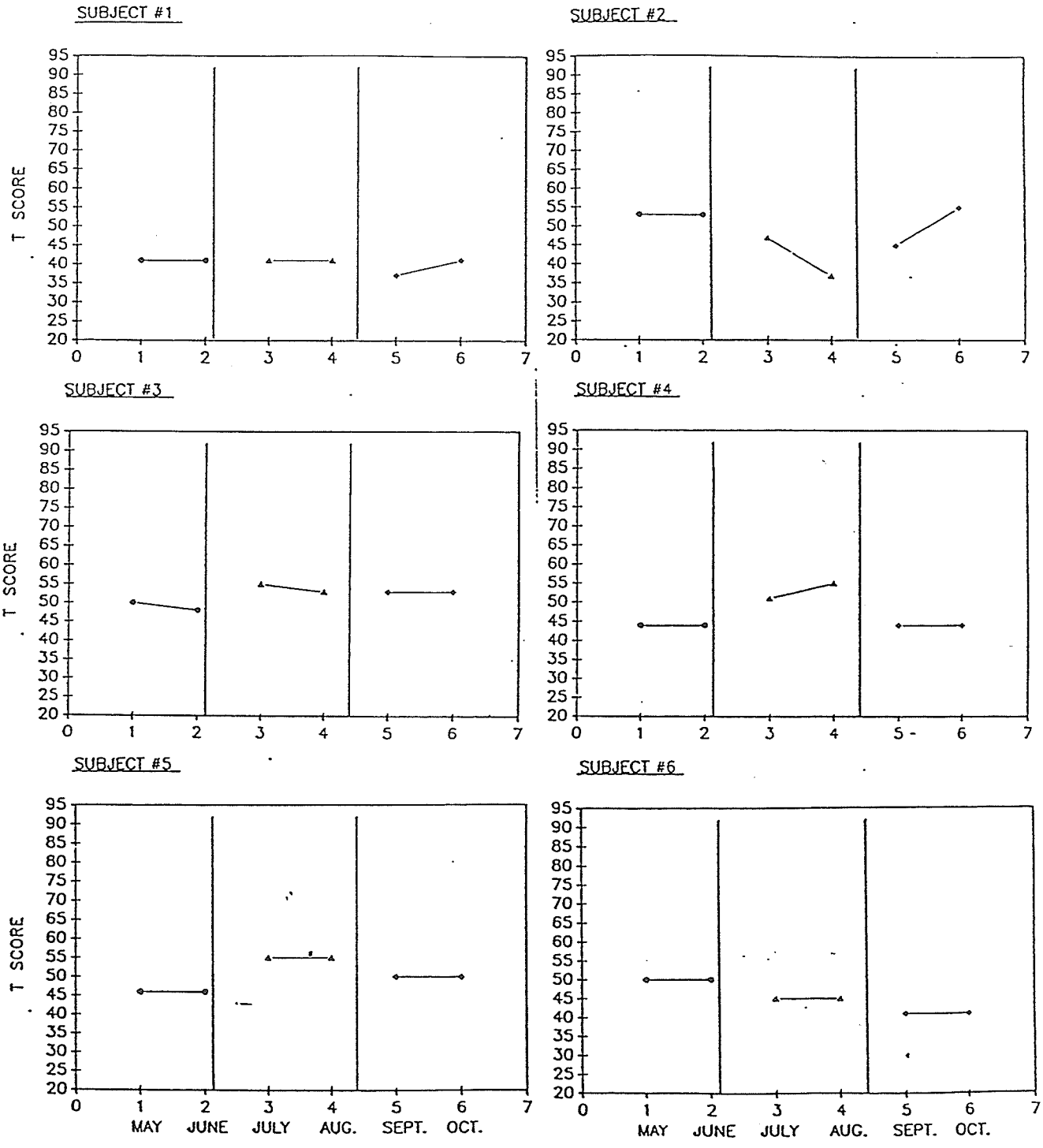


TABLE 3
CBCL: Summary of Visual Analysis

Subscale	Phase	Subject #1	Subject #2	Subject #3	Subject #4	Subject #5	Subject #6
Aggressive	1 - 2	N/C	cons.dec.	cons.dec.	dec.trend	sl.inc.	N/C
	2 - 3	N/C	cont'd.dec.	cont'd.dec.	ret'n.to BL	sl.dec.	N/C
Depressed	1 - 2	sl.dec.	sl.inc.	cons.dec.	dec.trend	N/C	N/C
	2 - 3	N/C	N/C	cont'd.dec.	ret'n.to BL	N/C	N/C
Delinquent	1 - 2	temp.dec.	N/C	N/C	dec.trend	cons.inc.	sl.inc.
	2 - 3	N/C	dec.	N/C	ret'n.to BL	ret'n.to BL	N/C
Obsessive-	1 - 2	sl.dec.	dec.trend	cons.dec.	dec.trend	N/C	N/C
Compulsive	2 - 3	N/C	sl.inc.trend	sl.inc.	ret'n.to BL	N/C	N/C
Somatic-	1 - 2	N/C	dec.trend	cons.dec.	dec.trend	N/C	N/C
Complaints	2 - 3	N/C	temp.inc.; dec.trend	sl.cons.dec.	ret'n.to BL	N/C	N/C
Social	1 - 2	N/C	temp.dec.; inc.trend	sl. dec.	dec.trend	cons.inc.	N/C
withdrawal	2 - 3	N/C	sl.dec.	sl.dec.	ret'n.to BL	ret'n.to BL	N/C
Hyperactive	1 - 2	sl.dec.	temp.dec.	cons.dec.	dec.trend	sl.inc.	cons.inc.
	2 - 3	dec.trend	sl.dec.	N/C	ret'n.to BL	ret'n.to BL	ret'n.to BL
Uncommuni-	1 - 2	N/C	N/C	sl.dec.	dec.trend	N/C	sl.inc.
cative	2 - 3	N/C	N/C	N/C	ret'n.to BL	N/C	ret'n.to BL
Schizoid/	1 - 2	N/C	N/C	N/C	temp.inc.	N/C	N/C
Anxious	2 - 3	N/C	N/C	sl.dec.	ret'n.to BL	N/C	N/C
Behaviour	1 - 2	dec.	dec.	dec.	del.dec.	inc.	inc.
Prob.Total	2 - 3	N/C	sl.dec.	sl.dec.	ret'n.to BL	ret'n.to BL	ret'n.to BL
Social	1 - 2	sl.inc.trend	del.dec.	N/C	sl.inc.trend	inc.	sl.inc.
Comp.Scale	2 - 3	sl.dec.	inc.trend	N/C	ret'n.to BL	ret'n.to BL	ret'n.to BL
School	1 - 2	sl.inc.	N/C	N/C	sl.dec.	N/C	sl.inc.
	2 - 3	dec. to bel. BL	N/C	sl.inc.	ret'n.to BL	sl.dec.	ret'n.to BL
Social	1 - 2	sl.inc.trend	sl.temp.inc.	sl. temp.dec.	del.sl.inc.	sl.dec.	sl.inc.
	2 - 3	N/C	sl.temp.inc.	sl.dec.	ret'n.to BL	ret'n.to nr BL	ret'n.to BL
Activities	1 - 2	N/C	dec.trend	sl.temp.inc.	inc.trend	inc.	sl.dec.
	2 - 3	sl.temp.dec.	inc.trend	N/C	ret'n.to BL	sl.dec.	sl.dec.

Key: increase = inc.
decrease = dec.
delayed = del.
temporary = temp.
consistent = cons.
return to baseline levels = ret'n.to BL
slight = sl.
trend = trend
No Change = N/C

iii) Daily symptoms: The PQ and ARR

Subjects in the present study were also contacted by the experimenter on a weekly basis to complete the Physician's Questionnaire (PQ) and the Adverse Reactions Report (ARR). These instruments provided a less structured format for data collection and permitted the recording of more qualitative information on a day to day basis. This information is generally consistent with what has been reported quantitatively. Some subtle symptoms, however, may not have been recorded by the instruments employed in the current study.

No major differences between experimental and control subjects were reported during phase 1 or phase 3 of the study. During phase 2, however, a number of minor behavioural and somatic problems were reported by the parents of all 4 experimental subjects but neither of the controls. Irritability, nervousness, and moodiness was reported for 3 of the 4 experimental subjects while an increase in oppositional or defiant behaviour was indicated for all experimental subjects. Stomach pains and indigestion was reported in 3 subjects following medication withdrawal while 2 had problems with skin irritations (itchiness), diaphoresis, eye lid irritation and slight ptosis (droop), and difficulty getting their eyes to focus. Oculogyria was reported during medication withdrawal by one of the experimental subjects. This term refers to the temporary upward rolling movement of both eyes. Oculogyric crisis (OCG) is the term given to this condition when the eyes remain fixed in an upwardly deviated position. All of these problems were reported during the early weeks of the medication withdrawal phase and are thought to be associated with medication cessation. None of these complains were registered by control

subjects. These symptoms, which are thought to be attributable to the effects of medication withdrawal, may need to be added to the current definition of the withdrawal emergent syndrome.

iv) Summary of withdrawal symptom investigation

Overall results of the current study indicate that withdrawal from haloperidol for TS patients is likely to result in a sharp increase in TS symptoms, particularly simple motor tics. Onset of TS symptoms usually occurs within 2 weeks of medication withdrawal and may be quite dramatic. Current results also suggest, however, that these symptoms usually subside rather quickly and rarely last more than 4 weeks. Three of the 4 experimental subjects had their TS symptoms stabilize near baseline levels while they were medication free during phase 2 of the study.

Physical symptoms that occur as a result of medication withdrawal include a number of behavioural and somatic problems such as irritability, nervousness, modiness, oppositional behaviour, stomach pains, indigestion, skin irritations, diaphoresis, visual acuity problems, and oculogyria. Results also indicate, however, that experimental subjects were less depressed, experienced fewer obsessive-compulsive symptoms and were less hyperactive and less socially withdrawn when they were medication free as compared to when they were on haloperidol. These findings are consistent with results indicating a high degree of symptom variability for those subjects undergoing haloperidol cessation as compared to those who remain on medications continually.

3) Interobserver-reliability (IOR)

Each phase of the study was two months long and all symptoms were closely monitored throughout each phase. The SCL-90-R, ARR, and TSGS were completed on a weekly basis by each subject with help from their parents. The CBCL was completed on a monthly basis by each subject's parents. In addition, the experimenter contacted the parents of each subject on a weekly basis to complete the PQ and ARR and to assist and consult with the data collection process. The TSGS, CBCL, and SCL-90-R were also completed by the experimenter with each subject on a monthly basis to check reliability between subject, experimenter, and parental ratings. Portions of these interactions with each subject were videotaped and rated for tic symptomatology by trained personnel who were blind to the purpose of the experiment and to experimental condition. These ratings took place at the end of the six month period of data collection and provided reliability data regarding subject, parental, experimenter, and independent observer ratings.

The accuracy of observations is critical to the validity of studies of behaviour. There are many sources of error that can affect observation accuracy. These include response definition, distractions in the observational situation, and poorly trained, unmotivated, or incompetent observers (Hawkins & Datson, 1975). Poorly designed, cumbersome data sheets for recording purposes or observer bias, either conscious or unconscious, may also be of concern (Martin & Pear, 1978). It is necessary to conduct interobserver-reliability (IOR) estimates to assess the presence and magnitude of these sources of error.

There are a number of methods available to assess the reliability of data gathered by different observers. One of the most common estimates of IOR is gathered by calculating the percent agreement (number of agreements divided by total of agreements plus disagreements, times 100). This method was employed to calculate the IOR in the present study not only because of its common general use, but also because of the nature of the instruments employed in the current study and due to the fact that this method had been used in the initial development and validation of some of the instruments used in the study.

Harcherik et al. (1984) in their development of the TSGS examined the percent agreement between raters. These scores were calculated by defining an agreement as being within a range of plus or minus one on each symptom dimension. The identical procedure was used in the present study. Results indicate that the agreement for the TSGS in the present study ranged from 94.5% to 100%. The overall average for the IOR of the TSGS between experimenter and parent/subject ratings was 76.5%. Average agreement for each subject ranged from 66.6% to 84%. Kazdin (1975) has suggested that by convention IOR should be between 80 and 100%. This suggestion however, is based on an assumption that a binary distinction between an event happening or not happening is being made. An IOR estimate of 76.5% with the use of dichotomous-ordinal rating scales as in the present study, is quite acceptable.

The criterion used to define an agreement for the SCL-90-R was the same as that for the TSGS. A range of plus or minus one for each symptom score was defined as an agreement. Using this criterion, the range for parent/subject and experimenter agreement was 50 to 100% with the average

IOR estimate being 80.6%. The average reliability scores for each subject ranged from 61.8% to 98.0% and overall, the IOR for the SCL-90-R is quite good in the present study.

A smaller range of options were available as responses to questions on the CBCL. For this reason, an exact agreement was required in the calculation of the reliability of scores. Individual scores ranged from 61.7% to 96.2% with the average IOR estimate being 77.1%. The average reliability scores for individual subjects ranged from 72.2% to 85.5% and indicates a reasonably high IOR estimate for the CBCL between parent/subject and experiment ratings.

An exact agreement was also required for the YSR because of its similarity in scoring the CBCL. The YSR and the CBCL were compared to provide an estimate of the IOR between subject and parent. The range of scores was from 68.1% to 91.1% with the average estimate being 76.3%. Average ratings of individual subjects ranged from 70.3% to 88.2% and indicate a reasonably good IOR rate between subject and parent.

Segments of a number of subject-experimenter interactions were videotaped during the course of the study. Two blind, independent observers (01 and 02) who were trained in the use of the instruments involved in the study and had had specialized training and experience with TS were asked to provide independent ratings of each subject's behaviour. For the interactions that were videotaped and used for IOR purposes, the agreement between the subject and experimenter ratings ranged from 54.5% to 100% with an average agreement of 80%. Ratings of agreement between the individual subjects and 01 ranged from 63.6% to 100% with an average of

83.2%. For O2, the IOR ranged from 54.5% to 100% with the average being 83.2%. The overall agreement between the experimenter and O1 and O2 was 85.6% and 87.4% respectively. The range of scores for both sets of observations was 66.6% to 100%. The range of agreement scores between O1 and O2 was 81.8% to 100% and the overall average between the independent observers was 92.3%. This suggests that the overall reliability of observations and scores between subjects, parents, experimenter, and independent observers is quite good.

4) Sampling Bias

The present study employed a very small number of TS patients as subjects. The issue of sampling bias needs to be addressed in order to interpret the present results in the most meaningful way, and to assess the relative probability of particular sampling biases accounting for current results. The representativeness of this small sample of TS patients must also be evaluated and considered in the context of result generalizability.

There are 65 to 70 diagnosed cases of TS in the province of Manitoba. Forty-one of these patients are directly involved in treatment with the Tourette Syndrome Clinic at the St. Boniface General Hospital, and all were contacted regarding participation in the present study. Of the initial 41 patients, 23 were not taking any medications to control their TS symptoms at the time of the study. The remaining 18 patients were actively involved in pharmacotherapeutic treatment utilizing medications such as haloperidol, clonidine, pimozide, propanolol, thyroxin, and various combinations of these and other drugs. A total of 7 patients met the inclusion criteria for the present study. Three of these patients refused to participate as

experimental subjects in the present study due to previous "disasters" that had occurred as a result of medication cessation. Two of these individuals however, agreed to participate as control subjects while the third declined all participation in the study. Three others indicated that they too had experienced intense discomfort with medication cessation, and agreed to participate as experimental subjects only on the condition that medication use could be resumed immediately if symptoms became severe. There was only one subject who routinely took a "drug holiday" as part of his standard treatment program. This subject also reported having experienced some discomfort during medication free periods and agreed to participate under the same conditions as the other experimental subjects.

Global ratings of symptom severity were available for all TS patients involved in treatment at the TS Clinic. These ratings were based on the TSGS Global Score and ranged from 0 to 100. The overall mean global score for all patients was 23.6, which is near the upper end of the "mild" catagory symptom severity. The patients who were eventually placed on medications reported slightly higher overall severity scores on initial presentation to the clinic staff (i.e. prior to medication being prescribed) than did those patients who ultimately remained medication free. The average global scores were 21.2 and 26.1 respectively for each group. The subjects who participated in the presnt study were in no way different from the larger group of TS patients known to the TS Clinic. The average TSGS global score for these patients at the beginning of the study was 19.2, which is near the upper end of the "mild" catagory and close to the overall group average of 23.6. The average global score of subjects in the present study prior to their initial medication use was 27.8, which is

consistent with the overall average of 26.1 for those patients who eventually came to use medications on a regular basis.

It is thought that the subjects in the present study are generally representative of the TS patients in treatment at the TS Clinic. Sampling bias in the present study is held to a minimum by including all but one of the patients who met the inclusion criteria. Subjects were, in general, similar each other and similar to those that have been involved in other studies of TS. Symptom severity at time of diagnosis falls within one standard deviation of the mean as outlined by the TSGS (Harcherik et al., 1984), and while on medications, symptom severity for the current group of subjects falls near the upper end of the "mild" catagory and is similar to other groups of patients in the literature on TS. Results of the current study are therfore not seen as being attributable to biases in the sampling procedures used in the present design.

VIII. DISCUSSION

1) Haloperidol cessation and TS symptoms

Many serious physiological conditions have been associated with the long term use of neuroleptic agents such as haloperidol (Brunn, 1984; Englehardt & Polizos, 1978; Fog et al., 1982; Gualitari & Hawk, 1980; Klawans et al., 1982; Shapiro et al., 1978; Shapiro & Shapiro, 1982). The risk of exposure to these serious long range side effects is thought by some, to be reduced through the prudent implementation of intermittent periods of medication cessation in long term treatment planning. For many TS patients, however, medication cessation leads to an increase in the symptoms of their disorder, as well as a number of more dramatic physical effects which are thought to be part of the withdrawal emergent syndrome. These symptoms make medication-free periods very difficult or intolerable for many patients. Since TS is most often diagnosed in childhood (Fulton et al., 1987) and since haloperidol is the most common treatment for those who are placed and remain on medications (Brunn, 1984; Cohen et al., 1979; Fulton et al., 1987; Shapiro et al., 1978; Shapiro & Shapiro, 1982; Wiener, 1984) many TS patients are likely to remain on haloperidol for a long period of time and are therefore exposed to the risks involved with the long term use of neuroleptic agents.

The present study was concerned with investigating the onset, severity, and duration of the withdrawal emergent syndrome and differentiating these

symptoms from those of TS. A small number of TS patients who were on low doses of haloperidol were examined over a six month period. During this time the four experimental subjects were medication free for the third and fourth months. Control subjects remained on medication throughout the study.

Results indicated that medication cessation may result in a symptom increase in some, but not all, aspects of TS. Experimental subjects reported a sharp increase in simple motor tics which was associated with medication cessation. A greater degree of TS symptom variability was reported by experimental subjects as compared to controls which suggests that an instability of TS symptoms is likely associated with medication withdrawal. For 2 of the 4 subjects, however, the TS symptom increase and period of instability lasted 3 to 4 weeks and then returned to near baseline levels. These results suggest that there are occasions during the course of the TS disorder when no medications are necessary to achieve symptom control. This is consistent with the nature of the disease in which the symptoms tend, periodically, to wax and wane on their own accord. This particular characteristic of the Tourette disorder continues to make research on TS difficult and points out the need for researchers to follow TS patients closely over long periods of time.

2) Haloperidol cessation and withdrawal symptoms

In the current study, both TS symptoms and withdrawal effects were monitored and scored on a weekly basis over a six month period. It was expected that experimental subjects would experience a number of withdrawal symptoms which could be observed, scored, and recorded using the

instruments employed for the collection of quantitative data throughout the study. Results, however, did not indicate any clear or consistent differences between experimental and control subjects on the quantitative rating scales where it was anticipated that withdrawal symptoms would emerge. The SCL-90-R somatic complaints scale, for example, not only indicated that there were no differences between experimental and control subjects but also reflected that there was a slight overall decrease in somatic complaints across all subjects during phase 2 of the study. Somatic complaints were expected to increase for experimental, but not control, subjects during this phase of the experiment. Parental ratings of somatic complaints as recorded monthly by the CBCL indicated that there was more variability for experimental than control subjects, but also that no increase in somatic complaints was evident for either experimental or control subjects during phase 2 of the experiment. Considering the results of the SCL-90-R and the CBCL only, it does not appear that haloperidol cessation results in the development of somatic complaints or symptoms of the withdrawal emergent syndrome for these TS patients.

3) Additional withdrawal symptoms

The quantitative results of both the SCL-90-R and the CBCL are not entirely consistent with the weekly qualitative reports that were gathered and recorded using the ARR. In the compilation of the qualitative data, it was clear that a number of minor behavioural and somatic problems were being reported by the parents of all the experimental subjects but neither of the controls. Among these reported difficulties were irritability, nervousness, moodiness, oppositional or defiant behaviour, stomach pains,

indigestion, skin irritatations, diaphoresis, eye lid irritation and slight ptosis (droop), eye focussing problems and oculogyria. The fact that none of these difficulties were experienced by either of the control subjects not only supports the attribution of these symptoms to the effects of medication cessation but also strengthens the argument for possible inclusion of these symptoms with a revised definition of the withdrawal emergent syndrome.

The question of the differences between the quantitative and qualitative data warrants discussion. It seems that the quantitative data collection procedures not only failed to record what was being reported qualitatively, but did so with a high degree of inter-observer reliability. Upon closer examination of the data recording procedures however, these results are not as discrepant and incompatible as they initially appear. Both the SCL-90-R and the CBCL require that an overall rating score be assigned in order to summarize a period of time, one week and one month respectively. The ARR on the other hand, inquires into the details of any occurrence of difficulties over the previous seven days. In this way, each encounter or event is recorded individually on the ARR and reflects a more day by day data collection process than does the SCL-90-R or the CBCL. The occurrence of one or two somatic complaints over a seven day period may not be sufficient to elevate a seven day or one month summary score. Perhaps even a slight decrease may be explained by examining other results which indicate that experimental subjects reported decreases in levels of depression, decreases in obsessive-compulsive behaviours, decreases in hyperactivity, and decreases in levels of social withdrawal. These global improvements which seem to be associated with medication cessation may have

removed the "complaint" aspect from somatic difficulties or influenced the overall perception of the period of time in question. For these reasons it is thought that the ARR provides a more accurate reflection of the adverse reactions to medication withdrawal than does the somatic complaint subscale of the SCL-90-R or the CBCL. Revisions to the definition of the withdrawal emergent syndrome are suggested from the ARR data collected in the present study.

4) Neuropsychological Testing

Neuropsychological testing was conducted with each of the 4 experimental subjects in the study. Testing sessions were scheduled such that each individual would be tested twice, once while on haloperidol and once while medication free. Since the assessments were scheduled to be approximately 8 weeks apart for each subject, it was necessary to attempt to control for practice effects. The order in which subjects were tested was alternated such that subjects #1 and #4 were first tested while they were on haloperidol, then re-assessed 8 weeks later when they were medication free. Subjects #2 and #3 were first tested when they were medication free, then re-tested 8 weeks later when they had returned to medication use. Unfortunately, from a research point of view, subject #2 did not return to medication use after his drug holiday and was therefore unable to provide neuropsychological test data reflecting his individual functioning while on haloperidol. Results from neuropsychological assessments conducted both while on and off haloperidol are available for subjects #1, #3, and #4. Summaries of these results, and the results of off haloperidol testing with subject #2 are presented along with concomitant ratings of TS symptoms as provided by the TSGS total scores (see appendix J).

The close temporal proximity of testing sessions make the neuropsychological test results in the current study very difficult to interpret. Practice effects are difficult to estimate and do not affect all types of tests equally. Similarly, the attribution of specific test results to the effects of haloperidol may not always be appropriate and symptom levels of the TS disorder must also be considered in the analysis of the neuropsychological test data.

Despite these limiting factors, the current neuropsychological test results are worthy of discussion. In general, it does not appear that haloperidol adversely affects the neuropsychological functioning of the current sample of TS patients. The single exception to this may be visual-motor skills as assessed by the Bender-Gestalt test. Two of the three subjects performed much more poorly while on haloperidol as compared to when they were medication free. Their TS symptoms, conversely, were less severe while they were on medications. The third subject, however, performed much better on the Bender-Gestalt Test when on haloperidol as compared to medication free. While both performances by this subject were quite poor, it is thought that his medication free results were adversely affected by severe TS symptoms at the time of testing. In light of these results, it seems possible that visual-motor skills may be slightly affected in an adverse way by haloperidol medication.

Practice effects are thought to account for many of the considerable differences between first and second testing scores for the same subject. There were some differences however, that seem to reflect a positive effect of haloperidol on neuropsychological functioning. These were consistent between subjects regardless of the scheduling of testing sessions. All

three subjects performed better on the Seashore Rhythm test while they were on haloperidol. This test requires attention, concentration, short term memory recognition, and the ability to sustain a speeded pace in working toward task completion. Haloperidol was also associated with a generally improved performance on the WISC-R coding subtest, Trail Making Tests A and B, and the name writing task (both hands) of the Lateral Dominance Examination. All of these tests assess attention, concentration, and the ability to maintain a speeded course of action in a race against the clock. Interestingly, all these subtests are timed tasks which along with attention and concentration are the most often cited school and learning problems experienced by children with TS (Shady et al., 1987).

Previous research has indicated that haloperidol may result in adverse effects on learning as assessed by a cognitive battery if doses of the medication were above the optimal dose (Campbell, Anderson, Meier, Cohen, Small, Samit, Sachar, 1978). No adverse cognitive effects on learning are thought to result from the use of an optimal dose of haloperidol (Campbell et al., 1978) and any negative effects of haloperidol on cognition have been shown to be a function of dose rather than of the neuroleptic itself (Werry & Aman, 1975). Results of the current study are consistent with these findings and are further suggestive of some improvements for this group of TS patients in the areas of attention, concentration, short term memory, and the ability to maintain a speeded performance throughout a timed task.

5) Theoretical conclusions

The symptoms of the withdrawal emergent syndrome have been described as "nausea, vomiting, diaphoresis, ataxia, various combinations of oral dyskenesias (tongue and lips), and dystonic movements of the extremities, head, and trunk" (Weiner, 1984, p. 839). It is of special concern to TS patients because it is most likely to occur on withdrawal from a low-dose and high-potency drug such as haloperidol (Engelhardt & Palizos, 1978) which is frequently used in the treatment of TS.

Results of the current study suggest that there may be other symptoms in addition to those described by Weiner (1984) which are associated with haloperidol withdrawal. Experimental subjects in the current project reported a number of difficulties such as oppositional or defiant behaviours (including irritability, nervousness, and moodiness), stomach pains, indigestion, skin irritations, diaphoresis, eye lid irritation and slight ptosis, eye focussing problems and oculogyria. All of these problems were attributed to medication withdrawal by the experimental subjects in the current study. This assessment of cause is strengthened by the fact that neither of the control subjects experienced any of these symptoms and reported no discomfort of any kind during phase 2 of the study. It is also important to note, however, that not all of the experimental subjects experienced all of these withdrawal symptoms. Furthermore, the small number of subjects involved in the present research does not offer the clear and sufficient evidence that is desirable for results to be generalized to the overall population of patients who may have occasion to experience a withdrawal from haloperidol. Results do suggest, however, that young male TS patients undergoing an intermittant

cessation of treatment with haloperidol are likely to experience some symptoms of withdrawal. These would most probably include irritability, moodiness, and an increase in oppositional or defiant behaviours. Other symptoms of withdrawal may include nervousness, stomach pains, indigestion, itchiness, eye lid irritation and slight ptosis, and eye focusing problems. The diaphoresis which was reported by two of the four experimental subjects is presently included in the list of symptoms described as the withdrawal emergent syndrome. Results of the current study suggest that a number of other symptoms could be included as associated features in the clinical definition of the withdrawal emergent syndrome.

6) TS treatment considerations

Results of the current study have a number of practical implications for the treatment of TS. It was noted during the process of recruiting subjects for the current study, in which all known TS patients in Manitoba were contacted, that many individuals reported an attempted period of medication cessation in their treatment history. These were almost invariably reported as "a disaster" which required the resumption of medication use within a very short period of time. Most of these patients expressed extreme reservation regarding the notion of medication cessation and declined to participate in the present study. The recruitment experience is consistent with results of a national survey which indicates that most patients remain on medications quite consistently throughout their treatment history (Fulton et al., 1987). In addition, the fact that a number of TS patients had had severe withdrawal reactions in the past and refused to participate in the present study because of this, indirectly

strengthens the case for revisions to be made to the definition of the withdrawal emergent syndrome. The patients who agreed to participate in the present study may have been those who had previously had less severe withdrawal reactions and felt that they were able to tolerate a medication free period. Those who had experienced severe withdrawal symptoms may have been those who declined to participate in the present study.

It is suspected that the "disaster" described by many TS patients in conjunction with medication cessation is likely a combination of TS symptom exacerbation and the effects of the withdrawal emergent syndrome. These symptoms may become discouraging if not overwhelming in a very short period of time, especially if there does not appear to be any relief in sight, and may strongly mitigate against the notion of a drug holiday. Given that intermittent medication free periods may be desirable in the long term treatment of TS with haloperidol, the results of the present study may provide hope for some TS patients. It does not appear that either the exacerbation of TS symptoms or the symptoms of withdrawal last for longer than 3 to 4 weeks. Following this period it appears that both TS symptomatology and other aspects of physiological and psychological health return to pre-medication levels.

There is also evidence from the current study which suggests that some aspects of the TS patient's psychological well-being may actually be improved during medication free periods. Bruun (1982) has suggested that some dysphoria and depression may be associated with the use of haloperidol in the treatment of TS. Current results indirectly support this contention as all 4 experimental subjects reported decreases in levels of depression associated with medication withdrawal. Control subjects did not report any

change in levels of depression throughout the experiment. In addition, obsessive-compulsive behaviours, hyperactivity, and levels of social withdrawal were all reported as being affected in a positive way by medication cessation. Control subjects tended to report slight increases in these difficulties during the summer months which supports the assertion that these improvements in psychological well-being are associated with medication cessation.

Results of the current study therefore imply that medication cessation may be a more viable option in the long term treatment of TS than it is presently considered to be. Furthermore, there may be a number of benefits to an individual's psychological well-being that are associated with periods of medication cessation in the long term treatment of TS.

7) Future Research

The secrets of TS remain elusive to researchers. The bizarre nature of the disorder, the waxing and waning of symptoms, and the wide range of individual differences in TS patients all conspire to confound experimental strategies and misguide the researcher. Results from even the best designed research may be rendered uninterpretable (Bruun, 1984).

TS research is required from the genetic-molecular level right through to the social-behavioural conduct of TS patients. In particular the areas of genetic transmission and penetrance seem promising as does the considerable research effort devoted to understanding the neurochemestry and neuroanatomy of the disorder. Much progress has been made in some areas, very little in others. The enormous undertaking of an array of

dedicated researchers from many disciplines will eventually lead from questions to answers as progress is made through multidisciplinary research.

The current research highlighted the need to record day by day changes in symptoms even in a relatively long term study. Very important data may otherwise be missed. Inter-observer reliability data is also very important to collect. Many TS patients seem, at times, to be completely unaware of their tics and are often not as accurate with self report instruments as the researcher would like them to be. These and many other pitfalls of self-report, paper and pencil instruments, and behavioural observation research methods will continue to plague and limit the usefulness of macro-level behavioural research in the natural history of TS. The relevance of each of these studies will lie not in their ability to definitively summarize all aspects of TS, but rather in their modest achievement of fitting as one small piece of the enormous puzzle, which is Tourette Syndrome.

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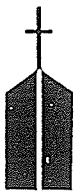
APPENDICES



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PATIENT INFORMATION AND CONSENT FORM

A comparison of neuropsychological functioning on and off haloperidol.

I understand that the criteria that must be met in order to be involved in the current study are as follows:

1) I must have been diagnosed as having Tourette Syndrome (TS).,

2) I must be on haloperidol and no other treatment for TS.,

3) I must have been on haloperidol for a minimum period of two months and an optimal dosage level must have been established.,

4) I must take haloperidol on a regular and consistent basis when medication for TS is being administered.,

5) I must take a "drug holiday" (i.e. be medication free) for a minimum period of four weeks during the year.,

6) I must be at least nine years of age.,

7) I must sign this consent form.

I am aware that investigators at the TS Clinic are interested in studying the side effects of haloperidol, and that neuropsychological testing will take place on two occasions during the experiment. In addition, I understand that I will be asked to complete certain questionnaies at weekly visits throughout the study.

I am aware that the total length of the study is 18 weeks. I am also aware that my participation in the study is entirely voluntary. I will be free to withdraw from the study at anytime and should I do so, this will have no effect on my future treatment at the TS Clinic. I am also aware that all information about me recorded during the study will be strictly confidential. My name will not be entered in computer data and my name will not appear in any publications resulting from the study.

If I am under 18, the study has been discussed with both me and my parents or guardian, who will sign below.

DATE: _____ PATIENT'S SIGNATURE: _____

DATE: _____ WITNESS' SIGNATURE: _____

I have read the consent form, which my child has read, understood, and signed. I consent to my child's participation in the study and have had an opportunity to ask any questions about it I may have had, as has my child.

DATE: _____ PARENT OR GUARDIAN'S SIGNATURE: _____

DATE: _____ WITNESS' SIGNATURE: _____

APPENDIX B

INVESTIGATOR	PROJECT 0122	IND 8705	STUDY	SUBJECT	FORM SEQ	SCREEN ID

SYMPTOM CHECKLIST (SCL-90) (Page 1 of 3)

SUBJECT'S INITIALS (F/M/L)	BIRTHDATE (Mo/Da/Yr)	SUBJECT NO.
TODAY'S DATE (Mo/Da/Yr)	VISIT Baseline Week 1 2 3 4	

BM USE ONLY

RECEIVED STAMP

INSTRUCTIONS: *Listed below are some symptoms or problems that people sometimes have. Please read each one carefully and decide how much the symptoms bothered or distressed you DURING THE PAST WEEK, INCLUDING TODAY.*

Decide how much the symptom affected you. **NOT AT ALL? A LITTLE? MODERATELY? QUITE A BIT? EXTREMELY?** *and place a check in the appropriate column to the right.*

HOW MUCH WERE YOU BOTHERED BY THE FOLLOWING SYMPTOMS? *(Do not leave out any items.)*

SYMPTOMS	Not At All 1	A Little 2	Moder-ately 3	Quite A Bit 4	Ex-treme-ly 5	SYMPTOMS	Not At All 1	A Little 2	Moder-ately 3	Quite A Bit 4	Ex-treme-ly 5
1. Headaches.						16. Hearing voices that other people do not hear.					
2. Nervousness or shakiness inside.						17. Trembling.					
3. Unwanted thoughts, words, or ideas that won't leave your mind.						18. Feeling that most people cannot be trusted.					
4. Faintness or dizziness.						19. Poor appetite.					
5. Loss of sexual interest or pleasure.						20. Crying easily.					
6. Feeling critical of others.						21. Feeling shy or uneasy with the opposite sex.					
7. Idea that someone else can control your thoughts.						22. Feeling of being trapped or caught.					
8. Feeling others are to blame for most of your troubles.						23. Suddenly scared for no reason.					
9. Trouble remembering things.						24. Temper outbursts that you could not control.					
10. Worried about sloppiness or carelessness.						25. Feeling afraid to go out of your house alone.					
11. Feeling easily annoyed or irritated.						26. Blaming yourself for things.					
12. Pains in heart or chest.						27. Pains in lower back.					
13. Feeling afraid in open spaces or on the streets.						28. Feeling blocked in getting things done.					
14. Feeling low in energy or slowed down.						29. Feeling lonely.					
15. Thoughts of ending your life.						30. Feeling blue.					

INVESTIGATOR	PROJECT	IND	STUDY	SUBJECT	FORM SEQ	SCREEN ID
	4022	6705				

SYMPTOM CHECKLIST (SCL-90) (Page 2 of 3)

BM USE ONLY	RECEIVED STAMP

SUBJECT'S INITIALS (F/M/L)	BIRTHDATE (Mo/Da/Yr)
SUBJECT NO.	TODAY'S DATE (Mo/Da/Yr)

INSTRUCTIONS: *Listed below are some symptoms or problems that people sometimes have. Please read each one carefully and decide how much the symptoms bothered or distressed you DURING THE PAST WEEK, INCLUDING TODAY.*

Decide how much the symptom affected you. **NOT AT ALL? A LITTLE? MODERATELY? QUITE A BIT? EXTREMELY?** *and place a check in the appropriate column to the right.*

HOW MUCH WERE YOU BOTHERED BY THE FOLLOWING SYMPTOMS? *(Do not leave out any items.)*

SYMPTOMS	Not At All 1	A Little 2	Moder-ately 3	Quite A Bit 4	Ex-treme-ly 5	SYMPTOMS	Not At All 1	A Little 2	Moder-ately 3	Quite A Bit 4	Ex-treme-ly 5
31. Worrying too much about things.						46. Difficulty making decisions.					
32. Feeling no interest in things.						47. Feeling afraid to travel on buses, subways or trains.					
33. Feeling fearful.						48. Trouble getting your breath.					
34. Your feelings being easily hurt.						49. Hot or cold spells.					
35. Other people being aware of your private thoughts.						50. Having to avoid certain things, places or activities because they frighten you.					
36. Feeling others do not understand you or are unsympathetic.						51. Your mind going blank.					
37. Feeling that people are unfriendly or dislike you.						52. Numbness or tingling in parts of your body.					
38. Having to do things very slowly to insure correctness.						53. A lump in your throat.					
39. Heart pounding or racing.						54. Feeling hopeless about the future.					
40. Nausea or upset stomach.						55. Trouble concentrating.					
41. Feeling inferior to others.						56. Feeling weak in parts of your body.					
42. Soreness of your muscles.						57. Feeling tense or keyed up.					
43. Feeling that you are watched or talked about by others.						58. Heavy feelings in your arms or legs.					
44. Trouble falling asleep.						59. Thoughts of death or dying.					
45. Having to check and double-check what you do.						60. Overeating.					

INVESTIGATOR	PROJECT 0022	IND 8705	STUDY	SUBJECT	FORM SEQ	SCREEN ID

SYMPTOM CHECKLIST (SCL-90) (Page 3 of 3)

SUBJECT'S INITIALS (F/M/L)	BIRTHDATE (Mo/Da/Yr)
SUBJECT NO.	TODAY'S DATE (Mo/Da/Yr)

BM USE ONLY — RECEIVED STAMP

INSTRUCTIONS: *Listed below are some symptoms or problems that people sometimes have. Please read each one carefully and decide how much the symptoms bothered or distressed you DURING THE PAST WEEK, INCLUDING TODAY.*

Decide how much the symptom affected you. **NOT AT ALL? A LITTLE? MODERATELY? QUITE A BIT? EXTREMELY?** *and place a check in the appropriate column to the right.*

HOW MUCH WERE YOU BOTHERED BY THE FOLLOWING SYMPTOMS? *(Do not leave out any items.)*

SYMPTOMS	Not At All 1	A Little 2	Moder-ately 3	Quite A Bit 4	Ex-treme-ly 5	SYMPTOMS	Not At All 1	A Little 2	Moder-ately 3	Quite A Bit 4	Ex-treme-ly 5
61. Feeling uneasy when people are watching or talking about you.						76. Others not giving you proper credit for your achievements.					
62. Having thoughts that are not your own.						77. Feeling lonely even when you are with people.					
63. Having urges to beat, injure or harm someone.						78. Feeling so restless you couldn't sit still.					
64. Awakening in the early morning.						79. Feelings of worthlessness.					
65. Having to repeat the same actions such as touching, counting, washing.						80. Feeling that familiar things are strange or unreal.					
66. Sleep that is restless or disturbed.						81. Shouting or throwing things.					
67. Having urges to break or smash things.						82. Feeling afraid you will faint in public.					
68. Having ideas or beliefs that others do not share.						83. Feeling that people will take advantage of you if you let them.					
69. Feeling very self-conscious with others.						84. Having thoughts about sex that bother you a lot.					
70. Feeling uneasy in crowds, such as shopping or at a movie.						85. The idea that you should be punished for your sins.					
71. Feeling everything is an effort.						86. Feeling pushed to get things done.					
72. Spells of terror or panic.						87. The idea that something serious is wrong with your body.					
73. Feeling uncomfortable about eating or drinking in public.						88. Never feeling close to another person.					
74. Getting into frequent arguments.						89. Feelings of guilt.					
75. Feeling nervous when you are left alone.						90. The idea that something is wrong with your mind.					

CHILD'S NAME _____ BIRTH DATE _____

CHILD BEHAVIOR CHECKLIST ..For ages 4-16

Child's age	Child's sex [_]boy [_]girl		Parent's type of work (Please be specific - e.g. teacher, laborer, Father _____ Mother _____
This form filled out by: [_] Mother [_] Father [_] Other _____	Date		

I.A. Please list the sports your child most likes to take part in: Eg. bike riding, fishing, swimming, baseball

[_] none

a. _____

b. _____

c. _____

B. Compared to Others of the same age, about how much time does he/she spend?

	Don't Know	Less Than Average	Avg	More Than Avg
a.	[_]	[_]	[_]	[_]
b.	[_]	[_]	[_]	[_]
c.	[_]	[_]	[_]	[_]

C. Compared to others of the same age, how well does he/she do each one?

	Don't Know	Below Avg	Avg	Above Avg
a.	[_]	[_]	[_]	[_]
b.	[_]	[_]	[_]	[_]
c.	[_]	[_]	[_]	[_]

II.A. Please list your child's favourite hobbies, activity, games, other than sports: Eg. books, dolls, piano, crafts (Do not include TV)

[_] none

a. _____

b. _____

c. _____

B. Compared to Others of the same age, about how much time does he/she spend?

	Don't Know	Less Than Average	Avg	More Than Avg
a.	[_]	[_]	[_]	[_]
b.	[_]	[_]	[_]	[_]
c.	[_]	[_]	[_]	[_]

C. Compared to others of the same age, how well does he/she do each one?

	Don't Know	Below Avg	Avg	Above Avg
a.	[_]	[_]	[_]	[_]
b.	[_]	[_]	[_]	[_]
c.	[_]	[_]	[_]	[_]

III.A. Please list any organizations, clubs, teams or groups your child belows to:

[_] none

a. _____

b. _____

c. _____

B. Compared to Others of the same age, how active is he/she in each?

	Don't Know	Less Active	Avg	More Active
a.	[_]	[_]	[_]	[_]
b.	[_]	[_]	[_]	[_]
c.	[_]	[_]	[_]	[_]

IV.A. Please list any jobs or chores your child has. Eg. making beds, paper route, babysitting, etc.

[_] none

a. _____

b. _____

c. _____

B. Compared to others of the same age, how well does he/she carry them out?

	Don't Know	Below Avg	Avg	Above Avg
a.	[_]	[_]	[_]	[_]
b.	[_]	[_]	[_]	[_]
c.	[_]	[_]	[_]	[_]

V. 1. About how many close friends does your child have?

[_] none [_] 1 [_] 2 or 3 [_] 4 or more

2. About how many times a week does your child do things with them?

[_] less than 1 [_] 1 or 2 [_] 3 or more

VI. Compared to other children his/her age, how well does your child:

	Worse	About Same	Better
a. Get along with his/her brothers & sisters?	[_]	[_]	[_]
b. Get along with other children?	[_]	[_]	[_]
c. Behave with his/her parents?	[_]	[_]	[_]
d. Play and work by himself/herself?	[_]	[_]	[_]

VII.1. Current school performance-for children aged 6 or older:

[_] Does not go to school

	Failing	Below Avg	Avg	Above Avg
a. Reading or English	[_]	[_]	[_]	[_]
b. Writing	[_]	[_]	[_]	[_]
c. Arithmetic or Math	[_]	[_]	[_]	[_]
d. Spelling	[_]	[_]	[_]	[_]
Other academic e._____	[_]	[_]	[_]	[_]
subjects: (Eg. f._____	[_]	[_]	[_]	[_]
history, science, foreign language) g._____	[_]	[_]	[_]	[_]

2. Is your child in a special class?
[_] no [_] yes - what kind?

3. Has your child ever repeated a grade?
[_] no [_] yes - grade and reason

4. Please describe any academic or other problems your child has in school.
[_] none

VIII. Below is a list of items that describe children. For each item that describes your child NOW OR WITHIN THE PAST 12 MONTHS, please circle the 2 if the item is VERY TRUE or OFTEN TRUE of your child. Circle the 1 if the item is SOMEWHAT or SOMETIMES TRUE of your child. If the item is NOT TRUE of your child, circle the 0.

0 1 2 1. Acts too young for age
0 1 2 2. Allergy (describe) _____
0 1 2 3. Argues a lot
0 1 2 4. Asthma
0 1 2 5. Behaves like opposite sex
0 1 2 6. Bowel movements outside toilet
0 1 2 7. Bragging, boasting
0 1 2 8. Can't concentrate, can't pay attention for long
0 1 2 9. Can't get his/her mind off certain thoughts; obsessions (describe) _____
0 1 2 10. Can't sit still, restless or hyperactive
0 1 2 11. Clings to adults or too dependent
0 1 2 12. Complains of loneliness
0 1 2 13. Confused or seems to be in a fog
0 1 2 14. Cries a lot
0 1 2 15. Cruel to animals
0 1 2 16. Cruelty, bullying or meanness to others
0 1 2 17. Day-dreams or gets lost in his/her thoughts
0 1 2 18. Deliberately harms self or attempts suicide
0 1 2 19. Demands a lot of attention
0 1 2 20. Destroys his/her own things
0 1 2 21. Destroys things belonging to his/her family or other children
0 1 2 22. Disobedient at home
0 1 2 23. Disobedient at school
0 1 2 24. Doesn't eat well
0 1 2 25. Doesn't get along with other children
0 1 2 26. Doesn't seem to feel guilty after misbehaving
0 1 2 27. Easily jealous
0 1 2 28. Eats or drinks things that are not food (describe)
_____
0 1 2 29. Fears certain animals, situations, or places, other than school (describe) _____
_____
0 1 2 30. Fears going to school
0 1 2 31. Fears he/she might think or do something bad
0 1 2 32. Feels he/she has to be perfect
0 1 2 33. Feels or complains that no one loves him/her
0 1 2 34. Feels others are out to get him/her
0 1 2 35. Feels worthless or inferior
0 1 2 36. Gets hurt a lot, accident-prone
0 1 2 37. Gets in many fights
0 1 2 38. Gets teased a lot
0 1 2 39. Hangs around with children who get in trouble

0 1 2 40. Hears things that aren't there (describe) _____

_____

0 1 2 41. Impulsive or acts without thinking
0 1 2 42. Likes to be alone
0 1 2 43. Lying or cheating
0 1 2 44. Bites fingernails
0 1 2 45. Nervous, highstrung, or tense
0 1 2 46. Nervous movements or twitching (describe) _____

_____

0 1 2 47. Nightmares
0 1 2 48. Not liked by other children
0 1 2 49. Constipated, doesn't move bowels
0 1 2 50. Too fearful or anxious
0 1 2 51. Feels dizzy
0 1 2 52. Feels too guilty
0 1 2 53. Overeating
0 1 2 54. Overtired
0 1 2 55. Overweight
56. Physical problems without known medical causes:
0 1 2 a. Aches or pains
0 1 2 b. Headaches
0 1 2 c. Nausea, feels sick
0 1 2 d. Problems with eyes (describe) _____
0 1 2 e. Rashes or other skin problems
0 1 2 f. Stomachaches or cramps
0 1 2 g. Vomiting, throwing up
0 1 2 h. Other (describe) _____

0 1 2 57. Physically attacks people
0 1 2 58. Picks nose, skin, or other parts of body (describe) _____

_____

0 1 2 59. Plays with own sex parts in public
0 1 2 60. Plays with own sex parts too much
0 1 2 61. Poor school work
0 1 2 62. Poorly coordinated or clumsy
0 1 2 63. Prefers playing with older children
0 1 2 64. Prefers playing with younger children
0 1 2 65. Refuses to talk
0 1 2 66. Repeats certain acts over and over; compulsions (describe)

_____

0 1 2 67. Runs away from home
0 1 2 68. Screams a lot
0 1 2 69. Secretive, keeps things to self
0 1 2 70. Sees things that are't there (describe) _____

_____

_____

0 1 2 71. Self-conscious or easily embarrassed
0 1 2 72. Sets fires
0 1 2 73. Sexual problems (describe) _____

_____

0 1 2 74. Showing off or clowning
0 1 2 75. Shy or timid
0 1 2 76. Sleeps less than most children
0 1 2 77. Sleeps more than most children during day and/or night (describe) _____

0 1 2 78. Smears or plays with bowel movements
0 1 2 79. Speech problem (describe)_____

0 1 2 80. Stares blankly
0 1 2 81. Steals at home
0 1 2 82. Steals outside the home
0 1 2 83. Stores up things he/she doesn't need (describe) _____

_____

0 1 2 84. Strange behaviour (describe) _____

_____

0 1 2 85. Strange ideas (describe) _____

_____

0 1 2 86. Stubborn, sullen, or irritable
0 1 2 87. Sudden changes in mood or feelings
0 1 2 88. Sulks a lot
0 1 2 89. Suspicious
0 1 2 90. Swearing or obscene language
0 1 2 91. Talks about killing self
0 1 2 92. Talks or walks in sleep (describe) _____
0 1 2 93. Talks too much
0 1 2 94. Teases a lot
0 1 2 95. Temper tantrums or hot temper
0 1 2 96. Thinks about sex too much
0 1 2 97. Threatens people
0 1 2 98. Thumb-sucking
0 1 2 99. Too concerned with neatness or cleanliness
0 1 2 100. Trouble sleeping (describe) _____
0 1 2 101. Truancy, skips school
0 1 2 102. Underactive, slow moving, or lacks energy
0 1 2 103. Unhappy, sad, or depressed
0 1 2 104. Unusually loud
0 1 2 105. Uses alcohol or drugs (describe) _____
0 1 2 106. Vandalism
0 1 2 107. Wets self during the day
0 1 2 108. Wets the bed
0 1 2 109. Whining
0 1 2 110. Wishes to be of opposite sex
0 1 2 111. Withdrawn, doesn't get involved with others
0 1 2 112. Worrying
0 1 2 113. Please write in any problems your child has that were not listed above: _____

_____

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NOTICE

AVIS

DIRECT OBSERVATION FORM

For each item that describes the child's behavior during the observational period, circle the
- 0 if the item was not observed
- 1 if there was a very slight or ambiguous occurrence
- 2 if there was a definite occurrence with mild to moderate intensity and less than three minutes duration
- 3 if there was a definite occurrence with severe intensity or greater than three minutes duration

For each behavior problem observed, score only the item that most specifically describes the behavior

0 1 2 3 b_1 Acts too young for age
0 1 2 3 b_2 Makes odd noises
0 1 2 3 b_3 Argues
0 1 2 3 4. Behaves like opposite sex
0 1 2 3 5. Defiant or talks back to staff
0 1 2 3 6. Bragging, boasting
0 1 2 3 b_7. Doesn't concentrate or doesn't pay attention for long
0 1 2 3 b_8. Can't get mind off certain thoughts; obsessions (specify) _____

_____

0 1 2 3 b_9. Doesn't sit still, restless, or hyperactive
0 1 2 3 10. Clings to adults or too dependent
0 1 2 3 11. Confused or seems to be in a fog
0 1 2 3 b_{12}. Cries
0 1 2 3 13. Fidgets
0 1 2 3 b_{14} Cruelty, bullying, or meanness
0 1 2 3 b_{15} Daydreams or gets lost in thoughts
0 1 2 3 b_{16} Deliberately harms self
0 1 2 3 b_{17}. Demands or tries to get attention of staff
0 1 2 3 b_{18} Destroys own things
0 1 2 3 19 Destroys property belonging to others
0 1 2 3 b_{20}. Disobedient
0 1 2 3 b_{21} Disturbs other children
0 1 2 3 22. Doesn't seem to feel guilty after misbehaving
0 1 2 3 b_{23}. Shows jealousy
0 1 2 3 24. Eats or drinks things that are not food (specify):

_____

_____

0 1 2 3 b_{25}. Shows fear of specific situations or stimuli (specify) _____

_____

0 1 2 3 b_{26}. Says no one likes him/her
0 1 2 3 b_{27}. Says others are out to get him/her
0 1 2 3 b_{28} Expresses feelings of worthlessness or inferiority
0 1 2 3 b_{29}. Gets hurt, accident prone
0 1 2 3 b_{30} Gets in physical fights
0 1 2 3 b_{31} Gets teased
0 1 2 3 32. Hears things that aren't there (specify): _____

_____

0 1 2 3 33. Impulsive or acts without thinking
0 1 2 3 a_{34}. Isolates self from others
0 1 2 3 35. Lying or cheating
0 1 2 3 36. Bites fingernails
0 1 2 3 37. Nervous, high-strung, or tense
0 1 2 3 38. Nervous movements or twitching (specify): ___

_

0 1 2 3 39. Overconforms to rules
0 1 2 3 40. Too fearful or anxious
0 1 2 3 41. Physically attacks people
0 1 2 3 42. Picks nose, skin, or other parts of body (specify)

_____

_____

0 1 2 3 b_{43} Falls asleep
0 1 2 3 44. Apathetic or unmotivated
0 1 2 3 45. Refuses to talk
0 1 2 3 b_{46} Disrupts group
0 1 2 3 b_{47} Screams
0 1 2 3 48. Secretive, keeps things to self
0 1 2 3 49. Sees things that aren't there (specify) _____

_____

0 1 2 3 50. Self-conscious or easily embarrassed
0 1 2 3 a_{51} Sexual problems (specify) _____

_____

0 1 2 3 b_{52}. Shows off or clowns
0 1 2 3 b_{53} Shy or timid behavior
0 1 2 3 b_{54}. Explosive behavior
0 1 2 3 55. Demands must be met immediately, easily frustrated
0 1 2 3 56. Inattentive, easily distracted
0 1 2 3 57. Stares blankly
0 1 2 3 b_{58} Acts like feelings are hurt when criticized
0 1 2 3 59. Steals
0 1 2 3 60. Stores up things he/she doesn't need (specify):

_____

_____

0 1 2 3 61. Strange behavior (specify): _____

_____

0 1 2 3 62. Strange ideas (specify): _____

_____

0 1 2 3 63. Stubborn, sullen, or irritable
0 1 2 3 64. Sudden changes in mood or feelings
0 1 2 3 b_{65}. Sulks
0 1 2 3 66. Suspicious
0 1 2 3 67. Swearing or obscene language
0 1 2 3 68. Talks about killing self
0 1 2 3 69. Talks too much
0 1 2 3 b_{70}. Teases
0 1 2 3 71. Temper tantrums or hot temper
0 1 2 3 72. Seems preoccupied with sex
0 1 2 3 73. Threatens people
0 1 2 3 74. Too concerned with neatness or cleanliness
0 1 2 3 75. Underactive, slow moving, or lacks energy
0 1 2 3 76. Unhappy, sad, or depressed
0 1 2 3 77. Unusually loud

0 1 2 3 76. Overly anxious to please
0 1 2 3 79. Whining
0 1 2 3 80. Withdrawn, doesn't get involved with others
0 1 2 3 81. Worrying
0 1 2 3 a_{82} Thumb-sucking
0 1 2 3 a_{83}. Fails to express ideas clearly
0 1 2 3 a_{84}. Impotent
0 1 2 3 a_{85} Tattles
0 1 2 3 b_{86}. Compulsions, repeats behavior over & over (specify): _____

_____

0 1 2 3 a_{87}. Easily led by peers
0 1 2 3 b_{88} Clumsy, poor motor control
0 1 2 3 b_{89} Doesn't get along with peers

0 1 2 3 a_{90} Runs out of class (or similar setting)
0 1 2 3 91 Behaves irresponsibly (specify): _____

_____

0 1 2 3 a_{92} Bossy
0 1 2 3 b_{93} Plays with younger children
0 1 2 3 a_{94}. Complains
0 1 2 3 b_{95} Afraid to make mistakes
0 1 2 3 a_{96} Acts like poor loser
97 Other problems (specify)
0 1 2 3 _____
0 1 2 3 _____
0 1 2 3 _____

SUPPLEMENTARY INSTRUMENTS

— for office use only —
IDENTIFICATION #

YOUTH SELF-REPORT — FOR AGES 11-18

YOUR AGE	YOUR SEX ☐ Boy ☐ Girl	GRADE IN SCHOOL	YOUR NAME
YOUR RACE ☐ Black ☐ White ☐ Other (specify) _____	TODAY'S DATE Yr. _____ Mo. _____ Day _____		PARENT'S TYPE OF WORK (Please be specific—for example: auto mechanic, high school teacher, homemaker, laborer, lathe operator, shoe salesman, army sergeant.) FATHER'S TYPE OF WORK: _____ MOTHER'S TYPE OF WORK: _____
	DATE OF BIRTH Yr. _____ Mo. _____ Day _____		

I. Please list the sports you most like to take part in. For example: swimming, baseball, skating, skate boarding, bike riding, fishing, etc.

☐ None

	Compared to others of your age, about how much time do you spend in each?			Compared to others of your age, how well do you do each one?		
	Less Than Average	Average	More Than Average	Below Average	Average	Above Average
a. _____	☐	☐	☐	☐	☐	☐
b. _____	☐	☐	☐	☐	☐	☐
c. _____	☐	☐	☐	☐	☐	☐

II. Please list your favorite hobbies, activities, and games, other than sports. For example: cards, books, piano, crafts, autos, etc. (Do not include T.V.)

☐ None

	Compared to others of your age, about how much time do you spend in each?			Compared to others of your age, how well do you do each one?		
	Less Than Average	Average	More Than Average	Below Average	Average	Above Average
a. _____	☐	☐	☐	☐	☐	☐
b. _____	☐	☐	☐	☐	☐	☐
c. _____	☐	☐	☐	☐	☐	☐

III. Please list any organization, clubs, teams or groups you belong to.

☐ None

	Compared to others of your age, how active are you in each?		
	Less Active	Average	More Active
a. _____	☐	☐	☐
b. _____	☐	☐	☐
c. _____	☐	☐	☐

IV. Please list any jobs or chores you have. For example: Paper route, babysitting, making bed, etc.

☐ None

	Compared to others of your age, how well do you carry them out?		
	Below Average	Average	Above Average
a. _____	☐	☐	☐
b. _____	☐	☐	☐
c. _____	☐	☐	☐

SUPPLEMENTARY INSTRUMENTS

V. 1. About how many close friends do you have? ☐ None ☐ 1 ☐ 2 or 3 ☐ 4 or more

2. About how many times a week do you do things with them? ☐ less than 1 ☐ 1 or 2 ☐ 3 or more

VI. Compared to others of your age, how well do you:

	Worse	About the same	Better
a. Get along with your brothers & sisters?	☐	☐	☐
b. Get along with other kids?	☐	☐	☐
c. Get along with your parents?	☐	☐	☐
d. Do things by yourself?	☐	☐	☐

VII. Current school performance

☐ I do not go to school

	Failing	Below Average	Average	Above Average
a. English	☐	☐	☐	☐
b. Math	☐	☐	☐	☐
Other subjects: c. _____	☐	☐	☐	☐
d. _____	☐	☐	☐	☐
e. _____	☐	☐	☐	☐
f. _____	☐	☐	☐	☐
g. _____	☐	☐	☐	☐

VIII. Below is a list of items that describe kids. For each item that describes you now or within the past 6 months, please circle the 2 if the item is very true or often true of you. Circle the 1 if the item is somewhat or sometimes true of you. If the item is not true of you, circle the 0.

0 1 2 1. I act too young for my age
0 1 2 2. I have an allergy (describe) _____
0 1 2 3. I argue a lot
0 1 2 4. I have asthma
0 1 2 5. I act like the opposite sex
0 1 2 a 6. I like animals
0 1 2 7. I brag
0 1 2 8. I have trouble concentrating or paying attention
0 1 2 9. I can't get my mind off certain thoughts (describe): _____
0 1 2 b 10. I have trouble sitting still
0 1 2 b 11. I'm too dependent on adults
0 1 2 12. I feel lonely
0 1 2 13. I feel confused or in a fog
0 1 2 14. I cry a lot
0 1 2 a 15. I am pretty honest
0 1 2 16. I am mean to others
0 1 2 17. I daydream a lot
0 1 2 18. I deliberately try to hurt or kill myself
0 1 2 b 19. I try to get a lot of attention
0 1 2 20. I destroy my own things
0 1 2 21. I destroy things belonging to others
0 1 2 22. I disobey my parents
0 1 2 23. I disobey at school
0 1 2 24. I don't eat as well as I should
0 1 2 25. I don't get along with other kids
0 1 2 26. I don't feel guilty after doing something I shouldn't
0 1 2 27. I am jealous of others
0 1 2 a 28. I am willing to help others when they need help
0 1 2 29. I am afraid of certain animals, situations, or places, other than school (describe) _____

SUPPLEMENTARY INSTRUMENTS

1 2 30. I am afraid of going to school
1 2 31. I am afraid I might think or do something bad
1 2 32. I feel that I have to be perfect
1 2 33. I feel that no one loves me
1 2 34. I feel that others are out to get me
1 2 35. I feel worthless or inferior
1 2 36. I accidently get hurt a lot
1 2 37. I get in many fights
1 2 38 I get teased a lot
1 2 39. I hang around with kids who get in trouble
1 2 40. I hear things that nobody else seems able to hear (describe) _____

_____

_____

1 2 [b] 41. I act without stopping to think
1 2 42. I like to be alone
1 2 43. I lie or cheat
1 2 44. I bite my fingernails
1 2 45. I am nervous or tense
1 2 46. Parts of my body twitch or make nervous movements (describe)

_____

_____

1 2 47. I have nightmares
1 2 48. I am not liked by other kids
1 2 [a] 49. I can do certain things better than most kids
1 2 50. I am too fearful or anxious
1 2 51. I feel dizzy
1 2 52. I feel too guilty
1 2 53. I eat too much
1 1 2 54. I feel overtired
1 1 2 55. I am overweight
56. Physical problems without known medical cause:
1 1 2 a. Aches or pains
1 1 2 b. Headaches
1 1 2 c. Nausea, feel sick
1 1 2 d. Problems with eyes (describe):

_____

1 1 2 e. Rashes or other skin problems
1 1 2 f. Stomachaches or cramps
1 1 2 g. Vomiting, throwing up
1 1 2 h. Other (describe): _____

_____

1 1 2 57. I physically attack people
1 1 2 [b] 58. I pick my skin or other parts of my body (describe) _____

_____

0 1 2 [a] 59. I can be pretty friendly
0 1 2 [a] 60. I like to try new things
0 1 2 61. My school work is poor
0 1 2 62. I am poorly coordinated or clumsy
0 1 2 63. I would rather be with older kids than with kids my own age
0 1 2 64. I would rather be with younger kids than with kids my own age
0 1 2 65. I refuse to talk
0 1 2 66. I repeat certain actions over and over (describe) _____

_____

0 1 2 67. I run away from home
0 1 2 68. I scream a lot
0 1 2 69. I am secretive or keep things to myself
0 1 2 70. I see things that nobody else seems able to see (describe)

_____

_____

0 1 2 71. I am self-conscious or easily embarrassed
0 1 2 72. I set fires
0 1 2 [a] 73. I can work well with my hands
0 1 2 74. I show off or clown
0 1 2 75. I am shy
0 1 2 76. I sleep less than most kids
0 1 2 77. I sleep more than most kids during day and/or night
(describe) _____

_____

0 1 2 [a] 78. I have a good imagination
0 1 2 79. I have a speech problem (describe): _____

_____

0 1 2 [a] 80. I stand up for my rights
0 1 2 81. I steal things at home
0 1 2 82. I steal things from places other than home
0 1 2 83. I store up things I don't need (describe) _____

_____

0 1 2 84. I do things other people think are strange (describe): _____

_____

0 1 2 85. I have thoughts that other people would think are strange (describe) _____

_____

0 1 2 [b] 86. I am stubborn
0 1 2 87. My moods or feelings change suddenly

SUPPLEMENTARY INSTRUMENTS

0	1	2	[a]88.	I enjoy being with other people
0	1	2	89.	I am suspicious
0	1	2	90.	I swear or use dirty language
0	1	2	91.	I think about killing myself
0	1	2	[a]92.	I like to make others laugh
0	1	2	93.	I talk too much
0	1	2	94.	I tease others a lot
0	1	2	95.	I have a hot temper
0	1	2	96.	I think about sex too much
0	1	2	97.	I threaten to hurt people
0	1	2	[a]98.	I like to help others
0	1	2	99.	I am too concerned about being neat or clean
0	1	2	100.	I have trouble sleeping (describe) _____
0	1	2	101.	I cut classes or skip school
0	1	2	[b]102.	I don't have much energy
0	1	2	103.	I am unhappy, sad, or depressed
0	1	2	104.	I am louder than other kids
0	1	2	105.	I use alcohol or drugs other than for medical conditions (describe): _____
0	1	2	[a]106.	I try to be fair to others
0	1	2	[a]107.	I enjoy a good joke
0	1	2	[a]108.	I like to take life easy
0	1	2	[a]109.	I try to help other people when I can
0	1	2	110.	I wish I were of the opposite sex
0	1	2	111.	I keep from getting involved with others
0	1	2	112.	I worry a lot

Please write down anything else that describes your feelings, behavior, and interests

PROTOCOL | SITE | SUBJ

PHYSICIAN'S QUESTIONNAIRE / DOSAGE (Follow-Up)

SUBJECT'S INITIALS (F/M/L)	BIRTHDATE (Mo/Da/Yr)	
SUBJECT NO.	TODAY'S DATE (Mo/Da/Yr)	INTERVIEWER'S NAME

CLINIC USE ONLY	RECEIVED STAMP

VISIT (Circle)

Week: 1 2 3 4

1. DEGREE OF GLOBAL PSYCHOPATHOLOGY
How ill is this subject now, compared to your experience with other psychiatric patients of this type?

Circle —

1 Not Ill
2 Very Mild
3 Mild
4 Moderate
5 Moderate - Severe
6 Severe
7 Extremely Severe

2. HOW MUCH HAS SUBJECT CHANGED SINCE STUDY ONSET? (Circle)

	a.) In doctor's opinion	b.) In subject's opinion
Very Much Better	1	1
Much Better	2	2
A Little Better	3	3
No Change	4	4
A Little Worse	5	5
Much Worse	6	6
Very Much Worse	7	7

3. DID SUBJECT HAVE ADVERSE REACTION(S) SINCE PREVIOUS EVALUATION? (Circle) 1 Yes 2 No
If YES, please complete an ADVERSE REACTION form.

4. DID SUBJECT HAVE SYMPTOMS SINCE LAST VISIT DUE TO INTERCURRENT ILLNESS? (Circle) 1 Yes 2 No
If YES, please specify illness, severity of symptoms, and start/stop date:

INTERCURRENT ILLNESS	SEVERITY (Circle)	START DATE (Mo/Da/Yr)	STOP DATE (Mo/Da/Yr)	COMMENTS
	1 = Mild 2 = Moder. 3 = Severe			
	1 = Mild 2 = Moder. 3 = Severe			

If medication was administered for intercurrent illness, enter information on CONCOMITANT MEDICATIONS AND PROCEDURES form.

PRESCRIPTION							COMPLIANCE TO LAST PRESCRIPTION (Check)
DATE TO BEGIN (Mo/Da/Yr)	REGIMEN PER DAY	TOTAL NUMBER CAPSULES PER DAY	Reason, If Dose Changed From Last Rx (Check)				
			INCREASE		*DECREASE*		
			Lack of Therapeutic Effect 1	For Further Improvement 2	Side Effects 3	Maint. of Improvement 4	
							☐ Yes ☐ No
							☐ Yes ☐ No

Yes *Subject compliance equals that prescribed.*

No *Explain non-compliance fully below. (Missed doses; Subject changed dose, etc. Explain with reason(s), date(s), and number of capsules from that prescribed. Use Comments if necessary.)*

WHEN APPLICABLE, STATE LAST DATE STUDY MEDICATION TAKEN (Mo/Da/Yr) _____
(If subject lost to follow-up, enter date of last visit.)

COMMENTS:

ADVERSE REACTION REPORT

SUBJECT'S INITIALS (F/M/L)	BIRTHDATE (Mo/Da/Yr)	SUBJECT NO.	☐ CHECK, If NONE

Report signs / symptoms below. Use additional forms as needed. All information must be completed. CIRCLE THE APPROPRIATE NUMBER.

NAME OF SYMPTOM	SEVERITY (Circle One)	DATE	OUTCOME OF SUBJECT TO SYMPTOM (Circle One)	SOURCE (Circle One)	ACTION TAKEN AS RESULT OF SYMPTOM (Study Rx Only)	IS SYMPTOM RELATED TO . . . (Check)	NO 1	Possibly 2	Probably 3	Yes 4	Unknown 5
	1 Mild 2 Moderate 3 Severe	ONSET (Mo/Da/Yr) CEASED (Mo/Da/Yr)	1 Alive with symptom present 2 Recovered 3 Still under treatment for symptom 4 No follow-up 5 Death	1 Symptoms spontaneously reported by subject 2 Symptoms elicited by investigator 3 Investigator observed signs 4 Other — explain in comments	1 NONE 2 Reduce dose 3 Suspend Rx 4 Discontinue Rx 5 Other — specify in comments	Test Drug?					
						Concomitant Drug(s)? *					
						Drug — Drug Interaction?					
						Subject's Clinical State?					
	1 Mild 2 Moderate 3 Severe	ONSET (Mo/Da/Yr) CEASED (Mo/Da/Yr)	1 Alive with symptom present 2 Recovered 3 Still under treatment for symptom 4 No follow-up 5 Death	1 Symptoms spontaneously reported by subject 2 Symptoms elicited by investigator 3 Investigator observed signs 4 Other — explain in comments	1 NONE 2 Reduce dose 3 Suspend Rx 4 Discontinue Rx 5 Other — specify in comments	Test Drug?					
						Concomitant Drug(s)? *					
						Drug — Drug Interaction?					
						Subject's Clinical State?					
	1 Mild 2 Moderate 3 Severe	ONSET (Mo/Da/Yr) CEASED (Mo/Da/Yr)	1 Alive with symptom present 2 Recovered 3 Still under treatment for symptom 4 No follow-up 5 Death	1 Symptoms spontaneously reported by subject 2 Symptoms elicited by investigator 3 Investigator observed signs 4 Other — explain in comments	1 NONE 2 Reduce dose 3 Suspend Rx 4 Discontinue Rx 5 Other — specify in comments	Test Drug?					
						Concomitant Drug(s)? *					
						Drug — Drug Interaction?					
						Subject's Clinical State?					
	1 Mild 2 Moderate 3 Severe	ONSET (Mo/Da/Yr) CEASED (Mo/Da/Yr)	1 Alive with symptom present 2 Recovered 3 Still under treatment for symptom 4 No follow-up 5 Death	1 Symptoms spontaneously reported by subject 2 Symptoms elicited by investigator 3 Investigator observed signs 4 Other — explain in comments	1 NONE 2 Reduce dose 3 Suspend Rx 4 Discontinue Rx 5 Other — specify in comments	Test Drug?					
						Concomitant Drug(s)? *					
						Drug — Drug Interaction?					
						Subject's Clinical State?					

COMMENTS:

Identify on CONCOMITANT MEDICATIONS form.

FORM T

CRC 349 T

Appendix A. Tourette's Syndrome Global Scale (TSGS)

NAME _____ DATE _____ RATER _____

CODE FOR FREQUENCY

1 = 1 or less in 5 min

2 = 1 in 2–4.9 min

3 = from 1 in 1.9 min to 4 in 1 min

4 = 5 or more in 1 min

5 = virtually uncountable

	FREQUENCY (F)						DISRUPTION (D)					
	None	Rarely	Occasionally	Frequently	Almost Always	Always	Camouflaged	Audible or Visible No Problem	Some Problem	Impaired Functioning	Cannot Function	
SIMPLE MOTOR (SM): Nonpurposeful, tics, jerks and/or movements	0	1	2	3	4	5	1	2	3	4	5	FXD = ___
COMPLEX MOTOR (CM): Purposeful, thoughtful actions (systematic actions), rituals, touching self, others, or objects	0	1	2	3	4	5	1	2	3	4	5	FXD = ___
SIMPLE PHONIC (SP): Nonpurposeful noises, throat clearing, coughing	0	1	2	3	4	5	1	2	3	4	5	FXD = ___
COMPLEX PHONIC (CP): Purposeful, insults, coprolalia, words, distinguishable speech	0	1	2	3	4	5	1	2	3	4	5	FXD = ___

BEHAVIOR (B) (conduct)

0 No problem
5 Subtle problems normal peer, school, and family relations
10 Some problems, at least one relationship area impaired
15 Clear impairment in more than one area
20 Serious impairment, affects all areas
25 Unacceptable social behavior, constant supervision

MOTOR RESTLESSNESS (MR)

0 Normal movement
5 Adventitial movements, visible no problem
10 Increased motor restlessness, clearly visible, some problem
15 Clear motor restlessness, moderate problem
20 Mostly in motion but occasionally stops, impaired functioning
25 Nonstop motion, clearly cannot function

SCHOOL AND LEARNING PROBLEMS

0 No problem
5 Low grades
10 Should be or in some special classes, or repeated
15 All special classes
20 Special School
25 Unable to remain in school, home bound

WORK AND OCCUPATION PROBLEMS

0 No problem
5 Stable job, some difficulty
10 Serious problems
15 Lost lots of jobs
20 Almost never employed
25 Unemployed

((SM + CM)/2) + ((SP + CP)/2) + ((B + MR + SCHOOL OR WORK PROBLEMS) × ⅓) = GLOBAL SCORE

Appendix B. Instructions and Scoring of Tourette's Syndrome Global Scale (TSGS)

Use of the TSGS requires the rater to have clinical experience with TS patients and knowledge of the range of TS symptomatology. Information for making a rating is based on a synthesis of the clinician's observation along with patient, parent, and school reports for the past week. Whether or not a patient is on medication is not taken into consideration.

Scoring: The TSGS has two major domains which contribute equally to the total (global) score. The first domain consists of ratings of motor and phonic tics; the second domain is an overall social functioning score.

The rating of tics is subdivided into four subcategories, based on clinical experience with TS: simple motor tics (SMT), complex motor tics (CMT), simple phonic tics (SPT), and complex phonic tics (CPT). These are defined in Appendix C. Each type of tic category is rated on a two-factor scale: frequency (F) of the tics in this category and disruptiveness (D) of tics in this category. Frequency (F) is scored on a 6-point scale, ranging from 0, no tics of this category are present, to 5, uncountable number of tics of this type are present. Disruption (D) is also scored on a 6-point scale, from 0, the tics cause no disruption or socially recognized disturbance for the patient, and are camouflaged, to 5, the symptoms make functioning impossible while they are present. An infrequently occurring symptom class (such as explosive coprolalia or head banging) may thus be rated with a low frequency score (e.g. 2) and a very high disruption score (e.g. 5); similarly, a very frequent tic such as eye blinking many times a minute may have a high frequency score (e.g. 5) but a low disruption score (e.g. 2). The total TSGS tic score is derived by summing the Frequency × Disruption scores (F × D) for each of the four tic categories and then dividing by two. The lowest score is zero, indicating the absence of any TS tic symptoms at the time of rating; the highest score is 50.

The social functioning domain in the TSGS consists of ratings of three broad problem areas: general behavior, motor restlessness, and school or work functioning. Each of these domains of functioning is rated from 0, for no problems in this area (superior functioning) to 25, for profound problems in this area. The simple summation of the scores for each of these domains would lead to a total score of 75; to achieve comparability with the tic score maximum of 50, the total social functioning score is divided by ½, leading to a minimal score of 0 (superb social functioning) and a maximum score of 50 (extreme disturbances in social functioning).

The TSGS Global Score is the sum of the TSGS total tic score (the sum of the F × D scores for each of the four categories, divided by 2) and the TSGS social functioning score (the sum of the scores for each of the three social functioning domains divided by ½). The minimal score is 0 (no tics, superb functioning) and the maximal score is 100 (uncountable, highly disruptive tics and devastated functioning). Based on clinical experience to date, the TSGS scores can be subdivided into mild, moderate, severe, and extreme TS (see Table 2).

Appendix C. Symptom Description and Scoring Codes

CODE FOR FREQUENCY

1. 1 or less in 5 min
2. 1 in 2 to 4.9 min
3. 1 to 4 in 1 to 1.9 min
4. 5 or more in 1 min
5. Virtually uncountable

CODE FOR DISRUPTION

1. Camouflaged: Some tics, but untrained person would not recognize (*Example:* tossing hair back)
2. Audible/visible no problem: Recognizable but does not interfere (*Example:* picking at hair, throat clearing)
3. Some problem: Significant problem but functioning continues (*Example:* interrupted speech, head-jerks, interruptions while reading)
4. Impaired function: Symptom definitely a problem (*Example:* prolonged complex movements, series of nonstop tics)
5. Cannot function: Cannot do anything when symptom is present

DESCRIPTION OF MOTOR SYMPTOMS

Simple Motor Tics:

Rapid, Darting, "Meaningless": Eyeblinking, grimacing, nose twitching, lip pouting, shoulder shrugs, arm jerks, head jerks, abdominal tensing, rapid kicks, finger movements, jaw snaps, tooth clicking, frowning, rapid jerking of any part of body

Complex Motor Tics:

Slower, "Purposeful": Hopping, clapping, touching objects or others or self, throwing, arranging, gyrating and bending, "dystonic" postures, biting mouth, lip, arm, headbanging, thrusting arms, striking out, picking scabs, writhing movements, rolling eyes to the ceiling, holding funny expressions, sticking out the tongue, kissing, pinching, writing over-and-over the same letter or word, pulling back on a pencil while writing, tearing paper or books

Copropraxia: "Giving the finger"—cursing through gestures

Appendix C (*continued*)

DESCRIPTION OF PHONIC SYMPTOMS

Simple Phonic Symptoms: Fast, "Meaningless" Sounds:
Whistling, coughing, sniffling, spitting, screeching, barking, grunting, gurgling, clacking, hawking, hissing, sucking, uh-uh, eeee, ah-uh, ah, and innumerable other sounds

Complex Phonic Symptoms: Language
Words, Phrases, Statements: Shut up, stop that, OK. I've got to. I'm going to better—right? Right. What makes me do this. How about it. Now you've seen it, all right, oh boy
Rituals: Counting rituals. Repeating a phrase until it is "just right"
Speech Atypicalities: Unusual rhythms, tone, accents, intensity of speech
Coprolalia: Obscene and aggressive words and statements

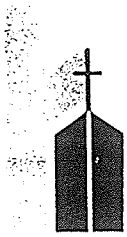
SOCIAL FUNCTIONING

I. *Behavior:* Provocative, argumentative, poor frustration tolerance, temper fits (with three main areas of interaction; peers, school or authority figures and family relations)
0: No problems, normal relationships
1–4: Somewhat more than normal behavior problems
5: Subtle problems, no particular relationship threatened
6–9: Strained relationships
10: Visible problem, at least one relationship impaired
11–14: Degree of impairment (*Example:* If OK relationship in school and peers but not with family, 14)
15: Clear impairment in more than one area
16–19: Degree of impairment
20: Serious impairment affects all areas, occasional interactions
21–24: Degree and number of social interactions (*Example:* Older brother and patient have good relationship)
25: Unacceptable social behavior, no attempt at good social interaction. Cannot be trusted, constant supervision

II. *Motor Restlessness:* Increased motor activity, more than normal movement for task
0: Normal movement for task—good concentration
1–4: Something more than normal
5: Adventitial, occasional, increased movement, mostly fine motor, visible, but no problem
6–9: More frequent but still no problem
10: Increased motor restlessness, clearly visible (*Example:* e.g. shaking, fidgety, would be trouble at dinner table or movies), mild interference
11–14: Greater degree of interference
15: Clear motor restlessness, fidgetting, hyperactive, some impairment (intervention)
16–19: Greater degree of impairment
20: Mostly in motion but occasionally stops, impaired direction, difficulty with structure, functioning greatly impaired
21–24: Fewer stops, greater impairment
25: Nonstop motion, impaired concentration, unable to sit still, always in motion, clearly cannot function

III. (A) *School and Learning Problems:*
0: No problem, at grade level, doing at least average work
1–4: Degree of borderline grades (*Example:* 4 Cs)
5: Low grades: Cs + Ds—not working up to potential
6–9: Degree of failing (*Example:* 2Fs might be an 8)
10: Should be or is in some special classes, special teacher, learning laboratory, tutor, or repeated grade
11–14: Degree of special help (*Example:* Special class for 2 subjects might be 12)
15: All special classes or repeated more than one grade
16–19: Degree of learning (*Example:* If very little learning, 19)
20: Special school
21–24: Having trouble in special school
25: Unable to remain in school, home bound, unable to learn

III. (B) *Work and Occupational Problems*
0: Have job, no problems
1–4: Occasional problem
5: Has held down job for at least 6 months, some problems doing work, getting along with co-workers, or taking orders
6–9: Shorter duration and/or degree of problems
10: Poor functioning, changed jobs a few times in the past year. Serious problems (2 or 3 jobs)
11–14: Number of jobs or seriousness of problems
15: Cannot hold a job for long, lost lots of jobs
16–19: Number of jobs, or seriousness of problems
20: Almost never employed, sporatic employment, out of work 2–3 months
21–24: Number of months out of work
25: Unemployed—did not work for 6 or more months



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QUESTIONNAIRE INSTRUCTIONS

Participation in research projects often involves a great deal of record keeping and filling out of questionnaires. The present study is no exception. In order to minimize confusion and streamline the data collection process, it may be useful for you to refer to this guide which will specify which questionnaires are to be filled out on a weekly basis and which are to be filled out on a monthly basis. It will also specify how to complete the questionnaires and by whom they should be completed. While most of this information is quite evident from the dates on the questionnaires, this guide might be useful in both the organization of your data collection procedures and in the understanding of the objectives of this research.

If you have any questions or problems with the completion of the questionnaires, please do not hesitate to contact me at the number listed below. Thank you very much for your cooperation.

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I. WEEKLY MEASURES

The majority of the data collection for this project is completed on a weekly basis. The weekly measures are all stapled together and dated for each seven day period at the top of the front page. The questionnaires which are to be filled out on a weekly basis are:

1) Tourette's Syndrome Global Scale (TSGS)
2) Adverse Reaction Report (ARR)
3) Symptom Checklist 90 (SCL-90).

1. THE TOURETTE'S SYNDROME GLOBAL SCALE (TSGS):

This questionnaire is used to keep track of the TS symptoms over a one week period. It is not really as complicated as it looks on first glance. The basic idea is to get a score out of 25 for each of the following eight categories:

1) Simple motor tics
2) Complex motor tics
3) Simple phonic tics
4) Complex phonic tics
5) Behaviour (Conduct)
6) Motor Restlessness
7) School and Learning Problems
8) Work and Occupational Problems

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1. THE TOURETTE'S SYNDROME GLOBAL SCALE (TSGS) (continued):

For categories 1 to 4, those involving the Simple motor, Complex motor, Simple phonic and Complex phonic tics, a score out of 25 is derived by carrying out the following procedures:

1) Rate the frequency (F) of occurrence for the tic on the Frequency Scale which ranges from 0 to 5.

0 - None
1 - Rarely
2 - Occasionally
3 - Frequently
4 - Almost always
5 - Always

2) Next, rate the disruption (D) that is caused by the tic's occurrence on the Disruption Scale which ranges from 1 to 5.

1 - Camouflaged
2 - Audible or Visible - No Problem
3 - Some Problem
4 - Impaired Functioning
5 - Cannot Function

3) Finally, multiply the frequency (F) by the disruption (D) at the end of each line for a score out of 25. F x D = _____. Complete this procedure for categories 1, 2, 3, and 4.

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1. THE TOURETTE'S SYNDROME GLOBAL SCALE (TSGS) (continued):

4) Categories 5 to 8 are simple and straightforward. Just rate, from 0 to 25, the level of problems in each of these areas that are the result of having TS. Any number from 0 to 25 may be used. If, for example, behaviour problems are somewhere in between clear impairments (15) and serious impairments (20), assign a score of 17 or 18, or whatever seems to best reflect the level of behaviour problems.

5) For clarification purposes, the two pages that follow the front page of the TSGS, that is, pages 158 and 159, provide more in-depth and understandable descriptions of the various category contents.

The TSGS can usually be completed in just a couple of minutes after an understanding of the questionnaire has been gained.

2. ADVERSE REACTION REPORT (ARR):

This report is used to monitor whether or not an individual has had an adverse or negative reaction to their medication or to the withdrawal of a medication.

If an individual has had an adverse reaction then:

1) Name the symptom

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2. ADVERSE REACTION REPORT (ARR) (continued):

2) Rate the severity of the symptom (mild, moderate or severe)

3) Record date of onset and date symptom ceased

Disregard the other categories on the form.

If no adverse reaction has taken place, then check appropriate box at the top right corner of the form.

3. SYMPTOM CHECKLIST 90 (SCL-90):

This questionnaire is designed to be a self report measure. However, it requires a fairly high reading level as it was developed basically for adult populations. In order for a younger person to understand the questions in the SCL-90, parents will likely have to provide some assistance for TS patients who are less than 14 years of age. For example, items regarding headaches, appetite, pains and crying are easily understood and scored by all age groups; however, other items such as feeling self-conscious may require some explanation to younger participants. Parents should try to explain, as best they can, what is meant by any given question.

Other items will simply be inappropriate for certain age groups. These items which often refer to sexual matters should be scored "not at all" (1).

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3. SYMPTOM CHECKLIST 90 (SCL-90) (continued):

There are three pages to the SCL-90, but it can usually be completed in about 15-20 minutes after a bit of practice.

II. MONTHLY MEASURES

There are two questionnaires to be filled out on a monthly basis. These are the CHILD BEHAVIOUR CHECKLIST (CBCL) and the YOUTH SELF REPORT (YSR). The CBCL is to be filled out by the parents alone. The YSR is for the youth to fill out on his own to the best of his ability. Parents may help the youth in completing the YSR but should restrict their input to explaining the meaning of certain words or concepts. The idea of the YSR is for the youth to give his individual perceptions of the items contained in the YSR.

Both of these questionnaires are quite straightforward and self-explanatory. However, it should be noted that on Page 3 of the CBCL the instructions indicate that items should be responded to on the basis of the child's behaviour over the last 12 months. Parents should disregard the 12 month indicator and base their responses on the child's behaviour on the 1 month period in question.

It will probably take about half of an hour to complete the CBCL and about the same for the YSR.

III. ADDITIONAL MEASURES

1. WEEKLY DATA COLLECTION:

The experimenter will telephone each participant once a week and go through the four questions on the Physician's Questionnaire (see enclosed). The following questions will be asked:

1) "How were _____'s Tourette's Symptoms over the last week?"

Rate on the following scale:

1. Not ill
2. Very mild
3. Mild
4. Moderate
5. Moderate-severe
6. Severe
7. Extremely severe

2) "How much have the symptoms changed over the last week?"

Rate on the following scale:

1. Very much better
2. Much better
3. A little better
4. No change

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1. WEEKLY DATA COLLECTION (continued):

5. A little worse
6. Much worse
7. Very much worse

3) "Did _____ have any adverse reactions to his medication or the withdrawal of his medication over the last week?"

YES or NO

4) "Did _____ have any other illnesses over the last one week period?"

YES or NO

2. MONTHLY DATA COLLECTION:

Monthly in-home visits will also be conducted by the experimenter. During these sessions the experimenter will collect data regarding the symptoms that the individual has experienced over the last one month period. The experimenter will complete a CBCL, SCL-90 and TSGS for each month during the experiment based on the information gathered during these visits.

All data collection materials will be collected at the end of each

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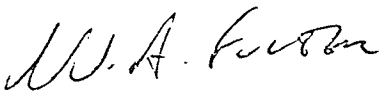
2. MONTHLY DATA COLLECTION (continued):

month. The experiment will run from May to October, 1987. Final results of the study should be available in the Spring of 1988.

Thank you again for your cooperation.



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APPENDIX J

SUMMARY OF NEUROPSYCHOLOGICAL TESTING

NAME: S #1 AGE: 9.1 DATE TESTED: 1987-06-24

LATERAL DOMINANCE = Lt

WISC-R

Verbal Tests

Information	10
Similarities	9
Arithmetic	8
Vocabulary	10
Comprehension	8
(Digit Span)	(5)

Performance Tests

Picture Completion	11
Picture Arrangement	16
Block Design	14
Object Assembly	15
Coding	9

Verbal IQ	94
Performance IQ	121
Full Scale IQ	106

BENDER GESTALT

Total Score = 5

Age Group = 7.0 to 7.5

SEASHORE RHYTHM TEST

Errors = 6 Rank = 0

SPEECH SOUNDS PERCEPTION TEST

Error = 11 Rank = 2

TRAIL MAKING TESTS

Trails A: Time = 12" Errors = 0 Rank = 0

Trails B: Time = 29" Errors = 1 Rank = 0

HALSTEAD CATEGORIES TEST

Errors = 20 Rank = 0

TACTUAL PERFORMANCE TEST

TPT time (total) = 7:54 Rank = 1

TPT memory = 5 Rank = 0

TPT location = 3 Rank = 1

APHASIA SCREENING TEST

Errors = 9 Rank = 1

Suppressions: Auditory Rt = 0 Lf = 0

Tactile Rt = 0 Lf = 0

Visual Rt = 8 Lf = 0

TAPPING TEST

M - D = 44.8 Rank = 0

M - ND = 37.8 Rank = 0

GRIP STRENGTH

D = 23.1 Rank = 0

ND = 24.2 Rank = 0

NAME WRITING

D = 13" Rank = 1

ND = 14" Rank = 0

TSGS TOTAL = 33

ON/OFF HALOPERIDOL = ON

SUMMARY OF NEUROPSYCHOLOGICAL TESTING

NAME: S #1 AGE: 9.3 DATE TESTED: 1987-08-25

LATERAL DOMINANCE = Lt

WISC-R

Verbal Tests

Information	14
Similarities	8
Arithmetic	6
Vocabulary	10
Comprehension	12
(Digit Span)	(9)

Performance Tests

Picture Completion	15
Picture Arrangement	16
Block Design	12
Object Assembly	19
Coding	12

Verbal IQ	100
Performance IQ	133
Full Scale IQ	118

BENDER GESTALT

Total Score = 1

Age Group = 10:6 to 10:11

SEASHORE RHYTHM TEST

Errors = 9 Rank = 0

SPEECH SOUNDS PERCEPTION TEST

Error = 8 Rank = 1

HALSTEAD CATEGORIES TEST

Errors = 17 Rank = 0

TACTUAL PERFORMANCE TEST

TPT time (total) = 5:47 Rank = 1

TPT memory = 6 Rank = 0

TPT location = 4 Rank = 1

APHASIA SCREENING TEST

Errors = 6 Rank = 1

Suppressions: Auditory Rt = 0 Lf = 0

Tactile Rt = 0 Lf = 0

Visual Rt = 0 Lf = 0

TAPPING TEST

M - D = 43.8 Rank = 0

M - ND = 36.4 Rank = 0

GRIP STRENGTH

D = 28.6 Rank = 0

ND = 28.6 Rank = 0

NAME WRITING

D = 18" Rank = 1

ND = 41" Rank = 2

TSGS TOTAL = 23

ON/OFF HALOPERIDOL = OFF

TRAIL MAKING TESTS

Trails A: Time = 18" Errors = 0 Rank = 1

Trails B: Time = 54" Errors = 2 Rank = 1

SUMMARY OF NEUROPSYCHOLOGICAL TESTING

NAME: S #2 AGE: 10:8 DATE TESTED: 1987-08-30

LATERAL DOMINANCE = Rt

WISC-R

Verbal Tests

Information	13
Similarities	16
Arithmetic	14
Vocabulary	12
Comprehension	12
(Digit Span)	(12)

Performance Tests

Picture Completion	15
Picture Arrangement	16
Block Design	16
Object Assembly	13
Coding	7
Verbal IQ	120
Performance IQ	124
Full Scale IQ	125

BENDER GESTALT

Total Score = 1

Age Group = 10:6 to 10:11

SEASHORE RHYTHM TEST

Errors = 8 Rank = 1

SPEECH SOUNDS PERCEPTION TEST

Error = 4 Rank = 0

TRAIL MAKING TESTS

Trails A: Time = 29" Errors = 0 Rank = 2

Trails B: Time = 31" Errors = 0 Rank = 0

HALSTEAD CATEGORIES TEST

Errors = 20 Rank = 0

TACTUAL PERFORMANCE TEST

TPT time (total) = 5:27 Rank = 1

TPT memory = 4 Rank = 1

TPT location = 4 Rank = 1

APHASIA SCREENING TEST

Errors = 2 Rank = 1

Suppressions: Auditory Rt = 0 Lf = 0

Tactile Rt = 0 Lf = 0

Visual Rt = 0 Lf = 0

TAPPING TEST

M - D = 43.8 Rank = 0

M - ND = 42.2 Rank = 0

GRIP STRENGTH

D = 36.3 Rank = 0

ND = 38.5 Rank = 0

NAME WRITING

D = 15" Rank = 1

ND = 34" Rank = 1

TSGS TOTAL = 14

ON/OFF HALOPERIDOL = OFF

SUMMARY OF NEUROPSYCHOLOGICAL TESTING

NAME: S #3 AGE: 10:4 DATE TESTED: 1987-07-29

LATERAL DOMINANCE = Rt

WISC-R

Verbal Tests

Information	5
Similarities	9
Arithmetic	4
Vocabulary	6
Comprehension	7
(Digit Span)	(5)

Performance Tests

Picture Completion	7
Picture Arrangement	7
Block Design	8
Object Assembly	6
Coding	1

Verbal IQ	77
Performance IQ	72
Full Scale IQ	72

BENDER GESTALT

Total Score = 7

Age Group = 6.6 to 6.11

SEASHORE RHYTHM TEST

Errors = 7 Rank = 1

SPEECH SOUNDS PERCEPTION TEST

Error = 4 Rank = 0

HALSTEAD CATEGORIES TEST

Errors = 44 Rank = 1

TACTUAL PERFORMANCE TEST

TPT time (total) = 12:23 Rank = 2

TPT memory = 3 Rank = 1

TPT location = 3 Rank = 1

APHASIA SCREENING TEST

Errors = 10 Rank = 3

Suppressions: Auditory Rt = 0 Lf = 0

Tactile Rt = 0 Lf = 0

Visual Rt = 0 Lf = 0

TAPPING TEST

M - D = 50 Rank = 0

M - ND = 38.8 Rank = 0

GRIP STRENGTH

D = 29.7 Rank = 0

ND = 27.5 Rank = 0

NAME WRITING

D = 13" Rank = 1

ND = 38" Rank = 2

TSGS TOTAL = 46

ON/OFF HALOPERIDOL = OFF

TRAIL MAKING TESTS

Trails A: Time = 32" Errors = 0 Rank = 2

Trails B: Time = 69" Errors = 0 Rank = 2

SUMMARY OF NEUROPSYCHOLOGICAL TESTING

NAME: S #3 AGE: 10:6 DATE TESTED: 1987-09-29

WISC-R

Verbal Tests

Information	6
Similarities	9
Arithmetic	5
Vocabulary	6
Comprehension	8
(Digit Span)	(7)

Performance Tests

Picture Completion	9
Picture Arrangement	8
Block Design	10
Object Assembly	7
Coding	5

Verbal IQ	80
Performance IQ	85
Full Scale IQ	81

BENDER GESTALT

Total Score = 4

Age Group = 8.0 to 8.5

SEASHORE RHYTHM TEST

Errors = 5 Rank = 0

SPEECH SOUNDS PERCEPTION TEST

Error = 6 Rank = 1

TRAIL MAKING TESTS

Trails A: Time = 29" Errors = 0 Rank = 2

Trails B: Time = 54" Errors = 0 Rank = 1

LATERAL DOMINANCE = Rt

HALSTEAD CATEGORIES TEST

Errors = 37 Rank = 1

TACTUAL PERFORMANCE TEST

TPT time (total) = 10:14 Rank = 1

TPT memory = 4 Rank = 1

TPT location = 3 Rank = 1

APHASIA SCREENING TEST

Errors = 8 Rank = 2

Suppressions: Auditory Rt = 0 Lf = 0

Tactile Rt = 0 Lf = 0

Visual Rt = 0 Lf = 0

TAPPING TEST

M - D = 47.2 Rank = 0

M - ND = 36.4 Rank = 1

GRIP STRENGTH

D = 24 Rank = 0

ND = 22 Rank = 0

NAME WRITING

D = 15" Rank = 1

ND = 41" Rank = 2

TSGS TOTAL = 34

ON/OFF HALOPERIDOL = ON

SUMMARY OF NEUROPSYCHOLOGICAL TESTING

NAME: S #4 AGE: 10:5 DATE TESTED: 1987-06-30

WISC-R

Verbal Tests

Information	7
Similarities	8
Arithmetic	6
Vocabulary	6
Comprehension	5
(Digit Span)	(4)

Performance Tests

Picture Completion	11
Picture Arrangement	5
Block Design	8
Object Assembly	9
Coding	6

Verbal IQ	79
Performance IQ	85
Full Scale IQ	80

BENDER GESTALT

Total Score = 8

Age Group = 6 to 6.5

SEASHORE RHYTHM TEST

Errors = 2 Rank = 0

SPEECH SOUNDS PERCEPTION TEST

Error = 3 Rank = 0

LATERAL DOMINANCE = Rt

HALSTEAD CATEGORIES TEST

Errors = 89 Rank = 3

TACTUAL PERFORMANCE TEST

TPT time (total) = 6:28 Rank = 1

TPT memory = 5 Rank = 0

TPT location = 4 Rank = 1

APHASIA SCREENING TEST

Errors = 6 Rank = 1

Suppressions: Auditory Rt = 0 Lf = 0

Tactile Rt = 0 Lf = 0

Visual Rt = 0 Lf = 0

TAPPING TEST

M - D = 46 Rank = 0

M - ND = 42.8 Rank = 0

GRIP STRENGTH

D = 26.4 Rank = 0

ND = 23.1 Rank = 0

NAME WRITING

D = 8 Rank = 0

ND = 11 Rank = 0

TSGS TOTAL = 23

ON/OFF HALOPERIDOL = ON

TRAIL MAKING TESTS

Trails A: Time = 28" Errors = 1 Rank = 3

Trails B: Time = 88" Errors = 2 Rank = 3

SUMMARY OF NEUROPSYCHOLOGICAL TESTING

NAME: S #4 AGE: 10:7 DATE TESTED: 1987-08-25

WISC-R

Verbal Tests

Information	10
Similarities	8
Arithmetic	7
Vocabulary	5
Comprehension	6
(Digit Span)	(5)

Performance Tests

Picture Completion	14
Picture Arrangement	10
Block Design	8
Object Assembly	12
Coding	3
Verbal IQ	82
Performance IQ	95
Full Scale IQ	87

BENDER GESTALT

Total Score = 4

Age Group = 8 to 8.5

SEASHORE RHYTHM TEST

Errors = 14 Rank = 1

SPEECH SOUNDS PERCEPTION TEST

Error = 4 Rank = 0

LATERAL DOMINANCE = Rt

HALSTEAD CATEGORIES TEST

Errors = 70 Rank = 2

TACTUAL PERFORMANCE TEST

TPT time (total) = 6:38 Rank = 1

TPT memory = 5 Rank = 0

TPT location = 5 Rank = 0

APHASIA SCREENING TEST

Errors = 7 Rank = 1

Suppressions: Auditory Rt = 0 Lf = 0

Tactile Rt = 0 Lf = 0

Visual Rt = 0 Lf = 0

TAPPING TEST

M - D = 43.2 Rank = 0

M - ND = 49.4 Rank = 0

GRIP STRENGTH

D = 33.0 Rank = 0

ND = 38.5 Rank = 0

NAME WRITING

D = 21 Rank = 2

ND = 41 Rank = 2

TSGS TOTAL = 23

ON/OFF HALOPERIDOL = OFF

TRAIL MAKING TESTS

Trails A: Time = 30" Errors = 1 Rank = 2

Trails B: Time = 96" Errors = 1 Rank = 3